

Brazilian Guideline on Geriatric Cardiology – 2026

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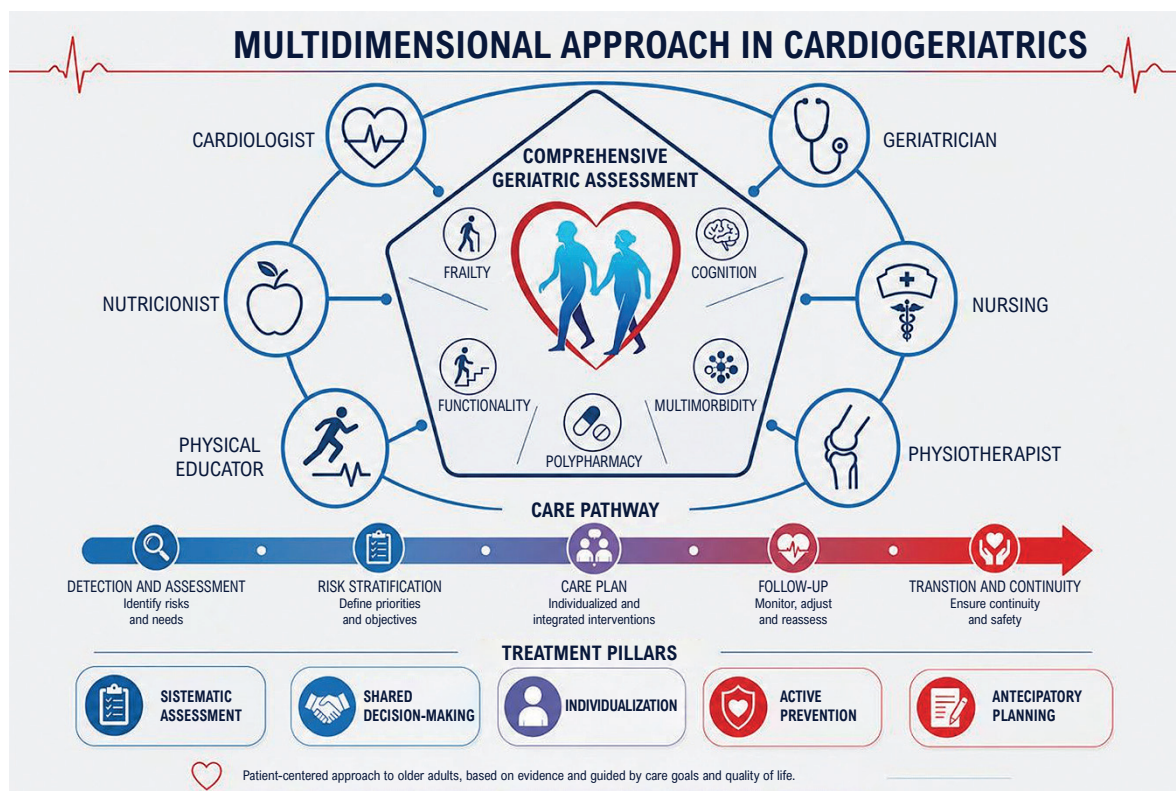
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1. The Pioneering Role of Brazilian Geriatric Cardiology

In 2002, while leading the Geriatric Cardiology Study Group (GEBRAC) of the Brazilian Society of Cardiology (SBC), we identified an important gap: there were no guidelines specifically targeting older adults. With the participation of Dr. Claudia F. Gravina and the unrestricted support of Prof. José Carlos Nicolau, we brought together 51 specialists from across Brazil who, over the course of 3 days in São Pedro, São Paulo, developed the world's first guideline specifically dedicated to geriatric cardiology. Published in 2002 in *Arquivos Brasileiros de Cardiologia*, the document has had a major impact and is widely cited and consulted in the scientific literature to this day.

In 2010, the SBC Geriatric Cardiology Department (DECAGE), with the support of Dr. Jadelson Andrade, gathered

Guidelines

more than 100 professionals to produce the II Brazilian Geriatric Cardiology Guidelines, in partnership with the Brazilian Society of Geriatrics and Gerontology (SBGG) and with the collaboration of international experts. In 2014, we presented the guidelines during a joint session of the American College of Cardiology (ACC) in Washington, D.C.

In 2019, a new update of the SBC Geriatric Cardiology Guidelines was published under the editorship of Gilson Soares Feitosa-Filho, José Maria Peixoto, and José Elias Soares Pinheiro.

We have now reached the III SBC Geriatric Cardiology Guidelines, edited by Izo Helber, José Maria Peixoto, and José Carlos da Costa Zanon, which once again demonstrate an innovative spirit by presenting, for the first time, a dedicated chapter on syncope in older adults.

More than two decades later, that pioneering initiative from 2002 remains alive and continues to evolve, reaffirming the leading role of Brazilian geriatric cardiology.

The Central Illustration of the 2026 Brazilian Guideline on Geriatric Cardiology summarizes the care philosophy that underpins this document. At its core, older patients and their families—represented by the DECAGE visual identity—are encompassed by the Comprehensive Geriatric Assessment, whose domains (frailty, cognition, functional status, multimorbidity, and polypharmacy) guide all cardiovascular decision-making. Surrounding this core, the multidisciplinary co-management ring highlights the need for shared care, recognizing that the complexity of older adults with cardiovascular disease requires multiprofessional support. The care pathway at the bottom depicts the continuum of care—from prevention and immunization to diagnostic screening, optimized treatment, individualized interventions, and palliative care—while the five supporting pillars consolidate the principles that underpin the Guideline recommendations. In summary, the Central Illustration reinforces its key message: cardiovascular care in aging should be person-centered, data-informed, and guided by goals of care and quality of life.

2. General Aspects of Old Age, Risk Factors, and Prevention

There has been a marked increase in the number of older adults worldwide in recent decades, particularly in low- and middle-income countries.¹ It is estimated that, by 2030, approximately 22% of the world's population will be over 60 years of age, nearly double the 12% observed in 2015.² Among all age groups, those over 80 years of age will experience the greatest growth—their numbers are expected to triple by 2050.² Brazil is in line with this global trend: according to the 2022 Brazilian Institute of Geography and Statistics (IBGE) census, the population aged over 65 years grew by 57.4% compared with 2010. One of the main drivers of this phenomenon is the increase in life expectancy. In 2000, life expectancy was 71.1 years; by 2023, it had reached 76.4 years, and it is projected to reach 83.9 years by 2070.³ The growing population of older adults will increase both the incidence and the prevalence of cardiovascular diseases (CVDs), which are major risk factors for myocardial infarction (MI), stroke, heart failure (HF), arrhythmias, and thromboembolism.⁴

The aging of the world's population has been accompanied by an increasing prevalence of age-related CVDs. HF, for example, affects 1%–2% of the adult population in developed countries, and exceeds 10% among individuals aged 70 years or older.⁵ Similarly, the prevalence of atrial fibrillation (AF) increases progressively with age, reaching 10%–17% among individuals aged 80 years or older.⁶ Aging is a complex biological process characterized by the progressive loss of physiological integrity and increased vulnerability to disease and death.⁷

Cardiac aging is an important nonmodifiable risk factor for CVD, contributing to the growing global burden of these conditions.⁸ With increasing longevity, a higher prevalence of HF with preserved ejection fraction (HFpEF), AF, and ischemic heart disease is expected.^{9–13} Although traditional risk factors contribute to this process, cardiac aging is primarily driven by interconnected molecular mechanisms, including oxidative stress, mitochondrial dysfunction, impaired autophagy, epigenetic alterations, inflammation, and fibrosis.^{14–17} These processes promote structural remodeling and functional deterioration even in apparently healthy older individuals and may contribute to worse cardiovascular prognoses.¹⁸ In this context, understanding the intrinsic mechanisms of cardiac aging is essential for the development of preventive and therapeutic strategies capable of preserving cardiovascular health.

2.1. Age-related Changes in Cardiac Structure and Function

2.1.1. Structural and Functional Changes

Cardiac aging is characterized by left ventricular hypertrophy, diastolic dysfunction, reduced functional reserve, myocardial fibrosis, extracellular matrix remodeling, increased arterial stiffness, and impaired endothelial function. Although ejection fraction is generally preserved, there is a progressive decline in intrinsic contractility associated with reduced β -adrenergic responsiveness and alterations in intracellular Ca^{2+} handling. Diastolic changes are more pronounced: early left ventricular diastolic filling progressively declines beginning in adulthood and may decrease by approximately 50% by age 80, while the contribution of atrial contraction to ventricular filling increases.¹⁹

These changes favor the development of HFpEF and AF, conditions often associated with aging.^{20,21} Among the main alterations are left ventricular hypertrophy, impaired diastolic function, left atrial enlargement, myocardial fibrosis, and, in some individuals, cardiac amyloidosis, generally with preserved ejection fraction.²²

2.1.2. Organ-Level Changes

With advancing age comes structural remodeling of the heart, characterized primarily by increased left ventricular wall thickness related to cardiomyocyte loss and compensatory hypertrophy, as well as increased mechanical stress and interstitial fibrosis.²³ The aging heart exhibits an increased ventricular mass-to-volume ratio, associated with reduced ventricular dimensions and asymmetric hypertrophy, particularly due to thickening of the interventricular septum.²³ Similar changes may occur in the right ventricle, although they are generally less pronounced.

In the atria, increased dependence on atrial contraction for ventricular filling, associated with structural remodeling and fibrosis, promotes atrial enlargement and the development of AF. Left atrial size is directly related to the risk of this arrhythmia.²⁴ Thus, age-related cardiac remodeling, particularly left ventricular hypertrophy and left atrial enlargement, plays a central role in the pathophysiology of HFpEF and AF.²⁵

As discussed above, aging, including cardiovascular aging, is a natural and inevitable process; however, identifying individuals with accelerated aging remains challenging. Recent studies indicate that aging is not uniform across individuals and may be influenced by lifestyle habits and metabolic, environmental, genetic, and epigenetic factors. Furthermore, interventions such as lifestyle changes, pharmacological treatments, and therapies targeting the mechanisms of aging may delay or even partially reverse cardiovascular aging, reinforcing the concept that this process may be partially modifiable.²⁶

2.1.3. Promotion of Healthy Aging

The World Health Organization (WHO) defines healthy aging as “the process of developing and maintaining the functional ability that enables well-being in older age”. Promoting healthy aging requires an integrated approach that combines lifestyle changes, health technologies, and patient-centered care strategies. Among the key interventions is the American Heart Association (AHA)'s Life's Essential 8, which encompasses eight components for cardiovascular risk reduction: smoking cessation, healthy diet, regular physical activity, weight management, blood pressure (BP) control, cholesterol management, glycemic control, and adequate sleep.²⁷⁻²⁹

Digital technologies widen the potential for prevention and monitoring in older adults. Telemedicine, telehealth, wearable devices, and remote monitoring can facilitate the assessment of physiological parameters and physical activity, contributing to the early identification of abnormalities and the promotion of healthy habits.^{30,31} In this context, objective measures of physical activity, such as step count and exercise duration, have been associated with better functional capacity and lower cardiovascular risk.³⁰

Care of older adults with CVD should include systematic screening for geriatric syndromes and individualized assessment of functional status, frailty, cognition, nutritional status, comorbidities, polypharmacy, life expectancy, and patient preferences.^{31,32} The comprehensive geriatric assessment (CGA) may help identify vulnerabilities and guide multidisciplinary interventions, balancing cardiovascular prevention, therapeutic safety, functional independence, and quality of life.³³⁻³⁵ Although the CGA is detailed and typically used in specialized settings for high-risk older adults, geriatric screening focuses on early detection and prevention, enabling proactive management before substantial decline occurs.

CVDs are influenced by both modifiable and non-modifiable risk factors. Modifiable risk factors include smoking, inadequate diet, sedentary lifestyle, excessive alcohol consumption, hypertension, dyslipidemia, diabetes mellitus (DM), obesity, and stress. Non-modifiable risk factors include age, sex, and genetics.

Aging is one of the main risk factors for CVD because it leads to structural and functional changes in the heart and blood vessels, including cardiac fibrosis, reduced functional capacity, endothelial dysfunction, arterial stiffness, and

chronic inflammation. These changes increase vulnerability to conditions such as HF, AF, and atherosclerosis.

However, recent studies indicate that individuals do not all age the same way and that aging may be influenced by lifestyle habits as well as metabolic, environmental, and genetic-epigenetic factors. Furthermore, interventions such as lifestyle changes, pharmacological treatment, and therapies targeting the mechanisms of aging may delay or even reverse part of cardiovascular aging, supporting the idea that this process may be partially modifiable.²⁶

The follow-up of older adults and the development of a care plan through CGA are essential for a comprehensive patient assessment. One of the areas of the CGA is the prevention of inappropriate polypharmacy, which requires a systematic approach based on regular medication review, rational deprescribing, and coordination of care across different levels of service. Mental health has a substantial impact on CVD in older adults, making the screening and diagnosis of depression, anxiety, and social isolation of paramount importance. Frailty increases susceptibility to functional loss, falls, prolonged hospitalization, institutionalization, and mortality.³⁶

2.2. Particularities in the Evaluation of Older Adults: When and How Should a Comprehensive Geriatric Assessment Be Performed?

According to the latest data from IBGE, the older adult population continues to grow rapidly, a phenomenon widely known in cardiology for several years.³ It is also well established that this population is heterogeneous; therefore, relying solely on chronological age for decision-making in health care is no longer acceptable. These differences encompass functional capacity, life trajectory, comorbidities, and lifelong habits maintained by the older adult. Accordingly, older adults present physiological, pathological, and psychosocial particularities that often render traditional clinical assessments inadequate.³⁷

In this context, the CGA has emerged as a fundamental pillar for the assessment, follow-up, and development of the care plan for older adults. More than a simple set of assessments, the CGA is a multidimensional diagnostic process that seeks to identify risk factors, enable the early diagnosis of diseases and conditions associated with aging, and evaluate functional capacity, cognitive function, socioeconomic status, nutritional status, emotional and spiritual health, and care preferences. Its primary objective is to develop an individualized and comprehensive care plan aimed at optimizing quality of life, preserving autonomy, and promoting healthy aging.³⁸

2.2.1. Particularities of Older Adults and the Comprehensive Geriatric Assessment

The assessment of older adults requires a comprehensive approach, since chronological age does not necessarily reflect biological age, functional reserve, or degree of vulnerability. The heterogeneity of this population, associated with the high prevalence of multimorbidity and polypharmacy, increases the risk of drug interactions, adverse events, and iatrogenesis.³⁸⁻⁴¹

In addition, diseases may present with atypical or nonspecific manifestations. MI, infections, and other acute

conditions may occur without classic signs, while delirium may be the first manifestation of an underlying disease. Similarly, depression and cognitive impairment may manifest predominantly through functional or behavioral changes, hindering diagnosis based on conventional assessment.

Functional status is one of the main markers of health in aging. Loss of independence in basic, instrumental, and advanced activities of daily living is associated with a higher risk of adverse events and should be systematically assessed. In this setting, frailty, characterized by reduced physiological reserve and increased vulnerability to stressors, plays a central role in risk stratification and therapeutic planning.

Cognitive impairment, mood disorders, social isolation, bereavement, socioeconomic conditions, and the quality of the support network may also directly interfere with treatment adherence, decision-making, functional status, and quality of life. Therefore, these aspects should be incorporated into the clinical assessment, together with comorbidities, nutritional status, polypharmacy, and environmental conditions.

Finally, therapeutic goals in older adults should be individualized, prioritizing, according to the clinical context, the preservation of autonomy, function, quality of life, and dignity. Thus, the CGA becomes an essential tool for recognizing vulnerabilities that may remain hidden during conventional assessment and for guiding a care plan corresponding to the needs, values, and preferences of the older adult.

Therefore, given this level of complexity and these particularities, when should the CGA be performed? This assessment is particularly indicated for:^{37,40}

- Advanced age (> 75–80 years);
- Frailty or risk of frailty (identified through screening);
- Multiple comorbidities and/or polypharmacy;
- Recent or progressive functional decline;
- Cognitive alterations or a diagnosis of dementia;
- Frequent hospitalizations or recurrent falls;
- Transition of care;
- Situations requiring complex decision-making.

2.2.2. Conducting the Comprehensive Geriatric Assessment: Essential Domains

The CGA is a multidimensional and interdisciplinary process designed to identify clinical, functional, cognitive, nutritional, psychological, and social problems that may go unnoticed during a conventional assessment. Its application should be individually planned and may take place over two or more visits and involve different health care professionals, depending on the needs identified.^{37,40}

2.2.2.1. Domains of the Comprehensive Geriatric Assessment

Assessment of basic activities of daily living, such as bathing, dressing, eating, continence, and transfers, may be performed using instruments such as the Katz and Barthel scales; while instrumental activities of daily living, such as meal preparation, shopping, medication management, and financial management, may be assessed using the Lawton

and Brody scale. Mobility and fall risk can be assessed using the Five Times Sit-to-Stand Test and gait speed (usually 3–4 meters, with a normal completion time of up to 8 seconds).

2.2.2.2. Cognitive Assessment

Screening for cognitive impairment and dementia may be performed using instruments such as the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). In hospital settings, the Confusion Assessment Method (CAM) assists in delirium screening.

2.2.2.3. Nutritional Status Assessment

Assessment of unintentional weight loss, malnutrition, chewing or swallowing difficulties, and conditions that impair food intake may be conducted using the Mini Nutritional Assessment (MNA).

2.2.2.4. Psychological Assessment

Depression, anxiety, mood changes, and social isolation may be identified through directed history taking and, when necessary, with the use of instruments such as the Geriatric Depression Scale (GDS).

2.2.2.5. Social and Environmental Assessment

For assessment of the family support network, housing conditions, socioeconomic status, social and leisure activities, and caregiver burden, specific instruments such as the Zarit Burden Interview may be used.⁴²⁻⁴⁵

2.2.2.6. Medication Review

Polypharmacy, potentially inappropriate medications, drug interactions, therapeutic duplication, and medication adherence problems may be identified using tools such as the Beers Criteria and the STOPP/START criteria, with deprescribing strategies incorporated when appropriate.^{39,46}

2.2.2.7. Comorbidities and Sensory Impairment

Chronic diseases, incontinence, pressure injuries, and visual and hearing impairments may be actively assessed using simple tests that can be performed in the office setting.^{37,40}

2.2.2.8. Existential Issues

For the identification of values, beliefs, sources of hope, and personal priorities, instruments such as FICA (Faith, Importance, Community, and Action) and HOPE (Sources of Hope, Organized Religion, Personal Spirituality, and Effects on Medical Care) may be used. This approach contributes to shared care planning, including advance directives and the definition of therapeutic goals.^{47,48}

2.2.3. Why is the Standard Assessment Not Enough? Comparing the Comprehensive Geriatric Assessment with the Traditional Approach

In older adults, the complexity of their health conditions and the atypical presentation of disease make the standard clinical

approach insufficient for developing a truly optimized care plan. By failing to consider aging-related issues, including frailty, fall risk, early cognitive impairment, and caregiver burden, the standard assessment fails to prevent adverse outcomes, including mortality, and to promote quality of life, well-being, and longer survival.

2.2.4. Benefits of the Comprehensive Geriatric Assessment: Outcomes

The CGA facilitates the identification of geriatric problems and underdiagnosed conditions, enabling early and individualized interventions. Its main benefits include the detection of frailty, sarcopenia, risk of falls, malnutrition, incontinence, depression, and cognitive impairment, as well as the identification of social problems and caregiver burden.^{37,38}

By directing interventions toward functional capacity, the CGA may help preserve or restore independence, improve quality of life, and reduce complications. The systematic medication review may reduce polypharmacy and the risk of adverse events, while interventions addressing mobility, the environment, and social support may reduce falls, hospitalizations, and institutionalization.

Another fundamental benefit is the promotion of person-centered care. Incorporating individual values, preferences, expectations, and goals favors shared decision-making and allows treatment intensity to be tailored to the patient's clinical and functional status. In advanced or irreversible conditions, this approach facilitates the definition of proportionate goals of care and the preservation of dignity.

The CGA also recognizes the caregiver as a fundamental part of the care process. Identifying caregiver burden enables the provision of support and strategies that promote the continuity and sustainability of home care.

2.2.5. Final Considerations

The CGA is an integral part of the assessment and planning of the care of older adults, complementing the conventional clinical approach by incorporating functional, cognitive, nutritional, psychological, social, and existential dimensions. Although time-consuming and often requiring interdisciplinary participation, it allows vulnerabilities that might otherwise remain hidden to be identified and provides guidance for individualized interventions. Its primary goal is not simply to prolong life, but to preserve autonomy, function, safety, quality of life, and dignity, aligning therapeutic decisions with the needs and values of the older adult.

2.3. Frailty: When and How to Screen it?

Aging is a complex biological process determined by multiple intrinsic and extrinsic factors. It is characterized by disturbances in cellular homeostasis, deterioration of tissue function, and physiological dysregulation of the organism.³⁶ Conventionally, aging has been attributed to the cumulative deterioration of multiple tissues. The systemic and organ-specific changes due to aging combine with those caused by CVD, resulting in an increased prevalence of clinical vulnerability syndromes such as sarcopenia, cachexia, and frailty (Figure 2.1).

2.3.1. The Relationship between Frailty and Cardiovascular Disease

Frailty is a syndrome resulting from the aging process, characterized by impaired ability of the body to respond adequately to physical, mental, and social stress.⁴⁹ This condition causes greater susceptibility to functional decline, falls, prolonged hospitalization, institutionalization, and mortality.⁵⁰⁻⁵² The association between frailty and CVD is bidirectional,⁵³ as both share common etiological factors and have outcomes that interact with one another. In other words, CVD is a risk factor for frailty, and frailty is a risk factor for CVD (Figure 2.1).

Their epidemiological relationship is also intense. Among older adults with CVD, the prevalence of frailty ranges from 25% to 60% and may reach as high as 80% in select groups, such as patients with HF.^{51,54,55} Frailty also increases disease severity and contributes to worse CVD-related outcomes,⁵⁵ due to a higher incidence of adverse events during procedures and hospitalization, including bleeding, thromboembolic events, and readmissions, and is associated with a substantially increased risk of mortality, regardless of age or the underlying CVD.^{50,56}

Cross-sectional studies have found a strong association between frailty and CVD among community-dwelling older adults, with odds ratios (OR) ranging from 2.7 to 4.1.⁵⁶ Furthermore, subclinical cardiovascular abnormalities detected by noninvasive examinations (left ventricular hypertrophy on echocardiography, regional wall motion abnormalities, electrocardiographic [ECG] alterations, systolic hypertension, increased carotid intima-media thickness, evidence of stroke on magnetic resonance imaging [MRI], and ankle-brachial index [ABI] < 0.8) have each been associated with frailty and mortality.⁵⁷ One explanation for this association is that CVDs and frailty share common pathophysiological mechanisms, including inflammation, thrombosis, and elevated levels of factor VIII, D-dimer, and C-reactive protein.^{58,59}

2.3.2. Patients Who Should Be Assessed for Frailty

The objective of frailty screening in older adults with CVD is to establish an initial risk profile for epidemiological and therapeutic perspectives (whether invasive or noninvasive) in order to reduce the risk of mortality, functional decline, and impaired quality of life. Although several medical and academic societies have issued recommendations regarding which older adults with CVD should undergo screening, there is still no consensus. Nevertheless, there is substantial agreement regarding the underlying concepts.

The AHA does not have a formal recommendation but has cited recommendations similar to those issued in 2019 by the Task Force of the International Conference on Frailty and Sarcopenia Research, which recommends that health care professionals identify and screen all older adults for frailty using a validated instrument appropriate to the specific clinical setting (strong recommendation). Ideally, the screening instrument should exclude disability as part of the screening process. Individuals who screen positive for frailty should undergo a more comprehensive clinical assessment to identify the underlying mechanisms and signs of frailty

Guidelines

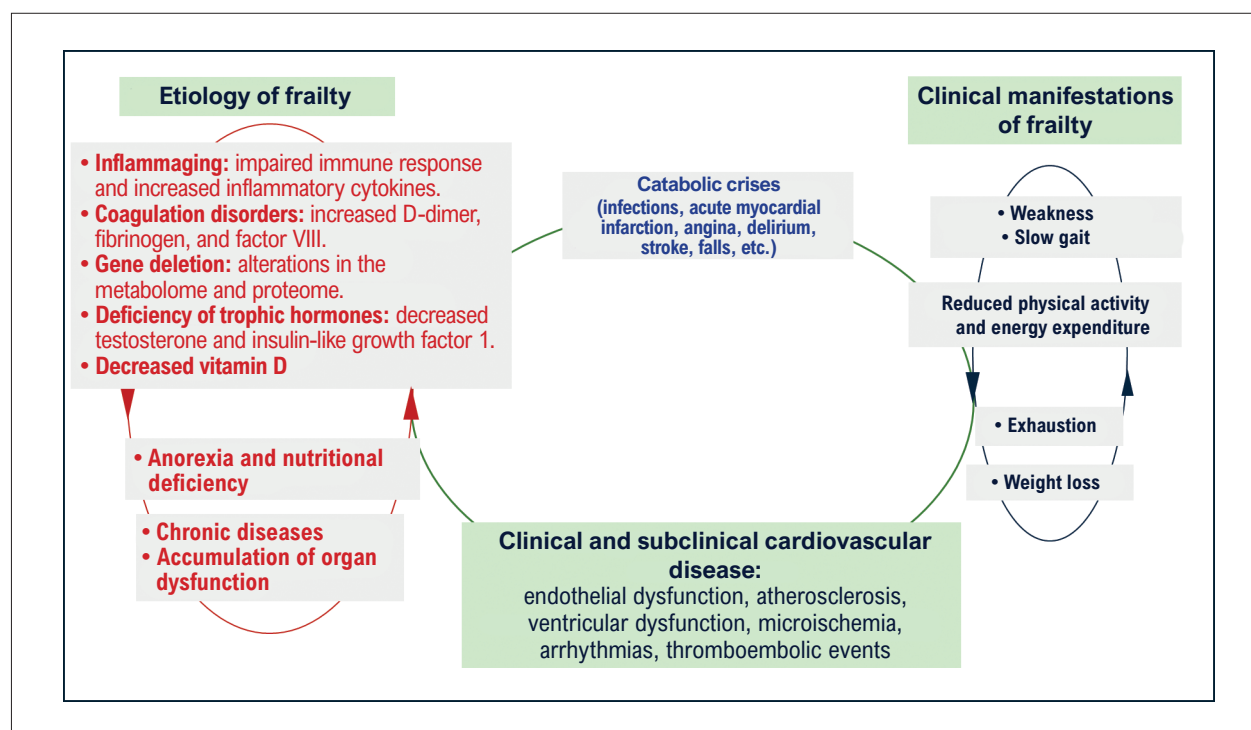


Figure 2.1 – Interactive cycle between the etiologic factors shared by cardiovascular disease and frailty, which act systemically, causing subclinical and clinical changes that interact with one another, perpetuating the harmful cycle between these conditions.

(strong recommendation). The European Society of Cardiology (ESC),⁶⁰ in turn, recommends screening individuals aged 65 years or older who have special conditions, as well as all adults over the age of 70. Based on the recommendations of these two societies and the Task Force, we propose the following recommendations for frailty screening in older adults with CVD, encompassing the concepts and criteria most frequently cited in the literature.

2.3.3. Individuals Who Should Be Screened for Frailty^{51,61,62}

- All older adults with CVD aged 70 years old or older.
- Older adults with CVD aged 65 years or older with special clinical conditions, such as:
 - Older adults receiving social assistance because of health problems, home health care services, hospitalization, or residing in long-term care facilities;
 - Individuals with significant unintentional weight loss (eg, more than 5% over one year or more than 3 kg over three months).
- Patients with multiple chronic conditions or specific diseases, such as:
 - DM;
 - Chronic obstructive pulmonary disease (COPD) or other debilitating respiratory diseases;
 - Stroke;
 - Neurodegenerative diseases (eg, dementia syndromes and Parkinson disease);

- HFpEF or HF with reduced ejection fraction (HFrEF);
- Cancer;
- Chronic kidney disease (CKD);
- HIV infection.

d) Patients scheduled to undergo cardiac interventions, including:

- Transcatheter aortic valve implantation (TAVI);
- Heart surgery (coronary artery bypass grafting [CABG], valve replacement);
- Percutaneous coronary intervention (PCI);
- Patients with acute coronary syndrome (ACS), such as ST-segment elevation MI (STEMI) and non-ST-segment elevation MI (NSTEMI);
- Patients with indication for implantation of cardiac electronic devices, including Pacemakers, cardiac resynchronization therapy (CRT) devices, and implantable cardioverter-defibrillators (ICDs).

2.3.4. Instruments for Frailty Screening in Older Adults with Cardiovascular Disease

There is broad agreement among geriatric and cardiology societies that instruments used to identify frailty should have high sensitivity and specificity, be practical and quick to administer, and be validated for the patient's specific clinical context, which may vary considerably. More than 60 frailty screening scales have been described in the literature, but most have been validated in populations

that differ substantially with respect to disease, age group, and ethnicity.

The AHA⁵¹ does not currently endorse a specific frailty assessment instrument, but both the ESC⁶⁰ and the Task Force of the International Conference on Frailty and Sarcopenia Research⁶¹ recommend several instruments that are also frequently used in AHA publications. These recommendations are intended to maximize both diagnostic sensitivity and specificity. Accordingly, the ESC recommends different instruments depending on risk profile and clinical population.

Based on these factors, we have divided older adults into two groups: Group A – individuals with systemic diseases (HF, acute MI [AMI], AF, and hypertension) who require epidemiological risk assessment; Group B – individuals scheduled to undergo medium- or high-complexity procedures (aortic valve implantation, CABG, or valve replacement) who require risk assessment. For Group A, instruments that assess physical frailty are recommended⁶⁰ (eg, the Fried or Johns Hopkins Frailty Phenotype or the Short Physical Performance Battery), while patients in Group B are better evaluated using multidimensional frailty assessment instruments (eg, the Frailty Index, the Multidimensional Prognostic Index derived from the CGA, or the Edmonton Frail Scale [EFS]). However, these instruments are more time-consuming and complex. When rapid screening is required, the Clinical Frailty Scale (CFS) – a simplified version of the Frailty Index – or the Essential Frailty Toolset is recommended.

2.3.4.1. Group A: Physical Frailty Scales

- Fried or Johns Hopkins Physical Frailty Phenotype⁴⁹: assesses weight loss, exhaustion, weakness (handgrip strength), slow gait (gait speed), and previous energy expenditure. Advantages: It has been widely used in the literature, within numerous epidemiological studies and assessments across different areas. It is one of the most commonly used research instruments and has been validated for diverse ethnicities and special populations. Disadvantages: It requires equipment (a dynamometer and stopwatch) and space for the walking test. Assessment of energy expenditure using the original questionnaire requires time and adequate comprehension, limiting its use in clinical practice. Some authors have replaced this item with the sit to stand test,⁶² or with the following question: “Compared with the past month, do you feel that you have greater difficulty or are no longer able to perform your daily activities?”;
- Short Physical Performance Battery (three items)⁶³: an instrument consisting of three physical activity tasks involving balance (standing in three different positions), weakness (standing up from a chair), and gait (5-minute walk test). Advantages: Assess several physical aspects involving muscular function and the peripheral and central nervous systems. It has been widely used in the literature and validated in multiple languages and populations.

Disadvantages: It requires time and adequate space to perform the assessments, as well as equipment (a dynamometer and stopwatch).

2.3.4.2. Group B: Multidimensional Frailty Scales

- CFS:⁶⁴ a 9-point scale used for rapid assessment of clinical vulnerability. Advantages: Easy to administer and does not require measurement equipment. It has been widely used in population-based studies and, particularly, for preoperative risk assessment. Disadvantage: Interpretation of the criteria is subjective and requires prior knowledge of the patient's basic and instrumental activities of daily living;
- EFS⁶⁵: most often used in acute care hospital settings. It consists of 11 items encompassing cognition, general health, independence, and social support. Scores are interpreted as follows: 0–4 (not frail), 5–6 (vulnerable), 7–8 (mild frailty), 9–10 (moderate frailty), and 11 (severe frailty). Advantages: Quick to administer and validated in multiple populations. Disadvantages: More suitable for patients in hospital settings; administration may be more time-consuming in emergency settings; requires specialized training; and has relatively lower sensitivity than other instruments;
- Essential Frailty Toolset⁶⁶: a 4-item instrument that encompasses functional testing, laboratory parameters, and cognitive assessment. Advantages: Quick to administer with no subjective components. It has demonstrated high specificity for mortality in patients undergoing TAVI and valve replacement surgery. Disadvantages: Requires laboratory testing and additional time to complete the cognitive assessment using an appropriate questionnaire. It is most frequently used in studies evaluating preoperative risk.

2.3.4.3. Frailty Markers^{51,60}

Five individual criteria, which are components of comprehensive frailty assessment instruments, may also be used individually as frailty markers. They provide a fast method for identifying individuals at high risk for frailty, who should subsequently undergo a more comprehensive assessment using the instruments recommended above.

- Slow gait: the patient stands behind the starting line and is instructed to walk at a comfortable pace beyond the 5-meter finish line. The stopwatch is pressed with the first step after the starting line and again with the first step after crossing the finish line. The average of three attempts is recorded. Slow: < 0.83 m/s (> 6 s); Very slow: < 0.65 m/s (> 7.7 s); and Extremely slow: < 0.50 m/s (> 10 s);
- Weakness: handgrip strength is measured three times in both the dominant and nondominant hands using a dynamometer. The patient should be instructed to exert maximal grip strength each time. The highest value obtained for the dominant hand is recorded. Men: < 30 kg and women: < 20 kg;

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- Self-reported or measured unintentional weight loss of ≥ 4.54 kg (10 pounds) during the previous year;
- Nutritional impairment: serum albumin concentration < 3.5 g/dL;
- Anemia: hemoglobin concentration < 13 g/dL in men and < 12 g/dL in women.

In summary, frailty is a clinical syndrome with high prevalence among older adults with CVD. It acts synergistically in the progression and incidence of CVD and is considered an important risk factor for poor outcomes and mortality. Older adults with CVD aged 65 years or older should be assessed for frailty when special clinical conditions are present, while all adults over 70 years of age should undergo frailty screening regardless of clinical status. At present, no single instrument is specifically recommended for assessing frailty across all groups of older adults with CVD. Physical frailty instruments are recommended for patients requiring epidemiological risk assessment, while multidimensional frailty instruments are recommended for individuals requiring risk assessment before medium- or high-complexity procedures.

2.4. Polypharmacy: How to Prevent it?

The progressive increase in life expectancy observed in recent decades has been accompanied by a higher prevalence of chronic noncommunicable diseases, including hypertension, DM, CVD, osteoarticular disorders, and neurodegenerative diseases.⁶⁷ These conditions frequently coexist in the same individual, resulting in a condition of multimorbidity that requires continuous clinical follow-up and long-term therapeutic interventions.

In this context, there has been a marked increase in the number of medical prescriptions and the concomitant use of multiple medications, a situation known as polypharmacy.⁶⁸ This phenomenon is particularly prevalent among older adults due to the greater clinical complexity involved, that care is provided by multiple health care professionals and specialties, the fragmentation of care, and the difficulty of systematically reviewing treatments that accumulate over time. Furthermore, self-medication and the prolonged use of medications initially prescribed for acute conditions contribute to the progressive increase in the number of medications used.

Although polypharmacy may be clinically appropriate in certain situations, particularly in the management of multiple chronic diseases, inappropriate polypharmacy represents a major public health issue. The concomitant use of multiple medications is associated with an increased risk of drug interactions, adverse reactions, prescribing errors, and poor treatment adherence. These risks are further amplified by the pharmacokinetic and pharmacodynamic changes inherent to the aging process.

The evidence indicates that inappropriate polypharmacy is associated with poorer quality of life, a higher incidence of adverse events, increased hospitalization rates, functional and cognitive decline, and higher health care costs.^{69,70} Complex therapeutic regimens may also compromise the autonomy of older adults, hinder the effective management

of chronic diseases, and reduce the effectiveness of proposed interventions.

Given this scenario, polypharmacy should be understood not merely as a consequence of the multimorbidity associated with aging but as a clinical and organizational challenge requiring specific prevention and management strategies. Accordingly, it is essential to discuss the factors associated with its occurrence, as well as clinical approaches aimed at rationalizing medication use, conducting regular prescription reviews, and promoting patient-centered care in order to reduce risks and optimize therapeutic benefits.

2.4.1. Concepts and Classifications of Polypharmacy

The scientific literature does not provide a single, universally accepted definition of polypharmacy. The most widely used quantitative definition refers to the concomitant use of five or more medications.⁷¹ Additionally, some authors define excessive polypharmacy or hyperpolypharmacy as the use of 10 or more medications, a condition associated with a significantly increased risk of adverse events.⁷²

However, more recent approaches have suggested a qualitative distinction between appropriate polypharmacy and inappropriate polypharmacy.⁷³ Appropriate polypharmacy occurs when all prescribed medications have a clear clinical indication, proven efficacy, an acceptable safety profile, and are in line with the patient's therapeutic goals. In contrast, inappropriate polypharmacy involves medications without a current indication, therapeutic duplication, inappropriate dosages, or medications whose risks outweigh their expected benefits.

2.4.2. Epidemiology of Polypharmacy

International studies indicate that the prevalence of polypharmacy among individuals aged 65 years or older ranges from 40% to 60% and can exceed 70% in hospital settings and long-term care facilities.^{74,75} Time-trend analyses have found a progressive increase in the use of multiple medications in recent decades, reflecting changes in prescribing patterns and in the epidemiological profile of populations.⁷⁶

In Brazil, studies conducted in primary health care settings have found a high prevalence of polypharmacy, particularly among older adults, women, and individuals with lower educational attainment. In addition, the frequent use of potentially inappropriate medications, which further increases the risks associated with polypharmacy, has been observed.

2.4.3. Factors Associated with Polypharmacy

Multimorbidity is the main determinant of polypharmacy, particularly when disease-specific guidelines result in cumulative prescribing without adequate consideration of treatment burden and drug interactions.⁷¹ Fragmentation of care, involving multiple prescribers and limited coordination, favors duplications, medications with similar mechanisms, and failure to conduct periodic medication reviews.⁷⁷ Self-medication, including herbal medicines, supplements, and over-the-counter medications, also contributes to increased medication burden and unrecognized interactions.⁷⁸

Polypharmacy is associated with an increased risk of adverse reactions, drug interactions, functional and cognitive decline, falls, and poorer treatment adherence, and may contribute to preventable hospitalizations.⁷⁹⁻⁸¹ Excessive polypharmacy is also associated with higher mortality, particularly among frail older adults and those with multimorbidity.⁷⁴

2.4.4. Evidence-Based Strategies for Preventing Polypharmacy

Prevention of inappropriate polypharmacy involves systematic medication review, deprescribing, the use of explicit criteria, a multidisciplinary approach, and education of patients and caregivers.

Periodic medication review allows assessment of medication indication, efficacy, safety, dose, and duration, as well as identification of therapeutic duplications and interactions.⁸²

Deprescribing, when performed in a planned and individualized manner, consists of reducing or discontinuing medications that provide no clinical benefit or pose potential risks and may reduce medication burden without a significant increase in adverse events.^{71,83}

The Beers Criteria and other prescribing tools assist in identifying potentially inappropriate medications for older adults.⁷⁹ Multidisciplinary care contributes to the optimization of pharmacotherapy and patient safety, while education of patients and caregivers promotes rational medication use, adherence, and reduction of self-medication.^{69,77}

2.4.5. Challenges and Future Perspectives

Despite the available evidence, implementing strategies to reduce polypharmacy faces challenges such as prescriber resistance, limited visit times, and the lack of integrated health information systems. Investment in continuing education, clinical decision support technologies, and patient-centered models of care is essential to address these challenges.

2.4.6. Conclusion

Polypharmacy represents a growing challenge in the health care of older adults, resulting from increased longevity, multimorbidity, and the complexity of clinical care. Although the concomitant use of multiple medications may be necessary in certain contexts, inappropriate polypharmacy is associated with important negative outcomes that directly affect quality of life, patient safety, and health care costs.

Preventing inappropriate polypharmacy requires a systematic approach based on regular prescription reviews, rational deprescribing, and coordination of care across different levels. Placing the patient at the center of the decision-making process and prioritizing nonpharmacological strategies are fundamental to promoting the rational use of medications.

In this context, it is essential that health care professionals incorporate practices aimed at the continuous evaluation of pharmacotherapy, recognizing polypharmacy as an indicator of quality of care. The adoption of these strategies contributes to safer, more effective care that is better aligned with the needs of the older adult population.

2.5. Current Overview of Depressive and Anxiety Disorders in Older Adults with Cardiovascular Disease

Depression and anxiety remain highly prevalent among patients with CVD, including coronary artery disease (CAD), HF, and others. Recent studies confirm that depression not only accompanies these conditions but also has a prognostic role: it is associated with a higher risk of adverse events, poorer treatment adherence, and worse quality of life.⁸⁴⁻⁸⁷

Recent estimates indicate that the prevalence of depression among patients with CVD ranges from 20% to 30%, depending on the diagnostic method, stage of disease, and presence of psychiatric comorbidities.⁸⁷⁻⁸⁹

Although treating depression may improve psychiatric symptoms, quality of life, and adherence to cardiovascular treatment, there is no robust evidence that any single antidepressant can, by itself, consistently reduce major adverse cardiovascular events (MACEs) or mortality across all clinical settings.⁹⁰⁻⁹³

2.5.1. Impact of Depression and Anxiety on Cardiovascular Risk: the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)

Initial findings from the ELSA-Brasil study have shown a significant association between depressive and anxiety disorders and an increased likelihood of CAD. In a study by Kemp et al.,⁹⁴ involving 15,105 adults aged 35 to 74 years, participants with major depression associated with anxiety were approximately three times more likely to have CAD, while depression alone doubled the risk and anxiety alone increased the risk by approximately 1.5-fold, even after adjusting for traditional risk factors such as smoking, hypertension, and dyslipidemia.

2.5.2. Initial Assessment

The initial assessment should include a thorough clinical history that takes into account the particularities of older adults, especially age-related pharmacokinetic and pharmacodynamic changes and the presence of frailty. This assessment should be complemented by basic laboratory tests, including a complete blood count, thyroid function tests, electrolytes, renal and hepatic function tests, and vitamin B12, in order to identify potentially reversible organic causes of depressive symptoms, such as hypothyroidism, anemia, and vitamin B12 deficiency.⁹⁵

After organic causes have been ruled out, a comprehensive cardiovascular evaluation is recommended, including assessment for HF, arrhythmias, AMI, angina, and valvular heart disease (VHD), as well as measurement of BP and heart rate and evaluation for signs of congestion. Depression screening should be incorporated into the cardiovascular assessment, particularly after coronary events, taking into account cardiovascular conditions that may influence the presentation and management of symptoms.⁹⁶

The assessment should also include comorbidities and medications in use, including prescription, over-the-counter, and herbal products, with attention to potential drug interactions and the risk of QT-interval prolongation.

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and arrhythmias, particularly in patients with CVD or polypharmacy. Finally, the diagnosis should be confirmed and characterized using validated scales for screening and monitoring depression in older adults, together with a comprehensive clinical assessment.^{97,98}

2.5.3. Recommended Scales

The four scales most frequently used for the initial assessment are:

- Patient Health Questionnaire 2 (PHQ-2): used for rapid initial screening of depressed mood and anhedonia;⁹⁹
- Patient Health Questionnaire 9 (PHQ-9): used to assess the severity of depressive symptoms and follow up on treatment response;¹⁰⁰
- 15-item GDS (GDS-15): an instrument used to assess depression in older adults;¹⁰¹
- Hospital Anxiety and Depression Scale (HADS): useful in cardiology and general medical settings because it minimizes the influence of somatic symptoms.¹⁰²

2.5.4. Nonpharmacological Treatment of Depression in Older Adults with Cardiovascular Disease

Nonpharmacological interventions are fundamental to the management of depression in older adults with CVD because of their favorable safety profile and benefits to overall health.¹⁰³⁻¹⁰⁶

Exercise-based cardiac rehabilitation is a key intervention, associated with reductions in mortality and hospitalization as well as improvements in functional capacity and quality of life.¹⁰⁷ Supervised exercise also produces clinically meaningful reductions in depressive symptoms, including in patients with cardiovascular comorbidities.¹⁰⁸ Its benefits include improved cardiorespiratory fitness, autonomic modulation, reduced inflammation, and psychosocial effects, as well as preservation of muscle mass and functional independence in older adults.

Cognitive behavioral therapy is a first-line treatment for depression, with short-term efficacy comparable to that of pharmacotherapy and the potential to reduce relapse.¹⁰⁹ Its combination with antidepressants may provide greater benefit, particularly in moderate depression. In older adults, cognitive behavioral therapy is particularly relevant when antidepressants are contraindicated, poorly tolerated, or associated with an increased risk of adverse effects.¹¹⁰

Electroconvulsive therapy remains indicated for severe or treatment-resistant depression and for cases associated with imminent risk, such as suicidal ideation. In older adults with CVD, including those with pacemakers or ICDs, electroconvulsive therapy can be performed safely with prior cardiovascular assessment, hemodynamic monitoring, and an experienced team. In pacemaker-dependent patients, appropriate device management and monitoring during and after the procedure are recommended to reduce the risk of arrhythmias and electromagnetic interference.¹¹¹

2.5.5. Pharmacological Treatment of Depression in Older Adults with Cardiovascular Disease

Before initiating antidepressant treatment in older adults with CVD, a clinical and laboratory safety assessment is recommended, including ECG, with evaluation of the QT interval, conduction, and rhythm; renal and hepatic function, to guide drug selection and dose adjustment; and electrolytes, particularly potassium, magnesium, and sodium, given the risk of arrhythmias and hyponatremia associated with some antidepressants. Blood glucose and lipid profiles may be assessed according to the individual's cardiometabolic risk.

2.5.5.1. Major Adverse Cardiovascular Events and the Cardiovascular Safety of Antidepressants

The cardiovascular safety of antidepressants is often assessed using the composite outcome of MACEs, which generally includes cardiovascular death, nonfatal AMI, and nonfatal stroke, although its components may vary across studies.

Clinical trials and meta-analyses indicate a favorable cardiovascular safety profile for selective serotonin reuptake inhibitors (SSRIs) in patients with CVD, without a consistent increase in MACEs. For example, the SADHART-CHF study demonstrated the cardiovascular neutrality of sertraline with regard to MACEs in patients with depression and HF.^{112,113} The AHA also recognizes the importance of treating depression in patients with CVD and identifies SSRIs as an option with a favorable cardiovascular safety profile.¹⁰⁷

These data support a preference for SSRIs, particularly sertraline, in older adults with CVD. Vortioxetine has also demonstrated a favorable cardiovascular safety profile, although evidence specifically based on MACEs is more limited in this population.

However, these findings should be interpreted cautiously in geriatrics, because cardiovascular studies frequently underrepresent frail older adults and may fail to address outcomes that are particularly relevant to this population, such as orthostatic hypotension, hyponatremia, syncope, falls, and functional decline. Accordingly, a “start low and go slow” strategy is recommended, with individualized drug selection, clinical monitoring and, when indicated, ECG monitoring, in addition to nonpharmacological interventions.^{84,112,113}

2.5.5.2. Pharmacological Treatment: Principles for Selecting Antidepressants in Older Adults with Cardiovascular Disease

The choice of antidepressant should balance clinical efficacy and cardiovascular safety, taking into account age-related pharmacokinetic and pharmacodynamic changes, polypharmacy, the risk of drug interactions, frailty, falls, and multimorbidity. Treatment should be individualized based on the patient's cardiovascular profile, comorbidities, medications in use, renal and hepatic function, risk of QT-interval prolongation, history of treatment response and tolerability, and patient preferences (Table 2.1).

Table 2.1 – Selection and use of antidepressants in older adults with cardiovascular disease

Antidepressant	Reference dose in older adults with CVD	Certainty of evidence (GRADE)*	Strength of recommendation**	Main clinical considerations
Sertraline	25–200 mg/day	Moderate	Strong in favor	First choice in CVD; strongest cardiovascular evidence among SSRIs.
Escitalopram	5–10 mg/day	Moderate	Strong in favor	Good tolerability; attention to QT prolongation in at-risk patients.
Citalopram	10–20 mg/day	Low	Conditional	Dose-dependent QT prolongation risk; monitoring required in select patients.
Vortioxetine	5–15 mg/day	Low	Conditional	Alternative to SSRIs; possible cognitive benefit; limited cardiovascular evidence.
Mirtazapine	7.5–30 mg/day	Low	Conditional	Useful for insomnia and loss of appetite; risk of sedation and orthostatic hypotension.
Bupropion SR/XL	150–300 mg/day	Low	Conditional	Useful for avoiding sexual dysfunction and weight gain; monitor BP.
Venlafaxine XR	37.5–150 mg/day	Low	Conditional against routine use	May increase BP and HR; avoid in uncontrolled hypertension and decompensated heart failure.
Desvenlafaxine	50–100 mg/day	Very low	Conditional against routine use	Limited evidence; may increase BP and HR.
Trazodone	25–150 mg/day	Very low	Conditional against routine use	Preferentially used for insomnia; risk of sedation, falls, and hypotension.
Vilazodone	10–30 mg/day	Very low	Conditional against routine use	Insufficient evidence in CVD; individualized use.
Tricyclics	Nortriptyline 10–75 mg/day (exceptional)	Low	Strong against routine use	High cardiovascular and anticholinergic risk; avoid in older adults with CVD.

BP: blood pressure; CVD: cardiovascular disease; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HR: heart rate; SR: sustained release; SSRI: selective serotonin reuptake inhibitor; XL: extended release; XR: extended release. Note: Doses should be individualized according to frailty, renal and hepatic function, comorbidities, polypharmacy, and drug interactions. Low starting doses and slow titration are recommended.^{90,118–131} *Certainty of evidence (GRADE): assessed based on risk of bias, consistency, precision, indirectness of evidence, and clinical applicability. **Strength of recommendation: based on the balance between benefits and risks in the target population (strong or conditional, in favor of or against).

2.5.5.3. Selective Serotonin Reuptake Inhibitors and Cardiovascular Safety in Older Adults with Cardiovascular Disease

SSRIs are considered the treatment of choice for depression in older adults with CVD because of their favorable cardiovascular profile, lower proarrhythmic potential, and lower anticholinergic burden compared with tricyclic antidepressants. The SADHART-CHF study found that sertraline is neutral with regard to MACEs in patients with HF, while meta-analyses in patients with CAD have not identified a consistent increase in mortality or cardiovascular events associated with SSRIs.^{112,114,115}

Sertraline has the strongest body of cardiovascular safety evidence among SSRIs in patients with established heart disease and is particularly appropriate for those at higher cardiovascular risk. Escitalopram also has good tolerability and low potential for drug interactions, although evidence regarding MACEs is less robust than that for sertraline.^{112,116}

Despite the overall cardiovascular safety of SSRIs, citalopram and escitalopram may cause dose-dependent QT-interval prolongation, particularly in older adults with CVD, electrolyte disorders, arrhythmias, or concomitant use of other medications that prolong ventricular repolarization.¹¹⁷ In these patients, individualized assessment of arrhythmic risk is recommended, including baseline ECG and periodic monitoring when indicated, as well as assessment and correction of electrolyte abnormalities. For escitalopram, the dose should be limited to 10 mg/day in older adults, in accordance with applicable safety recommendations.¹¹⁷

The choice of antidepressant should take into account the cardiovascular profile, comorbidities, polypharmacy, and frailty. Low starting doses and gradual titration are recommended, with preference given to medications with greater experience of use in patients with CVD, particularly sertraline, together with individualized clinical follow-up.¹¹⁷

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2.5.5.4. Cardiometabolic Considerations in the Selection of Antidepressants for Older Adults with Cardiovascular Disease

The systematic review and network meta-analysis by Pillinger et al.¹³² analyzed 151 randomized controlled trials (RCTs) involving more than 58,000 participants, comparing 30 antidepressants with regard to their cardiometabolic, hemodynamic, and physiological effects. The analysis found considerable heterogeneity among the different molecules, reinforcing the need for individualized therapy in older adults with CVD (Table 2.2).

2.5.5.5. Safety and the Management of Depression in Older Adults with Cardiovascular Disease

Treatment of depression in older adults with CVD requires particular attention to polypharmacy, frailty, and age-related pharmacokinetic and pharmacodynamic changes. Key considerations include the risks of bleeding, hyponatremia, drug interactions, and cardiovascular events.¹³³⁻¹³⁵

SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) may increase the risk of bleeding, particularly gastrointestinal bleeding, by reducing platelet serotonin. This risk is higher during the first months of treatment and in patients receiving concomitant acetylsalicylic acid, dual antiplatelet therapy (DAPT), or anticoagulants, as well as in those with a history of gastrointestinal bleeding or greater frailty.¹³⁶⁻¹³⁸ Individualized assessment of bleeding risk is recommended, along with consideration of gastroprotection when indicated and counseling of patients and family members regarding signs of bleeding.

Hyponatremia, frequently associated with the syndrome of inappropriate antidiuretic hormone secretion, is another clinically relevant adverse effect of SSRIs and SNRIs in older adults. The risk is higher in frail patients, women, individuals with low body weight, renal failure, those using thiazide diuretics, and those with a previous history of hyponatremia.^{137,138} Sodium levels should be measured before treatment initiation and reassessed during the first few weeks

in patients at higher risk. In the presence of clinically significant hyponatremia, the need for continued antidepressant treatment should be reassessed, concomitant medications reviewed, and alternatives with a lower risk, such as bupropion or mirtazapine, considered depending on clinical context.¹³⁸

Drug interactions should also be systematically assessed. Potent CYP2D6 inhibitors, such as paroxetine, fluoxetine, and bupropion, may increase exposure to beta-blockers metabolized through this pathway, such as metoprolol, favoring bradycardia and hypotension.¹³⁸ In such cases, antidepressants with lower interaction potential should be considered, and BP and heart rate monitored, with ECG performed when symptoms or arrhythmic risk factors are present.

Finally, structured clinical reassessment is recommended 6 to 12 weeks after initiating or adjusting an antidepressant, addressing therapeutic response, adherence, adverse effects, cardiovascular risk, bleeding, changes in sodium levels, hypotension symptoms, arrhythmias, and falls. Assessment should incorporate validated scales, such as the PHQ-9 or the GDS-15, and consider continuation or addition of psychotherapy, cardiac rehabilitation, and psychosocial interventions.¹³⁶

2.6. Cardiology and Palliative Care in Geriatric Patients: Implementation, Timing, and Target Population

2.6.1. Definition of Target Population and Clinical Condition

The implementation of palliative care (PC) in geriatric cardiology should focus on older adults (≥ 60 years) and the oldest-old (≥ 80 years) with advanced cardiovascular conditions. Current guidelines recommend PC for all patients with HF, not only those with Stage D disease, representing an important shift in the paradigm of care.^{139,140} The priority target population includes patients with advanced HF (stages C/D, New York Heart Association [NYHA] functional class III-IV), recurrent hospitalizations, CAD with refractory angina not eligible for revascularization, severe VHD without indication

Table 2.2 – Cardiometabolic profiles of the antidepressants most commonly used in geriatric cardiology

Antidepressant	Weight	Total cholesterol	Blood glucose	Heart rate	Blood pressure
Sertraline	Mild	No change	No change	Neutral/Mild	Neutral
Escitalopram	Mild	No change	No change	Neutral	Neutral
Citalopram	Mild	No change	No change	Neutral	Neutral
Vortioxetine	Neutral	No change	No change	Neutral	Neutral
Mirtazapine	Weight gain	Mild increase	Mild increase	Neutral	Neutral
Bupropion	Weight loss	No change	No change	Mild increase	Neutral
Venlafaxine	Mild decrease	Increase	No change	Increase	Increase
Desvenlafaxine	Mild decrease	Increase	No change	Increase	Increase

Source: based on Pillinger et al.¹³²

for surgical or percutaneous intervention, and advanced pulmonary hypertension (WHO functional classes III-IV), as well as patients who are not candidates for transplantation and have electronic devices, such as an ICD with recurrent shocks, or left ventricular assist devices.^{139,141,142}

Geriatric complexity should be incorporated into the decision to implement PC. The presence of frailty (CFS ≥ 5), cognitive impairment or moderate to severe dementia, multimorbidity, and polypharmacy are markers that increase the risk of adverse events and underscore the need for an approach centered on quality of life.^{140,143}

2.6.2. Intervention Models and Components of Care

The implementation strategy for PC varies among specialized multidisciplinary team models, integrated cardiology models through co-management in HF or geriatrics outpatient settings, primary PC delivered by the cardiology team with consultative support, and home-based PC.¹³⁹⁻¹⁴¹ The distinction between primary PC (provided by all clinicians) and specialized PC (secondary-level care) is essential for the appropriate allocation of resources.¹⁴²

The core components include systematic assessment of symptoms such as dyspnea, pain, fatigue, anxiety, and depression, using validated tools such as the Kansas City Cardiomyopathy Questionnaire (KCCQ), Minnesota Living with Heart Failure Questionnaire (MLHFQ), and Edmonton Symptom Assessment System (ESAS).^{139,140,143} Advance care planning and the establishment of therapeutic goals are central pillars, as are device management (including ICD deactivation when appropriate), symptom- and safety-focused deprescribing, and caregiver support.¹⁴⁰

2.6.3. Timing of Initiation and Eligibility Criteria

Current guidelines have evolved from a prognosis-only approach to a needs-based approach, allowing earlier integration of PC.¹⁴¹ An international Delphi study identified are disease-based, needs-based, and time-based criteria for referral to specialized PC.¹⁴² The main criteria are described below.

a) Disease-based criteria:

- Two or more unplanned hospitalizations within 3 months or less;¹⁴²
- NYHA functional class III-IV with KCCQ < 50 ;^{140,142}
- Ineligibility for advanced therapies (transplantation, left ventricular assist devices);¹⁴²
- Continuous home inotropic therapy;¹⁴²
- Persistent severe left ventricular dysfunction;¹⁴²
- Cardiorenal syndrome;¹⁴²
- Cardiac cachexia;¹⁴²
- Intolerance to guideline-directed medical therapy (GDMT);¹⁴²

b) Needs-based criteria:

- Severe refractory physical or emotional symptoms;¹⁴²
- Significant functional limitation;¹⁴²

- Difficulty in decision-making;¹⁴²
- Poor social support;¹⁴²
- Mental health challenges;¹⁴²
- Need for advance care planning;¹⁴²

c) Time-based criteria:

- Clinician-estimated life expectancy ≤ 6 months.¹⁴²
- Persistently elevated biomarkers, such as B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP), despite optimized therapy, as well as geriatric markers, including recent functional decline, sarcopenia, and frailty, should be interpreted as warning signs for the early introduction of a palliative approach.^{140,143}

2.6.4. Evidence of Benefits

The incorporation of PC into the management of HF is associated with improved outcomes, including better quality of life and symptom management (dyspnea, pain), improved functional class, lower rates of depression and anxiety, improved use of advance directives, lower health care utilization, fewer hospital admissions, shorter hospital stays, and lower health care costs.^{139,144-146} Studies show that PC services improve symptoms and HF functional class, as well as spiritual well-being and social support, in addition to reducing anxiety, depression, and social isolation.¹⁴³

However, it is important to note that clinical trials have had heterogeneous results. The Palliative Care in Heart Failure (PAL-HF) study found greater benefits regarding quality of life, anxiety, depression, and spiritual well-being compared with usual care, but other trials have reported mixed or negative results, suggesting that formal PC interventions should be tailored to the needs and preferences of individual patients and caregivers.¹⁴⁰

2.6.5. Considerations Specific to Geriatric Patients

In geriatric patients, the PC approach should incorporate a CGA, including frailty, cognition, functional status, and geriatric syndromes.¹⁴³ The presence of multimorbidity, polypharmacy, and social determinants of health (housing stability, access to fresh food, availability of transportation) may accelerate disease progression and influence PC goals and outcomes.^{141,143}

The “surprise question” (“Would you be surprised if this patient were to die within the next year?”) has been used as a screening tool to identify patients close to the end of life. In a series of patients with advanced HF, the 1-year mortality rate was approximately 50% among patients for whom the answer was “not surprised,” compared with only 10% among those for whom the answer was “surprised.”^{147,148}

2.6.6. Barriers and Challenges

Despite current recommendations, referral rates to PC among patients with HF remain suboptimal, and referrals are often made later than for patients with cancer.¹³⁹ Factors that explain these delays include inconsistent and limited education

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in PC among cardiovascular health care professionals, an insufficient supply of PC specialists (particularly those trained in cardiovascular PC) relative to the growing HF population, challenges in identifying patients who would benefit from PC, and confusion among patients, who frequently equate PC with hospice care.¹³⁹

2.7. Vaccination in Older Adults: Which Vaccines are Recommended?

2.7.1. Objective of Vaccination of Older Adults

- Reduction of morbidity and mortality from infectious diseases;
- Prevention of decompensation of chronic diseases;
- Reduction of cardiovascular events associated with infections;
- Promotion of healthy and functional aging.

Changes in the immune system related to aging contribute significantly to the increased incidence and severity of infections and cardiovascular outcomes in older adults. Vaccine effectiveness in this population is also recognized to be generally lower than that observed in younger adults due to immunosenescence.^{149,150}

Strategies to optimize vaccine response (increased antibody concentrations and efficacy) include the use of higher antigen doses (high-dose influenza vaccine) or adjuvants (respiratory syncytial virus [RSV] and herpes zoster vaccines). In addition to these technologies, for the prevention of infections caused by polysaccharide-encapsulated bacteria (pneumococci, meningococci, and *Haemophilus influenzae*), conjugate vaccines should be preferred because they induce a more effective, robust, and durable T-cell-dependent immune response, with the induction of immunologic memory, and should therefore be prioritized over polysaccharide vaccines.¹⁵¹

In addition to technological advances, there is a critical need to increase awareness of the importance of vaccination throughout life, beyond the pediatric setting. Vaccination coverage among older adults remains suboptimal, highlighting the need for vaccine prescription as part of the standard of care, as well as institutional strategies and public policies that promote active recommendation and access to immunization.

2.7.2. Vaccination of Older Adults Should Be Incorporated as a Mandatory Component of Clinical Care, with Shared Responsibility Among the Entire Health Care Team and as an Indicator of Quality of Care

a) General principles:

- Every individual aged 60 years or older should have their vaccination status assessed;
- In addition to the newer and more widely recognized vaccines recommended for this age group, other vaccines are also important and prevent diseases that affect this population, such as accidental tetanus;

- An individualized approach is also important. Considering comorbidities, frailty, and clinical risk, vaccines not routinely recommended for this age group (hepatitis A, measles, mumps, and rubella [MMR], and yellow fever, among others) may be indicated or contraindicated depending on the underlying condition;
- Every medical visit is an opportunity to prescribe vaccination.

b) Vaccination assessment during the medical visit should include:

- Documented vaccination history: vaccines not recorded on the vaccination card are not considered valid, and vaccination is recommended in such cases, with no harm to the patient;
- Comorbidities: vaccines not routinely recommended for the patient's age group may be indicated, and consultation of the Brazilian Society of Immunizations (SBIIm) special immunization schedules for each comorbidity and for immunosuppressed individuals (due to disease or treatment) is recommended (Table 2.3);
- History of events supposedly attributable to vaccination or immunization (ESAVI): rarely contraindicates vaccination, except in cases of anaphylaxis following the vaccine in question;
- Epidemiological situation: vaccines not routinely indicated may be recommended during outbreaks (MMR, hepatitis A, meningococcal disease, *Haemophilus influenzae* type b);
- Documentation in medical record: vaccination history, prescribed vaccines, and updates;
- Reporting: mandatory reporting of ESAVIs;
- Arthus reaction: a type III hypersensitivity reaction mediated by immune complexes that occurs at the antigen injection site in previously sensitized individuals. Typically lasting 4 to 12 hours after vaccination, it should not be confused with vaccine allergy, cellulitis, or injection-related abscess, and is easily controlled with antihistamines.¹⁵²

2.7.3. Vaccines Included in the Vaccination Schedule for Older Adults of the Brazilian Society of Immunizations (SBIIm) and the Brazilian Society of Geriatrics and Gerontology (SBGG)

- Influenza:¹⁵⁵
 - Influenza vaccination is universally recommended for older adults;
 - High-dose influenza vaccines are preferred; if unavailable, standard-dose vaccines should be used;

See Table 2.4 for recommendations;

- Covid-19:¹⁵⁶
 - According to the updated recommendations of the Brazilian Ministry of Health;
 - See Table 2.4 for recommendations;

Table 2.3 – Additional vaccines to the routine immunization schedule for older adults with comorbidities and/or immunosuppression according to underlying disease, immunosuppression, solid organ transplantation, and use of immunosuppressants^{153,154}

Special group	ADDITIONAL recommended vaccines, in addition to the routine immunization schedule for older adults	Vaccines available at CRIE
Diabetes	–	Influenza; COVID-19; PPSV23
Chronic heart disease and/or chronic lung disease	–	Influenza; COVID-19; PPSV23
Chronic liver disease	Hepatitis A	Influenza; COVID-19; Hepatitis A; Hepatitis B; PPSV23
Chronic kidney disease	Hepatitis A	Influenza; COVID-19; PPSV23; Hepatitis B
Anatomic or functional asplenia, hemoglobinopathies, storage diseases, and other conditions associated with splenic dysfunction	Hepatitis A; Hib; MenACWY; MenB	Influenza; COVID-19; Hepatitis A; Hepatitis B; PCV13; PPSV23; Hib; MenACWY; MenB
People living with HIV/AIDS	MenACWY; MenB; Hepatitis A; Hib	Influenza; COVID-19; PCV13; PPSV23; Hib; Hepatitis A; Hepatitis B; MenACWY; MenB
Active oncologic diseases	MenACWY; MenB; Hepatitis A; Hib	Influenza; COVID-19; PCV13; PPSV23; Hib; Hepatitis A; MenB
Autoimmune diseases leading to immunosuppression	MenACWY; MenB; Hepatitis A; Hib	PCV13; PPSV23; MenC; Hib; Hepatitis B; Hepatitis A; if at epidemiological risk: yellow fever, according to Ministry of Health recommendations
Individuals receiving immunosuppressants	MenACWY; MenB; Hepatitis A; Hib	PCV13; PPSV23; MenC; Hib; Hepatitis B; Hepatitis A
Candidates for or recipients of solid organ transplantation	MenACWY; MenB; Hepatitis A; Hib	PCV13; PPSV23; MenACWY; Hib; Hepatitis B; Hepatitis A
Hematopoietic stem cell transplant recipients	–	PCV13; PPSV23; MenACWY; Hib; Hepatitis B; Hepatitis A
Household contacts of immunosuppressed individuals	MMR; chickenpox	Influenza; MMR; chickenpox

CRIE: Centros de Referência para Imunobiológicos Especiais (Special Immunobiological Reference Centers); Hib: Haemophilus influenzae type b vaccine; MenACWY: meningococcal conjugate vaccine against serogroups A, C, W, and Y; MenB: meningococcal vaccine against serogroup B; MenC: meningococcal conjugate vaccine against serogroup C; MMR: measles, mumps, and rubella; PCV13: 13-valent pneumococcal conjugate vaccine; PCV15: 15-valent pneumococcal conjugate vaccine; PCV20: 20-valent pneumococcal conjugate vaccine; PPSV23: 23-valent pneumococcal polysaccharide vaccine; Td: adult tetanus and diphtheria adsorbed vaccine; Tdap: tetanus, diphtheria, and acellular pertussis (adult formulation). Source: Manual dos Centros de Referência para Imunobiológicos Especiais (Manual of the Special Immunobiological Reference Centers);¹⁵³ Calendários de vacinação SBIIm pacientes especiais – 2025 (2025 SBIIm vaccination schedules for special patients).¹⁵⁴

- Pneumococcal vaccines:^{155,157}
 - Preferred strategy: single dose of the 20-valent pneumococcal conjugate vaccine (PCV20);
 - Previously vaccinated individuals may still benefit from PCV20;
 - No additional PPSV23 dose is required after PCV20;
 - Alternative: sequential schedule (PCV13 or PCV15 followed by PPSV23);
 - Simultaneous administration with other vaccines is permitted;
- See Table 2.4;
- RSV:¹⁵⁵
 - Recombinant/adjuvanted RSV vaccine and recombinant RSV A and B vaccine;
 - Dosing schedule: single dose;
 - Recommended for individuals aged 60 years or older, especially those at increased risk of severe disease or decompensation of underlying disease;
 - Routinely recommended for all individuals aged 70 years or older, regardless of the presence of risk factors;

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- See Table 2.4;
- Adjuvanted herpes zoster vaccine:¹⁵⁵
 - Dosing schedule: two doses (2-month interval);
 - Recommended regardless of previous history of the disease;
- Interval between a herpes zoster episode and vaccination: the vaccine may be administered immediately after resolution of the episode, considering the risk of missed vaccination opportunities and therefore better adherence, or after 6 months, at the physician's discretion;

Table 2.4 – Vaccination of older adults (≥ 60 years): a practical guide for clinical decision-making¹⁵⁶

Vaccine	Indication	Preferred strategy	Schedule	Simultaneous administration	Contraindications	Availability
Influenza	Routine	Prefer high-dose vaccine; if unavailable, standard-dose vaccine	Annual dose	Yes	Severe allergy (anaphylaxis) to a vaccine component or previous dose	SUS (standard dose) and private sector (both)
Covid-19	Routine	According to the current annual schedule ¹	According to the current annual schedule	Yes	Severe allergy (anaphylaxis) to a vaccine component or previous dose	SUS
Pneumococcal	Routine	PCV20	Single dose	Yes	Severe allergy (anaphylaxis) to a vaccine component or previous dose	Private sector
	Alternative:	PCV13 or PCV15 + PPSV23	Sequential schedule	Yes		
Respiratory syncytial virus	Routine	LE	Single dose	Yes	Severe allergy (anaphylaxis) to a vaccine component or previous dose	Private sector
Herpes zoster (recombinant)	Routine	LE	2 doses (0–2 months)	Yes	Severe allergy (anaphylaxis) to a vaccine component or previous dose	Private sector
Tdap/Td	Routine	Tdap preferred for boosters	Booster every 10 years	Yes	Severe allergy (anaphylaxis) to a vaccine component or previous dose	Td (SUS); Tdap (private sector and SUS for health care professionals)
		Primary vaccination (unvaccinated)	Tdap–Td–Td			
Hepatitis B	Routine	–	3 doses (0–1–6 months)	Yes	Severe allergy (anaphylaxis) to a vaccine component or previous dose; thrombocytopenic purpura after a previous dose	SUS (hepatitis B) and private sector (hepatitis A and B)
Yellow fever	According to epidemiological risk ²	Individual risk-benefit assessment ³	Single dose	Yes	See note ⁴	SUS and private sector

NA: not applicable; PCV13/PCV15: 13- or 15-valent pneumococcal conjugate vaccine; PCV20: 20-valent pneumococcal conjugate vaccine; PPSV23: 23-valent pneumococcal polysaccharide vaccine; SUS: Brazilian Unified Health System; Td: tetanus and diphtheria; Tdap: tetanus, diphtheria, and acellular pertussis (adult formulation). Source: Calendário de vacinação do idoso [Vaccination schedule for older adults]. São Paulo: SBIIm; 2025.¹⁵⁶

- See Table 2.4;
- Adult tetanus, diphtheria, and acellular pertussis vaccine (Tdap) and/or adult tetanus-diphtheria vaccine (Td):^{155,158}
 - Pertussis is a serious disease among older adults, and the prevalence of accidental tetanus is higher in this age group;
 - Tdap is preferred for booster doses every 10 years;
 - Primary vaccination: one dose of Tdap followed by two doses of Td (0–2–4 to 8 months);
 - See Table 2.4;
- Hepatitis B:^{155,158}
 - Dosing schedule: three doses (0–1–6 months);
 - For individuals who have started the vaccination series, complete it while maintaining an interval of 4 months between the second and third doses;
 - See Table 2.4;
- Yellow fever:^{155,158}
 - The vaccine is not contraindicated for immunocompetent older adults;
 - However, physicians should assess the individual risk-benefit ratio given the rare risk (0.25–0.4 per 100,000 doses) of vaccine-associated viscerotropic disease;
 - If the risk of infection exceeds the risk of a serious adverse event, vaccination should be recommended, provided there are no contraindications;
 - Concomitant administration with all vaccines recommended for older adults is permitted;
 - Contraindications: allergy to egg protein and/or other vaccine components; immunosuppression due to disease or treatment; sickle cell disease receiving hydroxyurea (vaccinate only if neutrophil count is > 1,500 cells/mm³); history of thymic disorders (myasthenia gravis, thymoma, congenital athymia, or prior thymectomy);
 - See Table 2.4;
- Yellow fever (note):
 - Specific contraindications:
 - immunosuppression due to disease or treatment;
 - sickle cell disease receiving hydroxyurea (vaccinate if neutrophil count is > 1,500 cells/mm³);
 - history of thymic disorders (myasthenia gravis, thymoma, absence or removal of the thymus);
 - allergy to egg protein and/or other vaccine components.

2.8. Benefits of Physical Activity: How Should Physical Activity Be Prescribed? 27

Regular physical activity is associated with reduced all-cause mortality and cardiovascular, metabolic, functional, and psychocognitive benefits. Physically active individuals have a lower risk of CVD, a better metabolic profile, a lower prevalence of depressive symptoms, and better cognitive

performance.¹⁵⁹ Regular exercise contributes to the control of hypertension, primarily by reducing peripheral vascular resistance, and also improves the lipid profile, reduces adiposity, promotes glycemic control, and decreases the risk of CAD and mortality.¹⁶⁰

From a cardiovascular perspective, exercise improves functional capacity and the efficiency of the cardiovascular and respiratory systems by increasing oxygen uptake and utilization, lowering heart rate and BP at a given workload, and decreasing myocardial oxygen demand.¹⁶¹ These effects increase exercise tolerance and facilitate the performance of activities of daily living.

Physical activity also improves muscle strength, mobility, balance, and functional capacity, contributing to the maintenance of independence and reducing the risk of falls. It is also associated with improved cognitive function, reduced symptoms of depression and anxiety, and better quality of life and psychological well-being.¹⁶² Epidemiological evidence consistently demonstrates an association between higher levels of physical activity and lower cardiovascular risk, with a reduction of approximately 30%–40% in the risk of developing CVD among more active individuals, regardless of age, sex, or population group.¹⁶¹

In aging, maintaining adequate levels of physical activity is one of the primary strategies for preserving functional capacity and slowing age-related decline. In older adults, exercise contributes to maintaining strength, balance, mobility, and independence, while also playing an important role in the prevention and treatment of frailty, maintenance of bone health, and potentially preservation of cognitive function.^{106,163}

Fall prevention is one of the most relevant benefits in this population. Meta-analyses of RCTs demonstrate that structured exercise programs reduce the rate of falls by approximately 23% (rate ratio 0.77; 95%CI 0.71–0.83) and the risk of experiencing at least one fall by 15% (risk ratio [RR] 0.85; 95%CI 0.81–0.89) among community-dwelling older adults.¹⁶⁴ The benefit is particularly relevant in individuals at increased risk of falls and those with frailty and may also reduce the severity of fall-related consequences.^{164,165}

The relationship between physical activity and mortality follows a dose-response pattern, with benefits observed even at volumes below those currently recommended.¹⁶⁶ These findings reinforce its role as a central component of health promotion and cardiovascular prevention throughout aging.

Exercise prescription should be individualized according to functional capacity, clinical status, comorbidities, frailty, habitual level of physical activity, and individual goals.^{106,161,163} For older adults, aerobic exercise, muscle-strengthening exercises, and balance training should be combined, with flexibility and functional exercises added when appropriate. Modality, intensity, volume, and progression should be tailored to individual characteristics and limitations, with gradual progression to maximize safety, adherence, and functional benefits.^{106,163}

Thus, physical activity is one of the main nonpharmacological interventions for promoting healthy aging, contributing not only to cardiovascular prevention but also to preservation of autonomy, reduction of falls, maintenance of cognitive

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function, and improvement of mental health and quality of life.¹⁶⁴⁻¹⁶⁶

- Benefits of regular exercise:
- Improved physical fitness and overall health;
- Improved bone density;
- Increased muscle strength;
- Improved balance, posture, and flexibility;
- Improved weight control;
- Improved mood;
- Improved sleep quality;
- Reduced stress.

2.8.1. How Should Physical Activity Be Prescribed?

Exercise prescription in older adults, particularly frail individuals, should be preceded by an individualized clinical and functional assessment to identify comorbidities, functional limitations, cardiovascular risk, and risk of falls, thereby guiding the selection of the most appropriate and safe exercise modality and intensity. The CGA may contribute to this stratification, particularly in frail older adults or those with multimorbidity. Complementary examinations, such as ECG, echocardiography, and exercise stress testing (EST), should be requested according to the clinical history, symptoms, physical examination, and cardiovascular risk, rather than routinely in all individuals.^{161,166}

International recommendations advise older adults to engage in 150–300 minutes per week of moderate-intensity aerobic activity, 75–150 minutes of vigorous-intensity activity, or an equivalent combination. Exercise prescription should be individualized according to patient preferences, functional capacity, physical limitations, clinical conditions, and goals, using the principles of frequency, intensity, time, and type (FITT).¹⁶⁷

The exercise program should preferably be multicomponent, combining aerobic activity, strength training, and balance exercises, with flexibility and functional training included when appropriate.^{163,168-171} Aerobic activity may include walking, cycling, swimming, or other modalities compatible with functional capacity. Strength training should involve the major muscle groups, ideally on at least 2 days per week, with gradual progression of the load according to tolerance and clinical response. Strength training is particularly important in frail older adults and those with sarcopenia, contributing to the preservation or recovery of muscle mass and function.^{106,171}

Balance exercises should be incorporated regularly, particularly in older adults with impaired mobility or an increased risk of falls. Flexibility and mobility exercises may complement the program, contributing to range of motion and the performance of everyday activities.^{165,170}

Progression should be gradual, initially prioritizing adaptation to exercise frequency and duration and subsequently increasing intensity according to individual tolerance. Warm-up and cool-down periods may be incorporated into sessions, particularly when they contribute to greater comfort and preparation for exercise. In frail older adults, those with advanced sarcopenia or dementia, and

institutionalized older adults, the program should be adapted to cognitive, functional, and clinical limitations, prioritizing simple, supervised exercises targeting strength, balance, mobility, and functional tasks.^{169,171}

There is no single training volume or resistance-training model that applies to all older adults. Intensity, number of sets and repetitions, and frequency should be individualized and progressively adjusted. Even lower-volume programs can provide benefits when performed consistently and with appropriate progression. In frail older adults, strength training is an essential component for attenuating age-related loss of muscle mass and function and preserving functional independence.^{106,171,172}

Table 2.5 summarizes the recommendations for prescribing physical exercise for older adults.^{169,173}

2.9. Vitamin D Supplementation

2.9.1. Physiology and the Importance of Vitamin D

Vitamin D acts as an essential fat-soluble hormone for multiple organ systems, including bone metabolism, muscle function, the immune system, the brain, and the heart. Its endogenous synthesis occurs primarily through sun exposure (more than 90%), while exogenous sources include food and supplements, producing vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Its action is mediated by the vitamin D receptor, present in various tissues, promoting intestinal calcium absorption and influencing cellular differentiation and immune function.¹⁷⁴ Vitamin D deficiency compromises bone mineral density, increases the risk of falls and fractures, and affects muscle strength and balance, all of which are critical factors in the older adult population.^{174,175}

2.9.2. Vitamin D Deficiency in Aging

Increasing longevity brings with it challenges related to nutritional disorders, CVD, hypertension, DM, and cancer.

Table 2.5 – Prescription of physical activity for older adults

Modality (type)	Frequency	Intensity	Time
Aerobic	3/5 × per week	Light/moderate	150/300 min light or 75/150 min vigorous
Muscle strength training	> 2 × per week	-	20/30 min/session
Balance	> 3 × per week	Individualized	10/20 min/session
Flexibility	> 2 × per week	Light/moderate	10/15 min/session
Functional activity	Daily	Light/moderate	Variable

Several factors contribute to vitamin D deficiency with aging, such as reduced cutaneous production due to skin aging, decreased mobility and sun exposure, social isolation, reduced fat mass (which influences bioavailability), and declining renal function.¹⁷⁴

2.9.3. Serum Level Assessment

Measurement of serum 25(OH)D levels is recommended for specific risk groups, including adults over 75 years of age, individuals with osteometabolic diseases, CKD, pregnant or breastfeeding women, and individuals with risk factors for osteoporosis. Optimal values vary according to population type: levels above 20 ng/mL are considered adequate for the healthy general population up to 60 years of age, while levels between 30 and 60 ng/mL are recommended for risk groups, including older adults. Levels above 100 ng/mL are considered toxic.¹⁷⁵⁻¹⁷⁷

2.9.4. Supplementation Recommendations for Older Adults

For adults 75 years of age or older, the Endocrine Society suggests empiric vitamin D supplementation because of its potential to reduce mortality, without requiring routine screening of serum levels.¹⁷⁸ Empiric supplementation may include daily intake of fortified foods, vitamin formulations containing vitamin D, or daily supplements.¹⁷⁸ In clinical trials finding a mortality benefit, doses ranged from 400 to 3333 IU/day, with a weighted average of approximately 900 IU/day.¹⁷⁸ Daily supplementation with lower doses is preferred over intermittent high-dose regimens (less frequent than weekly), because an increased risk of falls and fractures has been associated with monthly or annual high-dose regimens.^{174,177,178}

For the general population aged 19 to 70 years, the U.S. National Academy of Medicine recommends a daily intake of 600 IU, increasing to 800 IU/day for individuals older than 70 years.¹⁷⁵ The tolerable upper intake threshold has been established at 4000 IU/day, although subsequent studies suggest that doses at this level may be associated with adverse events.¹⁷⁵ The American Geriatrics Society (AGS) suggests a minimum serum 25(OH)D level target of 30 ng/mL in older adults, particularly frail individuals at increased risk of falls, injuries, and fractures.¹⁷⁵

2.9.5. Evidence of Benefits and Limitations

Large RCTs, such as VITAL (25,871 participants) and D-Health (21,315 participants), conducted predominantly in generally healthy populations, have not found a benefit of vitamin D supplementation for the prevention of cardiovascular events, cancer, or DM.^{178,179} In VITAL, supplementation with 2000 IU/day for a median of 5.3 years also did not reduce the incidence of falls or fractures.¹⁷⁸

Consistent with these findings, a recent 2026 meta-analysis including 69 clinical trials and 153,902 participants found little or no effect of calcium and/or vitamin D supplementation on the prevention of fractures and falls in adults, predominantly community-dwelling individuals without high baseline risk.¹⁷⁹

However, in individuals aged 75 years or older, vitamin D supplementation is probably associated with a small reduction in all-cause mortality, without a significant benefit on fractures and without a consistent increase in adverse events.¹⁷⁸ Subgroup analyses suggest a possible reduction in falls with usual doses of vitamin D, but not with high doses.¹⁷⁸

The most consistent evidence of benefit for the combination of vitamin D and calcium focuses on fracture reduction, particularly hip fractures, especially in institutionalized older adults or those at higher risk of deficiency of these nutrients.^{178,180} When indicated, calcium supplementation should take dietary intake into account and be individualized, avoiding unnecessary supplementation.^{174,175}

In individuals with CKD, the indication for vitamin D and, particularly, its active analogs should be individualized according to renal function, calcium, phosphorus, and parathyroid hormone levels, and the stage of kidney disease. Routine use of active forms of vitamin D is not recommended for all patients with CKD.¹⁷⁷

2.9.6. When Not to Recommend Vitamin D Supplementation

Vitamin D supplementation is not recommended in the situations described below:

- Healthy individuals aged 19 to 74 years without risk factors: there is no robust evidence of benefits from supplementation or population screening in this age group;¹⁵⁷⁻¹⁵⁹
- Already elevated serum levels: when levels exceed 100 ng/mL, supplementation should be discontinued because of the risk of toxicity, including hypercalcemia;
- Hypercalcemia or hyperphosphatemia: contraindicated in patients with elevated serum calcium or phosphate levels;
- Hypersensitivity to components of the formulation;
- Intermittent megadoses: very high doses administered at prolonged intervals (monthly or annually) are not recommended, as studies suggest a paradoxical increase in the risk of falls among older adults;^{174,177,178}
- Sole purpose of delaying aging: there is no scientific evidence supporting this effect.

2.10. Surgical Risk Assessment in Older Patients: What Should Be Considered?

Population aging has made older adults the main group of patients undergoing surgery. In this age group, perioperative risk depends less on chronological age than on physiological reserve, frailty, comorbidities, and functional capacity.

Preoperative assessment should extend beyond cardiovascular risk stratification, incorporating functional, cognitive, nutritional, social, and medication-related aspects in order to identify modifiable vulnerabilities and guide targeted interventions. This approach increases surgical safety and promotes better functional recovery.

The 2024 SBC Guideline for Perioperative Cardiovascular Evaluation provides the technical framework for risk

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calculation and indication for examinations. This chapter, prepared by the SBC DECAGE, complements that model by incorporating the principles of multidimensional geriatric assessment, frailty assessment, and shared decision-making.

In the postoperative period, follow-up should encompass cardiovascular complications, delirium, functional decline, malnutrition, and medication-related adverse events, prioritizing early mobilization, medication review, and interdisciplinary rehabilitation.

- **Objective:** To provide practical recommendations for the perioperative assessment and management of older adults undergoing noncardiac surgery, from a geriatric cardiology perspective, aligned with the 2024 SBC guideline and classified according to the GRADE system (strength and quality of evidence).
- **Topics addressed:** (1) CGA; (2) cardiovascular stratification; (3) frailty; (4) functional capacity; (5) additional tests; (6) multidisciplinary decision-making; (7) delirium and cognition; (8) clinical and pharmacological optimization; and (9) risk-benefit analysis and goals of care.

The focus is on promoting an integrated, individualized, and older adult-centered assessment, balancing risk, benefit, and quality of life.

2.10.1. Comprehensive Geriatric Assessment

The CGA is an important tool in the perioperative assessment of older adults, as it enables the identification of vulnerabilities and better organization of care, with a positive impact on outcomes such as delirium and functional recovery.¹⁸¹ International and national guidelines recommend its incorporation – or at least structured geriatric screening – into the preoperative assessment of select older adults.^{182–185} The CGA will be discussed in detail in a specific chapter of this guideline.

Recommendation	Strength of recommendation	Certainty of evidence
Comprehensive geriatric assessment, including functional, cognitive, nutritional, and social status and polypharmacy, is suggested as part of the preoperative evaluation of older adults, particularly those undergoing intermediate- or high-risk surgery or presenting with geriatric vulnerabilities, to guide targeted optimization and delirium prevention.	CONDITIONAL	MODERATE

2.10.2. Cardiovascular Risk Stratification in Older Adults

Cardiovascular risk stratification is one of the pillars of preoperative assessment and should follow the sequential approach proposed by the 2024 SBC Guideline for Perioperative Cardiovascular Evaluation. This guideline maintains the Revised Cardiac Risk Index (RCRI) as the primary clinical tool for estimating the probability of MACEs (MI, acute pulmonary edema, severe arrhythmias, or cardiovascular death) in noncardiac surgery.¹⁸⁵

The RCRI uses six simple clinical variables (type of surgery, CAD, HF, cerebrovascular disease, creatinine > 2 mg/dL, and insulin-dependent diabetes) and categorizes risk as low (0 points), intermediate (1–2 points), and high (≥ 3 points). Although widely validated, it has limitations in older adults, in whom diminished physiological reserve and the presence of frailty may lead to an underestimation of actual risk.^{185,187}

For populations with multiple comorbidities, functional dependence, or undergoing high-risk surgical procedures, the SBC recommends considering complementary tools such as the Myocardial Infarction or Cardiac Arrest Model (MICA) or the Gupta Perioperative Cardiac Risk Calculator, which incorporate variables such as age, renal function, the American Society of Anesthesiologists classification, and functional dependence.^{185,188}

In older adults, the assessment should always integrate the clinical risk score with functional capacity (estimated in metabolic equivalents [METs] or by the Duke Activity Status Index [DASI]) and individualized clinical judgment, taking into account frailty, polypharmacy, and nutritional status. Therefore, risk stratification should not be viewed as an isolated step but rather as part of an integrated and multidimensional approach.^{105,189}

Recommendation	Strength of recommendation	Certainty of evidence
The use of validated clinical risk scores, preferably the RCRI, is recommended as the basis for preoperative cardiovascular risk stratification, without replacing clinical assessment and functional capacity assessment. In selected cases, MICA or the Gupta score may be considered as complementary tools.	STRONG	MODERATE

2.10.3. Frailty Assessment

Frailty represents a state of biological vulnerability resulting from the decline of multiple physiological systems, leading to reduced homeostatic reserve and a greater risk of adverse outcomes after surgery. It is recognized as an independent predictor of mortality, perioperative complications, length of hospital stay, and institutionalization in older adults.

Frailty screening should be a routine component of preoperative evaluation, particularly before intermediate- or high-risk surgical procedures. Several validated instruments are available, with the CFS, the Risk Analysis Index (RAI), and the Fried Frailty Phenotype being the most commonly used. The CFS stands out for its clinical applicability and strong correlation with mortality and functional loss.^{64,185,190}

Observational studies and meta-analyses show that frail patients have a 2- to 4-fold higher risk of cardiovascular events and major complications, regardless of RCRI score. Early identification allows optimization of clinical conditions, adjustment of expectations, and support for shared decision-making regarding perioperative management.^{184,191}

International guidelines and the 2024 SBC guideline recommend that frailty be assessed and documented preoperatively and used for risk communication and multidisciplinary planning.^{182,183,187,192}

Recommendation	Strength of recommendation	Certainty of evidence
Preoperative assessment and documentation of frailty using a validated instrument (eg, CFS, RAI, or Fried criteria) are recommended in older adults undergoing intermediate- or high-risk surgery, with the results used to guide risk communication, optimization, and shared decision-making.	STRONG	MODERATE

2.10.4. Functional Capacity (Metabolic Equivalents/Duke Activity Status Index)

Functional capacity is one of the most important predictors of perioperative cardiovascular risk, reflecting the patient's overall physiological reserve. In older adults, functional capacity often correlates not only with age or comorbidities but also with the interaction among sarcopenia, frailty, and multiple chronic diseases.

The 2024 SBC guideline recommends estimating functional capacity whenever possible, as values < 4 METs are associated with a higher risk of cardiac events and major complications. When subjective assessment is uncertain, structured tools such as the DASI should be used, as they allow quantifying functional capacity with good reproducibility. A DASI score < 34 points correlates with an increased risk of cardiovascular events within 30 days and higher mortality.^{193,194}

The 2024 AHA/ACC guideline recognizes the DASI as the preferred instrument (Class IIa) for estimating functional capacity in patients undergoing noncardiac surgery, considering it superior to subjective assessments.¹⁰⁵ The 2022 ESC guideline recommends functional assessment as an essential step in risk stratification,

guiding the need for complementary examinations only when the results suggest possible changes to management strategies.¹⁸⁹

In older patients, functional capacity should be interpreted in light of locomotor limitations, osteoarticular diseases, and sensory deficits, in order not to underestimate it. Whenever possible, this information should be supplemented with objective measures of mobility, gait speed, or the sit to stand test, which correlate strongly with the risk of complications and mortality.^{103,165}

Recommendation	Strength of recommendation	Certainty of evidence
A structured preoperative assessment of functional capacity, preferably using the Duke Activity Status Index (DASI), is recommended. A threshold of < 4 metabolic equivalents or a DASI score < 34 should be considered indicative of increased risk, with the results used to guide the need for additional testing and clinical optimization.	STRONG	MODERATE

2.10.5. Additional Tests

Requests for additional tests should follow the principle of clinical utility: they should only be performed when the results may change management strategies (eg, delaying surgery for optimization, indicating or avoiding revascularization, adjusting anesthesia or monitoring strategies, or intensifying surveillance). In older adults, indications should take into account functional capacity, surgical type and risk, symptoms, and pretest probability.^{105,165,187,189}

- *Transthoracic echocardiography (TTE)*: indicated in the presence of new symptoms or worsening HF, dyspnea of unclear etiology, a significant murmur suggestive of moderate-to-severe VHD, or when no recent TTE (≈12 months) is available in a patient with known VHD whose clinical status has changed. It is not routinely indicated in asymptomatic and stable patients.
- *Stress testing (EST, stress echocardiography/MRI, myocardial scintigraphy)*: consider when functional capacity is < 4 METs or uncertain and the surgical risk is intermediate or higher, provided the result may change management strategies (eg, lead to revascularization, postponement of surgery or selection of a less invasive technique, or intensification of therapy). Avoid indiscriminate screening.
- *Coronary artery calcium score (CACS)/coronary computed tomography angiography (CCTA)*: CCTA may

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be considered in select patients with an intermediate pretest probability of CAD, when functional methods are inconclusive or unavailable, and the findings influence management strategies. Do not use routinely for screening in low-risk patients.

- **Biomarkers (BNP/NT-proBNP and troponin):** in older adults at high clinical risk (CAD/congestive HF/CKD, low functional capacity) or those undergoing intermediate- or high-risk surgery, preoperative BNP/NT-proBNP measurement may be performed to refine risk stratification and guide monitoring. Serum troponin may also be measured preoperatively (baseline) and monitored postoperatively in high-risk patients to detect myocardial injury after noncardiac surgery, which is associated with a worse prognosis.^{195,196}
- **Coronary revascularization:** indicated only according to standard cardiology criteria (refractory angina, high-risk CAD), regardless of surgery, and not as a routine strategy to reduce perioperative risk.

Recommendation	Strength of recommendation	Certainty of evidence
Complementary examinations are suggested only when their results may change management. Transthoracic echocardiography may be considered in patients with new symptoms, clinical deterioration, suspected valvular heart disease, or no recent evaluation; stress testing may be considered in patients with functional capacity < 4 metabolic equivalents or uncertain functional capacity before intermediate- or high-risk surgery; and preoperative BNP/NT-proBNP measurement and perioperative troponin monitoring may be considered in high-risk patients to refine risk stratification and surveillance. Indiscriminate screening should be avoided.	CONDITIONAL	MODERATE

BNP: B-type natriuretic peptide; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

2.10.6. Multidisciplinary Discussion and Shared Decision-Making

The perioperative assessment and management of older adults should involve structured multidisciplinary interaction among cardiology, geriatrics, surgery, anesthesiology, nursing, and physical therapy teams, with active participation by the patient and family members. This approach integrates cardiovascular, functional, cognitive, and social aspects, providing a comprehensive view of the risks and benefits of the intervention.

The 2024 SBC Guideline proposes the concept of the Perioperative Risk Team, responsible for coordinating communication among specialties, standardizing management, and optimizing preoperative clinical preparation.¹⁶⁵ As well as cardiovascular risk, this team should also discuss the potential for functional recovery, patient preferences, overall prognosis, and goals of care.

Shared decision-making is particularly important in frail older adults or those with multiple comorbidities, in whom functional impact and quality of life may be more relevant than mortality risk alone. International guidelines, such as the CPOC/BGS 2021 and AHA/ACC 2024 guidelines, emphasize that surgical decisions should be made jointly with the patient and their family, based on clear information regarding risks, benefits, and therapeutic alternatives.^{105,183,197}

When available, an interdisciplinary case conference (geriatrics, cardiology, surgery, anesthesiology, and rehabilitation team) is considered best practice. This approach reduces variability in management, improves alignment among specialties, and increases patient satisfaction, even in high-risk situations.^{198,199}

Recommendation	Strength of recommendation	Certainty of evidence
Assessment of older adults, particularly those with frailty or multiple comorbidities, by a multidisciplinary perioperative team (cardiology, geriatrics, surgery, and anesthesiology) is suggested, together with shared decision-making regarding surgical management that considers risk, prognosis, and individual values.	CONDITIONAL	MODERATE

2.10.7. Risk of Delirium and Postoperative Cognitive Complications

Postoperative delirium is one of the most frequent complications in older adults, occurring in 15% to 50%

of cases, depending on the type of surgery and patient vulnerability. It is characterized by an acute disturbance of attention and level of consciousness and is associated with increased mortality, functional decline, institutionalization, and poorer quality of life.²⁰⁰

Preoperative identification of risk factors, such as advanced age, preexisting dementia, benzodiazepine use, alcohol abuse, polypharmacy, visual or hearing disorders, malnutrition, anemia, and major surgery, is essential for implementing preventive strategies.^{201,202}

Brief cognitive screening (eg, the Mini-Cog or the MoCA) should be performed during the preoperative assessment in order to identify preexisting cognitive impairment, which increases the risk of delirium and postoperative cognitive dysfunction.²⁰¹ Prevention should be based on multimodal nonpharmacological interventions, known to reduce the incidence and duration of delirium: frequent reorientation, a calm and well-lit environment, use of eyeglasses and hearing aids, adequate pain control, correction of hydroelectrolytic disturbances, maintenance of normal sleep, and early mobilization.²⁰³

Medications such as benzodiazepines and anticholinergics should be avoided whenever possible. Routine prophylactic use of antipsychotic medications is not recommended.^{201,203} An interdisciplinary approach (nursing, physical therapy, geriatrics, and cardiology) is decisive for early detection and appropriate management.^{204,205}

Recommendation	Strength of recommendation	Certainty of evidence
Preoperative assessment of the risk of delirium is suggested for all older adults, together with the implementation of nonpharmacological preventive measures (reorientation, sleep management, sensory stimulation, early mobilization, hydration, and adequate pain management). Routine use of benzodiazepines and anticholinergic medications should be avoided.	CONDITIONAL	MODERATE

2.10.8. Preoperative Optimization of Clinical Conditions and Medications

Preoperative optimization in older adults seeks to stabilize chronic conditions, correct modifiable vulnerabilities, and adjust medication regimens to reduce complications

and accelerate recovery.^{79,105,165,189} The SBC 2024 flow recommends that elective surgery be postponed whenever potentially reversible clinical decompensation is present, maintaining urgency as the determining factor.¹⁶⁵

- **HF and CAD:** prioritize euvolemia, symptom control, and GDMT, including beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), angiotensin II receptor-neprilysin inhibitors (ARNIs), mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter-2 inhibitors (SGLT2i), when applicable. Avoid initiating beta-blockers immediately before surgery; continuation is recommended in patients already receiving and tolerating them. Coronary revascularization should be performed only for standard cardiology indications, not as a routine risk-reduction strategy.
- **Anemia and nutritional status:** investigate and treat iron deficiency anemia and other causes of anemia (intravenous iron may be used when the time to surgery is short).²⁰⁶ Screen for malnutrition (eg, MNA–Short Form) and consider protein-calorie supplementation and vitamin D replacement when deficiencies are identified. Anemia and malnutrition are associated with an increased risk of delirium, infection, and functional loss.
- **Pulmonary disease (COPD/asthma) and smoking:** optimize bronchodilation/inflammation therapy (long-acting muscarinic antagonists [LAMA], long-acting beta-agonists [LABA], or inhaled corticosteroid, according to phenotype), treat exacerbations, and institute smoking cessation (ideally 4 weeks or more before surgery). Encourage preoperative respiratory physical therapy when available.^{207,208}
- **Blood glucose and DM:** aim for safe glycemic control (avoid hypoglycemia); in general, use moderate glycemic targets (≈ 140 – 180 mg/dL) in hospitalized patients. Adjust insulin and hypoglycemic agents on the day of the procedure according to institutional protocols.²⁰⁹
- **Renal function and electrolytes:** correct hydroelectrolytic disturbances, review nephrotoxic medications, and adjust drug doses according to glomerular filtration rate (GFR). Carefully manage hydration to prevent acute kidney injury.
- **Obstructive sleep apnea:** screen patients with clinical suspicion of obstructive sleep apnea (eg, using the STOP-Bang questionnaire); recommend perioperative continuous positive airway pressure when indicated and increase postoperative surveillance.
- **Medication review (polypharmacy):** perform a comprehensive medication review focusing on the 2023 Beers Criteria (benzodiazepines, anticholinergics, hypnotics, nonsteroidal anti-inflammatory drugs [NSAIDs], and long-acting sulfonyleureas), as well as drug interactions and duplications. Prioritize deprescribing potentially inappropriate medications, particularly in frail individuals.^{79,198}

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- *Antithrombotic agents and other drug classes:* follow the 2024 SBC Guideline to adjust antiplatelet and anticoagulant agents according to the procedure-related bleeding risk and individual thrombotic risk. Statins should be continued; consider initiating statin therapy before vascular surgery. Consider suspending the morning dose of ACEIs/ARBs before surgical procedures with higher hemodynamic risk, according to institutional protocols and the patient's clinical profile.¹⁶⁵

Recommendation	Strength of recommendation	Certainty of evidence
Postponement of elective surgical procedures is recommended to allow correction/stabilization of decompensated conditions (congestive heart failure, chronic obstructive pulmonary disease/asthma, poor glycemic control, and fluid and electrolyte disturbances); treatment of anemia and malnutrition; smoking cessation; screening for and management of obstructive sleep apnea; and medication review, focusing on potentially inappropriate medications (2023 Beers Criteria). Continuation of indicated cardiovascular therapies (eg, statins and beta-blockers already in use) and adjustment of antithrombotic therapy according to risk are also recommended.	STRONG	MODERATE

2.10.9. Individualized Risk-Benefit Analysis and Objectives of Care

The decision to proceed with surgery in older adults should be based on an individualized risk-benefit assessment that integrates not only cardiovascular parameters but also life expectancy, functional status, quality of life, and personal preferences. Age alone is not a contraindication to surgery, but the benefit of an invasive intervention depends on the likelihood of meaningful functional recovery and the expected impact on symptoms and well-being.

The 2024 SBC Guideline emphasizes that clinical decisions should be shared among the physician, the patient, and their family, with clear communication regarding risks, benefits, and therapeutic alternatives.¹⁶⁵ This approach is particularly relevant in frail older adults and those with cognitive impairment or multiple comorbidities, in whom complications may result in permanent functional dependence.^{105,189}

Objective tools such as frailty scales (CFS), functional assessment (DASI), and prognostic indices (eg, the Charlson Comorbidity Index or the Clinical Prediction of Mortality) help estimate overall prognosis and support proportionate decision-making. However, these data should always be interpreted in light of the patient's individual values and goals.¹⁰³

When risks outweigh the benefits, or when the procedure is not in line with the patient's personal goals (eg, comfort, autonomy, symptom control), nonsurgical strategies or a conservative/palliative approach should be considered. The participation of a multidisciplinary team and, when necessary, PC services, contributes to ethical, person-centered decision-making.^{183,210,211}

Recommendation	Strength of recommendation	Certainty of evidence
An individualized risk-benefit assessment before surgery is recommended in older adults, integrating cardiovascular risk, life expectancy, functional status, and patient preferences, with shared decision-making and consideration of less invasive alternatives or palliative care when surgery is not aligned with the patient's goals of care.	STRONG	MODERATE

2.10.10. Executive Summary of Recommendations: Surgical Risk Assessment in Older Patients

Domain assessed	Summary of recommendation	Strength of recommendation	Certainty of evidence
Comprehensive geriatric assessment	Perform a multidimensional assessment (functional, cognitive, nutritional, social, and medication-related) in older adults at intermediate or high risk or with geriatric vulnerability; use the findings to optimize care and prevent delirium.	CONDITIONAL	MODERATE
Cardiovascular risk stratification (RCRI and similar tools)	Use the RCRI as the primary score in conjunction with functional assessment; consider MICA/Gupta in complex cases.	STRONG	MODERATE
Frailty	Assess and document frailty (Clinical Frailty Scale, Risk Analysis Index, Fried criteria); use the results for risk communication and shared decision-making.	STRONG	MODERATE
Functional capacity (metabolic equivalents/ Duke Activity Status Index)	Assess functional capacity using a structured instrument (DASI < 34 or < 4 METs = high risk); use the results to determine examinations and management strategies.	STRONG	MODERATE
Complementary examinations	Order examinations only if the results may change management strategies; consider B-type natriuretic peptide/troponin in high-risk patients.	CONDITIONAL	MODERATE
Multidisciplinary discussion and shared decision-making	Implement an integrated perioperative team (cardiology, geriatrics, surgery, anesthesiology); ensure shared decision-making with the patient and their family.	CONDITIONAL	LOW
Delirium and cognitive complications	Implement risk screening and nonpharmacological preventive measures (sleep optimization, reorientation, early mobilization, hydration); avoid benzodiazepines.	CONDITIONAL	MODERATE
Clinical and pharmacological optimization	Correct decompensated conditions, treat anemia and malnutrition, promote smoking cessation, review polypharmacy (Beers Criteria 2023), and continue essential therapies.	STRONG	MODERATE
Risk-benefit and objectives of care	Integrate cardiovascular risk, functional status, and personal goals; consider less invasive management or palliative care when appropriate.	STRONG	MODERATE

DASI: Duke Activity Status Index; METs: metabolic equivalents; MICA: Myocardial Infarction or Cardiac Arrest; RCRI: Revised Cardiac Risk Index.

2.11. Diabetes Mellitus: Diagnostic and Treatment Parameters in Frail Older Adults

DM is a highly prevalent condition among older adults. Among its different subtypes, type 2 DM (T2DM) is the most frequent and will be discussed in greater detail in this section. Current data indicate that 24% of individuals aged 65 to 99 years have it, totaling 158.3 million cases worldwide.²¹² The prevalence is even higher among frail individuals, reflecting a bidirectional relationship between frailty and DM.²¹³

There are no differences in the diagnostic criteria for DM in older adults compared with younger individuals: (1) fasting plasma glucose ≥ 126 mg/dL; or (2) random plasma glucose ≥ 200 mg/dL associated with disease symptoms; or

(3) 2-hour post-load plasma glucose ≥ 200 mg/dL during a 75-g oral glucose tolerance test; or (4) glycated hemoglobin (HbA1c) $\geq 6.5\%$.²¹⁴

The importance of adequate glycemic control is based on the prevention of microvascular and macrovascular complications over the medium and long term.^{215,216} However, clinical trials have failed to find benefits of intensive glycemic control in older adults with T2DM, particularly those with longer disease duration and CVD.²¹⁷⁻²¹⁹ These studies suggest a U-shaped relationship, in which both hypoglycemia and hyperglycemia are associated with adverse outcomes.

Accordingly, in individuals with more advanced age, it is recommended that glycemic targets be individualized

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according to comorbidities, functional status, autonomy, frailty, and life expectancy²²⁰⁻²²⁶ (Table 2.6). Given the marked heterogeneity of this patient population, performing a CGA is recommended, including frailty screening tools appropriate to the clinical setting.^{49,64,227-229} Identifying frailty is fundamental for guiding individualized nonpharmacological and pharmacological treatment while minimizing the risk of iatrogenic complications.

It is recommended that management of older adults with T2DM involve a multidisciplinary team to provide psychosocial assessment, DM education, identification of barriers to treatment adherence, nutritional planning, rehabilitation, and disability management.²²⁴⁻²²⁶ For nonfrail older adults and those without geriatric syndromes, recommendations do not meaningfully deviate from those for the general population, with a suggested HbA1c target < 7.5%. Even so, age-related pharmacokinetic and pharmacodynamic changes and iatrogenic risk should be taken into account.⁷⁹

Among the medications available, those that reduce cardiovascular risk and slow the progression of kidney disease, such as glucagon-like peptide-1 receptor agonists (GLP-1), may be suggested. SGLT2i may also be indicated, as they provide the same benefits as well as reducing adverse HF outcomes.²³⁰⁻²³⁶ In a meta-analysis including 93,502 participants, with a mean age over 60 years (in most studies), the use of GLP-1 receptor agonists and SGLT2i was associated with lower rates of CVD and MACEs, even among individuals

aged 75 years or older. However, except for the PIONEER-6 trial, which had a mean follow-up of 1.3 years, all studies included in the meta-analysis had follow-up periods exceeding 2 years. This should be taken into consideration in frail individuals with limited life expectancy.^{237,238}

Given these considerations, we recommend an approach similar to that proposed by the Brazilian Diabetes Society (SBD), which individualizes therapy according to the severity of frailty and nutritional status. For frail underweight individuals and HbA1c < 10%, the medications of choice are dipeptidyl peptidase-4 inhibitors. This recommendation is based on the favorable safety profile of this class, which does not lead to weight loss and carries a low risk of hypoglycemia.^{239,240} (conditional recommendation/moderate evidence level).

For frail patients with normal body mass index and HbA1c < 10%, other drug classes may be considered, such as metformin and SGLT2i, since these promote weight loss, particularly in patients at nutritional risk. In individuals with higher body fat percentage and sarcopenia, whose excess weight restricts functional capacity, GLP-1 receptor agonists may be considered on an individualized basis.^{241,242} In these cases, the time required to achieve therapeutic benefit and the risks of anorexia and loss of muscle mass, which may be particularly harmful in patients with more advanced frailty, should be considered. At present, evidence supporting the use of GLP-1 receptor agonists in frail older adults remains scarce.

Table 2.6 – Glycemic targets for diabetes in older adults

Health condition and characteristics	Rational	HbA1C target	CGM target	Fasting or preprandial glycemia	Glycemia before bedtime
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer life expectancy	< 7.0–7.5%	TIR 70–180 mg/dL of 70% and TBR < 4%	80–130 mg/dL	80–180 mg/dL
Complex/Intermediate (multiple coexisting chronic illnesses, or two or more impairments in ADLs, or mild to moderate cognitive impairment)	Variable life expectancy. Consider: - Severity of comorbidities - Cognitive and functional limitations - Frailty - Risk-benefit balance of diabetes medications - Individual preference	< 8.0%	TIR 70–180 mg/dL of 50% and TBR < 1%	90–150 mg/dL	100–180 mg/dL
Very complex/poor health (long-standing or end-stage chronic illnesses, moderate to severe cognitive impairment, or two or more ADL impairments)	Limited remaining life expectancy makes benefits minimal.	Avoid HbA1c-based targets; decisions should be based on preventing hypoglycemia and symptomatic hyperglycemia.		100–180 mg/dL	110–200 mg/dL

AADLs: activities of daily living; CGM: continuous glucose monitoring; HbA1c: glycated hemoglobin; TBR: time below range; TIR: time in range. Adapted from American Diabetes Association Professional Practice Committee for Diabetes.²²³

Nevertheless, individualized use may be justified based on the rationale that adaptive weight loss may provide potential benefits in quality of life.²⁴³

Other drug classes, such as sulfonylureas and peroxisome proliferator-activated receptor gamma agonists, may also be indicated. Currently, sulfonylurea use is less frequently recommended because of the risk of hypoglycemia and lower potential for cardiovascular and renal protection.⁷⁹ However, given the economic reality of Brazil and the indirect benefits associated with improved glycemic control, this drug class continues to be widely used.

Pioglitazone may be used safely in older adults provided that certain precautions are observed, such as avoiding it in patients with HF, osteoporosis, or bladder cancer. In addition, it offers the advantages of being weight-neutral and having a low risk of hypoglycemia. A meta-analysis published in 2020 found that pioglitazone reduced the risk of MACEs. However, this was accompanied by a significant increase in hospitalizations for HF. This further restricts its use, given the safety profiles of other drug classes.²⁴⁴⁻²⁴⁹

For patients presenting with higher glycemic levels (HbA1c > 10%), insulin therapy at a dose of 0.1–0.2 U/kg is recommended, either as monotherapy or associated with other agents, with slow dose titration (except in hyperglycemic emergencies). This more cautious approach is recommended because hypoglycemia in older adults may result in adverse consequences, including falls, seizures, cardiovascular events, dementia, and frailty.³⁷⁻⁴¹ Evidence suggests that ultra-long-acting basal insulin is associated with a lower risk of hypoglycemia than NPH insulin.²⁵⁰

Finally, in patients with advanced frailty, limited life expectancy, and an indication for PC, the focus should shift to symptom control related to hyperglycemia, which may be achieved with low-dose basal insulin.^{229,251} In conclusion, older adults with T2DM benefit from a multidimensional approach that allows safer, more individualized treatment.

3. Cardiovascular Risk Stratification in Older Adults

3.1. Subclinical Atherosclerosis Investigation: is it Worth it for Older Adults?

Population aging and longer life expectancy have made the management of dyslipidemia in older adults an increasingly important topic in clinical practice. Dyslipidemia, characterized by abnormalities in plasma lipid levels, is one of the main modifiable risk factors for CVD, with atherosclerosis being its most prevalent manifestation. In older adults, however, the decision to treat dyslipidemia extends beyond strict low-density lipoprotein cholesterol (LDL-c) targets and requires an individualized assessment that considers not only chronological age but also functional status, frailty, comorbidities, and patient preferences.

Recent studies stress that the treatment of dyslipidemia in older adults should follow a patient-centered approach, prioritizing quality of life and the net benefits of therapy. Guidelines from the SBC²⁵² (Figure 3.1), the ESC,²⁵³ and the AHA/ACC²⁵⁴ underscore the importance of risk stratification and shared decision-making, particularly in individuals older than 75 years.^{253,264}

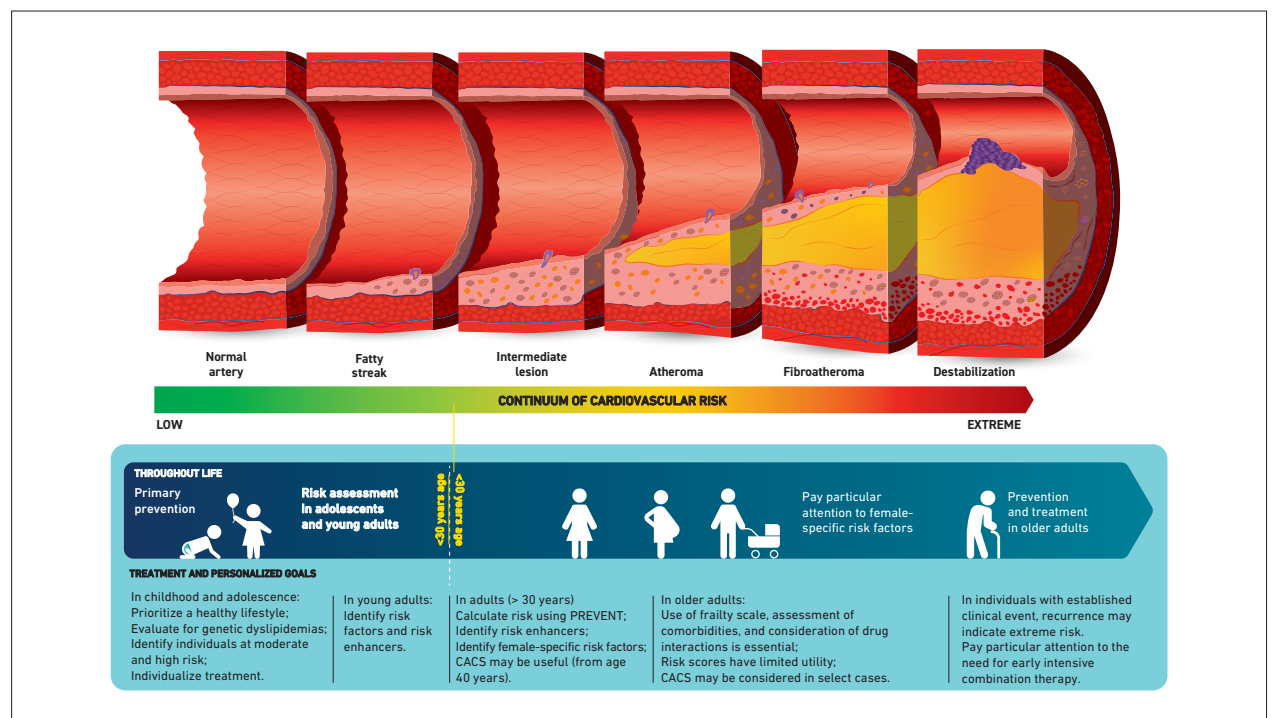


Figure 3.1 – Evolution of atherosclerotic disease throughout life. CACS: Coronary Artery Calcium Score. Source: Rached et al.²⁵²

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3.1.1. Particularities of the Older Adult Population: Risk Stratification

The prevalence of dyslipidemia increases with age and is frequently accompanied by subclinical atherosclerosis and other metabolic conditions, such as DM and metabolic syndrome. In addition, polypharmacy, which is common among older adults, may contribute to secondary dyslipidemia, particularly through the use of medications such as thiazide diuretics, beta-blockers, and corticosteroids. Polypharmacy should also be considered when selecting lipid-lowering therapy, as some therapeutic options have greater potential for drug interactions.

Frailty, defined as a biological syndrome characterized by diminished physiological reserves and increased vulnerability to stressors, is a key determinant in the management of dyslipidemia in older adults. Studies show that frail patients have higher risk of medication-related adverse events, underscoring the need for a CGA before initiating or intensifying lipid-lowering therapy.²⁵³

Moreover, the heterogeneity of the older adult population requires that therapeutic approaches extend beyond chronological age, taking into account biological age, functional status, and life expectancy. For example, a functionally independent 80-year-old patient with no comorbidities may benefit from more aggressive therapeutic targets, whereas another patient of the same age with advanced frailty may derive little benefit from that approach.²⁵³

3.1.2. Decisions about better treatment: subclinical atherosclerosis

The decision to treat dyslipidemia in older adults should be based on a careful analysis of cardiovascular risk, life expectancy, comorbidities, and patient preferences. Recent guidelines emphasize the importance of individualized treatment and shared decision-making, particularly in individuals over 75 years of age.²⁵²⁻²⁵⁷

Primary prevention of CVD in older adults remains a subject of considerable debate, especially due to the heterogeneity of this population and the need to balance risks and benefits. RCTs have provided important evidence regarding the impact of statins in reducing cardiovascular events among older adults without established CVD, although results vary according to patients' risk profiles and duration of follow-up.

Within this framework of individualized cardiovascular risk assessment in older adults, cardiovascular risk stratification using the PREVENT algorithm (Figure 3.2) remains applicable, with treatment targets determined according to this stratification method (Figure 3.3).

The assessment for the presence of subclinical atherosclerosis becomes fundamental in the evaluation of older adults.²⁵⁸ CVDs are the leading cause of disability and premature death in older adults. By itself, the identification of subclinical atherosclerosis places the older adult in the high cardiovascular risk category, with much stricter treatment targets.

3.1.3. Final Considerations

Preventing CVD in older adults requires an individualized approach, based on robust evidence and in line with the

patient's preferences. While primary prevention should be carefully weighed in terms of the risks and benefits, secondary prevention provides clear and consistent benefits, even in older patients. In the context of primary prevention (individuals who have not yet experienced clinically manifest cardiovascular events), the identification of subclinical atherosclerosis provides a solid basis for decision-making, highlighting the importance of individualized therapeutic targets and the use of combination therapy in high-risk cases. Therapeutic decision-making should be shared, based on a careful assessment of functional status, frailty, and comorbidities. Recent guidelines emphasize that, in older adults, individualized treatment is essential to maximize benefits and minimize risks.

3.2. Primary Prevention of Dyslipidemia: is it Worth it?

3.2.1. Cardiovascular Risk Assessment in Primary Prevention in Older Adults

CVD risk increases with age,²⁵⁹ as does the risk of noncardiovascular mortality, inevitably reducing life expectancy. However, the strength of the association between risk factors and cardiovascular events diminishes with aging. Because age is the factor with the greatest weight in determining risk, the absolute risk of cardiovascular events rises with age.²⁵⁹ Older risk scores did not take into account the competing risk of death from noncardiovascular causes, which could overestimate risk and, consequently, the predicted benefit of therapeutic interventions in older adults.²⁶⁰ Most risk equations were developed for populations under the age of 80 years, including the risk models used globally by the WHO.²⁶¹ The PREVENT score, for example, is intended for individuals up to 79 years of age,^{262,263} although it performed well in an older population in one study.²⁶⁴ In Europe, SCORE2-OP was developed to estimate cardiovascular risk in individuals aged 70 years or older.²⁶⁵ The score was calibrated for four regions according to country-specific cardiovascular mortality rates in Europe, with the rates from moderate-risk regions being the closest to Brazilian rates. According to SCORE2-OP for moderate-risk European regions, the 10-year risk of cardiovascular death, nonfatal MI, or nonfatal stroke in individuals aged 80 years or older is invariably $\geq 20\%$, making this population a high-risk subgroup.²⁶⁵

In addition to traditional risk factors, such as hypertension, T2DM, dyslipidemia, and obesity, older adults have other factors, including exposure to tobacco, alcohol, and air pollution; comorbidities such as CKD, hyperuricemia, and cognitive disorders; as well as geriatric conditions such as frailty, depression, and disability.²⁶⁶ These conditions are associated with increased oxidative stress and structural and electrical cardiac changes, as well as genetic and epigenetic factors that may be involved in the development of CVD in older adults.²⁶⁶

3.2.2. Management of Dyslipidemia in Older Adults in Primary Prevention

The management of CVD risk factors should be carefully assessed to balance benefits and risks in this population.

Population-based data from China since the country's economic reforms suggest increasing trends in BP, cholesterol, and DM, with a slight decline in smoking among men. Projections of future trends in CVD risk factors may help guide prevention policies and change the landscape of aging.²⁶⁷ The benefits of treatment may differ in individuals with limited life expectancy,²⁶⁸ whereas older adults generally have a higher risk of adverse events and medication side effects.^{269,270} Therefore, it is essential to identify those individuals most likely to benefit from preventive treatment.

The decision to initiate lipid-lowering treatment for primary prevention in older adults should take into account certain particularities, such as the pharmacokinetics of medications, the more limited evidence of clinical benefit in certain age groups due to the lack of studies in these populations, and the high prevalence of subclinical atherosclerosis in individuals over the age of 65 years.

The Cardiovascular Health Study (CHS) found clinical atherosclerosis in more than 30% of participants, with prevalence increasing with age.²⁷¹ Lipid concentrations also change with aging.²⁷² Total cholesterol is highest up to the sixth decade of life and declines slightly thereafter; however,

the prevalence of hypercholesterolemia remains high in older adults, with 25% of men and 42% of women having total cholesterol levels above 240 mg/dL.²⁷³ Even in genetic forms of dyslipidemia, there are no marked elevations in total cholesterol, triglycerides, and LDL-c, while dyslipidemias secondary to hypothyroidism, DM, glucose intolerance, obesity, nephrotic syndrome, and the use of medications such as thiazide diuretics and nonselective beta-blockers are common.

High cholesterol levels are associated with an increased risk of CAD in middle-aged adults and young-old individuals. This association weakens with age and may even reverse – a phenomenon known as the “cholesterol paradox,”²⁷⁴ which is a consequence of frailty or the presence of comorbidities such as cancer. Thus, the apparent increase in mortality associated with low cholesterol levels in older adults may be related to multiple factors, including malnutrition, frailty, and chronic diseases that simultaneously lower cholesterol levels and increase the risk of death.²⁷⁵

Despite the stronger evidence regarding the role of dyslipidemia in the pathogenesis of atherosclerosis and CAD from observational and experimental studies in

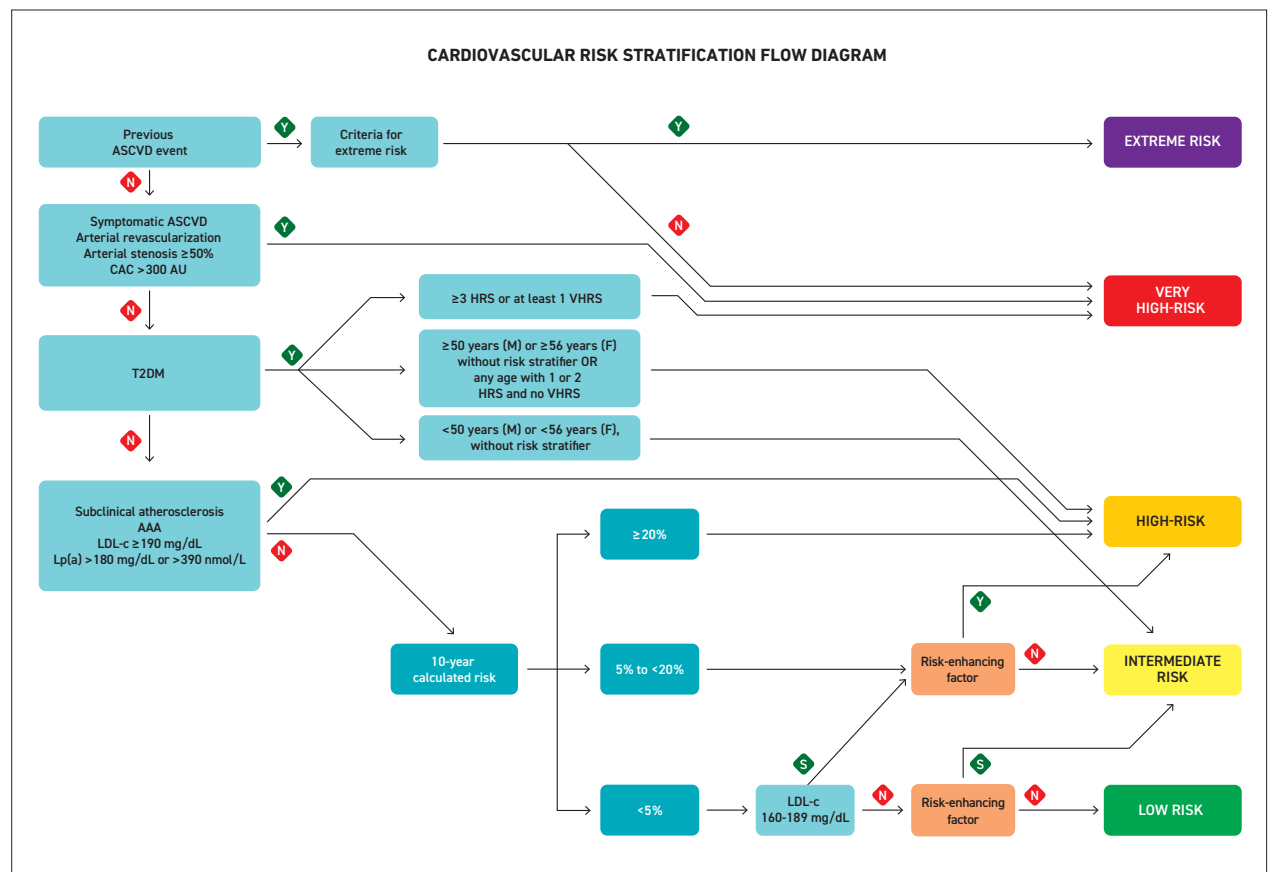


Figure 3.2 – Risk stratification (2025 Brazilian guidelines). AAA: abdominal aortic aneurysm; ASCVD: atherosclerotic cardiovascular disease; CAC: coronary artery calcium; F: female; HRS: high-risk stratifier; LDL-c: low-density lipoprotein cholesterol; Lp(a): lipoprotein(a); M: male; N: no; T2DM: type 2 diabetes mellitus; UA: Agatston units; VHRS: very-high-risk stratifier; Y: yes. Source: Rached et al.²⁵²

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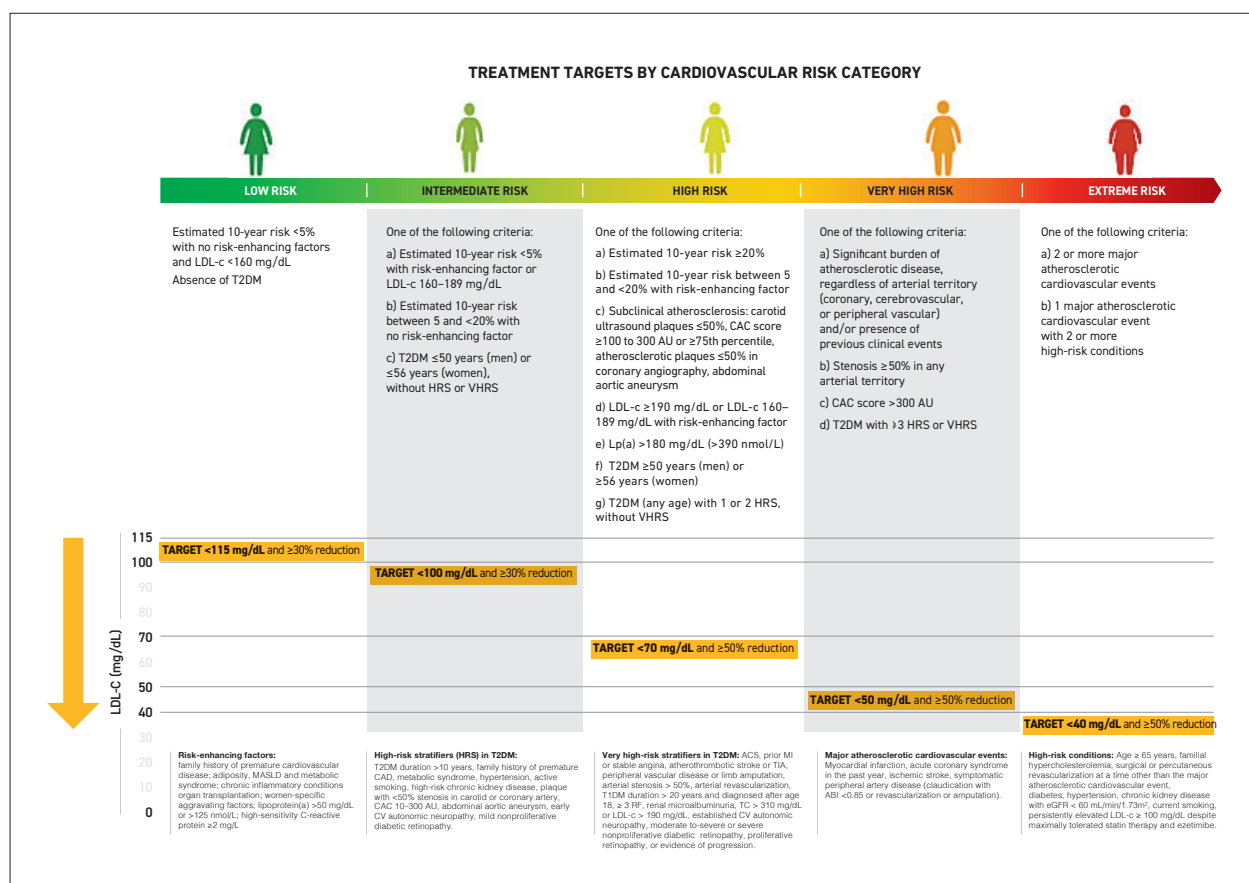


Figure 3.3 – Therapeutic targets according to estimated risk. ABI: ankle-brachial index; ACS: acute coronary syndrome; AML: acute myocardial infarction; AU: Agatston units; CACS: Coronary Artery Calcium Score; CAD: coronary artery disease; CV: cardiovascular; eGFR: estimated glomerular filtration rate; HRS: high-risk stratifier; LDL-c: low-density lipoprotein cholesterol; Lp(a): lipoprotein(a); MASLD: metabolic dysfunction-associated steatotic liver disease; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; TC: total cholesterol; TIA: transient ischemic attack; VHRS: very-high-risk stratifier. Source: Rached et al.²⁵²

middle-aged individuals,²⁷⁶ subsequent studies have provided important information that may support the decision to treat the older population as well.²⁷⁷ In older adults, the treatment of dyslipidemia should take into account the patient's physical and mental health, socioeconomic conditions, family support, existing comorbidities, and concomitant medications, which may interact with lipid-lowering agents, influencing treatment adherence and maintenance.

3.2.2.1. Nonpharmacological Treatment

Guidelines for nonpharmacological therapy should follow the same principles applied to younger adults, following caloric, protein, and vitamin requirements and the recommendation of regular physical activity.²⁵² The scientific evidence supporting lifestyle changes in older adults is solid and clear about its overall benefits, with high-to moderate-certainty recommendations for improving quality of life and preventing chronic diseases, even when initiated later in life.

Recommendations for nonpharmacological treatment	Strength of recommendation	Certainty of evidence
Guidelines for nonpharmacological therapy should follow the same principles applied to younger adults, following caloric, protein, and vitamin requirements and the recommendation of regular physical activity. The importance of smoking cessation and moderation of alcohol consumption should be emphasized.	STRONG	HIGH

3.2.2.2. Pharmacological Treatment

3.2.2.2.1. Statins

Statins are the medications of choice in this population. Data from the Prospective Studies Collaboration, which pooled the results of 61 prospective observational studies,²⁷⁸ found an association between total cholesterol and vascular mortality in nearly 900,000 individuals with no history of vascular disease, aged 40 to 89 years. Regarding CAD mortality, each reduction of approximately 39 mg/dL in total cholesterol was associated with improved survival, ranging from 21 per 10⁵ person-years in the fifth decade of life to 380 per 10⁵ person-years in the ninth decade.

The PROspective Study of Pravastatin in the Elderly at Risk (PROSPER) trial assessed the impact of cholesterol reduction with statins in older men and women aged 70 to 82 years. In that study, among patients at high cardiovascular risk (preexisting CVD or a high-risk equivalent), pravastatin 40 mg/day reduced coronary mortality by 24% over a mean follow-up of 3.2 years.²⁷⁹

The Heart Protection Study (HPS), which included a large number of individuals older than 65 years, found a significant reduction in coronary and cerebrovascular events among patients receiving simvastatin 40 mg/day.²⁸⁰

An exploratory analysis of the Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER)²⁸¹ involving participants aged 70 years or older (n = 5,695) without CVD but with C-reactive protein ≥ 2 mg/L found that rosuvastatin 20 mg/day reduced the relative risk of the primary outcome by 39% with no reduction in mortality. In the HOPE-3 trial, in which half of the participants were older than 65 years (mean age 71 years), without CVD and with one additional risk factor (men) or two additional risk factors (women older than 60 years), there was an approximately 25% reduction in the coprimary outcomes, with consistent benefits across the analyzed subgroups.²⁸²

The Cholesterol Treatment Trialists (CTT) meta-analysis found a 16% relative reduction in vascular events among patients older than 75 years receiving statin therapy.²⁸³

The STAREE (Statins in Reducing Events in the Elderly) trial,²⁸⁴ a randomized, double-blind, placebo-controlled clinical trial, is investigating the effects of statin therapy on the primary prevention of cardiovascular events and reduction of mortality in healthy older adults aged 70 years or older. Results from related studies show that statin use in older adults is not associated with an increased risk of dementia or Alzheimer's disease and, in some settings, may even confer protection. However, in the United States, the U.S. Preventive Services Task Force states that there is insufficient evidence to support the treatment of dyslipidemia in older adults aged 75 years or older with no prior history of CVD, and that treatment decisions should be individualized.²⁸⁵ The use of cardiovascular risk assessment tools, such as the Systematic Coronary Risk Evaluation 2–Older Persons (SCORE2-OP), adopted by the ESC to estimate cardiovascular risk in individuals older than 70 years, may assist in therapeutic decision-making for this population. This score incorporates factors such as age, BP, total cholesterol, high-density lipoprotein cholesterol, smoking

status, and sex to predict the 10-year risk of fatal and nonfatal cardiovascular events.²⁶⁵ The score also allows us to estimate the number of CVD-free life-years gained by lowering LDL-c by 1 mmol/L (39 mg/dL).

Three systematic reviews (searching the EMBASE, MEDLINE, Cochrane Central Register of Controlled Trials, and Web of Science databases through January 2021) identified 7,617 references, of which 29 studies were included.²⁸⁶ The following items were assessed: (1) the impact of hypercholesterolemia on mortality and MACEs in individuals older than 80 years; (2) the efficacy of statins in preventing cardiovascular events in this age group; and (3) the safety and tolerability of statins in this population. The review concluded that: (1) the association between hypercholesterolemia and cardiovascular events and mortality is weak in older patients; (2) in primary prevention, the usefulness of statins in octogenarians remains uncertain; and (3) statins should be considered with caution, taking into account overall physiological status and frailty, comorbidities, estimated cardiovascular risk, life expectancy, and individual preferences.

Based on the available evidence, treatment of dyslipidemia in older adults should be individualized, taking into account factors such as comorbidities, life expectancy, and possible drug interactions. Treatment should be recommended for older adults at high risk or very high risk, and treatment targets are similar to those established for younger adults.²⁵²

3.2.2.2.2. Nonstatin Treatment

Ezetimibe

The Ezetimibe Lipid-Lowering Trial on Prevention of Atherosclerotic Cardiovascular Disease in 75 or Older (EWTPIA 75) assessed the efficacy of lipid-lowering therapy with ezetimibe in preventing cardiovascular events in adults older than 75 years. Patients were randomized 1:1 to either usual treatment with lifestyle changes or open-label ezetimibe 10 mg/day. Ezetimibe significantly lowered the primary outcome, secondary outcomes, and coronary revascularization, with no differences in all-cause mortality or stroke. The substantial number of protocol violations and the open-label design of the study mean that results should be interpreted with caution.²⁸⁷

Bempedoic acid

A subgroup analysis of the CLEAR Outcomes trial included 2,107 (15%) patients aged 75 years or older (mean age, 78.3 [2.8]), of whom 30% were in primary prevention and 53% were women, statin-intolerant or unwilling to take statins. Bempedoic acid was found to be well tolerated, with efficacy and safety comparable to those observed in younger subgroups, and may be considered a viable strategy for the management of hypercholesterolemia.²⁸⁸

PCSK9-targeted therapies

Recently, the PCSK9 inhibitor evolocumab was tested in patients with atherosclerosis or DM but no prior MI or stroke, LDL-c levels of 90 mg/dL or more, and who had been receiving

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a stable statin dose for at least two weeks. Although the study did not include only older adults, patients older than 65 years derived the same benefits as younger participants. Evolocumab reduced the incidence of first 3-point MACE by 25% and 4-point MACE by 19% compared with placebo,²⁸⁹ making it another option for older adults. To date, there is no data for inclisiran.

The following recommendations apply to patients without ASCVD and with LDL-c levels between 70 and 189 mg/dL.²⁵⁷ Careful assessment of polypharmacy is key, with particular attention to the Beers Criteria regarding potentially inappropriate medications in older adults, including deprescribing criteria.⁷⁹

Recommendations for the management of dyslipidemia in older adults without ASCVD and with LDL-c levels between 70 and 189 mg/dL ^{252,257}	Strength of recommendation	Certainty of evidence
Up to 75 years of age, the management of dyslipidemia in older adults should follow the same recommendations as for younger adults.	STRONG	HIGH
After 75 years of age, lipid-lowering dosages should be individualized according to frailty, comorbidities, life expectancy, and polypharmacy.	STRONG	MODERATE
In adults older than 75 years without established ASCVD, LDL-c is associated with incident ASCVD and should be measured as part of cardiovascular risk stratification.	STRONG	MODERATE
In adults older than 75 years with LDL-c levels between 70 and 189 mg/dL, initiation of statins for primary prevention of atherosclerotic cardiovascular events is reasonable in individuals without life-limiting illnesses.	CONDITIONAL	MODERATE
In adults older than 75 years, the utility of cardiovascular risk equations for assessing 5- to 10-year ASCVD risk appears uncertain.	CONDITIONAL	MODERATE
In adults older than 75 years, risk models adjusted for competing risks may be considered to estimate ASCVD risk and the potential benefit of primary prevention with statins on an individual basis.	CONDITIONAL	MODERATE
In adults older than 75 years with LDL-c levels between 70 and 189 mg/dL for whom there is uncertainty regarding statin initiation, CACS is reasonable, and statins are not indicated if CACS = 0.	CONDITIONAL	MODERATE
In adults aged 76 to 80 years with LDL-c levels between 70 and 189 mg/dL and a CACS > 100 or above the 75th percentile for age, sex, and race, shared decision-making regarding statin initiation is reasonable.	CONDITIONAL	LOW
In adults older than 75 years without ASCVD, statin use to reduce ASCVD risk is reasonable despite the potential risk of statin-associated muscle symptoms.	CONDITIONAL	LOW
In adults older than 75 years without ASCVD, statin use to reduce ASCVD risk is reasonable despite the potential risk of new-onset T2DM.	CONDITIONAL	MODERATE
In adults older than 75 years without ASCVD, statin use to reduce ASCVD risk is reasonable despite the potential risk of medication-related cognitive impairment.	CONDITIONAL	MODERATE
In adults older than 75 years without ASCVD, validated mortality indices that include comorbidities and functional status are recommended to help clinicians incorporate the patient's remaining life expectancy into decisions regarding statin use for ASCVD prevention.	STRONG	MODERATE
In adults older than 75 years without ASCVD, integrating screening of frailty, dementia, and functional impairment into decisions regarding statin initiation for ASCVD prevention may be useful.	CONDITIONAL	MODERATE
In adults older than 75 years without ASCVD who are receiving statins, LDL-c monitoring every 3 to 12 months, as clinically indicated, is recommended.	STRONG	HIGH
In adults older than 75 years without ASCVD, shared decision-making should be used when making patient-centered decisions regarding statin therapy.	STRONG	LOW
In select adults older than 75 years without ASCVD for whom deprescribing is under consideration, shared decision-making among the clinician, patient, and/or caregiver is reasonable.	CONDITIONAL	LOW
In adults older than 75 years without ASCVD, discontinuation of statin therapy may increase the risk of cardiovascular events compared with continuation.	CONDITIONAL	MODERATE

In adults older than 75 years without ASCVD who have life-limiting conditions and an estimated survival time of less than 1 year, discontinuation of statin therapy to improve quality of life may be reasonable.	CONDITIONAL	MODERATE
In adults older than 75 years without ASCVD but with LDL-c levels above thresholds recommended by guidelines and additional risk factors, ezetimibe to reduce ASCVD risk may be considered.	STRONG	MODERATE
In adults older than 75 years without ASCVD and with intolerance to statins, bempedoic acid to reduce LDL-c levels and ASCVD risk may be considered.	CONDITIONAL	LOW
In adults older than 75 years without ASCVD and with intolerance to statins, PCSK9-targeted therapies to reduce LDL-c levels and ASCVD risk may be considered.	CONDITIONAL	LOW

ASCVD: atherosclerotic cardiovascular disease; CACS: coronary artery calcium score; LDL-c: low-density lipoprotein cholesterol; PCSK9: proprotein convertase subtilisin/kexin type 9; SAMS: statin-associated muscle symptoms; T2DM: type 2 diabetes mellitus.

3.3. Coronary Artery Calcium Score: is it Worth it for Older Adults?

CVDs remain the leading cause of morbidity and mortality among older adults worldwide, accounting for a substantial burden of hospitalizations, disability, and health care costs. This scenario is strongly influenced by the high prevalence of and prolonged cumulative exposure to classic risk factors, such as hypertension, DM, dyslipidemia, and smoking, as well as the presence of established or subclinical CAD.²⁹⁰ With progressive population aging, particularly in middle- and high-income countries, improving strategies for cardiovascular prevention, diagnosis, and risk stratification in this age group has become increasingly important.

However, cardiovascular risk assessment in older adults remains a major clinical challenge. Traditional scores based exclusively on clinical and laboratory variables, widely used in clinical practice, have important limitations in this population, mainly because chronological age is heavily weighted in their algorithms. Consequently, these models tend to overestimate cardiovascular risk in older individuals regardless of actual atherosclerotic burden, potentially leading both to overprescription of preventive therapies and to difficulty in individualizing clinical decisions.²⁶⁵ Moreover, the biological heterogeneity of aging, the coexistence of multiple comorbidities, and functional variability make an assessment based solely on conventional risk factors insufficient.

In this context, imaging methods capable of directly identifying and quantifying coronary atherosclerosis have gained prominence. The CACS, obtained using non-contrast computed tomography (CT), enables an objective quantification of the burden of coronary artery calcification, directly and reproducibly reflecting the presence of subclinical atherosclerosis.²⁹¹ Unlike clinical risk scores, CACS provides an anatomic measure of disease, integrating the cumulative effects of lifetime exposure to risk factors, making it particularly attractive in older populations.

Over recent decades, CACS has become established as a robust prognostic tool in middle-aged adults, demonstrating a strong association with future cardiovascular events, including MI and cardiovascular mortality. However, its

applicability in individuals aged 65 years or older remains controversial.²⁹² This is partly due to the high prevalence of coronary calcification in this age group, raising questions about the actual discriminatory value of the method, particularly in distinguishing physiological vascular aging from clinically relevant atherosclerosis. On the other hand, growing evidence suggests that the absence of coronary calcium (CACS = 0) retains a high negative predictive value even in older adults, while high scores are associated with a higher risk of events, highlighting the role of CACS as a risk refinement tool and an aid to clinical decision-making in this population.

Accordingly, incorporating CACS into the cardiovascular assessment of older adults has emerged as a promising strategy to complement traditional risk stratification models, enabling a more individualized approach aligned with the principles of evidence-based medicine and personalized prevention. A thorough understanding of its indications, limitations, and clinical implications is fundamental to optimize cardiovascular care in an increasingly large and complex older population.^{293,294}

The goal of this review is to critically analyze the scientific evidence published between 2020 and 2026 regarding the use of CACS in older adults, particularly in the presence of DM, SAH, and CAD, as well as to discuss recommendations from national and international guidelines.

3.3.1. Pathophysiological Bases of the Coronary Artery Calcium Score in Aging

Vascular aging is associated with arterial remodeling, chronic low-grade inflammation, and progressive calcium deposition within the arterial wall.²⁹⁴ Population-based studies have found that the prevalence of CACS > 0 exceeds 70% among individuals older than 70 years. However, calcification does not progress homogeneously and is accelerated by the presence of DM and hypertension.²⁹⁵

Coronary calcification represents a marker of cumulative atherosclerotic burden rather than simply a phenomenon of physiological aging.²⁹⁶ Therefore, objective quantification of CACS may help distinguish expected vascular aging from clinically relevant atherosclerosis.²⁹⁷

3.3.2. Prognostic Value of the Coronary Artery Calcium Score in Older Adults

Several recent studies have found that CACS has prognostic value independent of chronological age. Analyses from the Multi-Ethnic Study of Atherosclerosis (MESA) showed that older adults with high CACS have a significantly greater risk of cardiovascular events, while those with CACS = 0 maintain a favorable prognosis.²⁹⁸

Blaha et al. found that, among adults aged 65 years or older, CACS had greater discriminatory ability for coronary events than age alone.²⁹⁹ Similarly, European and North American studies have confirmed that CACS > 300 or > 400 Agatston units (AU) is associated with a risk comparable to that of patients undergoing secondary prevention.^{300,301}

3.3.3. Zero Calcium Score in Older Adults

The presence of CACS = 0 has consistently been associated with low cardiovascular risk, including in older adults.²⁹⁴ Recent meta-analyses have found that adults aged 65 years or older with CACS = 0 have an annual cardiovascular event rate under 1%.³⁰²

This finding has substantial clinical relevance, as it may help avoid aggressive pharmacological interventions in individuals at intermediate clinical risk, thereby reducing polypharmacy and adverse events.³⁰³

3.3.4. Coronary Artery Calcium Score in Older Adults with Diabetes Mellitus

Although DM has traditionally been considered a coronary risk equivalent, recent studies have found considerable heterogeneity among older adults with DM.³⁰⁴ Data from MESA indicate that up to 25% of older adults with DM have CACS = 0 and a significantly more favorable prognosis.³⁰⁵

On the other hand, CACS > 400 in older adults with DM is associated with a marked increase in cardiovascular mortality and coronary events, justifying the use of intensive therapies.³⁰⁶ Therefore, CACS enables more precise risk stratification within the diabetic population, helping to avoid both undertreatment and overtreatment.³⁰⁷

3.3.5. Coronary Artery Calcium Score and Hypertension

Hypertension is one of the main determinants of progression of vascular calcification.³⁰⁸ Observational studies have found a direct correlation between duration of hypertension, inadequate BP control, the magnitude of CACS.³⁰⁸

Among older adults with hypertension, elevated CACS is associated with a higher incidence of MI, HF, and cardiovascular mortality.³⁰⁹ Accordingly, CACS may help identify patients with apparently controlled hypertension who nevertheless have a high atherosclerotic burden.³¹⁰

3.3.6. Clinical Guidelines and Current Recommendations

The AHA/ACC guidelines recognize CACS as a useful tool for refining risk stratification in older adults, particularly in

cases of therapeutic uncertainty.³¹¹ For individuals aged 76 to 80 years without DM and with LDL-c levels between 70 and 189 mg/dL, CACS may be considered to assist clinical decision-making.³¹²

European guidelines and the 2025 Brazilian Guideline on Dyslipidemias and Prevention of Atherosclerosis also recommend CACS as a complementary method for individuals at intermediate risk, with no strict age limit.^{252,313}

3.3.7. Therapeutic Implications of the Coronary Artery Calcium Score in Older Adults

CACS plays an increasingly important role in individualizing therapeutic decision-making in older adults, particularly for the primary prevention of atherosclerotic CVD. Unlike traditional clinical risk scores, CACS provides an objective measure of coronary atherosclerotic burden, allowing risk reclassification and adjustment of treatment intensity.^{314,315}

3.3.7.1. Coronary Artery Calcium Score-Guided Statin Use

Several observational studies and expert consensus statements have shown that CACS is particularly useful when deciding whether to initiate statin use in older adults at intermediate or uncertain clinical risk. Among individuals aged 65 years or older without established CVD:

- CACS = 0 is associated with a very low short- and intermediate-term cardiovascular risk, even in the presence of traditional risk factors, allowing postponement or avoidance of statin initiation for primary prevention, particularly when there are concerns regarding polypharmacy and muscle-related adverse effects.³¹⁴
- CACS ≥ 100 or ≥ 75th percentile for age and sex identifies older adults at significantly increased cardiovascular risk for coronary events and is considered a strong indication for initiating or intensifying statin therapy, regardless of baseline LDL cholesterol levels.³¹⁵

Technical classification:

- CACS stratification (Agatston) is usually categorized as follows:
 - 0 = no CAC;
 - 1–99 = mild;
 - 100–299 = moderate;
 - 300 ≥ 400 = severe.

These categories help guide diagnostic and therapeutic priorities.

Recent studies indicate that older adults with high CACS have event rates similar to those observed in patients receiving secondary prevention, underscoring the need for intensive lipid-lowering therapy.³¹⁵ In addition, cost-effectiveness analyses suggest that a strategy based on CACS may reduce both undertreatment and unnecessary statin use among older adults at low cardiovascular risk.³¹⁴

3.3.7.2. Coronary Artery Calcium Score and aspirin Use in Primary Prevention

Aspirin use for primary prevention in older adults remains controversial, primarily due to the increased risk of gastrointestinal and intracranial bleeding. Recent studies have shown that CACS may help identify subgroups for whom the potential cardiovascular benefit of aspirin outweighs the risks.

Older adults with high CACS (≥ 400 AU) have a significantly higher cardiovascular risk and may represent a subgroup with a potential net benefit from aspirin use, provided that bleeding risk is carefully assessed.³¹⁶ On the other hand, individuals with low or zero CACS generally have risk of bleeding greater than the potential cardiovascular benefit, and aspirin use is therefore not recommended in this context.³¹⁶

These findings highlight the role of CACS as an additional risk stratification tool, enabling more precise and individualized decision-making regarding antithrombotic therapy in older adults.

3.3.7.3. Older Adult-Centered Approach: Frailty and Life Expectancy

Despite the usefulness of CACS, therapeutic decisions in older adults should always take into consideration factors beyond absolute cardiovascular risk. Elements such as frailty, multimorbidity, life expectancy, functional status, and patient preferences are all essential to avoid disproportionate interventions.³¹⁷

In frail older adults or those with limited life expectancy, even a high CACS may not justify aggressive therapy, particularly when the expected benefit is delayed. Therefore, CACS should be interpreted as a complementary tool integrated into the CGA.³¹⁷

3.3.8. Limitations and Controversies of the Coronary Artery Calcium Score in Older Adults

Despite its advantages, the use of CACS in older adults has important limitations and areas of controversy that should be considered in clinical practice.

3.3.8.1. High Prevalence of Positive Coronary Artery Calcium Score with Aging

One of the main challenges of CACS in older adults is the high prevalence of positive results. Population-based studies show that most individuals aged 75 years or older have some degree of coronary calcification.³¹⁸ This reduces the discriminatory ability of the test in the oldest age groups, particularly for low or intermediate scores.

Therefore, the mere presence of CACS > 0 in older adults should not automatically be interpreted as indicating high risk, and requires careful interpretation of the absolute score, age- and sex-adjusted percentile, and the clinical context.³¹⁸

3.3.8.2. Inability to Assess Noncalcified Plaques

Another important limitation is that CACS does not detect noncalcified atherosclerotic plaques, which may be

vulnerable and associated with acute events.³¹⁹ In older adults, although calcified plaques may be more prevalent, mixed or noncalcified plaques may play an even more relevant role, especially in patients with DM.

Therefore, low CACS does not completely rule out the presence of coronary atherosclerosis, and the examination is no substitute for more complete anatomical or function methods when coronary disease is suspected.³¹⁹

3.3.8.3. Limited Usefulness in Patients with Known Coronary Artery Disease

In older adults with established CAD or prior cardiovascular events, CACS has limited usefulness, since these individuals are automatically classified as high-risk patients and are candidates for intensive therapies.³²⁰ In these cases, CACS rarely changes clinical management and is not routinely recommended.³²⁰

3.3.8.4. Scarcity of Randomized Controlled Trials with the Oldest Old

Despite the large number of observational studies, few RCTs have assessed CACS-guided therapeutic strategies exclusively in older adults aged 75 years or older.³²¹ Most of the evidence comes from secondary analyses or age subgroups, limiting the generalizability of results for frail older adults and the oldest old.

Ongoing studies, such as the PREVENTABLE trial, may provide more robust data on the impact of preventive strategies based on atherosclerotic risk in the oldest old.^{257,318,320-331}

3.4. Use of Computed Tomography Angiography of the Coronaries Associated with Coronary Artery Calcium Score in Older Adults

CCTA has become established as a high-sensitivity noninvasive diagnostic method for detecting CAD, particularly in patients with stable chest pain and a low to intermediate pretest probability.^{79,332,333} At the same time, the CACS has become an important marker of atherosclerotic burden and a robust tool for cardiovascular risk stratification, including in older populations.^{334,335}

However, the routine application of these methods in older adults, particularly those over 65 years of age, remains controversial and requires careful consideration, taking into account the pathophysiological changes associated with aging, the higher prevalence of extensive coronary calcification, the technical limitations of CCTA, and the actual impact of the findings on clinical decision-making.^{333,336}

Overall, and in accordance with contemporary evidence and international guidelines, CCTA should not be used routinely as an investigative test in all older patients (65 years or older), even when combined with CACS.³³⁶⁻³³⁸ Indiscriminate use of CCTA in this population may result in nondiagnostic examinations, increased exposure to ionizing radiation and iodinated contrast material, and limited incremental clinical yield in individuals with a high calcified atherosclerotic burden.^{336,337}

Therefore, the combined use of CCTA and CACS should be individualized and guided by the pretest probability

of CAD, the presence and characteristics of symptoms, functional capacity, associated comorbidities, and, above all, the expectation that test results will effectively change clinical management.^{337,339}

3.4.1. Absence of Relevant Clinical Impact in Routine Use

A central principle of evidence-based medicine is that diagnostic testing should only be requested when there is a realistic possibility that the results will change therapeutic management.³⁴⁰ In older adults, optimized clinical management, including strict BP control, statin therapy, appropriate management of DM, and smoking cessation, is indicated in most clinical scenarios, regardless of additional anatomic evidence of coronary atherosclerosis.^{223,341}

Therefore, identification of atherosclerotic plaques by CCTA in asymptomatic older adults or those with atypical symptoms rarely results in meaningful changes in therapeutic strategy, limiting the clinical value of routine use of this examination in this population.^{338,341,342}

3.4.2. Critical Synthesis

Therefore, although CACS is a valuable tool for guiding therapeutic decisions in older adults, its use should be judicious, individualized, and integrated into the overall clinical assessment. The balance between cardiovascular benefit, risk of adverse events, and quality of life is essential when making decisions in this population.

3.4.3. Conclusion

Scientific evidence published between 2020 and 2026 indicates that CACS is a useful and safe tool for cardiovascular risk stratification in adults aged 65 years or older, particularly in the presence of DM and hypertension. When interpreted in the appropriate clinical context, CACS allows more individualized decision-making, avoiding both undertreatment and excessive medicalization.

3.5. When to Check the Ankle-Brachial Index?

The ABI is a noninvasive, low-cost method widely used in the diagnostic evaluation of peripheral artery disease (PAD), as well as a cardiovascular prognostic marker.³⁴³⁻³⁴⁶ Values ≤ 0.90 are considered diagnostic of PAD.^{344,345} Values ≥ 1.40 suggest noncompressible arteries, generally due to medial arterial calcification, a condition frequently observed in older adults and patients with DM and CKD.³⁴³ In these cases, an additional assessment using the toe-brachial index (TBI) and/or waveform analysis is recommended.³⁴⁴

The ABI has an approximate sensitivity of 75% and specificity of 86% for $\geq 50\%$ stenosis compared with angiography.³⁴⁷ However, its sensitivity may be reduced in older adults and in patients with DM or CKD.^{345,347,348} Therefore, when clinical suspicion is high and the ABI is normal or elevated, complementary diagnostic methods should be considered.

3.5.1. Physiology and Aging

Under normal hemodynamic conditions, ankle systolic BP (SBP) tends to be equal to or slightly higher than brachial SBP, so an ABI of approximately 1.0–1.3 is considered normal. In the presence of arterial stenosis or occlusion in the lower extremities, there is a drop in distal arterial pressure, resulting in a lower ABI. In older adults, two phenomena may change the interpretation:

- Higher atherosclerotic burden (lowering the ABI);
- Increased arterial stiffness and medial calcification (making tibial arteries less compressible and artificially increasing ankle pressure, resulting in a “high” ABI).

3.5.2. Diagnostic and Prognostic Performance

Resting ABI has a sensitivity of approximately 68%–84% and specificity of 84%–99% for the diagnosis of PAD.^{344,347,348} Although it performs well in clinical practice, its sensitivity is insufficient to rule out PAD in high-risk older adults, particularly in the presence of DM, CKD, or arterial calcification.³⁴⁸⁻³⁵¹ In patients with DM, the TBI may have greater sensitivity than the ABI and is particularly useful when the ABI is normal or elevated.³⁵⁰⁻³⁵² Thus, an ABI between 0.90 and 1.30 does not rule out PAD when clinical suspicion remains high.

In addition to its diagnostic value, the ABI has important prognostic value in geriatric cardiology. Low values are associated with an increased risk of cardiovascular events, CAD, stroke, HF, ischemic limb events, and cardiovascular and all-cause mortality.^{346,353-355} Elevated values, particularly > 1.30 – 1.40 , are also associated with increased mortality, reflecting the presence of noncompressible arteries and a greater atherosclerotic burden.^{346,355}

Thus, the ABI represents an important initial tool for the assessment of PAD and cardiovascular risk stratification in older adults. However, normal results should not be used in isolation to rule out PAD in high-risk individuals or those with high clinical suspicion, in whom complementary methods, such as the TBI and waveform assessment, may improve diagnostic accuracy.

3.5.3. When to Check the Ankle-Brachial Index

For diagnostic purposes, the ABI should be performed in older adults with symptoms or signs suggestive of PAD, including exertional pain or fatigue, walking impairment, diminished pulses, arterial bruits, BP asymmetry, poorly healing wounds or ulcers, and rest pain. The absence of typical claudication does not rule out PAD, as many older adults remain asymptomatic or present with atypical manifestations, particularly given limited mobility or comorbidities.^{343,345}

In opportunistic screening, ABI may be considered in individuals 65 years of age or older with increased atherosclerotic risk, particularly in the presence of smoking, DM, CKD, hypertension, dyslipidemia, atherosclerotic disease in another vascular bed, foot lesions, or walking impairment of undetermined cause.^{343,344} In asymptomatic

older adults without relevant risk factors, systematic screening is not recommended, and the indication should be individualized.

3.5.4. How to Measure and Interpret it

The technique used to measure the ABI is critical for accuracy. The preferred method uses continuous-wave Doppler (8–10 MHz), a calibrated sphygmomanometer, and appropriately sized cuffs. The patient should remain in supine position for 5–10 minutes in a quiet environment, with the cuff covering approximately 40% of the limb circumference and positioned approximately 2 cm above the ankle malleolus.³⁴⁵

The ABI should be calculated as the ratio of the higher ankle SBP obtained from either the posterior tibial or dorsalis pedis artery to the higher brachial SBP.^{342,345} The seated position should not replace the supine examination, as it may artificially increase the values; when the supine position is not tolerated, the position used should be documented and the result interpreted with caution.³⁴⁵

The sequence and conditions of the measurements should be standardized, with discrepant values between limbs repeated. Tremor, agitation, or difficulty remaining still may compromise the quality of the examination and require repetition or the use of complementary methods.^{346,347}

3.5.5. Classification

The classification most frequently used in contemporary guidelines (including PAD guidelines) is:

- Abnormal (PAD): $ABI \leq 0.90$;
- Borderline: $0.91\text{--}0.99$;
- Normal: $1.00\text{--}1.40$;
- Incompressible/suggestive of calcification: > 1.40 .

An $ABI > 1.40$ requires assessment using complementary methods, such as the TBI, toe pressure measurement, or Doppler waveform analysis. Likewise, a normal or borderline ABI does not conclude the investigation if symptoms persist, particularly in patients with DM, CKD, advanced age, skin wounds, or strong clinical suspicion. In these cases, exercise testing and/or arterial duplex ultrasonography are appropriate. It is important to emphasize the possibility of false-positive results with some simplified exercise criteria; therefore, post-exercise examinations should be interpreted within the clinical context and with appropriate laboratory expertise. Recent studies have identified a substantial number of false-positive results in healthy populations when a post-exercise ABI reduction higher than 20% is used as the diagnostic threshold.³⁵⁶

3.5.6. Automated (Oscillometric) Methods: When to Consider and When to Avoid

A meta-analysis of automated oscillometric devices (compared with Doppler) suggests good correlation,

with high specificity (approximately 96%) and moderate sensitivity (approximately 69%) for detecting PAD. This may support their use in screening situations where Doppler is unavailable, provided that borderline, symptomatic, or high-risk cases are confirmed by Doppler examination.³⁵⁷

In contrast, studies in patients with AF (a common arrhythmia in older adults) have found poor agreement between oscillometric and Doppler measurements, explicitly recommending that oscillometry not replace Doppler in these patients.³⁵⁸

The proposed strategy for the initial evaluation and complementary diagnostic assessment of PAD in older adults, based on ABI results and the clinical context, can be found in Figure 3.4.

3.5.7. Particularities of the Older Adult

Medial arterial calcification, more frequent in older adults and in patients with DM and CKD, may render the arteries noncompressible and produce a falsely elevated ABI. Thus, values ≥ 1.40 should be interpreted as indicating noncompressible arteries rather than normality, and the assessment should be complemented with the TBI, toe pressure, and, when available, waveform analysis.^{343-345,350}

Frailty, sarcopenia, osteoarthritis, and limited mobility may mask claudication, particularly in patients who walk little. In individuals 75 years of age or older with PAD, assessment of frailty, sarcopenia, nutritional status, and mobility can assist in risk stratification and individualized care.^{343,359-362}

Cognitive impairment, depression, diabetic neuropathy, and low physical activity may reduce the reliability of the history taking. In these patients, the absence of typical symptoms does not rule out PAD, and objective findings, such as diminished pulses, trophic lesions, and pain, should be given greater consideration.

The identification of PAD should trigger a comprehensive assessment of cardiovascular risk and a review of preventive measures, including lipid-lowering therapy, antithrombotic therapy when indicated, risk-factor control, and foot care. In older adults receiving multiple medications, these interventions should consider the risk of iatrogenesis and be individualized.^{343,363}

Cardiac rhythm irregularity may interfere with automated ABI measurements. In patients with AF, particularly older adults, caution is recommended when interpreting oscillometric measurements and, when possible, Doppler assessment should be preferred.³⁵⁸

The ABI can be used for comparison before and after revascularization, with an increase ≥ 0.15 representing an objective parameter of hemodynamic improvement. However, changes in the ABI do not replace imaging methods, particularly when restenosis or multisegmental disease is suspected.^{343,364}

Guidelines

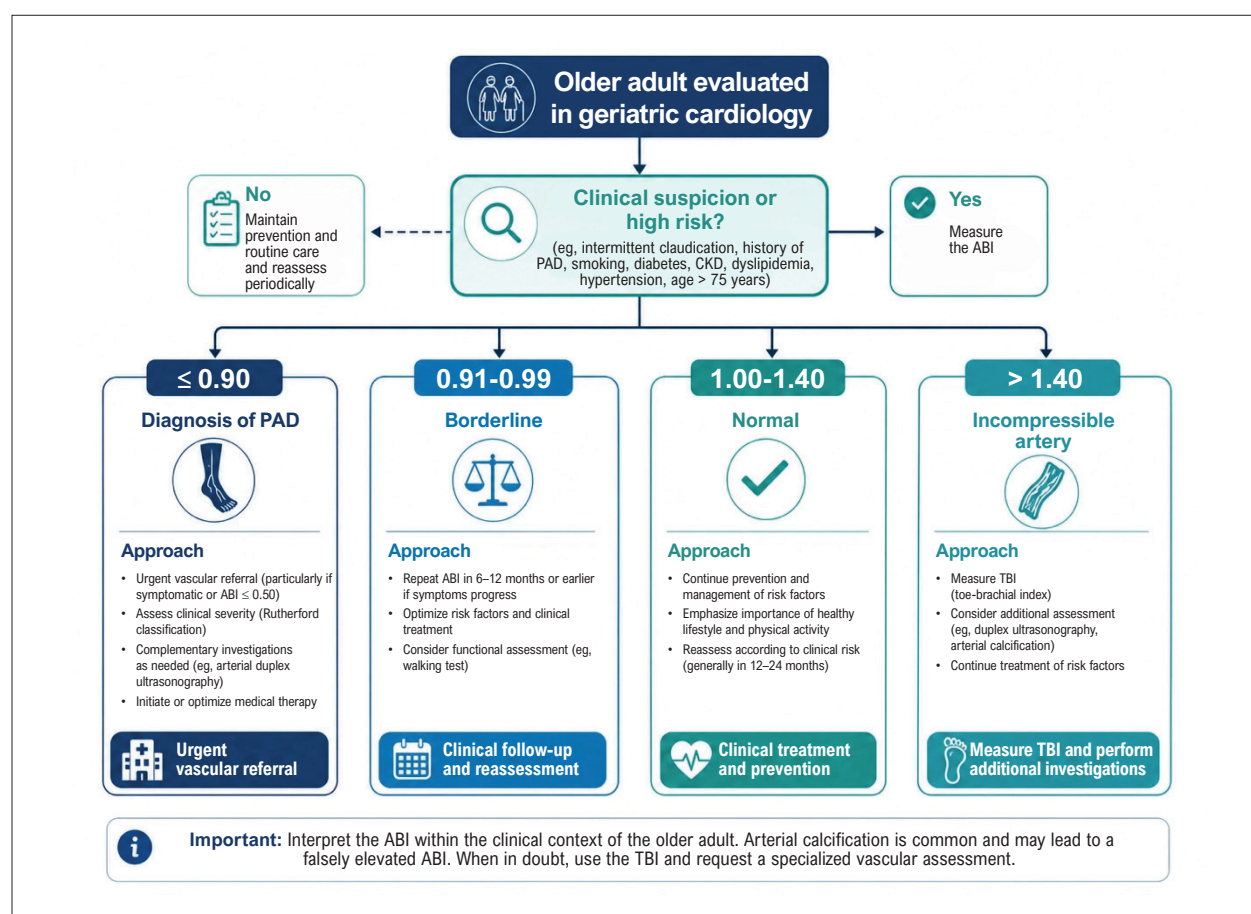


Figure 3.4 – Proposed strategy for the initial evaluation and complementary diagnostic assessment of peripheral artery disease in older adults. ABI: ankle-brachial index; CKD: chronic kidney disease; PAD: peripheral artery disease; TBI: toe-brachial index. Sources: ACC/AHA 2016 PAD Guideline; Sociedade Brasileira de Angiologia e Cirurgia Vascular (SBACV)

Recommendations for the diagnostic investigation of PAD in older adults	Strength of recommendation	Certainty of evidence
In older adults with symptoms, clinical signs, or physical examination findings suggestive of PAD, including intermittent claudication, pain at rest, trophic lesions of the lower extremities, or abnormal peripheral pulses, measurement of the resting ABI using Doppler ultrasound as the first noninvasive diagnostic test is recommended.	STRONG	MODERATE
In asymptomatic older adults at high cardiovascular risk or with established atherosclerosis in other vascular beds, opportunistic ABI measurement for the detection of concomitant PAD and improved prognostic stratification, particularly in the presence of age 65 years or older, diabetes mellitus, current or previous smoking, dyslipidemia, hypertension, chronic kidney disease, or atherosclerotic disease in another vascular bed is suggested.	CONDITIONAL	MODERATE

When the ABI is > 1.40 , or when there is strong suspicion of a falsely normal result due to arterial calcification or incompressible arteries, complementary evaluation with the toe-brachial index, digital pressure measurement, waveform analysis, and/or vascular Doppler ultrasonography is recommended.	STRONG	MODERATE	During follow-up of older adults with PAD, longitudinal clinical assessment, including evaluation of symptoms, functional status, peripheral pulses, and foot inspection, is suggested. After revascularization, structured surveillance with ABI measurement and arterial duplex ultrasonography according to the type of procedure and the clinical context is suggested.	CONDITIONAL	LOW
In older adults with symptoms suggestive of PAD and an ABI between 0.91 and 1.40, further investigation with post-exercise ABI testing and/or arterial duplex ultrasonography, rather than terminating the diagnostic assessment, is recommended.	STRONG	MODERATE			
In cases of borderline ABI (0.91–0.99), post-exercise ABI testing for diagnostic confirmation, depending on the clinical context, may be considered.	CONDITIONAL	LOW			
In older adults with diabetes mellitus, chronic kidney disease, frailty, impaired mobility, or cognitive impairment, a lower threshold for ABI measurement is suggested. When necessary, ABI assessment should be combined with the toe-brachial index, digital pressure measurement, or waveform analysis, recognizing that normal ABI values may not reliably exclude PAD in these groups.	CONDITIONAL	LOW			

ABI: ankle-brachial index; DM: diabetes mellitus; PAD: peripheral artery disease.

3.5.8. Limitations and Gaps

The evidence supporting diagnostic accuracy specifically in frail older adults, the oldest-old, institutionalized individuals, or those with dementia remains inferior to what would be desirable. Furthermore, much of the contemporary prognostic evidence is observational. Finally, available studies emphasize longitudinal follow-up but do not provide a single recommended interval for repeat ABI measurement in all asymptomatic older adults outside specific scenarios such as post-revascularization follow-up.^{364,365}

3.5.9. Conclusion

The ABI is the first-line noninvasive test for suspected PAD. In high-risk older adults, it can and should be used opportunistically, even in the absence of typical claudication. It is important to emphasize that, in older adults, the primary error is interpreting a “normal” or elevated ABI without taking into account arterial calcification, DM, CKD, frailty, and the unreliability of the clinical history. In practical terms, the ABI should be measured when there are symptoms, abnormal physical examination findings, a poorly healing wound, unexplained functional loss without a convincing musculoskeletal cause, or simply advanced age combined with atherosclerotic risk factors. If the ABI is > 1.40 , or if clinical suspicion remains high despite an ABI between 0.91 and 1.40, the next step should be using alternative methods for diagnostic complementation, such as the TBI, digital pressure measurement, Doppler waveform analysis, exercise testing, or duplex ultrasonography, depending on the clinical scenario.

4. Chronic Coronary Heart Disease

4.1. Introduction

The Brazilian population is aging. According to projections by IBGE in partnership with Fundação Oswaldo Cruz (Fiocruz), older adults are expected to account for approximately 30% of Brazil's population by 2050.³⁹⁰ In this context, chronic CAD has emerged as the leading cause of cardiovascular mortality in Brazil, accounting for a substantial share of hospitalizations and deaths within the Brazilian Unified Health System (SUS).³⁶⁶

Chronic CAD – also referred to as chronic coronary syndrome – encompasses a heterogeneous spectrum of clinical presentations, including stable angina, silent ischemia, ischemic ventricular dysfunction, and a history of stabilized ACS.³⁶⁷ The prevalence of this condition increases progressively with age, reaching epidemic proportions among individuals aged 70 years or older, with a direct impact on quality of life, functional capacity, and mortality.^{368,369}

Management of chronic CAD in older adults requires a thorough understanding of the pathophysiological, clinical, and pharmacological specificities that distinguish this age group from younger adults. Changes in physiological reserve, multiple comorbidities, polypharmacy, frailty, cognitive decline, and issues related to autonomy and decision-making make the management of this condition intrinsically more complex.

4.2. Peculiarities of the Diagnosis of Chronic Coronary Artery Disease in older Adults

4.2.1. Atypical Clinical Presentation

The clinical presentation of chronic CAD in older adults differs substantially from that observed in younger and middle-aged adults. Typical angina (oppressive precordial pain radiating to the left upper extremity, triggered by exertion and relieved by rest) is less frequent in this population.³⁷⁰ Aging is associated with alterations in nociceptive perception, reduced autonomic sensitivity, and changes in myocardial physiology that contribute to atypical or silent presentations of myocardial ischemia.³⁷⁰

The most common anginal equivalents in older adults include exertional dyspnea, disproportionate fatigue, syncope, dizziness, and worsening functional capacity without apparent cause.³⁷⁰ These manifestations are often attributed to other comorbidities, such as HF, COPD, or anemia, delaying diagnosis and exposing patients to an increased risk of acute ischemic events.³⁷⁰

Silent ischemia, defined as the absence of symptoms during objectively documented episodes of myocardial ischemia, occurs in up to 40% of older adults without a previous history of CAD,³⁶⁷ highlighting the importance of systematic investigation in this age group, even in the absence of classic anginal complaints. Ambulatory ST-segment monitoring studies have found that episodes of silent ischemia in older adults are more frequent, longer-lasting, and associated with a worse prognosis than in younger adults.³⁷¹

4.2.2. Limitations of the Exercise Stress Test

Conventional EST (treadmill or bicycle exercise testing) has important limitations in the evaluation of older adults with suspected chronic CAD.³⁷² The main limitations include:

- Reduced functional capacity: many older adults fail to achieve the target heart rate predicted for their age ($\geq 85\%$ of maximum heart rate) due to physical deconditioning, osteoarthritis, peripheral vascular disease, or neurological disorders, resulting in inconclusive test rates of up to 30%–40% in this population;³⁷⁰
- Baseline ECG abnormalities: left ventricular hypertrophy, left bundle branch block, digoxin use, and repolarization abnormalities complicate interpretation of ST-segment changes during exercise;³⁷⁰
- Reduced sensitivity and specificity: because of the factors above, the predictive value of exercise testing in older adults is lower than that observed in younger adults.³⁷⁰

Despite these limitations, EST retains prognostic value when feasible, particularly because of its ability to estimate functional capacity in METs and assess the hemodynamic response to exercise.³⁷⁰

4.2.3. Imaging Methods

Given the limitations of EST, cardiovascular imaging – with or without pharmacologic stress – is the preferred diagnostic strategy for older adults with suspected chronic CAD.³⁶⁷⁻³⁷⁰

Stress echocardiography (with dobutamine or exercise) enables simultaneous assessment of regional and global systolic function, VHD, and filling pressures, with good diagnostic accuracy in older adults, including those with multiple comorbidities.³⁷³ Myocardial perfusion scintigraphy (with dipyridamole or adenosine) is particularly useful in older adults unable to exercise, providing information on the extent and severity of ischemia as well as myocardial viability.³⁷³

CCTA has an expanding role in risk stratification of older adults with an intermediate likelihood of obstructive CAD, allowing noninvasive anatomic assessment with high sensitivity.³⁷⁴ However, the presence of extensive coronary calcification, highly prevalent in older adults, may limit image interpretation and lead to overestimation of the degree of stenosis.³⁷⁴ CACS is an incremental risk stratification tool that is particularly useful in older adults with intermediate risk factors.³⁷⁵

Cardiac MRI (CMR) provides comprehensive assessment of ischemia, myocardial viability, and ventricular function without exposure to ionizing radiation, making it a valuable option in centers with appropriate levels of expertise.³⁷⁶ Its limitations include limited availability, longer examination times, and the presence of incompatible metallic implants.

4.2.4. Cardiac Catheterization: Indications and Risks in Older Adults

Coronary cineangiography (cardiac catheterization) remains the gold standard for anatomic assessment of CAD and

is indicated when noninvasive methods suggest meaningful ischemia, when there is disagreement between clinical findings and functional testing, or when a revascularization strategy is being considered.³⁶⁷⁻³⁶⁹

In older adults, the risks associated with catheterization are greater than in younger adults because of vascular tortuosity and calcification, baseline renal dysfunction (with a higher risk of contrast-induced nephropathy), a higher prevalence of coagulopathies and bleeding, and reduced cardiovascular reserve.^{370,377} The rate of major complications (MI, stroke, or death) during diagnostic catheterization in adults aged 75 years or older is estimated at approximately 0.5%–1.0%, higher than that observed in younger adults.^{370,377}

Fractional flow reserve and the instantaneous wave-free ratio allow physiological assessment of intermediate coronary lesions during catheterization, helping to avoid unnecessary interventions in older adults, whose tolerance for the procedure is often more limited.³⁷⁰⁻³⁷⁷

4.2.5. Polypharmacy, Comorbidities, and Differential Diagnosis

Older adults with chronic CAD rarely present with the disease as an isolated condition. They typically have multiple concomitant comorbidities – hypertension, DM, HF, AF, CKD, COPD, anemia, and musculoskeletal disorders – which complicate the differential diagnosis and increase therapeutic complexity.³⁷⁰

Polypharmacy, defined as the concomitant use of five or more medications, is highly prevalent among older adults with CAD, affecting an estimated 50%–80% of this population.^{370,378} In addition to the risk of drug interactions and adverse effects, polypharmacy may mask or mimic CAD symptoms: bradycardia caused by beta-blockers or digoxin may be mistaken for syncope of another etiology; orthostatic hypotension induced by diuretics or antihypertensive medications may simulate ischemic equivalents; and the use of NSAIDs may precipitate HF decompensation or worsen renal function, altering the clinical condition.^{370,379}

The differential diagnosis of chest pain and dyspnea in older adults should include aortic stenosis (AS), hypertrophic obstructive cardiomyopathy, pulmonary embolism, esophageal spasm, cervical and thoracic spine osteoarthritis, hiatal hernia, and anxiety disorders.³⁷⁰

4.2.6. Frailty and Multidimensional Geriatric Assessment

Frailty syndrome, characterized by diminished physiological reserve and increased vulnerability to stress, affects approximately 30% of older adults with chronic coronary syndrome.^{103,370} Frailty is an independent predictor of mortality, hospitalization, postprocedural complications, and poorer quality of life in this population.¹⁰³

Frailty should be assessed systematically before any invasive therapeutic decision is made. The most commonly used instruments are the Fried Frailty Phenotype (criteria: unintentional weight loss, exhaustion, low physical activity, reduced handgrip strength, and slow gait speed)⁴⁹ and the CFS, which stratifies frailty into nine degrees based on functional

status and dependence.⁶⁴ The frailty index based on deficit accumulation is also widely used in research and can be adapted for clinical practice.³⁸⁰

The CGA extends beyond frailty and incorporates domains that are essential to the management of older adults with CAD, including cognitive function, mood and depression, basic and instrumental functional capacity, social support, nutritional status, risk of falls, and polypharmacy.¹⁸¹ The integration of CGA into cardiovascular decision-making is recommended by major international guidelines^{370,381} and represents a paradigm shift in the care of older adults with heart disease.

4.3. Peculiarities of the Treatment of Chronic Coronary Artery Disease in Older Adults

4.3.1. Pharmacological Treatment

Pharmacological treatment of chronic CAD in older adults follows the same general principles as adult guidelines,³⁶⁷⁻³⁶⁹ but with mandatory adaptations to minimize risks and optimize benefits in this population.

Beta-blockers: indicated for angina control and improvement of functional capacity in older adults with chronic CAD, particularly in those with left ventricular dysfunction or a history of MI.³⁸² The main precautions include bradycardia, orthostatic hypotension, and worsening of sexual function. Dose titration should be performed carefully, starting with low doses and increasing gradually according to tolerance.³⁸²

Statins and lipid-lowering therapy: high-intensity statin therapy is recommended for all older adults with established CAD, regardless of age.³⁶⁷⁻³⁶⁹ Observational studies and post hoc analyses of major clinical trials have found reductions in major cardiovascular events among patients older than 75 years with established CAD.³⁸³ Liver function, signs of myopathy, and interactions with drugs metabolized through CYP3A4, frequent in this age group, should be monitored.³⁸³

The 2025 Brazilian Guideline on Dyslipidemias and Prevention of Atherosclerosis²⁵² reaffirms that the absolute benefit of lipid-lowering therapy is greater in older adults because of the higher incidence of cardiovascular outcomes with advancing age. Lipid targets for older adults in secondary prevention are the same as those for younger patients (Table 4.1), with dose individualization according to frailty, comorbidities, and polypharmacy. Patients with chronic CAD are classified as being at very high risk (LDL-c < 50 mg/dL and ≥ 50% reduction) or extreme risk – defined as two or more major cardiovascular events or one event plus ≥ 2 high-risk conditions – for whom the LDL-c target is < 40 mg/dL.²⁵²

When high-intensity statin monotherapy is not enough to achieve targets – a common situation in older adults because of dose scaling – association with ezetimibe is recommended. If LDL-c levels remain above target or full-dose statins are not tolerated, bempedoic acid may be added; PCSK9 inhibitors are reserved for higher-risk patients in secondary prevention.^{252,340,384} Table 4.2 summarizes the expected reductions in LDL-c with the main therapeutic combinations.

Guidelines

Table 4.1 – Lipid targets by cardiovascular risk category (Brazilian Society of Cardiology, 2025)

Risk category	LDL-c target	LDL-c reduction	Non-HDL target	Apolipoprotein B target
Low	< 115 mg/dL	> 30%	< 145 mg/dL	< 100 mg/dL
Intermediate	< 100 mg/dL	> 30%	< 130 mg/dL	< 90 mg/dL
High	< 70 mg/dL	> 50%	< 100 mg/dL	< 70 mg/dL
Very high	< 50 mg/dL	> 50%	< 80 mg/dL	< 55 mg/dL
Extreme	< 40 mg/dL	> 50%	< 70 mg/dL	< 45 mg/dL

HDL: high density lipoprotein; LDL-c: low density lipoprotein cholesterol. Lipid targets in mg/dL. Extreme risk: ≥ 2 major cardiovascular events or 1 event plus ≥ 2 high-risk conditions.²⁵²

- **Antiplatelet therapy:** low-dose acetylsalicylic acid (75–100 mg/day) is recommended for all older adults with established CAD, unless formally contraindicated.³⁶⁷⁻³⁶⁹ The risk of gastrointestinal bleeding is substantially higher in older adults, so concomitant use of a proton pump inhibitor is recommended.³⁸⁵ DAPT should be considered only for a limited period after PCI, with particular attention to risk of bleeding, which increases with age.³⁶⁷⁻³⁶⁹

Table 4.2 – Expected reductions in low density lipoprotein cholesterol with lipid-lowering therapies (Brazilian Society of Cardiology, 2025)^{252,384}

Lipid-lowering therapy	Reduction in LDL-c
MIS	~30%
HIS	~50%
EZE	~20%
BA	~23%
EZE + BA	~38%
HIS + EZE	~60%
HIS + BA	~58%
HIS + BA + EZE	~68%
PCSK9mAb	~60%
PCSK9mAb + EZE	~70%
HIS + PCSK9mAb	~75%
HIS + EZE + PCSK9mAb	~80%
HIS + EZE + BA + PCSK9mAb	~86%

BA: bempedoic acid; EZE: ezetimibe; HIS: high-intensity statin; LDL-c: low-density lipoprotein cholesterol; MIS: moderate-intensity statin; PCSK9mAb: proprotein convertase subtilisin/kexin type 9 monoclonal antibody. Source: adapted from Rached et al.²⁵² and Blumenthal et al.³⁴⁰

- **ACEIs and ARBs:** indicated in older adults with chronic CAD associated with left ventricular dysfunction (ejection fraction $\leq 40\%$), DM, or uncontrolled hypertension.³⁶⁷⁻³⁶⁹ Renal function and serum potassium levels should be closely monitored because the risks of hyperkalemia and acute kidney injury are higher in older adults.³⁸⁶
- **Long-acting nitrates:** useful for symptomatic control of angina in older adults who do not achieve adequate symptom control with beta-blockers and/or calcium channel blockers (CCBs).³⁶⁷⁻³⁷⁰ Caution is required due to the risks of orthostatic hypotension, syncope, and headache, which may be particularly disabling in this age group.³⁷⁰
- **CCBs:** long-acting dihydropyridine CCBs (amlodipine, felodipine) are alternative or complementary options to beta-blockers for angina control.^{368,369} Nondihydropyridine CCBs (verapamil and diltiazem) should be avoided in older adults with left ventricular dysfunction or atrioventricular block.³⁷⁰
- **Ranolazine:** an additional antianginal option for older adults with refractory angina and has an acceptable safety profile, although data specific to octogenarians remain limited.³⁷⁰
- **Ivabradine:** may be considered in older adults who are in sinus rhythm with a heart rate ≥ 70 beats per minute (bpm) and who do not tolerate beta-blockers, particularly in the presence of left ventricular dysfunction.³⁶⁷⁻³⁷⁰

Recommendation	Strength of recommendation	Certainty of evidence
The use of high-intensity statins with dose scaling, either as monotherapy or in combination with additional lipid-lowering agents, is recommended in older adults at high or very high cardiovascular risk. ³⁸⁴	STRONG	MODERATE

4.3.2. Myocardial Revascularization in Older Adults

The decision to perform myocardial revascularization in older adults with chronic CAD is one of the most complex in contemporary cardiology, requiring consideration of multiple factors: coronary anatomy, ventricular function, comorbidities, frailty, patient preferences, and life expectancy.³⁶⁷⁻³⁷⁰

The ISCHEMIA trial (subanalysis of patients 75 years or older) found that an early invasive strategy did not reduce the incidence of major cardiovascular events compared with optimal clinical management in this age group, and that the symptomatic benefit of intervention was smaller in older adults than in younger patients.³⁸⁷ These findings reinforce the importance of optimal clinical management as the primary treatment strategy for older adults with stable chronic CAD and moderate ischemia.

Regarding PCI, the SENIOR trial showed that drug-eluting stents associated with a short course of DAPT (1 month) were superior to bare-metal stents in patients aged 75 years or older, reducing ischemic events without increasing bleeding risk.³⁸⁸ This finding supports the current recommendation favoring drug-eluting stents with short-duration DAPT in this population.

CABG remains the preferred strategy for older adults with severe multivessel CAD (particularly three-vessel disease or left main coronary artery involvement), complex CAD,³⁸⁹ DM,³⁹⁰ left ventricular dysfunction,³⁹¹ provided they have good functional reserve and are not at high surgical risk.^{367-370,392} However, operative mortality and complication rates from CABG increase progressively with age, reaching 5%–8% in select octogenarians.³⁹³ Preoperative frailty assessment using validated instruments is a key determinant in selecting appropriate surgical candidates.³⁷⁰

4.3.3. Cardiac Rehabilitation

Exercise-based cardiac rehabilitation is an intervention with proven efficacy in patients with established CAD, reducing cardiovascular mortality and hospitalizations while improving functional capacity and quality of life. Among older adults, the benefits of cardiac rehabilitation are proportionally equivalent or superior to those observed in younger adults, with additional gains in fall prevention, preservation of cognitive function, and reduction of frailty syndrome.³⁹⁴

Cardiac rehabilitation programs for older adults should be individualized, taking into account functional, musculoskeletal, and cognitive limitations, with moderate-intensity aerobic exercise, resistance training, and balance exercises.⁷⁹ Supervision by a multidisciplinary team, including a physical therapist, physical educator, nutritionist, and psychologist, is essential to ensure adherence and safety.⁷⁹ Common barriers to participation include transportation, cost, mobility limitations, and inadequate social support; these should be actively identified and addressed.³⁹⁴

4.3.4. Polypharmacy and the Prescribing Cascade

The prescribing cascade, a phenomenon in which an adverse effect from a medication is misinterpreted as a new disease and treated with an additional medication,

is particularly prevalent among older adults with chronic CAD.³⁹⁵ Identification and systematic review of prescriptions are essential components of clinical management.

The most recent version of the AGS Beers Criteria,³⁹⁵ lists medications that are potentially inappropriate for older adults. In chronic CAD, particular attention should be paid to NSAIDs (risk of worsening HF and gastrointestinal bleeding), Class IA and IC antiarrhythmic drugs (proarrhythmic risk), benzodiazepines (risk of falls and cognitive impairment), and tricyclic antidepressants (anticholinergic effects and orthostatic hypotension).³⁹⁵

The STOPP/START tool is also widely used to identify potentially inappropriate prescriptions (STOPP: medications to avoid) and therapeutic omissions (START: medications to initiate) in older adults with CAD.³⁸⁹ Regular medication review, ideally supported by a clinical pharmacist, is a recommended and cost-effective practice.^{334,335}

4.3.5. Individualized Therapeutic Targets

Therapeutic targets in older adults with chronic CAD should be individualized, taking into account life expectancy, degree of frailty, patient preferences, and associated comorbidities.

BP: the SPRINT trial found that more intensive systolic targets (< 120 mm Hg) reduced cardiovascular events in high-risk older adults, albeit at the cost of a higher incidence of hypotension, syncope, and mild acute kidney injury.³⁹⁰ The SPRINT Senior study assessed a cohort of 2,636 hypertensive patients aged 75 years or older and found that the arm with a more intensive SBP target (< 120 mm Hg) reduced the primary composite outcome by 34%.³³⁶ The STEP trial assessed older adults with hypertension in China, comparing an SBP reduction target of 130–150 mm Hg with a target of 110–130 mm Hg. After a median follow-up of 3.3 years, the study was terminated early because the more intensive SBP-lowering strategy proved superior in reducing cardiovascular outcomes.³³⁷ Recent meta-analyses also show that more intensive BP control in older adults with hypertension reduces the frequency of cardiovascular outcomes without increasing the rate of adverse events.^{338,339} Based on these findings, the 2025 Brazilian Guidelines of Hypertension recommend a target of < 130/80 mm Hg for the great majority of older adults with hypertension. For frail older adults, the oldest old, or those with conditions limiting life expectancy, BP should be reduced to the maximum level tolerated.^{339,340}

LDL-c: an LDL-c target of < 55 mg/dL is recommended for older adults with established CAD and high or very high cardiovascular risk by both Brazilian and international guidelines.^{252,341,367-369} Discontinuation of statin therapy in very frail older adults or those receiving PC may be considered following an individualized discussion with the patient and their family members, weighing potential benefits and risks.^{223,341,383}

Glycemia: in older adults with CAD and DM, more conservative glycemic targets (HbA1c 7.5%–8.5%) are preferable to minimize the risk of hypoglycemia, which in older patients may precipitate arrhythmias and ischemic events.³⁴²

Guidelines

Heart rate: a resting heart rate target of 55–60 bpm is reasonable for older adults with chronic CAD and preserved ventricular function, as long as symptomatic bradycardia or conduction blocks are absent.³⁶⁸

4.3.6. Multidisciplinary Approach and Palliative Care

Caring for older adults with advanced chronic CAD extends beyond the traditional model and requires a truly multidisciplinary approach that integrates cardiology, geriatrics, nursing, clinical pharmacy, nutrition, physical therapy, psychology, and social work.¹⁴¹

PC – aimed at relieving suffering, controlling symptoms, and improving quality of life – should be considered early in older adults with advanced chronic CAD, particularly those with severe ventricular dysfunction, refractory angina, or multiple recent hospitalizations.⁷¹ Early integration of PC does not imply withdrawing care but rather a shift in emphasis from prolonging life toward maximizing patient comfort and dignity.³³⁵

Advance care planning, including advance directives and the designation of a legal representative, should be encouraged for all older adults with chronic CAD in a supportive environment, with active participation of the patient and family members.³³⁵

Recommendation	Strength of recommendation	Certainty of evidence
A comprehensive geriatric assessment, including screening for frailty, cognitive function, functional capacity, and polypharmacy, is recommended for all older adults with chronic CAD before defining the therapeutic strategy. ^{372,381}	STRONG	MODERATE
In older adults with chronic CAD and atypical symptoms or anginal equivalents, systematic investigation for myocardial ischemia is recommended, even in the absence of typical angina. ^{367,371}	STRONG	MODERATE
The use of cardiovascular imaging methods (stress echocardiography or myocardial perfusion scintigraphy) as the preferred diagnostic strategy is recommended for older adults unable to achieve an adequate workload during exercise stress testing. ³⁷⁶	STRONG	MODERATE
In older adults with stable chronic CAD and moderate ischemia without limiting symptoms, optimized clinical management as the initial therapeutic strategy is recommended before considering revascularization. ³⁶⁸	STRONG	HIGH
The use of drug-eluting stents with short-duration dual antiplatelet therapy (1 month) is recommended for adults aged 75 years or older undergoing elective percutaneous coronary intervention. ³⁶⁹	STRONG	HIGH
High-intensity statin therapy is recommended for all older adults with established CAD, regardless of age, with an LDL-c target of < 55 mg/dL. ^{367,383}	STRONG	HIGH
Low-dose acetylsalicylic acid (75–100 mg/day) associated with a proton pump inhibitor is recommended for all older adults with established CAD and no formal contraindications. ²⁵²	STRONG	HIGH
Beta-blockers as first-line antianginal therapy are recommended in older adults with chronic CAD, particularly in those with a history of myocardial infarction or left ventricular dysfunction, with gradual dose titration. ³⁸²	STRONG	HIGH
Participation in supervised exercise-based cardiac rehabilitation programs adapted to functional limitations is recommended for older adults with chronic CAD. ^{386,387}	STRONG	MODERATE
Systematic and periodic medication review, with identification and discontinuation of potentially inappropriate medications according to the Beers Criteria or the STOPP/START tool, is recommended in older adults with chronic CAD. ^{388,389}	STRONG	MODERATE
Individualized blood pressure targets are recommended in older adults with chronic CAD (SBP 130–150 mm Hg in frail individuals or those aged 80 years or older), with active monitoring for orthostatic hypotension. ³⁹⁰	STRONG	MODERATE
Less intensive glycemic targets (HbA1c 7.5%–8.5%) are recommended for older adults with chronic CAD and diabetes mellitus at high risk of hypoglycemia. ³⁹²	STRONG	LOW
Preferential use of radial access is recommended in older adults undergoing diagnostic or therapeutic cardiac catheterization to reduce access-site bleeding complications. ⁴⁹	STRONG	MODERATE

Early integration of palliative care is recommended for older adults with advanced chronic CAD, refractory angina, or severe ventricular dysfunction, with a focus on symptom control and quality of life. ³⁹³	STRONG	LOW
Advance care planning, including discussions regarding advance directives, is recommended for all older adults with advanced chronic CAD. ³⁹³	STRONG	VERY LOW
Assessment of frailty using a validated instrument (Fried Frailty Phenotype or Clinical Frailty Scale) is recommended as an additional criterion when selecting older adults for surgical or percutaneous myocardial revascularization. ^{181,373}	STRONG	MODERATE
Shared decision-making involving the older adult, their family members or caregivers, and the health care team is recommended when defining the revascularization strategy, taking into account patient preferences, values, and life expectancy. ^{368,369,393}	STRONG	MODERATE
Avoiding nonsteroidal anti-inflammatory drugs is recommended in older adults with chronic CAD because of the risk of worsening renal function, elevated blood pressure, and heart failure decompensation. ³⁸⁸	STRONG	MODERATE

CAD: coronary artery disease; HbA1c: glycated hemoglobin; LDL-c: low-density lipoprotein cholesterol; SBP: systolic blood pressure.

4.4. General Considerations

4.4.1. Life Expectancy and Personalized Goals

Clinical decision-making in older adults with chronic CAD should incorporate a realistic estimate of individual life expectancy, taking into account not only chronological age but, more importantly, biological age – expressed by the presence or absence of frailty, functional status, and comorbidity burden.³⁷⁰ Robust, functionally independent 80-year-olds may benefit from aggressive interventions similarly to younger adults, while frail 70-year-olds with multiple comorbidities may benefit more from an approach centered on comfort and quality of life.³⁶⁸⁻³⁷⁰

The concept of time to benefit is particularly relevant in this context: some interventions – such as revascularization for asymptomatic multivessel CAD – improves survival only after several years of follow-up, a period that may exceed the life expectancy of frail older adults.³⁷⁰ Therefore, the marginal utility of each intervention should be weighed in light of the patient's own perspective and values.

4.4.2. Shared Decision-Making

Shared decision-making is an ethically and clinically superior approach to medical paternalism in the care of older adults with chronic CAD.³⁷⁰ It involves presenting clear and understandable information regarding risks, benefits, and therapeutic alternatives, followed by an open discussion of the patient's preferences and values.

Decision-support tools, such as informational brochures, educational videos, and risk calculators adapted for laypersons, may facilitate this process and improve decision-making quality, particularly among older adults with low educational attainment or mild cognitive impairment.³⁷⁰ The participation of family members or trusted caregivers, when authorized by the patient, is equally important.

4.4.3. Pre-Procedure Frailty

Systematic assessment of frailty before invasive cardiovascular procedures, including PCI, CABG, and TAVI, has become an

increasing priority in contemporary geriatric cardiology.^{103,370} According to a recent meta-analysis, frail older adults undergoing PCI have an approximately 3.5-fold higher risk of in-hospital mortality and an approximately 2.1-fold higher risk of all-cause mortality than non-frail older adults.³⁷⁷

Pre-procedural identification of frailty allows clinicians to (1) stratify risk more accurately; (2) select more appropriate candidates for intervention; (3) implement prehabilitation strategies that may improve functional status before the procedure; and (4) adjust the expectations of patients and their family members regarding outcomes.³⁷⁰

4.4.4. Deprescribing

Deprescribing is the deliberate and supervised process of reducing or discontinuing medications whose potential harms outweigh their expected benefits in the individual clinical context. It is an active therapeutic strategy rather than simply withholding care. In older adults with chronic CAD, deprescribing may improve quality of life, reduce adverse effects, and simplify complex dosing regimens that compromise adherence. Candidates for deprescribing include statins in patients with very limited life expectancy; acetylsalicylic acid in older adults without established CAD who are at high risk of bleeding; excessive antihypertensives causing orthostatic hypotension; and medications with anticholinergic effects that worsen cognitive decline.³³⁴ The process should be gradual, carefully monitored, and always conducted in partnership with the patient.

4.4.5. Integration with Geriatrics

Formal integration between cardiology and geriatrics, through collaborative care or co-management models, represents the current state of the art in the management of older adults with chronic CAD.^{181,381} Multidisciplinary teams involving geriatrics, clinical pharmacy, specialized nursing, and social work have better outcomes with respect to hospitalization prevention, comorbidity control, and patient satisfaction.^{181,381}

Guidelines

4.4.6. End-of-Life Care

In older adults with advanced chronic CAD – refractory to optimized therapy and associated with severe ventricular dysfunction or multiple hospitalizations within a short period – the transition to end-of-life care should be considered and discussed openly with the patient and their family members.⁷¹ This transition does not imply withdrawing care but rather redirecting it toward relief of suffering, maintenance of comfort, and preservation of dignity.

Symptoms such as dyspnea, refractory angina, anxiety, and depression should be actively treated during this stage, with judicious use of opioids for intractable dyspnea, benzodiazepines for anxiety, and antidepressants when indicated.⁷¹ The involvement of specialized PC teams, ideally at home or in dedicated PC units, improves quality of care during this stage of life.⁷¹

5. Acute Coronary Heart Disease

5.1. Clinical Manifestations

ACS remains one of the leading etiologies of morbidity and mortality worldwide. With progressive population aging, clinical management of ACS in older adults, defined as individuals older than 60 or 65 years, depending on the country's development, has become a major diagnostic and therapeutic challenge in clinical practice. Approximately 30% to 40% of patients hospitalized with ACS are over 75 years of age.^{33,396,97} NSTEMI is the most prevalent subtype among older adults, particularly those older than 75 years, accounting for the majority of ACS cases.³⁹⁶

Unstable angina is also frequent but generally carries a lower mortality risk compared with MI, whereas STEMI, although less frequent than NSTEMI, is associated with a higher risk of death.^{33,398} Type 2 MI (MI secondary to an imbalance between oxygen supply and demand without plaque rupture) is especially prevalent among older adults because of the high incidence of comorbidities such as HF, anemia, and infections. The prognosis of type 2 MI is worse than that of type 1, with higher long-term mortality, mainly due to the severity of the underlying diseases.³³

Among the distinctive characteristics of geriatric patients with ACS is the higher prevalence of comorbidities, including hypertension, DM, history of ACS and AMI, peripheral vascular disease, stroke, HF, and multivessel CAD.³⁹⁹ In addition to traditional comorbidities, geriatric factors (or geriatric syndromes) are important predictors of poor prognosis and should be incorporated into the clinical assessment. These syndromes, which reflect the biological complexity of aging, include frailty,^{400,401} multimorbidity, polypharmacy, and cognitive and functional impairment.³³

ACS in older adults frequently presents in an atypical and less classic manner than in younger patients. Although chest pain remains the most common symptom, data from the National Registry of Myocardial Infarction showed that only 40% of patients older than 85 years hospitalized with ACS reported chest pain, compared with 77% of those younger than 65 years.⁴⁰² Silent or asymptomatic ischemia is more frequent in older patients. Dyspnea is particularly frequent and is considered an anginal equivalent in older adults; studies show that up to 49% of patients aged 85 years or older present with dyspnea as their primary

symptom, even more frequently than chest pain.⁴⁰¹ Syncope and acute mental confusion are also important manifestations, with a prevalence rate of approximately 17% of older adults with ACS.^{33,398–403}

Older women have an even higher frequency of atypical symptoms and cognitive impairment, which may hinder symptom reporting, delay recognition and adequate treatment of ACS, and adversely affect prognosis.⁴⁰⁴

Among the less common manifestations, the most important are (a) unexplained falls; (b) abdominal or epigastric pain; (c) isolated palpitations, dizziness, intense weakness, or nonspecific malaise; (d) nausea and vomiting, which occur as atypical manifestations in approximately 24% of older adults; (e) isolated sweating (diaphoresis); and (f) initial presentation with acute HF or cardiogenic shock.^{401–403}

Risk stratification should always be performed in older adults with ACS, with the GRACE Score remaining the most extensively validated tool for this population, including those older than 80 years.⁴⁰⁵ Studies show that incorporating frailty assessment scales such as the CFS, the EFS, and the Fried Frailty Phenotype improves the accuracy of risk stratification using the GRACE Score. Among these tools, the EFS showed superior discrimination for all-cause mortality and prolonged hospitalization compared with the CFS and the Fried criteria and further improved risk discrimination when added to clinical risk scores.⁴⁰⁶

NSAIDs are associated with an increased risk of acute coronary events in older adults.^{401–407} Medications that increase bleeding risk, such as anticoagulants and antiplatelet agents, may precipitate ACS secondary to acute anemia or hemodynamic instability. The U.S. Food and Drug Administration contraindicates the use of prasugrel in patients aged 75 years or older except in very high-risk situations.⁴⁰⁷ Drug interactions are particularly relevant in older adults because of polypharmacy. For example, the combination of clopidogrel with CCBs may reduce the efficacy of the antiplatelet agent and increase the risk of ischemic events.^{401–407}

Early detection of ACS in older adults requires a heightened level of clinical vigilance, and it should be recognized that absence of pain and mental confusion may conceal ischemia. Risk stratification should extend beyond chronological age and incorporate frailty, comorbidities, functional status, and patient preferences.

Recommendation	Strength of recommendation	Certainty of evidence
It is recommended that ACS be suspected in older adults even in the absence of typical chest pain, particularly when sudden dyspnea, syncope, acute mental confusion, unexplained falls, nausea, vomiting, or acute functional decline is present.	STRONG	HIGH

It is recommended that older adults with ACS undergo assessment of frailty, cognition, functional status, and nutritional status as integral components of prognostic stratification and therapeutic decision-making.	STRONG	HIGH
It is recommended that the GRACE Score be used for initial risk stratification in older adults with ACS, preferably associated with frailty assessment instruments such as the Edmonton Frail Scale, Clinical Frailty Scale, or Fried criteria.	STRONG	MODERATE
It is recommended that cardiovascular and noncardiovascular comorbidities be systematically assessed in older adults with ACS, including heart failure, diabetes mellitus, chronic kidney disease, anemia, cerebrovascular disease, peripheral arterial disease, cognitive impairment, and multimorbidity.	STRONG	MODERATE
It is recommended that acute heart failure, acute pulmonary edema, or cardiogenic shock be recognized as possible initial manifestations of ACS in older adults, even in the absence of classic anginal symptoms.	STRONG	HIGH

ACS: acute coronary syndrome.

Conclusions:

- Atypical presentation of ACS is significantly more frequent in older adults, particularly those aged 75–85 years or older. Observational studies and multicenter registries have found a progressive decline in the prevalence of typical chest pain with advancing age, as well as a higher incidence of anginal equivalents and nonclassical manifestations;

Frailty and functional impairment are independently associated with increased mortality, prolonged hospitalization, cardiovascular complications, and functional loss following ACS. The CGA improves therapeutic individualization;

- The GRACE Score remains validated in older adults, including octogenarians. However, chronological age may overestimate risk, and incorporating frailty improves prognostic accuracy and therapeutic individualization;
- Multimorbidity is associated with worse prognosis, higher mortality, increased complications, and greater therapeutic complexity following acute coronary events;
- Older adults have a higher prevalence of ventricular dysfunction, multivessel disease, and atypical presentations, frequently presenting initially with acute HF.

5.2. Physical Examination

The physical examination of older adults with suspected ACS should be thorough and systematic, focusing on three main objectives:³³

- Risk stratification and identification of potential ACS-related complications;
- Identification of associated diseases or comorbidities;
- Suspicion and exclusion of differential diagnoses.

The initial priority is the rapid monitoring of vital signs, including noninvasive BP measurement in both upper extremities, pulse oximetry, cardioscopy associated with a 12-lead ECG, respiratory rate, and body temperature. Classic signs of congestive HF should be actively investigated, as they are associated with higher morbidity and mortality,^{33,408} including jugular venous distention, a third heart sound (gallop rhythm), pulmonary crackles, acute pulmonary edema, and lower-extremity edema.

Particular attention should be paid to cardiac auscultation for murmurs, as their presence may indicate ACS-related complications, associated diseases, or alternative diagnoses.^{33,326,409} A regurgitative systolic murmur heard at the mitral area or along the mid-to-lower left sternal border may indicate mitral regurgitation (MR) due to papillary muscle dysfunction or rupture and leads to a differential diagnosis with post-AMI mechanical complication of ventricular communicating shunt. A crescendo-decrescendo (“diamond-shaped”) systolic murmur heard at the aortic and accessory aortic areas, radiating to the sternal notch and carotid arteries, is consistent with aortic valve stenosis, a condition with high prevalence rates among older adults.

Guidelines

Hypotension is particularly concerning and may indicate cardiogenic shock or other high-risk conditions,³³ requiring concomitant assessment of additional signs of impaired organ perfusion, such as capillary refill time greater than 3 seconds, cold extremities, livedo reticularis, reduced urine output, and acute alteration in the level of consciousness. A complementary multimodal diagnostic assessment, including point-of-care ultrasound, should be used to differentiate among the four types of shock: cardiogenic, hypovolemic, distributive, and obstructive.^{33,326,409}

The physical examination is also essential to identify associated diseases or comorbidities, such as frailty, sarcopenia, COPD, dementia syndromes, sequelae of previous ischemic neurological events, hearing or visual impairment, and clinical signs secondary to nephropathy and liver disease.^{33,408} The suspicion and exclusion of differential diagnoses are an integral part of this process, prioritizing the investigation of conditions such as pulmonary embolism, aortic dissection, cardiac tamponade, and sepsis.

Recommendation	Strength of recommendation	Certainty of evidence
Monitoring (blood pressure, heart rate, respiratory rate, peripheral oxygen saturation, temperature, electrocardiogram).	STRONG	HIGH
Assessment of signs of heart failure (third heart sound, jugular venous distention, crackles).	STRONG	MODERATE
Auscultation for murmurs for associated conditions or mechanical complications.	STRONG	MODERATE
Assessment of organ perfusion and shock (capillary refill time, livedo, and urine output).	STRONG	MODERATE
Use of point-of-care ultrasound to distinguish chest pain and especially circulatory shock.	STRONG	HIGH

5.3. Diagnostic Approach in Emergency Care

ACS in older adults has important peculiarities due to atypical clinical presentation, physiological characteristics, multimorbidity, and frailty.^{33,410} The mortality rate of AMI in patients older than 75 years reaches one-third of cases,⁴¹⁰ approximately twice that observed in younger patients.⁴¹¹

Upon arrival at the emergency department, a 12-lead ECG should be the first diagnostic procedure performed, within 10 minutes of admission. In patients with NSTEMI, the ECG may be normal or nondiagnostic in up to 6% of cases, requiring early repetition in symptomatic patients and repetition within 6 hours in asymptomatic patients.^{396,412} In the GUSTO II study, left bundle branch block, left ventricular hypertrophy, and pacemaker rhythm were associated with a worse prognosis.⁴¹³ Interpretation should consider coronary occlusion equivalents (de Winter pattern, Wellens syndrome, and the Smith-modified Sgarbossa criteria).^{411,414}

5.3.1. Biomarkers

Troponins are the primary biomarkers for the diagnosis of MI. However, other cardiac and systemic conditions may alter troponin levels, including shock, sepsis, pulmonary embolism, stroke, takotsubo syndrome, and VHD.^{415,416} High-sensitivity cardiac troponin T has reduced sensitivity in older adults, particularly those over 70 years of age.⁴¹⁷

5.3.2. Noninvasive Examinations

These are used for diagnosis and risk stratification when the clinical condition suggests an ischemic syndrome despite a normal ECG and biomarkers. The indication for each test depends on the objectives of patient management.

EST may be useful in older adults at low or intermediate risk who are clinically and hemodynamically stable 9 to 12 hours after symptom onset, with no ECG abnormalities and negative biomarkers.⁴¹⁸ In older adults, functional limitations, an attenuated chronotropic response, and nonspecific baseline ECG abnormalities may compromise accuracy.⁴¹⁹

Echocardiography provides essential data on global ventricular function and segmental abnormalities and contributes to the differential diagnosis (aortic dissection, critical AS, and takotsubo syndrome).^{396,420}

Myocardial perfusion scintigraphy has an established role in low- to intermediate-risk patients, with a high negative predictive value (up to 98%) when results are normal.⁴²¹⁻⁴²³

CCTA assists in anatomical investigation, but extensive coronary calcification and arrhythmia may limit interpretation in older adults.⁴²⁴⁻⁴²⁶

Nuclear MRI assists in structural diagnosis and differentiation of other pathologies such as myocarditis, takotsubo syndrome, and AMI with nonobstructive coronary arteries.^{33,415,427}

Coronary angiography is the anatomical gold standard for confirming coronary obstruction, which influences clinical decision-making regarding revascularization, whether by angioplasty or surgery.³⁶⁸

Therapeutic decision-making should consider the high prevalence of CAD in this age group, as it tends to favor an invasive approach. However, older adults remain underrepresented in clinical trials, and the data to guide optimal management are lacking. Frailty, polypharmacy, and multimorbidity should also be taken into account.^{367,368} In the After Eighty study, patients older than 80 years randomized to an early invasive strategy

experienced a 24% reduction in major outcomes (AMI, urgent revascularization, or death).⁴²⁸

A systematic review and meta-analysis of patients older than 70 years with NSTEMI found that the invasive strategy reduced subsequent revascularization events by 59% and AMI by 25%. The incidence of stroke and HF was similar between the groups.⁴²⁹

Regarding vascular access, to reduce bleeding complications, the radial approach is preferred over the femoral approach.³⁶⁸

Recommendation	Strength of recommendation	Certainty of evidence
Electrocardiogram in the initial management of acute coronary syndrome.	STRONG	HIGH
Biomarkers, especially high-sensitivity troponin.	STRONG	HIGH
Exercise stress testing.	STRONG	MODERATE
Echocardiogram at rest.	STRONG	HIGH
Myocardial perfusion scintigraphy.	STRONG	HIGH
Coronary computed tomography angiography.	STRONG	HIGH
Nuclear magnetic resonance imaging.	STRONG	HIGH
Invasive coronary angiography.	STRONG	HIGH

5.4. Optimal Clinical Management

5.4.1. Antithrombotic Therapy in Older Adults

5.4.1.1. Antiplatelet Therapy

DAPT remains a cornerstone of the pharmacological treatment of ACS.

- *Aspirin*: should be initiated with a 300-mg loading dose (non-enteric-coated), followed by a maintenance dose of 81 to 100 mg/day.
- *Clopidogrel*: generally the P2Y₁₂ inhibitor of choice in older adults due to its more favorable safety profile. In the POPular AGE study, which randomized patients aged 70 years or older with NSTEMI, clopidogrel showed efficacy similar to that of ticagrelor or prasugrel, but with a significantly lower incidence of bleeding. When fibrinolytic therapy is administered to patients older than 75 years, the dose should be 75 mg without a higher loading dose.

- *Ticagrelor*: may be considered in select situations (STEMI or complex anatomy). The recommended regimen is an 180-mg loading dose followed by 90 mg twice daily.
- *Prasugrel*: carries a warning regarding the use of the full dose (10 mg/day) in patients older than 75 years. The Elderly ACS 2 study did not find superior results for prasugrel over clopidogrel in this age group. When indicated, a reduced dose of 5 mg may be considered in select patients.
- *Duration of DAPT*: traditionally, DAPT is recommended for at least 12 months after ACS. However, recent evidence suggests that shorter regimens may be appropriate in patients at high bleeding risk.

A 2024 meta-analysis showed that 3 months of DAPT after PCI in older adults does not compromise cardiovascular safety and significantly reduces the risk of bleeding.

5.4.1.2. Parenteral Anticoagulation

Therapeutic anticoagulation is recommended during the initial hospital stage of ACS, regardless of the reperfusion strategy adopted.

- *Unfractionated heparin*: useful in patients with major renal failure. An initial bolus of 60 IU/kg (maximum 4,000 IU) is recommended, followed by an infusion of 12 IU/kg/hour (maximum 1,000 IU/hour), adjusted to maintain the activated partial thromboplastin time between 60 and 80 seconds.
- *Enoxaparin*: requires dose adjustment in older adults or patients with renal dysfunction; when creatinine clearance is 15 to 30 mL/min, the dose should be 1 mg/kg/day. When used in conjunction with fibrinolysis in patients aged 75 years or older, the initial intravenous bolus should not be administered, and the subcutaneous dose should be reduced to 0.75 mg/kg every 12 hours.
- *Fondaparinux*: recommended dose is 2.5 mg subcutaneously once daily; contraindicated when creatinine clearance is < 30 mL/min.

5.4.1.3. Management of Patients with Concomitant Atrial Fibrillation

In older adults with chronic AF undergoing PCI, dual therapy (a direct oral anticoagulant [DOAC] associated with clopidogrel, without aspirin) has been shown to be superior to triple therapy in terms of safety. Triple therapy should be used only during the first few days, usually for up to 5 days or until hospital discharge. Apixaban is often preferred in older adults because of its favorable safety profile.

5.4.2. Fibrinolytic Therapy in Older Adults

Primary PCI is the preferred strategy in older adults with STEMI. When timely PCI is unavailable, fibrinolysis is an alternative. The STREAM and STREAM-2 studies found that half-dose fibrinolytic therapy in patients older than 75 years reduces bleeding complications while maintaining efficacy similar to that of primary PCI when administered early (within 3 hours of symptom onset).

Guidelines

Fibrinolytic agents: when PCI cannot be performed within approximately 120 minutes, full-dose alteplase or tenecteplase is recommended for patients younger than 75 years, and half-dose therapy for those aged 75 years or older, provided there are no contraindications.

Clopidogrel is the P2Y12 inhibitor indicated for patients undergoing fibrinolysis. In patients older than 75 years, an initial dose of 75 mg is recommended, followed by 75 mg daily.

5.4.3. Other Adjuvant Treatments

- **Beta-blockers:** initiate at low doses with gradual titration.
- **ACEIs and ARBs:** recommended in high-risk patients (left ventricular ejection fraction [LVEF] $\leq$ 40%, DM, hypertension, or history of AMI).
- **Aldosterone antagonists:** recommended in patients with LVEF $\leq$ 40% associated with HF or DM symptoms; MRAs reduce mortality and major cardiovascular events.
- **High-intensity statins:** should be initiated in all patients.
- **Nitrates:** sublingual nitrates are indicated for relief of ischemic pain and may be followed by intravenous administration in cases of persistent symptoms.
- **CCBs:** nondihydropyridine CCBs may be used in patients with recurrent ischemia who have contraindications to beta-blockers, provided there is no left ventricular dysfunction, risk of cardiogenic shock, or advanced atrioventricular block in the absence of a pacemaker.
- **Oxygen therapy:** supplemental oxygen is indicated in patients with oxygen saturation $<$ 90%, with the goal of improving myocardial oxygen delivery.
- **Analgesia:** intravenous morphine sulfate may be used in cases of persistent chest pain despite optimized anti-ischemic therapy. NSAIDs should be avoided during hospitalization for ACS due to the increased risk of adverse cardiovascular events.⁴¹⁵
- **Gastroprotection:** proton pump inhibitors are recommended in patients with a history of gastrointestinal bleeding or at high risk (older adults or those receiving anticoagulants).

5.4.4. Percutaneous Coronary Intervention

In ACS, sarcopenia, frailty, and geriatric syndromes have a negative impact on outcomes in patients undergoing PCI.^{397,430} In the management of older adults with ACS, treatment decisions should be individualized, taking into account individual characteristics in addition to cardiovascular factors, such as existing geriatric syndromes, frailty, sarcopenia, comorbidities, thrombotic and bleeding risks, cognitive status, quality of life, and the preferences of the patient and their family members.^{139,400,431,432}

In STEMI, although patients older than 75 years were excluded from several clinical trials, recommendations

for younger patients should be followed: culprit artery revascularization during the index procedure and complete revascularization within 45 days should be considered.^{415,433} In cases of cardiogenic shock, culprit-vessel revascularization with PCI should be the first option.⁴¹⁵

In NSTEMI, there is ongoing debate regarding invasive versus conservative management.^{33,415,433,434} The After Eighty study (patients 80 years or older) showed that the invasive strategy had a lower rate of the primary outcome (death or MI).⁴³⁵⁻⁴³⁸ Kunadian et al. (SENIOR-RITA), in patients aged 75 years or older, observed no statistically significant difference in cardiovascular death or nonfatal MI over 4.1 years of follow-up.⁴³⁹ However, a meta-analysis found that the invasive strategy was associated with a lower likelihood of recurrent MI.⁴⁴⁰ The FIRE study found a reduction in adverse outcomes in the complete revascularization group (15.7% vs. 21%; $p = 0.001$). It is recommended that treatment decisions be individualized; the invasive strategy reduces the likelihood of recurrent ischemia and the need for repeat revascularization.⁴⁴¹

Recommendation	Strength of recommendation	Certainty of evidence
In patients with NSTEMI and a high GRACE or TIMI score, an early invasive strategy is recommended.	STRONG	MODERATE
In older adults with STEMI within the reperfusion window, primary PCI is recommended.	STRONG	HIGH
In older adults with ACS presenting with cardiogenic shock, refractory angina, or electrical instability, an immediate invasive strategy is recommended.	STRONG	MODERATE
Consideration of geriatric syndromes and patient and family preferences is recommended when making treatment decisions for older adults with ACS.	STRONG	LOW

In the context described above, an early invasive strategy reduced recurrent ischemia and the need for myocardial revascularization in older adults.

A compilation of studies and meta-analyses has found a reduction in the composite outcome of death, recurrent MI, and disabling stroke.

Although an early invasive strategy has been found to reduce clinical events, in some older adults the intervention may be futile or associated with an increased risk of adverse outcomes.

Although geriatric syndromes are known to be important, they are not formally incorporated into risk assessment models.

5.4.5. Coronary Artery Bypass Graft

In CABG, morbidity and mortality among older patients have declined over the past two decades. However, geriatric-domain factors are not adequately incorporated into risk prediction scores.^{442,443} Some authors believe that geriatric factors should be incorporated into surgical risk assessment.⁴⁴⁴ A study involving 2,137,618 patients undergoing CABG found that frailty increased the risk of postoperative complications, mortality, and health care costs.⁴⁴⁵

In a subgroup analysis of the EXCEL study (patients aged ≥ 75 years), mortality was higher in the PCI group than in the CABG group (16.6% vs. 8.4% [OR 1.96; 95%CI 1.00–3.83]).^{446–448} Comparing CABG versus PCI showed that the incidence of all-cause mortality, AMI, stroke, or repeat revascularization was lower in the CABG group (26% vs. 34%; hazard ratio [HR] 0.75; 95%CI 0.60–0.94; $p = 0.01$).⁴⁴⁶

The impact of anatomic complexity showed that when the SYNTAX score was ≤ 22 , PCI was associated with lower mortality, whereas when the SYNTAX score was ≥ 33 , CABG was associated with lower mortality. The incidence of early stroke was higher in the CABG group.⁴⁴⁶ A meta-analysis with 10 years of follow-up found no difference in memory outcomes between the groups.⁴⁴⁹

In the GOPCABE trial, involving patients older than 75 years, there was no difference in the incidence of stroke or the need for dialysis between on-pump and off-pump CABG. Five-year mortality was similar between the groups (31% vs. 30%).⁴⁵⁰

Recommendation	Strength of recommendation	Certainty of evidence
In older adults with an indication for CABG, assessment of anatomic complexity and expected surgical risk is recommended.	STRONG	MODERATE
Integration of a systematic assessment of geriatric factors into CABG risk scores is recommended.	STRONG	LOW

6. Heart Failure

Unlike HF in younger adults, which typically presents with classic symptoms such as severe dyspnea and orthopnea, is frequently associated with an ischemic etiology, and predominantly involves reduced ejection fraction, HF in older adults often presents atypically and insidiously. Unexplained fatigue, mental confusion, recurrent falls, subtle functional decline, and cardiac cachexia take the place of more obvious signs, masked by comorbidities such as CKD, AF, and anemia. The frequent presentation of HFpEF results in early underdiagnosis, compounded by inflammaging (chronic low-grade inflammation inherent to aging), which accelerates cardiac remodeling and syndromic frailty.

The impact on quality of life is profound: a large share of older adults with HF lose autonomy in basic activities of daily living, facing social isolation, family dependence, and depression, with high rates of annual hospitalizations and readmissions. The prognosis worsens dramatically, driven by frailty, which doubles hospitalizations, triples the incidence of delirium, and limits quadruple therapy because of intolerance (hypotension and worsening renal function). The inflammatory interaction between HF and frailty creates a vicious cycle: proinflammatory cytokines (interleukin 6, tumor necrosis factor alpha) exacerbate sarcopenia and endothelial dysfunction, reducing survival.

This reality requires a holistic approach, including integrated geriatric assessment, age-adjusted biomarkers, community-based health education, and individualized therapy, to restore function and autonomy.

6.1. Peculiarities of the Diagnosis of Heart Failure in Older Adults

HF represents one of the greatest diagnostic challenges in geriatric clinical practice. The prevalence of HF increases progressively with age, affecting more than 10% of individuals aged 70 years or older, with a 2- to 3-fold increase after 65 years of age.⁴⁵¹ Population aging, together with the accumulation of comorbidities and improved control of predisposing CVDs, contributes to the growing prevalence of the condition.

Diagnosis in older adults is complicated by frequent atypical clinical presentations, the high burden of comorbidities, and the greater prevalence of HFpEF. The diagnostic pillars are the same as those used in younger adults – suggestive signs and symptoms, objective evidence of structural or functional cardiac abnormalities, and, ideally, demonstration of elevated filling pressures^{452,453} – but interpretation of clinical findings and complementary examinations requires adaptations specific to this age group.

6.1.1. Diagnostic Challenges Specific to Older Patients

In older adults, symptoms such as fatigue, exercise intolerance, edema, and dyspnea are often attributed to aging, sedentary lifestyle, or noncardiac diseases, resulting in underdiagnosis.^{451,454} Comorbidities such as COPD, obesity, venous insufficiency, AF, CKD, anemia, pulmonary

hypertension, and infiltrative cardiomyopathies may mimic, mask, or confound the clinical condition.^{451,455}

Two aspects deserve particular attention: (1) dyspnea may be absent in older adults with limited mobility because functional limitations prevent patients from reaching the level of exertion required to trigger it; and (2) natriuretic peptide levels tend to be higher in this age group even in the absence of HF because of the higher prevalence of AF, CKD, reduced lean body mass, and aging itself, reducing the specificity of these biomarkers.³⁷⁶ As a result, the so-called “gray zone” – intermediate values that are difficult to interpret – is more frequent in older adults. In these cases, interpretation should always be integrated with the clinical condition and echocardiogram.

6.1.2. Clinical Presentation and Physical Examination

6.1.2.1. Symptoms

The most useful symptoms remain orthopnea and paroxysmal nocturnal dyspnea.⁴⁵¹ Other symptoms include exertional dyspnea, fatigue, lower limb edema, and bendopnea (dyspnea when bending forward). In older adults, atypical presentations should be systematically recognized.^{456,457}

- Unexplained progressive functional decline;
- Mental confusion or delirium (cerebral hypoperfusion);
- Anorexia and weight loss (splanchnic congestion, cardiac cachexia);
- Recurrent falls (orthostatic hypotension, muscle weakness);
- Isolated chronic cough and nocturia.

6.1.2.2. Physical Examination

The main findings on physical examination are jugular venous distention, hepatojugular reflux, third heart sound, pulmonary crackles, peripheral edema, ascites, and displacement of the apex beat.⁴⁵¹ In older adults, interpretation requires caution: (a) the positive predictive value of the third heart sound is reduced; (b) lower limb edema is often multifactorial; (c) pulmonary crackles may be absent even with significant pulmonary congestion; and (d) elevated jugular venous pressure and a positive hepatojugular reflux are the most specific findings.⁴⁵⁵

6.1.3. Natriuretic Peptides

BNP and NT-proBNP are the most diagnostically relevant biomarkers in HF, particularly due to their high negative predictive value.

6.1.4. Transthoracic Echocardiography

TTE is the key examination for diagnostic confirmation and classification of the HF phenotype.^{140,456,457} In older adults, echocardiography is particularly important because HFpEF is more prevalent, making echocardiographic parameters of diastolic

function – particularly the E/e' ratio (a value ≥ 15 suggests elevated filling pressures), indexed left atrial volume, and tricuspid annular velocity – fundamental to the diagnosis.^{140,458} GLS and left atrial strain analysis can detect subclinical dysfunction even with preserved LVEF and help differentiate the pseudonormal pattern of diastolic dysfunction often found in older adults.¹⁴⁰

6.1.5. Diagnosis of Heart Failure with Reduced Ejection Fraction in Older Adults

The diagnosis of HFrEF follows a structured approach: clinical suspicion, initial assessment with biomarkers, echocardiographic confirmation of LVEF $< 50\%$, followed by etiological investigation.^{140,457,459} Approximately half of all cases are ischemic in etiology, justifying investigation for CAD in most patients with a recent diagnosis, save those with multiple severe comorbidities or who are not candidates for revascularization.

6.1.6. Diagnosis of Heart Failure with Preserved Ejection Fraction in Older Adults

HFpEF is the predominant form of HF in older adults, especially women older than 75 years with hypertension and AF.^{140,454} Diagnosis requires integration of signs and symptoms, natriuretic peptide levels, structural and functional echocardiographic findings, and, when uncertainty persists, additional testing.^{140,460-462}

The H2FPEF score integrates six variables and ranges from 0 to 9 points.⁴⁶³⁻⁴⁶⁵ A score ≥ 6 indicates probable HFpEF; 2–5 indicates intermediate probability, requiring stress echocardiography or right heart catheterization with hemodynamic assessment at rest or during exercise; and 0–1 indicates HFpEF is unlikely.^{140,376}

The ESC HFA-PEFF algorithm provides a structured three-step diagnostic approach (P: Pre-test assessment; E: Echocardiography and biomarkers; FF: Functional/hemodynamic assessment), applicable in cases of greater diagnostic complexity.⁴⁶⁶

Causes that are particularly relevant in older adults include transthyretin cardiac amyloidosis (ATTR-CA), prevalent in individuals older than 75 years and frequently underdiagnosed; hypertensive cardiomyopathy; degenerative VHD; and AF associated with atrial cardiomyopathy.¹⁴⁰ When infiltrative disease is suspected, CMR and technetium-99m pyrophosphate scintigraphy (for ATTR-CA) are highly relevant complementary diagnostic tools.^{140,457}

6.1.7. Initial Complementary Examinations

The initial assessment should systematically include a 12-lead ECG, chest radiography, natriuretic peptide measurement (BNP or NT-proBNP), and complete laboratory tests.^{140,456} The ECG is rarely normal in established HF, and a normal ECG has a high negative predictive value. Chest radiography has a sensitivity of 81% for acute HF, but up to 20% of cases show no radiographic signs of congestion.⁴⁵⁸

Table 6.1 presents the recommended complementary tests, their indications, and particularities in older patients, graded according to the GRADE system.

Table 6.1 – Recommended complementary tests, their indications, and particularities in older adults

Test	Main indication	Particularities in older adults	Strength of recommendation	Certainty of evidence
12-Lead electrocardiogram	Initial screening; identification of arrhythmias, overload, and blocks	AF present in 30%–50%; LBBB supports indication for CRT; high NPV when normal	STRONG	HIGH
BNP or NT-proBNP	Confirmation/exclusion of HF; prognostic stratification	Mandatory age-adjusted cutoff values (75 years: 1,800 pg/mL); AUC-ROC decreases with aging	STRONG	HIGH
Transthoracic echocardiogram	Diagnostic confirmation; classification by ejection fraction; diastolic function	Pseudonormal pattern is frequent; GLS and left strain aid in HFrEF diagnosis; $E/e' \geq 15$ suggests elevated filling pressures	STRONG	HIGH
Complete blood count	Anemia as an aggravating and precipitating factor	Present in 30% of older adults with HF; independent impact on functional status and prognosis	STRONG	HIGH
Creatinine, urea, eGFR	Assessment of cardiorenal syndrome; therapeutic adjustment	Acute decline in eGFR is common after initiation of ACEIs/ARBs – do not discontinue before assessment	STRONG	HIGH
Electrolytes (Na^+ , K^+ , Mg^{2+})	Disorders associated with diuretics and RAAS inhibitors; arrhythmic risk	Hypokalemia and hypomagnesemia potentiate digoxin toxicity in older adults	STRONG	HIGH
Ferritin + transferrin saturation	Iron deficiency – independent therapeutic target in HF	Iron deficiency occurs in up to 50% of older adults with HF; treatment improves functional capacity and quality of life	STRONG	HIGH
Blood glucose and HbA1c	Type 2 diabetes as a prevalent comorbidity and risk factor	Comorbid in 40% of older adults with HF; integrated management with SGLT2i	STRONG	HIGH
Cardiac magnetic resonance imaging	Select cases: suspected amyloidosis, myocarditis, infiltrative cardiomyopathy	Important for the diagnosis of TTR amyloidosis, prevalent in adults over 75 years of age	CONDITIONAL	LOW

ACEI: angiotensin-converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; AUC-ROC: area under the receiver operating characteristic curve; BNP: B-type natriuretic peptide; CRT: cardiac resynchronization therapy; eGFR: estimated glomerular filtration rate; GLS: global longitudinal strain; HbA1c: glycated hemoglobin; HF: heart failure; HFrEF: heart failure with preserved ejection fraction; LBBB: left bundle branch block; NPV: negative predictive value; NT-proBNP: N-terminal pro-B-type natriuretic peptide; RAAS: renin–angiotensin–aldosterone system; SGLT2i: sodium–glucose cotransporter 2 inhibitor; TTR: transthyretin. Source: Prepared by the authors based on references.^{140,376,451,456,457,460,463,465}

Guidelines

6.1.8. Differential Diagnosis

Given the nonspecific spectrum of symptoms, the differential diagnosis of HF in older adults is broad. The primary conditions to exclude include:

- Causes of dyspnea: COPD (coexisting in up to 30% of cases), pulmonary embolism, severe anemia, primary pulmonary hypertension, pleural effusion of other etiologies;
- Causes of edema: chronic venous insufficiency, nephrotic syndrome, lymphedema, CCB-induced edema, deep vein thrombosis;
- Causes of functional decline: hypothyroidism, anemia, major depression, sarcopenia, frailty syndrome, occult malignancy.

The coexistence of COPD and HF is particularly common in older adults; both conditions may exacerbate one another and share similar symptoms. An elevated BNP/NT-proBNP level associated with echocardiographic abnormalities is the primary distinguishing feature. Spirometry is recommended if the diagnosis is uncertain.^{451,456}

6.1.9. Particularities of the Older Adult in the Diagnostic Process

The distinction in diagnosing HF in older adults lies less in different formal criteria than in adaptations to their interpretation.^{451,456} It is essential to consider: (a) frailty, present in up to 45% of older adults hospitalized for HF, which interferes with clinical presentation, prognosis, and tolerance to therapy; (b) cognitive impairment, which may compromise history taking and treatment adherence; (c) polypharmacy, which increases the risk of drug interactions and adverse effects; and (d) multimorbidity, which broadens the differential diagnosis and reduces the specificity of biomarkers.^{452,453,463}

A multidisciplinary approach integrating cardiology, geriatrics, and a specialized multidisciplinary team has been shown to reduce readmissions and improve functional outcomes in older adults with HF.^{451,454} The CGA, including frailty screening (eg, Fried Frailty Phenotype or CFS) and cognitive, functional, and nutritional assessments, should be incorporated into the diagnostic process and therapeutic planning.

Recommendations for diagnosis of HF in older adults	Strength of recommendation	Certainty of evidence
For older adults with suspected HF, measurement of BNP or NT-proBNP using age-adjusted cutoff values to support the diagnosis or exclusion of HF (for exclusion of acute HF: NT-proBNP; for patients ≥ 75 years: NT-proBNP 1,800 pg/mL) is recommended. The estimated effect of the strategy is present according to the literature identified in this recommendation. ^{376,460}	STRONG	HIGH
For older adults with suspected HF and elevated natriuretic peptides, transthoracic echocardiography for diagnostic confirmation, assessment of ejection fraction, and phenotypic classification (HFrEF or HFpEF) is recommended. The estimated effect of the strategy is present. ^{140,456}	STRONG	HIGH
For older adults with preserved ejection fraction ($\geq 50\%$) and clinical suspicion of HFpEF, application of the H2FPEF score or the HFA-PEFF algorithm to support the diagnosis is recommended. In intermediate cases (H2FPEF score 2–5), stress echocardiography or invasive hemodynamic assessment is recommended. The estimated effect is probably present. ^{140,465}	STRONG	MODERATE
For older adults with suspected or confirmed HF, a comprehensive initial laboratory evaluation, including complete blood count, renal function, electrolytes, TSH, iron studies, and HbA1c, to identify precipitating factors, treatable comorbidities, and guide therapeutic adjustment is recommended. The estimated effect is present. ^{140,460}	STRONG	HIGH
For older adults with HF, comprehensive geriatric assessment, including screening for frailty, cognition, functional status, and polypharmacy, as an integral component of the cardiologic evaluation, using a multidisciplinary approach, is suggested. The estimated effect may be present according to the literature. ^{451,452,463}	CONDITIONAL	LOW
For older adults with suspected HFrEF (EF $< 50\%$), targeted etiological investigation, including assessment for coronary artery disease, valvular heart disease, transthyretin cardiac amyloidosis, and cardiomyopathies, is recommended; strong recommendation based on moderate-certainty evidence. The estimated effect is probably present. ^{140,457}	STRONG	MODERATE

BNP: B-type natriuretic peptide; EF: ejection fraction; HbA1c: glycated hemoglobin; HF: heart failure; HFimpEF: heart failure with improved ejection fraction; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; NT-proBNP: N-terminal pro-B-type natriuretic peptide; TSH: thyroid-stimulating hormone.

6.2. Peculiarities of the Treatment of Heart Failure in Older Adults

Physiological changes associated with aging pose specific challenges to the treatment of HF in older adults, particularly because of the high prevalence of multimorbidity and the functional and social particularities of this population.⁴⁵²

Older adults frequently present with lower BP levels, sarcopenia, frailty, and more severe HF at the time of diagnosis, as well as cognitive impairment and polypharmacy. In addition, limitations in social support and functional capacity may compromise treatment adherence and self-care. These factors increase the risk of medication intolerance, contraindications, and frequency of adverse events, thereby expanding the therapeutic challenge.^{467,468}

It should be emphasized that the major clinical trials in HF predominantly enrolled younger, male patients with reduced ejection fraction. In clinical practice, on the other hand, a greater proportion of older women with HFpEF is observed.

Accordingly, an approach integrating cardiovascular assessment, CGA, evidence-based therapy, and patient-centered multidisciplinary care is recommended.

6.2.1. Definition and Approach to Etiology

Identification of the etiology of HF is a fundamental step in management, since many causes are potentially treatable or modifiable. In older adults, establishing the etiology may be more challenging, often because of delayed presentation, less pronounced symptoms, and the coexistence of multiple etiologic factors.

In this population, the following conditions stand out: degenerative VHD, hypertensive cardiomyopathy, drug-induced cardiotoxicity, and infiltrative diseases, particularly cardiac amyloidosis, whose prevalence increases with aging.

6.2.2. General Principles of Pharmacological Treatment in Older Adults

What sets treatment in older adults apart is not the indication for therapies, but rather their initiation, the level of monitoring, and dose adjustments. It is important to consider several age-related pharmacokinetic changes, reduced muscle mass and GFR, increased baroreceptor sensitivity, lower homeostatic reserve, and polypharmacy itself.

- Pharmacological management in older adults with HF generally follows a few fundamental principles:
- Initiate therapy at lower doses than those used to assess the initial response and tolerability;
- Titrate slowly, every 1–2 weeks, according to symptoms, vital signs, renal function, electrolytes, and the patient's ability to adhere to follow-up;
- Nevertheless, pursue target doses with close monitoring;
- Periodically review polypharmacy and deprescribe medications that precipitate decompensation, conflict with priority therapies, or provide no clear benefit in light of clinical studies;
- Incorporate geriatric assessment, including frailty, cognition, functional status, social support, and goals of care, into therapeutic decision-making.

Deprescribing, including medication discontinuation or dose reduction to correct or prevent complications, is an active component of management in older adults. Medications that often precipitate decompensation and should be reviewed include NSAIDs, thiazolidinediones, nondihydropyridine CCBs (verapamil, diltiazem), dronedarone, and class I antiarrhythmic medications.

6.2.3. Correction of Precipitating Factors

HF decompensation is frequently associated with potentially preventable precipitating factors, such as infections, arrhythmias, excessive sodium and/or fluid intake, deterioration of renal function, use of deleterious medications (particularly NSAIDs), and nonadherence to pharmacological treatment. These factors are present in approximately 20% to 50% of patients with HFrEF.⁴⁶⁹

In older adults, poor treatment adherence is generally multifactorial, involving complex therapy regimens, greater susceptibility to adverse effects, cognitive impairment, and socioeconomic limitations. Polypharmacy, which is highly prevalent in this population, requires periodic medication reviews, with careful assessment of the risk-benefit balance and individualized, safe consideration of deprescribing when appropriate.⁴⁶⁸

Cognitive impairment stands out as a precipitating factor, as it may be present in up to 40% of patients with HF. It is associated with poorer quality of life, a higher number of hospitalizations, and increased mortality.⁴⁷⁰ Routine cognitive screening, as well as implementation of multidisciplinary care strategies, is therefore recommended.

Pharmacological treatment should not be determined by age alone, but rather by ejection fraction, clinical profile, and individual tolerability. Optimized pharmacological therapy for patients with HFrEF is also associated with improved clinical outcomes in the geriatric population, regardless of the degree of frailty, reinforcing the recommendation to implement evidence-based therapies whenever possible, even in older and frail patients.

Table 6.2 shows the impact of geriatric conditions on the clinical condition and prognosis of older adults.

Table 6.2 – Impact of geriatric conditions on the clinical condition and prognosis of older adults

Geriatric condition	Impact on heart failure	Clinical implications
Frailty	Associated with higher mortality and hospitalization rates	Geriatric assessment and multidisciplinary approach
Sarcopenia	Reduced functional capacity	Rehabilitation and nutritional support
Cognitive impairment	Reduced treatment adherence	Simplification of pharmacological regimen

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6.2.4. Pharmacological Treatment

6.2.4.1. Treatment of Heart Failure with Reduced Ejection Fraction in Older Adults

6.2.4.1.1. Four Pillars: Efficacy and Geriatric Adaptations

Subgroup analyses of the pivotal studies confirm that beta-blockers, ACEI/ARNI, MRA, and SGLT2i maintain consistent efficacy in older adults, with no significant heterogeneity of treatment effect according to age group.^{140,471} However, older adults are less likely to receive target doses and are more

likely to have interruptions, often avoidable with appropriate monitoring (Table 6.3).

6.2.4.1.2. Angiotensin Receptor-Neprilysin Inhibitor Versus Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blocker in Older Adults

Sacubitril/valsartan (ARNI) maintains a survival benefit over ACE inhibitors/ARBs in older adults with HFrEF, with no attenuation of benefit with advancing age, although at the cost of a higher risk of symptomatic hypotension, requiring careful monitoring of blood pressure and renal function in this population.

Table 6.3 – Four pillars of guideline-directed medical therapy for heart failure with reduced ejection fraction in older adults: doses, adaptations, and level of recommendation

Class	Medication/target dose	Initial dose in older adults	Main geriatric consideration	Strength of recommendation	Certainty of evidence
ARNI /ACEI	Sacubitril/valsartan 200 mg 2×/day	Sacubitril/valsartan: initiate 50 mg 2×/day ACEI: ½ of target dose	Symptomatic hypotension and falls. ARNI preferred over ACEI: lower risk of renal dysfunction and hyperkalemia; facilitates MRA titration. Monitor creatinine and K ⁺ before and after initiation	STRONG	HIGH
	Enalapril 20 mg 2×/day				
	Ramipril 10 mg/day				
Beta-blocker	Carvedilol 25 mg 2×/day	Carvedilol: 3.125 mg 2×/day Nebivolol: 1.25 mg/day	Titration guided by achieved heart rate rather than absolute dose. Consider chronotropic incompetence. Intermediate doses may be sufficient. Use caution in severe COPD	STRONG	HIGH
	Metoprolol succinate 200 mg/day				
	Nebivolol 10 mg/day				
MRA	Spirolactone 25–50 mg/day	Spirolactone or eplerenone: 12.5–25 mg/day	Risk of hyperkalemia and worsening renal function is amplified in older adults. Monitor K ⁺ and eGFR every 1–2 weeks during the first 4 weeks. Discontinue if K ⁺ > 5.5 mEq/L or eGFR < 30	STRONG	HIGH
	Eplerenone 25–50 mg/day				
SGLT2i	Dapagliflozin 10 mg/day	Same dose (adjustment for age not required)	Lower risk of renal dysfunction and hyperkalemia. Monitor for volume depletion in low-body-weight older adults or those receiving diuretics. Genitourinary infections are more frequent.	STRONG	HIGH
	Empagliflozin 10 mg/day				

ACEI: angiotensin-converting enzyme inhibitor; ARNI: angiotensin receptor–neprilysin inhibitor; COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; MRA: mineralocorticoid receptor antagonist; SGLT2i: sodium-glucose cotransporter 2 inhibitor. Source: Prepared by the authors based on references^{140,469,471–473}

In an analysis of Medicare beneficiaries, the 5-year survival benefit of ARNI over ACE inhibitors/ARBs persisted even after adjustment for real-world discontinuation rates, which were unexpectedly slightly higher with ACE inhibitors/ARBs (2.3% per month) than with ARNI (1.9% per month). The number needed to treat did not increase with age: 84 among individuals aged 66–74 years and 67 among those aged ≥ 85 years.⁴⁷⁴

In older adults, the lower incidence of worsening renal function and hyperkalemia facilitates the initiation and subsequent titration of MRAs.^{140,471} Treatment should be initiated with the lowest available dose, with particular attention to symptomatic hypotension, which is the primary limiting factor in this age group. A decline in estimated GFR of up to 30% after initiation is acceptable and does not justify discontinuation without clinical evaluation.¹⁴⁰

6.2.4.1.3. Beta-Blockers: Heart Rate-Guided Titration

In older adults, beta-blocker titration should be guided by the achieved heart rate rather than the absolute dose. The CIBIS-ELD study found that heart rate after short-term titration, rather than the bisoprolol dose itself, was the independent predictor of lower mortality.⁴⁷¹ Intermediate doses may be sufficient and are preferable to absence of treatment. Chronotropic incompetence, frequent in older adults, may limit titration. In such cases, lower doses are preferable to discontinuing the medication. Particular attention should be paid to fatigue and the risk of falls, both of which may be exacerbated in older adults.⁴⁷¹

In the SENIORS trial, nebivolol was evaluated in patients aged 70 years or older, regardless of ejection fraction, showing a reduction in the composite outcome of all-cause mortality or cardiovascular hospitalization, although no significant reduction in all-cause mortality was observed when analyzed separately.⁴⁷⁵

6.2.4.1.4. Mineralocorticoid Receptor Antagonists: Hypercalcemia and Renal Monitoring

The risk of hyperkalemia and worsening renal function associated with MRAs is amplified in older adults because of the higher prevalence of CKD and the concomitant use of ACEI/ARNI. A meta-analysis of patients older than 75 years from the RALES, EMPHASIS-HF, and TOPCAT trials found a 26% reduction in the composite outcome of cardiovascular death or hospitalization for HF with MRAs, with no age-related heterogeneity.⁴⁵³ An initial spironolactone dose of 12.5–25 mg/day and monitoring of serum potassium and estimated GFR at 1 and 4 weeks after initiation are mandatory.¹⁴⁰ Eplerenone is preferred in men because it does not cause gynecomastia.⁴⁷¹

6.2.4.1.5. Sodium-Glucose Cotransporter-2 Inhibitors: Advantages in the Geriatric Safety Profile

Among the four pillars of therapy, SGLT2i have the most favorable safety profile in the geriatric setting: they do not require age-related dose adjustment, have a lower risk of renal dysfunction, and do not cause hyperkalemia.^{472,473} A subgroup analysis of the DAPA-HF trial by age group, including 24.2% of participants older than 75 years, found a consistent reduction

in the risk of cardiovascular death or hospitalization for HF across all age groups (HR 0.68; 95%CI 0.53–0.88 in patients 75 years or older; p for interaction = 0.76).⁴⁷² The principal geriatric concern is volume depletion in low-body-weight older adults or those receiving concomitant loop diuretics.

6.2.4.1.6. Diuretics

The goal of diuretic therapy is to achieve and maintain euolemia using the lowest dose required to control symptoms. The guidelines recommend loop diuretics for congestion relief in patients with symptomatic HF, with a consistent indication across the entire spectrum of ejection fraction, including patients with mid-range and preserved ejection fraction.¹⁴⁰ Their use is associated with reduced hospitalizations for HF, although there is no robust evidence of mortality reduction from RCTs.¹⁴⁰

In older adults, diuretics should be prescribed more cautiously due to increased susceptibility to adverse effects, such as hypovolemia, worsening renal function, and electrolyte disturbances, particularly potassium abnormalities. In addition, they may aggravate clinical manifestations that are common in this population, such as postural hypotension and urinary incontinence.

Therefore, periodic clinical and laboratory monitoring is essential, particularly when diuretics are used in association with other therapies that affect hemodynamics and renal function, such as ACEI, ARNI, and SGLT2i.

6.2.4.1.7. Ivabradine

Ivabradine reduces heart rate by inhibiting If channels in the sinus node. It is indicated for symptomatic patients with HF and an ejection fraction $\leq 35\%$, in sinus rhythm and with a heart rate ≥ 70 bpm, despite optimized treatment or when beta-blockers are not tolerated, with the aim of reducing hospitalizations for HF and cardiovascular mortality.¹⁴⁰

Evidence in older adults is limited. In the SHIFT study, ivabradine consistently reduced the composite outcome of cardiovascular death and hospitalization for HF across age groups, without a significant increase in adverse events, although the study population was relatively young.⁴⁷⁶ In older subgroups (≥ 75 years), a trend toward benefit was observed, without statistical significance.

Regarding safety, the primary adverse effects include bradycardia, AF, arrhythmias, nausea, and visual phenomena (phosphenes), requiring careful monitoring, particularly in older patients.

6.2.4.1.8. Hydralazine and Nitrate

Evidence supporting the use of hydralazine associated with nitrates in HFrEF is based on clinical trials that predominantly included patients with a mean age between 57 and 61 years.¹⁴⁰

The V-HeFT I study (mean age approximately 57 years) found reduced mortality and improved functional status with hydralazine associated with isosorbide dinitrate. In V-HeFT II (mean age approximately 61 years), this strategy was inferior to enalapril in terms of mortality.⁴⁷⁷ The A-HeFT

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study, with a mean age of approximately 57 years, found significant reductions in mortality and hospitalizations, as well as improved quality of life, in patients with HFrEF receiving optimized therapy.⁴⁷⁸

Patients aged 75 years or older were underrepresented in these studies, and, in clinical practice, use in older adults is often limited by lower tolerability, particularly due to hypotension and related adverse effects.

6.2.4.1.9. Adjuvant Therapies

Iron deficiency is identified in up to 50% of older adults with HF and constitutes an independent therapeutic target. The FAIR-HF study found improvements in functional class, 6-minute walk test, and quality of life with intravenous ferric carboxymaltose replacement in patients with and without anemia, with no difference in adverse outcomes across age groups.⁴⁷¹

Digoxin has a limited role in older adults: it should be reserved for heart rate control in symptomatic AF or for improvement of refractory symptoms, at a maximum dose of 0.125 mg/day and with a target serum level ranging from 0.5 to 0.9 ng/mL. Reduced muscle mass and the high prevalence of CKD increase the risk of toxicity, which is aggravated by hypokalemia, hypomagnesemia, and interactions with amiodarone and antibiotics.⁴⁷¹

It may be considered in HFrEF, both in sinus rhythm and in the presence of AF with a rapid ventricular response, particularly when other therapeutic options are ineffective or poorly tolerated.⁴⁷¹

In the DIG study, digoxin reduced hospitalizations, including for HF, without a consistent effect on mortality, with similar benefit across different age groups. Its impact is more evident in patients with reduced ejection fraction and is limited in those with preserved ejection fraction.⁴⁷¹

In older patients, its use requires greater vigilance because of its narrow therapeutic margin, particularly in the presence of renal failure, low body weight, or hydroelectrolytic disturbances. The primary manifestations of toxicity include supraventricular and ventricular arrhythmias, as well as atrioventricular block.^{147,461,479,480}

6.2.4.1.10. Implantable Devices

In terms of implantable devices, current recommendations are based primarily on evidence from studies that included patients with a mean age between 60 and 70 years, with limited representation of the oldest old.

ICDs are indicated for the primary prevention of sudden death in patients with HF and an ejection fraction $\leq 35\%$, despite optimized medication therapy, with a life expectancy greater than 1 year and good functional status. CRT is recommended for patients with an ejection fraction $\leq 35\%$, sinus rhythm, wide QRS (especially ≥ 150 ms), and a left bundle branch block pattern, with persistent symptoms.⁴⁷⁹

In older patients, the decision to implant these devices should be individualized, taking into account frailty, comorbidities, life

expectancy, and the competing risk of nonarrhythmic mortality. Studies suggest that although the relative benefits may be maintained, the absolute effect may be attenuated at more advanced ages, particularly for ICDs, because of the higher prevalence of nonarrhythmic causes of death.

In the context of advanced therapies, heart transplantation and ventricular assist devices represent treatment options for patients with advanced HF refractory to optimal clinical management. However, the available evidence is derived predominantly from populations with a mean age under 65 years, with limited representation of the oldest old.

Heart transplantation remains the treatment of choice for eligible patients, providing significant improvements in survival and quality of life. However, advanced age, particularly over 70 years, is associated with a higher risk of perioperative complications, infections, and lower long-term survival, which is why many centers adopt stringent selection criteria for this age group.

Ventricular assist devices, in turn, have been increasingly used as destination therapy or as a bridge to decision, including in the oldest old. Observational studies indicate that individuals aged 70 years or older may experience clinical benefits in terms of symptom relief and quality of life, although with a higher incidence of adverse events, such as bleeding, infections, and thromboembolic events.

Accordingly, both heart transplantation and ventricular assist devices should be considered on an individualized basis in older adults, with careful assessment of frailty, comorbidities, social support, and life expectancy to ensure appropriate candidate selection and outcome optimization.

Nonpharmacological interventions are an essential component of HF management, with an even greater impact on older adults. These include education, nutritional support, smoking cessation, vaccination, and cardiovascular rehabilitation.⁴⁷⁹

6.2.5. Treatment of Heart Failure with Preserved Ejection Fraction in Older Adults

HFpEF is the predominant form of HF in older adults, especially women over 75 years of age, and represents the primary contemporary therapeutic challenge in geriatric cardiology. Its treatment differs structurally from that of HFrEF, with management of comorbidities and precipitating factors taking a central role (Table 6.4).^{147,461}

The EMPEROR-Preserved and DELIVER trials established SGLT2i as the pharmacological intervention with the greatest impact in HFpEF, reducing the composite outcome of hospitalization for HF or cardiovascular death by 18%–21%, regardless of DM and across the entire ejection fraction spectrum above 40%.^{147,461}

Finerenone, a nonsteroidal MRA, was established by the FINEARTS-HF trial as the second pharmacological pillar for HFpEF and HF with improved ejection fraction, alongside SGLT2i. Unlike steroidal MRAs, finerenone has a more favorable safety profile in older adults, with a lower risk of clinically severe hyperkalemia and no gynecomastia.⁴⁸⁰

The prespecified age subgroup analysis of FINEARTS-HF, which stratified patients into quartiles, including the oldest

Table 6.4 – Treatment of heart failure with preserved ejection fraction in older patients: Interventions, evidence, and geriatric Adaptations

Intervention	Primary evidence	Particularities in older adults	Strength of recommendation	Certainty of evidence
SGLT2i (dapagliflozin or empagliflozin)	EMPEROR-Preserved and DELIVER: 18%–21% reduction in the composite outcome of hospitalization for HF or cardiovascular death versus placebo; benefit independent of DM	No age-based dose adjustment required. Monitor for volume depletion in low-body-weight older adults. Benefit extended across the entire EF > 40% spectrum.	STRONG	HIGH
Loop diuretics	Congestion relief: reduction in dyspnea and edema. No prospective mortality trial in HFpEF.	Risk of volume depletion, orthostatic hypotension, and falls. Titrate for euvolemia; avoid hypotension. Monitor renal function and electrolytes.	STRONG	MODERATE
MRA (spironolactone or eplerenone)	TOPCAT: reduction in hospitalizations for HF (most consistent benefit in the Americas subgroup analysis). Effect most evident with EF at the lower end of the HFpEF range.	High risk of hyperkalemia in older adults. Monitor K ⁺ and eGFR 1–2 weeks after initiation. Contraindicated if eGFR < 30 or K ⁺ > 5.0.	CONDITIONAL	MODERATE
Finerenone (nonsteroidal MRA) 20–40 mg/day	FINEARTS-HF: (N = 6,001; follow-up, 32 months): 16% reduction in the composite outcome of cardiovascular death and total worsening HF events (RR 0.84; 95%CI 0.74–0.95; p = 0.007). First MRA with definitive evidence in HFpEF/HFimPEF. Benefit maintained with concomitant use of SGLT2i.	Prespecified age subgroup analysis: consistent efficacy across all quartiles, including patients 80 years or older (n = 1,412), with no significant interaction. Lower risk of hyperkalemia and gynecomastia than steroidal MRAs. Projection: gain of 2.0 event-free years for a 65-year-old patient.	STRONG	HIGH
Sacubitril/valsartan	PARAGON-HF: nonsignificant reduction in the primary outcome (p = 0.06); post hoc analyses suggest effect in women and in patients with EF < 57%.	May be considered in women and in patients with HFpEF with EF at the lower end. Lower risk of renal impairment than ACEIs/ARBs. Risk of hypotension.	CONDITIONAL	LOW
Physical exercise and cardiac rehabilitation	Clinically significant improvement in peak VO ₂ , functional capacity, and quality of life in HFpEF.	Adaptation to the physical limitations of older adults. Supervised rehabilitation emphasizing moderate-intensity aerobic exercise and resistance training. Assess frailty before prescribing.	STRONG	MODERATE

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; DM: diabetes mellitus; EF: ejection fraction; eGFR: estimated glomerular filtration rate; HF: heart failure; HFimPEF: heart failure with improved ejection fraction; HFpEF: heart failure with preserved ejection fraction; MRA: mineralocorticoid receptor antagonist; RR: relative risk; SGLT2i: sodium-glucose cotransporter 2 inhibitor; VO₂: oxygen consumption. Source: prepared by the authors based on references.^{140, 147, 461, 465, 480–482}

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quartile (≥ 80 years; $n = 1,412$), found consistent efficacy across all age groups, with no significant age-treatment interaction. The benefit of finerenone was maintained in patients receiving concomitant SGLT2i, suggesting potential synergy between the two agents and supporting their combination as the second therapeutic pillar in HFpEF.⁴⁸⁰

Strict BP control and titration of diuretics to achieve euvolemia are indispensable pillars in the management of HFpEF in older adults. Orthostatic hypotension, present in up to 30% of older adults with HF, should be systematically assessed, as it is a common cause of falls and syncope and may be aggravated by the concomitant use of multiple antihypertensive agents.¹⁴⁰

Supervised exercise and cardiac rehabilitation produce clinically meaningful increases in peak VO_2 , functional capacity, and quality of life in patients with HFpEF.^{401,461} Exercise prescription should be preceded by an assessment of frailty and adapted to the physical limitations of older patients, with an emphasis on moderate-intensity aerobic exercise and resistance training.⁴⁰¹

6.2.6. Safety Profile and Specific Care for Older Adults

A systematic analysis of adverse events in HF trials found that such events are common in patients with HF regardless of treatment, and that GDMT adds only a minimal incremental risk compared with placebo.⁴⁸¹ In older adults, however, reduced physiologic reserve amplifies the clinical impact of

adverse effects such as hypotension, hyperkalemia, worsening renal function, and falls.¹⁴⁰

6.2.7. Polypharmacy, Deprescribing, and Holistic Approach

Polypharmacy, defined as the concomitant use of five or more medications, is the rule rather than the exception in older adults with HF. In the Dutch CHECK-HF registry, each 10-year increase in age was associated with a 10%–29% reduction in the likelihood of receiving target doses of GDMT.⁴⁵³ At the same time, the likelihood of diuretic use increased by 32% per decade, reflecting the prioritization of symptom management over disease-modifying therapy.⁴⁷¹

The periodic review of the medication list should integrate routine clinical care. Medications that precipitate decompensation or have clinically relevant interactions with GDMT should be identified and replaced or discontinued whenever possible.¹⁴⁰ Tools such as the STOPP/START criteria are valuable aids in this review for older adults with HF (Table 6.5).

A CGA, including screening for frailty, cognition, functional status, nutritional status, social support, and goals of care, should guide therapeutic decision-making and follow-up planning.¹⁴⁰ The involvement of a multidisciplinary team specializing in HF and geriatrics has been shown to reduce readmissions and improve functional outcomes in this population (Figure 6.1).

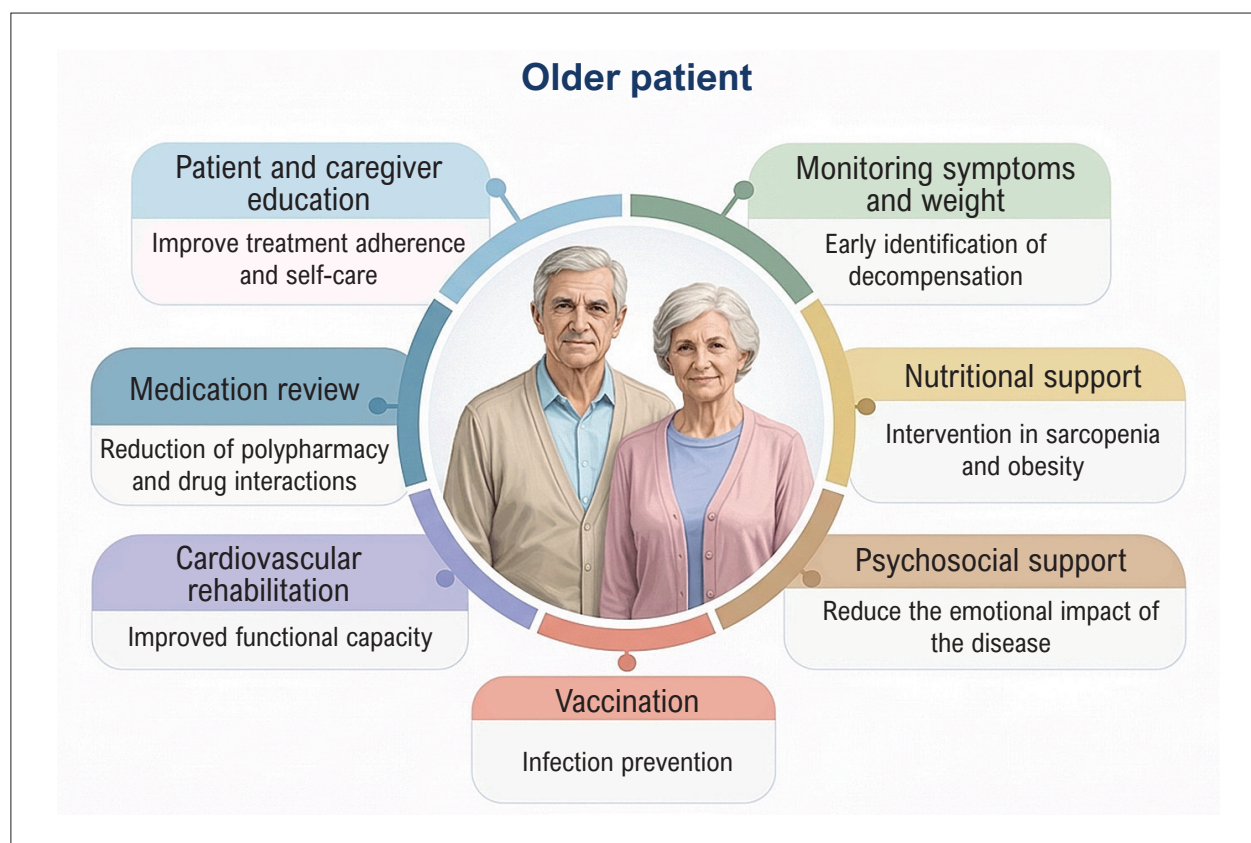


Figure 6.1 – Components of multidisciplinary heart failure management programs.

Table 6.5 – Summary of pharmacological treatment according to the GRADE system

Class	Medication	Initial dose	Maximum dose	Care of older adults	Safety in older adults	Strength of recommendation	Certainty of evidence
ACEI	Captopril	6.25 mg 3x/day	50 mg 3x/day	Monitoring renal function and potassium	Increased risk of orthostatic hypotension. Take at bedtime. Reduce diuretics. Greater susceptibility to renal dysfunction.	STRONG	HIGH
	Enalapril	2.5 mg 2x/day	10–20 mg 2x/day				
	Lisinopril	2.5–5.0 mg 1x/day	20–40 mg 1x/day				
	Perindopril	2.0 mg 1x/day	8.0–16 mg 1x/day				
	Ramipril	1.25–2.5 mg 1x/day	10 mg 1x/day				
ARB	Candesartan	4.0–8.0 mg 1x/day	32 mg	Monitoring renal function and potassium	Similar to ACEI use	STRONG	HIGH
	Losartan	25 mg 1x/day	50–100 mg				
	Valsartan	40 mg 2x/day	320 mg				
ARNI	Sacubitril/valsartan	50 mg 2x/day	200 mg 2x/day			STRONG	HIGH
Beta-blocker	Bisoprolol	1.25 mg 1x/day	10 mg 1x/day	Heart rate and blood pressure should guide dose adjustment	Caution with bradycardia and hypotension	STRONG	HIGH
	Carvedilol	3.12–5 mg 2x/day	50 mg/day				
	Metoprolol, succinate	12.5–25 mg	200 mg/day				
	Nebivolol	1.25 mg	10 mg				MODERATE
MRA	Spironolactone	12.5–25 mg	25–50 mg	Potassium monitoring	Increased risk of hyperkalemia. Monitor for gynecomastia and breast pain.	STRONG	HIGH
	Eplerenone	25 mg	100 mg	Potassium monitoring			

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SGLT2i	Finerenone	10 mg	20 mg	Avoid without creatinine clearance	Genital infection	STRONG	HIGH
	Dapagliflozin	10 mg					
	Empagliflozin	10 mg	25 mg				
Loop diuretic	Furosemide	20–40 mg/day 1 ou 2x/day	600 mg (usual 40–240 mg/day)	Initiate 20 mg/day	Monitor water balance and electrolyte disturbance	STRONG	LOW
	Torsemide	5–10 mg/day	10–200 mg/day				
	Bumetanide	0.5–1 mg/day	1–10 mg/day			WEAK	LOW
Thiazide	Hydrochlorothiazide	25 mg	200 mg/day (usual 12.5–100 mg/day)	Initiate 12.5–25 mg	Monitor volume status and electrolytes	WEAK	LOW
	Chlorthalidone	12.5 mg/day	50mg/day				
	Indapamide	2.5 mg/day	5.0 mg/day				
Potassium-sparing diuretic	Amiloride	5 mg/day	5–10 mg/day		Increased risk of hypercalcemia	WEAK	LOW

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor–neprilysin inhibitor; MRA: mineralocorticoid receptor antagonist; SGLT2i: sodium-glucose cotransporter 2 inhibitor.

Recommendations for treatment of heart failure in older adults	Strength of recommendation	Certainty of evidence
For older adults with HFrEF, guideline-directed medical therapy with the four fundamental pillars (ARNI or ACEI/ARB, beta-blocker, MRA, and SGLT2i) is recommended, starting with reduced doses and titrating every 1–2 weeks according to tolerability, with stringent monitoring of renal function, electrolytes, blood pressure, and heart rate. ^{140,471}	STRONG	HIGH
For older adults with HFrEF, preferential use of sacubitril/valsartan is recommended in detriment of an ACEI because of its lower risk of worsening renal function and hyperkalemia, facilitating MRA initiation and titration. ^{140,471}	STRONG	HIGH
For older adults with HFrEF receiving beta-blockers, guiding dose titration by the achieved heart rate rather than the absolute dose is recommended, given that intermediate doses may be sufficient and safer in this age group. ⁴⁷¹	STRONG	MODERATE
For older adults with HFpEF, the use of SGLT2i (dapagliflozin 10 mg/day or empagliflozin 10 mg/day) to reduce hospitalizations for HF and cardiovascular mortality is recommended, with benefit independent of the presence of diabetes mellitus. ^{147,461}	STRONG	HIGH
For older adults with HF and iron deficiency (ferritin < 100 ng/mL or transferrin saturation < 20%), intravenous ferric carboxymaltose is recommended to improve symptoms, functional capacity, and quality of life. ¹⁴⁰	STRONG	MODERATE

For older adults with HF, systematic assessment of polypharmacy and periodic medication review, including deprescribing of medications that precipitate decompensation, are suggested. ¹⁴⁰	CONDITIONAL	LOW
For older adults with HF, enrollment in a cardiac rehabilitation program and supervised physical exercise adapted to functional limitations and frailty status, with prior assessment of functional capacity, is suggested. ^{147,482}	CONDITIONAL	MODERATE

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor–neprilysin inhibitor; HF: heart failure; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; MRA: mineralocorticoid receptor antagonist; SGLT2i: sodium-glucose cotransporter 2 inhibitor.

6.2.8. Heart Failure with Preserved Ejection Fraction and Heart Failure with Reduced Ejection Fraction

Management of HF in older adults extends beyond the application of traditional guidelines, requiring a patient-centered approach that takes into account frailty, cognition, functional status, and individual preferences. As the population ages, it becomes imperative that diagnostic and therapeutic strategies evolve to address this clinical heterogeneity. Therefore, more than treating the disease, caring for older adults with HF requires understanding its complexity and the delivery of truly comprehensive care.^{57,479,483-486}

7. Hypertension in Older Adults

7.1. Physiopathological Mechanisms and Prevalence

7.1.1. Epidemiology

Hypertension is the most prevalent chronic cardiovascular condition among older adults. Its prevalence increases progressively with age, exceeding 60% among individuals aged 65 years or older and 75% in the eighth decade of life.^{339,401,487-490} In adults, the lifetime risk of developing hypertension is approximately 90%.^{401,487}

Another important characteristic is the predominance of isolated systolic hypertension, which accounts for more than 90% of cases after 70 years of age.⁴⁰¹ This BP phenotype primarily results from increased arterial stiffness.

Arterial hypertension affects approximately one-third of the world's population⁴⁸⁹ and, in older adults, remains the modifiable cardiovascular risk factor with the highest impact, contributing to more than 70% of cases of AMI, stroke, and HF.⁴⁰¹

7.1.2. Pathophysiology

The pathophysiology of hypertension in older adults is complex and multifactorial, centered on vascular aging. Both the international literature and the 2025 Brazilian Guideline consider arterial stiffness the predominant mechanism in the age-related increase in BP.^{339,490,491}

7.1.2.1. Arterial Stiffness and Hemodynamic Alterations

With aging, there is a progressive increase in the stiffness of the great arteries, especially the aorta, due to increased

collagen deposition, elastin degradation, medial calcification, and chronic inflammation.^{401,491-493} As a consequence of this reduction in arterial compliance, SBP values increase substantially.

Together with genetic predisposition, this vascular remodeling – which may be accelerated or not, depending on several associated factors – produces a characteristic hemodynamic pattern consisting of gradual progressive rise in SBP, stabilization followed by a gradual decline in diastolic blood pressure (DBP) after 50–59 years of age, and widening pulse pressure, an important marker of cardiovascular risk.^{401,490,491,494}

Increased pulse pressure and pulse wave velocity are important markers of vascular aging and the pathophysiology of isolated systolic hypertension.³³⁹

7.1.2.2. Endothelial Dysfunction

The aging process reduces endothelial nitric oxide synthase activity and nitric oxide bioavailability, leading to endothelial dysfunction and loss of endothelium-dependent vasodilation.⁴⁹⁵ This endothelial dysfunction reduces arterial vasodilatory capacity and helps increase BP as well as cardiovascular risk.

7.1.2.3. Increased Inflammatory Activity

Concomitantly with the vascular aging process, there may be a pathological increase in inflammatory activity, establishing a cycle that augments this damage. Several inflammatory markers, including C-reactive protein, interleukin 6, and tumor necrosis factor, among others, are elevated in this setting.⁴⁹⁶

7.1.2.4. Changes in Renal Sodium Handling

Renal aging leads to reduced glomerular filtration capacity, decreased natriuresis, altered responsiveness of the renin-angiotensin-aldosterone system, and increased salt sensitivity.^{493,497,498} All of these adaptations, together with the structural changes in the arterial bed, contribute to increased BP values.

7.1.2.5. Autonomic Dysfunction

Diminished baroreflex sensitivity and sympathetic-parasympathetic imbalance contribute to greater variability in BP and an increased risk of orthostatic hypotension.^{493,498}

In addition, autonomic dysfunction may also reduce the adaptive response through impaired heart rate variation, a mechanism likewise associated with greater variability in BP in older adults.

7.1.3. In-office and Out-of-Office Blood Pressure Measurement

Although traditional office BP measurement has served as the basis for most clinical studies, out-of-office monitoring, whether ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM), has become increasingly valued and is indicated for the diagnosis of hypertension in older adults. Self-measurement of BP, despite its limitations, should also be considered.^{449,507}

7.1.3.1. In-office Measurement

7.1.3.1.1. Casual or Office Blood Pressure

Office BP measurement is one of the most common procedures in medical practice. In most settings worldwide, a patient's BP is based on measurements obtained in the physician's office, which is often the only method available. Therefore, while recognizing the importance of out-of-office BP measurements, BP measurements obtained in clinical settings should be emphasized. Measuring BP using a standardized approach and clinically validated devices is extremely important.⁵⁰⁰

Several factors affect BP measurement in older adults because of greater BP variability and a few peculiarities:

- *Auscultatory gap*: the auscultatory gap can be avoided by estimating SBP using radial pulse palpation and inflating the cuff 20 to 30 mm Hg above that point. However, oscillometric devices may be preferable in older patients with auscultatory gaps because they are not affected by this phenomenon.⁵⁰¹
- *Pseudohypertension*: aging is accompanied by reduced arterial compliance and, consequently, increased arterial stiffness. Therefore, indirect sphygmomanometry may become inaccurate, giving rise to the concept of "pseudohypertension," which describes patients with a marked discrepancy between cuff-measured BP and directly measured BP.⁵⁰² The importance of this "phenomenon" has been questioned.⁵⁰³ However, in older patients for whom BP measured conventionally appears disproportionate to clinical findings, the Osler maneuver is recommended, as is referral to a specialized cardiovascular center.⁵⁰⁴
- *Orthostatic hypotension*: to identify orthostatic hypotension, defined as a reduction in SBP ≥ 20 mm Hg and/or DBP ≥ 10 mm Hg, BP should be measured in the supine position using the standard technique and again at 1 minute and 3 minutes after standing, ideally with the arm supported at heart level.^{500,505}
- *Unobserved automated office blood pressure measurement*: unobserved automated office BP measurement is a practical option for improving diagnosis

and guiding immediate therapeutic adjustments while the patient is still in the physician's office. Initially used in the SPRINT trial,⁵⁰⁶ it was also tested in Brazil using the same technology and protocol.⁵⁰⁷ It enables identification of a very common phenotype in older adults (white coat hypertension and the white-coat effect) and, when properly used, can prevent unnecessary treatment adjustments.

7.1.3.2. Out-of-Office Blood Pressure Measurement

7.1.3.2.1. Ambulatory Blood Pressure Monitoring

In older patients, ABPM may be very important in cases of suspected postural, postprandial, medication-induced, or situational hypotension, as well as in the evaluation of dysautonomias and syncope. It's important to note that the ABPM reference values adopted for older adults are the same as those for younger adults. In addition, assessments should take into account increased cardiovascular risk, reduced nocturnal BP dipping, increased pulse pressure, and an early morning BP surge, all common in older adults.⁵⁰⁰

7.1.3.2.2. Home Blood Pressure Monitoring

HBPM is an extremely important tool, particularly for periodic therapeutic control in older adults, contributing to a better prognosis. It is a feasible method for older adults, although it requires more careful training in individuals over 80 years of age, those with low educational attainment, cognitive impairment, or physical limitations requiring assistance from others. Telemonitoring may be used in such cases. Normal reference values do not differ from those established for the general adult population.⁵⁰⁰

7.1.4. Clinical and Complementary Assessment

Hypertension in older adults is one of the leading determinants of cardiovascular morbidity and mortality and is highly prevalent after 60 years of age. Clinical and complementary assessments should be comprehensive, taking into account the physiological aspects of aging, frailty, polypharmacy, and associated comorbidities in order to individualize diagnosis, treatment, and prognosis.⁴⁸⁹

The 2025 Brazilian Guidelines of Hypertension recommend a multidimensional approach that includes detailed history taking, targeted physical examination, laboratory and imaging evaluation, and global cardiovascular risk stratification.⁴⁸⁹ The objective is to identify end-organ damage, associated risk factors, and possible secondary causes of hypertension.

7.1.4.1. Clinical Assessment

Medical history should address cardiovascular symptoms, medication use, treatment adherence, family history, lifestyle habits, and assessment of functional status and cognition. Older adults with hypertension may present with nonspecific symptoms such as dizziness, weakness, and postural instability, often related to orthostatic hypotension or adverse effects of medications.⁵⁰⁸

The physical examination should include repeated BP measurements in both the seated and standing positions, using an appropriately sized cuff in a calm environment. It is recommended that BP be measured in both arms at the initial visit. An inter-arm difference greater than 15 mm Hg may indicate peripheral arterial disease.⁴⁸⁹ The 2024 ESC Guideline emphasizes the need to measure BP in the standing position and to investigate symptoms of postural hypotension, which is common in frail older adults.³³⁹

Examination of peripheral pulses, cardiac auscultation, and assessment for carotid and abdominal bruits are also essential components. In addition, nutritional assessment, cognitive screening (such as the MMSE), and gait testing are useful for detecting frailty and adapting antihypertensive treatment.⁵⁰⁷

7.1.4.2. Additional Tests

Laboratory and imaging tests are intended to identify end-organ damage and investigate risk factors or secondary causes. The 2025 Brazilian Hypertension Guideline³³⁹ recommends the routine basic tests listed in Table 7.1.

Imaging studies are indicated according to clinical suspicion. Echocardiography assesses left ventricular hypertrophy and diastolic dysfunction, while carotid ultrasonography detects atherosclerotic plaques. Microalbuminuria assessment is an early marker of hypertensive nephropathy and increased cardiovascular risk.⁴⁸⁹

ABPM and HBPM are increasingly valued in older adults and are superior to office BP measurement for predicting cardiovascular risk. Out-of-office BP monitoring is particularly useful in older adults for identifying different

BP phenotypes and, especially, for diagnosing and monitoring conditions such as orthostatic hypotension and postprandial hypotension.⁵⁰⁹

7.1.4.3. Cardiovascular Risk Stratification

Risk stratification in older adults should take into account age, comorbidities, renal function, and the presence of end-organ damage. The use of risk scores such as the ESC SCORE2-OP is recommended for adults aged 70 years or older. The 2025 Brazilian Guideline suggests an assessment that integrates laboratory and imaging tests.³³⁹

Management should prioritize individualized care, taking into account life expectancy, comorbidities, frailty, and treatment adherence. Polypharmacy should be reviewed periodically to reduce drug interactions and adverse effects. Nonpharmacological strategies – such as sodium restriction, adapted physical activity, and smoking cessation – remain pillars of treatment. Combining the traditional assessment with modern methods such as ABPM and echocardiography improves diagnostic accuracy and cardiovascular risk stratification.⁴⁸⁹

Finally, integration among the multidisciplinary team, the patient, and caregivers is essential to optimize BP control and reduce cardiovascular and cerebrovascular complications in older adults with hypertension.

7.1.5. Nonpharmacological Treatment

Nonpharmacological treatment of hypertension in older adults follows the same principles adopted for the general population.³³⁹ However, some particularities deserve attention:

Table 7.1 – Recommended complementary tests for older adults with hypertension

Test	Purpose
Complete blood count	Assess anemia and general health
Blood glucose and HbA1c	Screen for diabetes mellitus
Creatinine and GFR	Evaluate renal function
Serum potassium	Detect electrolyte abnormalities
Total cholesterol and fractions	Cardiovascular risk stratification
Urinalysis and albumin/creatinine ratio	Evaluate renal injury
ECG	Detect left ventricular hypertrophy or arrhythmias
Echocardiogram	Assess ventricular function and wall thickness
ABPM or HBPM	Identify masked hypertension or white coat hypertension
Carotid ultrasonography	Evaluate subclinical atherosclerosis
Fundoscopy	Detect hypertensive retinopathy
Functional assessment: orthostatic blood pressure measurement, walking test, cognitive and functional assessment	Assess frailty and tolerance to therapy

ABPM: ambulatory blood pressure monitoring; ECG: electrocardiogram; GFR: glomerular filtration rate; HbA1c: glycated hemoglobin; HBPM: home blood pressure monitoring.

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Health self-management education for older adults is considered the best nonpharmacological intervention for reducing BP in older adults with hypertension, followed by moderate-intensity aerobic exercise.⁵¹⁰

7.1.5.1. Multiprofessional and Social Support

Recommendation	Strength of recommendation	Certainty of evidence
It is recommended that management of hypertension in older adults be individualized, taking into account the presence of geriatric syndromes, such as frailty and sarcopenia, as well as the patient's clinical condition and functional status. ⁵⁶⁹	STRONG	MODERATE
Self-care education as a fundamental strategy for blood pressure control in older adults is recommended.	STRONG	MODERATE
Follow-up by a multidisciplinary team, including professionals such as nutritionists, physical educators, psychologists, and gerontologists, to promote integrated and individualized interventions is recommended. ^{510,512}	STRONG	MODERATE
Active involvement of family members and caregivers to improve adherence to nonpharmacological interventions and sustain lifestyle modifications is recommended.	STRONG	MODERATE

It is recommended that therapeutic planning take into account the patient's functional status, ability to perform activities of daily living, and personal preferences and goals of care.⁵¹¹

STRONG

MODERATE

7.1.5.2. Sodium Restriction and Increased Potassium Intake

Recommendation	Strength of recommendation	Certainty of evidence
Reduction of sodium intake is recommended as an effective strategy for lowering blood pressure and is particularly beneficial in older adults. ⁵¹³	STRONG	HIGH
It is recommended that serum sodium be monitored in older adults undergoing sodium restriction, particularly in the presence of factors that increase the risk of hyponatremia, such as age-related physiological changes, comorbidities, and the use of medications that may induce hyponatremia (eg, thiazide diuretics and selective serotonin reuptake inhibitors). ⁵¹⁴	STRONG	MODERATE
A dietary pattern combining reduced sodium intake with adequate potassium intake is recommended as it promotes blood pressure control. ⁵¹⁵	STRONG	HIGH

It is recommended that excessive potassium supplementation be avoided, particularly in older adults with renal dysfunction due to the risk of hyperkalemia. ⁵¹⁶	STRONG	MODERATE
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It is recommended that the modality, intensity, and progression of physical exercise be individualized according to the older adult's functional status, comorbidities, physical capacity, and safety.	STRONG	HIGH
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7.1.5.3. Weight Loss and Physical Activity

Recommendation	Strength of recommendation	Certainty of evidence
Assessment of sarcopenic obesity in older adults with hypertension is recommended, as it is an important cardiovascular risk factor and is associated with poorer blood pressure control. ⁵¹⁷	STRONG	HIGH
Isometric exercise is recommended as part of the physical exercise program, when clinically indicated, because of its benefits in reducing blood pressure and preserving muscle function and muscle mass. ⁵¹⁸	STRONG	MODERATE
Regular physical exercise is recommended to reduce blood pressure – both high-intensity interval training and moderate-intensity continuous training may be used, depending on the individual clinical assessment. ^{519,520}	STRONG	HIGH

7.1.6. Choice of Antihypertensive(s)

Pharmacological management of hypertension in older adults represents one of the major challenges in cardiology and requires an individualized approach, prioritizing a comprehensive patient assessment. Associated diseases, interactions with other drug classes, potential adverse events, frailty, and cognitive function should always be considered in therapeutic decision-making and in determining which medications to avoid in a particular older adult patient.

Pharmacological treatment should be initiated at low doses, with gradual increases and periodic reassessment, targeting intensive BP control and, consequently, reduced morbidity and mortality^{334,336,521} (Table 7.2).

Combination therapy, preferably as a single pill to facilitate adherence, is recommended for most patients and has been shown to be more effective in reducing BP and cardiovascular events.⁵²²⁻⁵²⁴ However, monotherapy may be considered as initial treatment in very frail individuals, the oldest old (> 80 years), or those with symptomatic orthostatic hypotension.

The risk of falls may increase after initiation of pharmacological treatment or following dose titration, particularly with the use of diuretics.⁵⁰⁷ RCTs have shown that chronic use of antihypertensive agents and BP control reduce adverse outcomes without increasing the risk of orthostatic hypotension or falls with injuries, even in patients who had orthostatic hypotension at initiation.⁵⁰⁷⁻⁵⁰⁹

Preferred medication classes for the treatment of hypertension in older adults are described below (Table 7.3).

1. Thiazide and thiazide-like diuretics (hydrochlorothiazide, chlorthalidone, and indapamide): may be used as first-line medications, either alone or associated with other antihypertensive agents. They are particularly useful in isolated systolic hypertension and in situations associated with increased preload.⁵²⁴ Their use requires caution and monitoring of electrolytes, renal function, and postural hypotension. RCTs have shown that low doses (< 25 mg of hydrochlorothiazide or equivalent) reduce mortality and cardiovascular outcomes while causing fewer adverse effects;⁵²⁵

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Table 7.2 – Pharmacological Treatment

Clinical appearance	Recommendation	Strength of recommendation	Certainty of evidence
Initiate at low doses and titrate gradually	Recommended	STRONG	HIGH
Combination therapy (preferably fixed-dose combination)	Recommended for most patients	STRONG	HIGH
Initial monotherapy	Consider in frail older adults (> 80 years) or those with orthostatic hypotension	CONDITIONAL	MODERATE
Monitoring for orthostatic hypotension and falls	Recommended	STRONG	HIGH

Table 7.3 – Pharmacological Classes

Medication class	Recommended clinical status	Strength of recommendation	Certainty of evidence
Thiazide and thiazide-like diuretics (hydrochlorothiazide, chlorthalidone, indapamide)	First-line therapy, alone or in combination; particularly effective in isolated systolic hypertension	STRONG	HIGH
ACEI (enalapril, ramipril, lisinopril, etc.)	First-line therapy, especially in heart failure, left ventricular dysfunction, and diabetes with microalbuminuria	STRONG	HIGH
ARB (losartan, valsartan, candesartan, etc.)	Alternative to ACEIs or in association with other classes; beneficial in older adults with diabetes mellitus and for stroke prevention	STRONG	HIGH
Dihydropyridine CCBs (amlodipine, felodipine)	First-line therapy, alone or in combination; effective in isolated systolic hypertension	STRONG	HIGH
Aldosterone receptor antagonist (spironolactone, eplerenone)	Resistant hypertension	STRONG	MODERATE
Beta-blockers (atenolol, metoprolol, bisoprolol)	Not first line, except in heart failure, coronary artery disease, or arrhythmias	WEAK	MODERATE
Alpha-blockers (doxazosin, clonidine)	Avoid as routine	STRONG (AGAINST)	MODERATE
Central α2-adrenergic receptor agonists (methyldopa, clonidine)	Avoid	STRONG (AGAINST)	MODERATE
Non-dihydropyridine CCBs, (verapamil, diltiazem)	Avoid in monotherapy for systolic hypertension	MODERATE (AGAINST)	LOW
Peripheral vasodilators (hydralazine)	Not recommended as first-line medication	WEAK (AGAINST)	LOW

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker.

2. ACEIs: they are considered effective despite age-related declines in renin levels. They may be used alone or in combination with a diuretic or a CCB. They are particularly useful in patients with HF or asymptomatic left ventricular dilation, and in patients with DM, especially those with concomitant microalbuminuria.⁵²⁶ They are generally well tolerated,

but cough, angioedema, and hyperkalemia are adverse effects that should be considered;

3. ARBs: their tolerability and efficacy profile is similar to that of ACEIs regarding cardiac and renal protection, especially in patients with DM. In addition, they have been found to reduce the risk of stroke in older adults with hypertension, with a significant protective effect

for this outcome.^{527,528} Hyperkalemia, acute kidney injury, hypotension, and, less frequently, cough, angioedema, and skin reactions have been reported and require monitoring;

4. Dihydropyridine CCBs: they are effective for treating hypertension in older adults, particularly for reducing SBP, common in this age group due to arterial stiffness. Long-acting CCBs have been shown to have efficacy comparable or superior to that of other antihypertensive classes in preventing cardiovascular events, primarily stroke. They have a favorable safety profile in older adults, with a low incidence of metabolic adverse effects, making them appropriate for patients with comorbidities such as DM or obesity.⁵²⁹⁻⁵³¹ The primary adverse effects are peripheral edema, headache, and flushing, which are less frequent with extended-release formulations. Short-acting preparations should be avoided due to the increased risk of acute cardiovascular events in older adults. CCBs may be used as monotherapy or in combination with other classes, such as ACEIs or ARBs;
5. Aldosterone antagonists (spironolactone, eplerenone): they are effective in reducing BP in older adults with resistant hypertension but require strict monitoring due to the risk of hyperpotassemia and worsening renal function, particularly in older adults with comorbidities. They are more effective than beta-blockers as fourth-line therapy for resistant hypertension;⁵³²
6. Beta-blockers: they are not recommended as first-line therapy for hypertension in older adults except in specific situations, such as CAD, HF, or arrhythmias. In older adults without these conditions, other drug classes should be prioritized because beta-blockers have limited efficacy and an unfavorable safety profile in older adults.⁵³³

Medication classes to avoid or use with caution in older adults:

1. Alpha-blockers (doxazosin): not routinely recommended because of the high risk of orthostatic hypotension and adverse effects;
2. Other centrally acting alpha-agonists (methyl dopa, clonidine) have a high risk of central nervous system adverse effects, bradycardia, and orthostatic hypotension;
3. Non-dihydropyridine CCBs (verapamil, diltiazem): low antihypertensive potency and increased risk of cardiac conduction disturbances and hypotension;
4. Peripheral vasodilators (hydralazine): not considered first-line agents, should be used with caution due to variable response and an increased risk of adverse effects (orthostatic hypotension, tachycardia, fluid retention, and precipitation of angina).⁵³⁴

7.1.7. Therapeutic Targets

Hypertension management in older adults and the establishment of therapeutic targets remain public health

priorities, particularly in light of global population aging. The focus on individualized care is essential, based on an assessment of the patient's mental and physical functional status, and chronological age alone should not determine treatment strategy. Antihypertensive medications should be adjusted every 4 weeks to avoid abrupt decreases in BP.

Recent meta-analyses^{337,338,518} have found that reducing SBP to values below 130 mm Hg significantly reduced combined cardiovascular events, all-cause mortality, and cardiovascular mortality without increasing severe adverse events. These findings suggest that BP control in functionally independent older adults should be as strict as that in younger adults. The SPRINT and STEP studies^{336,535} have shown the cardiovascular benefits of intensive BP control in older adults. The former included 9,361 participants over 75 years of age, divided into two groups. In the standard-treatment group, the target was SBP < 140 mm Hg, whereas in the intensive-treatment group, the target was SBP < 120 mm Hg. The intensive-treatment group experienced a significant reduction in cardiovascular events but also a slight increase in adverse events such as hypotension, syncope, bradycardia, and hydroelectrolytic disturbances. The SPRINT-MIND substudy⁵³⁶ analyzed brain MRI findings in adults with hypertension and found that intensive SBP control was associated with slower progression of cerebral white matter lesions, as well as a lower incidence of cognitive decline. Observational studies have also shown a progressive increase in cardiovascular risk as SBP exceeds 115 mm Hg.⁵³⁷

Nevertheless, the optimal SBP target for older adults remains uncertain. Most studies have predominantly enrolled relatively healthy older adults, with limited data on frail and institutionalized individuals, as they generally excluded older adults with major comorbidities such as recent stroke, HF requiring antihypertensive medications, CKD, clinical dementia, and loss of autonomy.^{336,535} The PARTAGE study assessed frail nursing home residents and did not find benefits from intensive BP reduction, with mortality risk reaching twice that observed in individuals over 80 years of age.³³⁶ Given the evidence above, these guidelines recommend a target BP of < 130/80 mm Hg for most older adults with hypertension. Excessive BP reduction in older adults may be harmful, presumably because of reduced perfusion of end organs, particularly among frail individuals or those with conditions that limit life expectancy.

7.1.8. Special Situations

7.1.8.1. Life Expectancy and Frailty Assessment

Frailty syndrome in older adults is characterized by diminished physiological reserve and increased vulnerability to stressors, with a higher risk of hospitalization, functional decline, and death. Now recognized as one of the major prognostic determinants in older adults, frailty improves the predictive capacity of traditional risk scores such as GRACE in ACS and 3C-HF in HF.^{405,538} Its impact on prognosis in patients with hypertension is substantial and is associated with a marked reduction in survival.⁵³⁹

Systematic assessment of frailty and life expectancy represents a fundamental component of hypertension management in older adults, guiding treatment intensity and therapeutic targets. Quantifying frailty using validated instruments rather than subjective clinical judgment is critical, as informal assessments have low accuracy.⁵⁴⁰ Among the available tools, the CFS, which has been validated for the Brazilian population, stands out for its excellent reproducibility and prognostic value in patients with hypertension.^{227,541}

It is important to recognize that frailty is not a dichotomous condition but rather that there is a spectrum of vulnerability. On the CFS, patients range from vulnerable (CFS 4) to severe frailty (CFS 7–9). This gradation is essential because the degree of frailty determines the therapeutic strategy.^{335,336}

Another crucial aspect is the assessment of life expectancy. It is estimated that approximately 3 years of treatment with intensive targets are required before clinically meaningful benefits can be observed. Therefore, patients with a life expectancy of less than 3 years are unlikely to benefit from intensive treatment strategies, and more lenient BP targets may be preferable.⁵⁴² A useful tool for this assessment is the ePrognosis website (<https://eprognosis.ucsf.edu/>), which provides prognostic calculators.⁵⁴³

In light of this evidence, we recommend individualized treatment for older adults with moderate to severe frailty (CFS 6–9) and/or a life expectancy of less than 3 years. In these patients, low-dose monotherapy should be initiated, with blood-pressure targets adjusted according to clinical tolerance.^{339,544}

It should be emphasized that frailty is potentially reversible under certain circumstances. Accordingly, when a frail older adult is identified, a CGA (or its abbreviated 10-TaGA version) should be performed to identify impaired domains and guide targeted interventions.⁵⁴⁵ Thus, before considering any intervention to be disproportionate in a frail older adult, it is absolutely necessary to assess its potential reversibility, as this may change both prognosis and therapeutic goals.

7.1.8.2. Major Neurocognitive Disorder (Dementia)

Hypertension during midlife increases the lifetime relative risk of dementia by 20%–54%, including both vascular dementia and Alzheimer's disease. The relationship between hypertension and cognitive decline manifests through multiple pathophysiological mechanisms, including small-vessel disease, lacunar infarctions, cerebral microbleeds, endothelial dysfunction, and neuroinflammation.⁵⁴⁶ The population impact of hypertension on dementia has been quantified using the population attributable fraction, which estimates the share of dementia cases that could be prevented by completely eliminating exposure to a given risk factor. The authors reported an adjusted population attributable fraction of 7.1%. This finding identifies hypertension as the second most important modifiable risk factor for dementia, second only to low educational attainment.⁵⁴⁷

Evidence from RCTs and meta-analyses has established the benefit of antihypertensive treatment in preventing cognitive impairment and dementia.^{548,549} In addition, more recent studies have shown that intensive BP targets provide greater

benefits than standard BP control.^{535,550} In 2025, the CRHCP-3 trial, which enrolled 33,995 individuals with uncontrolled hypertension randomized to a BP target of < 130/80 mm Hg versus usual care, found a 15% reduction in the risk of all-cause dementia over a 4-year follow-up period.⁵⁵¹

Based on this evidence, an SBP target of < 130 mm Hg in adults is recommended to reduce the risk of mild cognitive impairment and dementia.⁵⁵² Periodic cognitive monitoring using validated screening instruments is recommended in older adults with hypertension to enable early detection of cognitive impairment. The 10-CS is a quick and easy-to-administer cognitive screening tool.⁵⁵³

7.1.8.3. Polypharmacy and its Consequences

Polypharmacy, defined as the concomitant use of five or more medications, is highly prevalent in Brazil, affecting up to 29.4% of individuals over 80 years of age.^{554,555} Although polypharmacy is associated with an increased risk of iatrogenic complications and adverse outcomes, it should be emphasized that deprescribing is not always possible. A distinction should be made between inappropriate polypharmacy and appropriate or rational polypharmacy; in the latter, patients only take medications with well-established indications, and these therapies should be maintained.⁷⁴

Several consequences of polypharmacy in older adults with hypertension can be mitigated through simple strategies. Poor adherence may be prevented through the use of single-pill fixed-dose combination antihypertensive medications, medication schedules, and pill organizers.⁵⁵⁶

Some adverse effects that limit optimization of antihypertensive therapy, such as orthostatic hypotension and hyponatremia, may result from noncardiovascular medications, particularly psychotropic medications. These should be reviewed before reducing or discontinuing antihypertensive medications.^{557,558} Another critical consideration is the identification of medications that may elevate BP and contribute to prescribing cascades, in which additional antihypertensive medications are prescribed to treat this side effect, such as decongestants (phenylephrine and pseudoephedrine), mirabegron (used for urge urinary incontinence), and NSAIDs as well as antidepressants.⁵⁵⁹

Important drug interactions, such as that between amlodipine and simvastatin, can be identified using interaction checkers such as the Drug Interaction Checker (available free of charge through Medscape) and the drug interaction module of UpToDate (subscription required).⁵⁶⁰⁻⁵⁶²

Finally, one should remain alert to therapeutic inertia, a situation in which physicians fail to optimize antihypertensive therapy because of concerns regarding polypharmacy, even when there is room for adjustment. The presence of polypharmacy alone should not preclude pursuing appropriate therapeutic targets with proven cardiovascular benefit.^{334,336}

7.1.8.4. Deprescribing

Deprescribing should be undertaken with great caution. Inappropriate discontinuation of cardiovascular medications

may increase morbidity and mortality, as found in studies evaluating the withdrawal of statins and HF therapies.^{563,564}

RETREAT-FRAIL, the first RCT to evaluate the effects of deprescribing antihypertensive medications in older adults, enrolled 1,048 institutionalized adults aged 80 years or older with frailty and SBP < 130 mm Hg, who were randomized to antihypertensive dose reduction or usual care. After a mean follow-up of 38.4 months, there was no significant difference between the groups in the incidence of cardiovascular events or all-cause mortality. Although deprescribing was not associated with improved cognition, functional status, or quality of life, the study concluded that the gradual reduction of antihypertensive medications is safe in this patient population.⁵⁶⁵ In addition, reducing polypharmacy may provide additional benefits that were not directly assessed in the study, including improved treatment adherence and creases in costs, treatment complexity, and the risk of drug interactions.

Accordingly, deprescribing may be considered in older adults with advanced frailty, polypharmacy, and SBP < 130 mm Hg, provided that strict clinical monitoring is maintained.⁵⁶⁵

7.1.8.5. Orthostatic and Postprandial Hypotension

Orthostatic hypotension and postprandial hypotension affect approximately 20% of older adults. Orthostatic hypotension is defined as a decline in SBP of ≥ 20 mm Hg and/or DBP of ≥ 10 mm Hg within 5 minutes of changing from the supine to the standing position. Postprandial hypotension is characterized by a decline in SBP of ≥ 20 mm Hg 30 to 90 minutes after a meal.

In the pathophysiology of orthostatic hypotension, aging impairs the baroreceptor-mediated mechanisms that compensate for BP reduction, including increases in peripheral vascular resistance, venous return, and cardiac output.⁵⁶⁶ In postprandial hypotension, the release of intestinal vasodilatory peptides and splanchnic blood pooling are not adequately compensated by peripheral vasoconstriction, resulting in often nonspecific symptoms such as malaise, cold sweating, dizziness, and drowsiness after meals.⁵⁶⁷

Antihypertensive medications are the leading medication-related cause of orthostatic hypotension, with risk being more strongly related to the number of medications and their doses than to any specific drug class. The risk is highest during the first few weeks after treatment initiation or dose adjustment.^{566,567}

Management should prioritize nonpharmacological measures. For orthostatic hypotension, adequate hydration, physical conditioning, gradual postural changes, and compression stockings are recommended. For postprandial hypotension, although evidence is limited, recommendations include smaller, more frequent meals with reduced carbohydrate content; drinking cold water 30 minutes before meals; consuming caffeine (200–250 mg/day) to inhibit peripheral vasodilation; and not taking antihypertensive medications with meals. Pharmacological treatment is indicated for refractory symptomatic cases and includes fludrocortisone (to increase plasma volume)

or midodrine (an alpha-1 adrenergic agonist that improves vascular tone), with attention to supine hypertension as a potential adverse effect.^{568,569}

Older adults with dysautonomia may present with concomitant supine hypertension and orthostatic hypotension. In this situation, measures such as elevating the head of the bed, avoiding diuretics and excessive nighttime fluid intake, and the judicious use of short-acting antihypertensive agents at bedtime may help mitigate these problems.

Treatment of hypertension in frail older adults with symptomatic orthostatic hypotension should be individualized, initiating as low-dose monotherapy and aiming for more lenient BP targets.³³⁹ However, therapeutic inertia should be avoided in robust older adults or those with mild frailty, because a meta-analysis has found that the frequency of orthostatic hypotension does not increase with intensive treatment compared with standard treatment in this population. Indeed, there is evidence that appropriate treatment of hypertension may actually reduce the risk of orthostatic hypotension.⁵⁷⁰

7.1.8.6. Low Diastolic Blood Pressure and J-Curve

The most frequent hypertension phenotype in older adults is isolated systolic hypertension, resulting in clinical situations in which SBP remains above target while DBP is relatively low. In this setting, there is concern that intensifying antihypertensive therapy may reduce DBP excessively, potentially increasing cardiovascular risk. This concern stems from the J-curve phenomenon, based on observational studies and secondary analyses of clinical trials, suggesting that very low DBP values (< 70/60 mm Hg) are associated with an increased risk of AMI.^{571,572} This hypothesis is biologically plausible because coronary perfusion occurs during diastole, and very low DBP levels could compromise coronary blood flow, thereby promoting myocardial ischemia. However, observational studies find associations without establishing causality.

Evidence from RCTs finding the benefits of intensive BP control included exploratory subgroup analyses of patients with DBP < 60 mm Hg and found no increase in cardiovascular events.⁵⁷³ Supporting these findings, Arvanitis et al. investigated the relationship between DBP and cardiovascular events using Mendelian randomization analyses and found no evidence of a causal relationship between low DBP and increased cardiovascular risk, indicating that previously observed associations may be explained by confounding factors or reverse causality.

The reverse-causality hypothesis is particularly plausible in geriatrics, where low DBP reflects increased arterial stiffness and higher degrees of frailty, both of which are associated with higher cardiovascular risk. Therefore, low DBP should be interpreted as a risk marker rather than a cause.

In light of the current evidence, low DBP should not preclude optimization of antihypertensive therapy, although special caution is warranted in patients with clinically manifest CAD. Specific recommendations for the management of patients with chronic coronary syndrome are discussed in the corresponding chapter of these guidelines.³³⁹

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Recommendations for the management of hypertension in older adults in special situations	Strength of recommendation	Certainty of evidence
For older adults with moderate to severe frailty, life expectancy of less than 3 years, and symptomatic orthostatic hypotension, an individualized blood pressure target is recommended, aiming for the lowest well tolerated value.	STRONG	HIGH
Because the safety and efficacy of intensive blood pressure targets are uncertain in older adults with moderate to severe frailty, frailty should be assessed using validated instruments, such as the Clinical Frailty Scale, for diagnosis and severity classification.	STRONG	MODERATE
An SBP target of ≤ 130 mm Hg in adults with hypertension to reduce the risk of mild cognitive impairment and dementia is recommended.	STRONG	HIGH
Before initiating or intensifying antihypertensive therapy, patients should be assessed for orthostatic hypotension by measuring blood pressure in the supine position (after 5 minutes of rest) and again after standing for 3 minutes.	STRONG	MODERATE
It is recommended that deprescribing of antihypertensive medications be considered in older adults with moderate to severe frailty, who are institutionalized, have polypharmacy, and maintain SBP < 130 mm Hg.	STRONG	MODERATE
For older adults with polypharmacy, the use of fixed-dose combination antihypertensive medications in a once-daily single pill is recommended to improve treatment adherence.	STRONG	MODERATE

SBP: systolic blood pressure.

8. Valvular Heart Diseases

8.1. Mitral Regurgitation

8.1.1. Introduction and General Concepts

MR is among the most frequently diagnosed VHDs in contemporary clinical practice and represents a major cause of cardiovascular morbidity worldwide. MR is characterized by the abnormal backflow of blood from the left ventricle into the left atrium during ventricular systole, resulting from structural or functional abnormalities of the mitral valve apparatus. Its prevalence increases progressively with age, reflecting population aging and improved survival among patients with CVD. In Brazil, rheumatic heart disease (RHD) remains the leading cause of mitral valve disease. The Update of the Brazilian Guidelines for Valvular Heart Disease – 2020 recognize RHD as the most prevalent etiology of primary MR in Brazil, while the Cardiovascular Statistics – Brazil 2023 report that rheumatic disease is associated with more than 90% of cases of mitral stenosis (MS) and approximately 55%–60% of cases of MR.^{366,574}

Although Brazil currently lacks nationwide population-based echocardiographic registries capable of accurately estimating the prevalence of MR, international studies provide context for the global burden of the disease. In a population-based study conducted in the United States involving 11,911 individuals who underwent echocardiographic evaluation, the prevalence of moderate or severe VHD was 2.5% in the general population, increasing from 0.7% among individuals aged 18–44 years to 13.2% among those aged 75 years or older. MR was the most frequently observed moderate or

severe valvular lesion, with a prevalence of 1.7% (95%CI 1.4–2.0) in the study population.⁵⁷⁵ Furthermore, the overall prevalence of MR is approximately 10.4% when all grades of disease severity are considered. Among patients with isolated clinically significant MR, primary MR accounted for approximately 65% of cases, whereas secondary MR accounted for approximately 35%. Among patients with chronic primary MR, degenerative disease was responsible for approximately 61% of cases, representing the predominant mechanism of MR in developed countries.⁵⁷⁶ These findings contrast with the epidemiological profile in Brazil, where RHD remains an important cause of MR, although a progressive epidemiological transition is occurring, with an increasing contribution of degenerative and functional forms.

More recent international data corroborate the findings of individual population-based studies. In 2025, a meta-analysis including more than 6 million individuals from 20 population-based studies estimated the global prevalence of moderate or severe MR at 0.67% (95%CI 0.33–1.11), increasing progressively with age to approximately 2.85% and 6.45% at 70 and 90 years of age, respectively.⁵⁷⁷ These findings further underscore the well-established strong association between MR and population aging and reinforce the growing importance of the disease as a public health concern, directly related to increasing life expectancy. Comparison of the epidemiological profile in Brazil with that observed in developed countries highlights important differences in predominant etiology, age groups affected, pathophysiological mechanisms, and temporal trends (Table 8.1).

These differences, together with increasing international migration and the resulting changes in the epidemiological profile of VHD over recent decades, have direct implications

Table 8.1 – Key epidemiological differences in MR between Brazil and developed countries

Characteristic	Brazil	Developed countries
Predominant etiology of primary MR	Rheumatic	Degenerative
Estimated contribution of rheumatic etiology to MR	~55%–60%	< 30%
Typical age group	Young adults Middle-aged adults Older adults	Predominantly older adults
Main mechanism	Chronic rheumatic heart disease	Mitral valve prolapse Fibroelastic deficiency
Current trend	Epidemiological transition	Population aging

MR: mitral regurgitation.

for diagnosis, risk stratification, clinical follow-up, and treatment selection. An estimated 281 million people currently live outside their countries of origin, corresponding to approximately 3.6% of the global population. This phenomenon has contributed to the global redistribution of several CVDs, including RHD and other forms of VHD historically associated with specific geographic regions.^{578,579} Accordingly, the interpretation of international evidence and the formulation of recommendations in the current Guideline must necessarily consider the specific characteristics of the Brazilian population.

The mitral valve is a complex anatomical structure comprising the anterior and posterior leaflets, mitral annulus, chordae tendineae, papillary muscles, and left ventricular and left atrial myocardium. Abnormalities in any of these components may impair leaflet coaptation and result in MR. Consequently, understanding the pathophysiology of MR requires an integrated assessment of the entire mitral apparatus and its interaction with the left-sided cardiac chambers.⁵⁸⁰

MR is classified as primary or secondary. In chronic primary MR, regurgitation results from intrinsic structural abnormalities of the mitral valve or subvalvular apparatus, most notably rheumatic disease, mitral valve prolapse (MVP), myxomatous degeneration, fibroelastic deficiency, and mitral annular calcification (MAC). Acute forms, such as chordal rupture and infective endocarditis, should be considered within their specific clinical context and addressed separately. In secondary MR, regurgitation results from ventricular or atrial abnormalities that lead to loss of leaflet coaptation despite the absence of primary structural leaflet disease.^{574,581}

Over recent decades, advances in cardiovascular imaging, valve surgery, and transcatheter therapies have substantially improved the understanding of disease mechanisms and expanded diagnostic and therapeutic options. The development of three- (3D) and four-dimensional echocardiography, CMR, cardiac CT, and transcatheter repair techniques has enabled more detailed anatomical characterization of the mitral apparatus and more comprehensive assessment of patients with MR.⁵⁸²⁻⁵⁸⁴ Therefore, the current Update of the Brazilian Guidelines for Valvular Heart Disease – 2020 aims to integrate the scientific evidence published since 2020 and

provide contemporary recommendations for the diagnosis, risk stratification, follow-up, and treatment of chronic primary and secondary MR.

8.1.2. Key Changes between the 2020 and 2026 Guidelines

Since the publication of the Brazilian Guidelines for Valvular Heart Disease – 2020,⁵⁷⁴ significant advances have been made in the understanding of the pathophysiological mechanisms of MR, cardiovascular imaging modalities, risk-stratification strategies, and surgical and transcatheter treatment options. In parallel, the publication of RCTs, prospective multicenter registries, and contemporary observational studies has substantially expanded the evidence base available for the management of primary and secondary MR.⁵⁸⁵⁻⁵⁹³

Table 8.2 summarizes the key studies published between 2020 and 2026 that directly influenced the updated recommendations in these Guidelines and outlines the major conceptual, diagnostic, and therapeutic changes incorporated into the present update compared with the Brazilian Guidelines for Valvular Heart Disease – 2020.⁵⁷⁴ Collectively, this evidence reflects advances in scientific knowledge in the field, including recognition of atrial secondary MR as a distinct clinical entity,⁵⁸⁵ consolidation of specialized Heart Valve Center and Heart Team programs,⁵⁷⁴ expansion of the role of multimodality imaging,⁵⁹³ strengthening of the evidence supporting transcatheter edge-to-edge repair (TEER),⁵⁸⁶⁻⁵⁹⁰ and refinement of patient-selection criteria for surgical and percutaneous interventions.⁵⁸⁶⁻⁵⁹¹ The scope of this article encompasses primary and secondary MR and does not address dysfunction or degeneration of mitral valve prostheses.

8.1.3. Chronic Primary Mitral Regurgitation

8.1.3.1. Prevalence and Etiology

Among patients with clinically significant MR, approximately two-thirds have chronic primary MR.⁵⁷⁶ In developed countries, degenerative forms are the predominant etiology, accounting for approximately 60% of cases of chronic primary

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Table 8.2 – Key changes between the Brazilian Society of Cardiology 2020 and 2026 Guidelines

Topic	2020 ⁵⁷⁴	2026
Atrial secondary MR	Limited emphasis	Formally defined clinical entity with a dedicated section
Heart Valve Center	Limited concept	Central role in patient evaluation and treatment
Heart Team	Important	Mandatory framework for complex cases
Three-dimensional echocardiography	Complementary tool	Central component of anatomical and procedural assessment
Cardiac magnetic resonance imaging	Secondary role	Greater relevance for quantification and prognostic assessment
Asymptomatic primary MR	Classical criteria for intervention	Refined criteria for early intervention
TEER in primary MR	Alternative for high-risk patients	Strengthened recommendation in selected patients
TEER in ventricular secondary MR	More restrictive recommendation	Class I recommendation in selected patients after optimized GDMT
Atrial secondary MR	No specific algorithm	Dedicated diagnostic and therapeutic algorithm
Minimally invasive mitral valve surgery	Limited emphasis	Recommended in selected patients at experienced centers
Integrated multimodality imaging	Less emphasis	Formal strategy for the assessment of MR
Genetic evaluation in primary MR	Limited consideration	Included in the evaluation of selected cases

GDMT: guideline-directed medical therapy; MR: mitral regurgitation; TEER: transcatheter edge-to-edge repair.

MR.⁵⁷⁶ In contrast, RHD remains an important cause of MR in low- and middle-income countries, including Brazil.^{366,574,579} A progressive epidemiological transition has been observed in Brazil, with a proportional increase in degenerative forms associated with population aging, particularly at high-complexity urban centers.^{366,574}

MVP is the main clinical manifestation of degenerative mitral valve disease and affects 2%–3% of the general population.⁵⁹⁴ Although most individuals have a benign course, a subset develops progressive MR, cardiac remodeling, and ultimately requires valve intervention.^{584,594} In more advanced cases, particularly in the presence of myxomatous degeneration or fibroelastic deficiency, chordal rupture may occur, resulting in a flail mitral leaflet.^{595,596} In this setting, the affected leaflet edge loses its normal support and moves freely into the left atrium during systole, generally resulting in severe MR, more rapid clinical progression, and a greater likelihood of valve intervention.^{597,598}

Recent studies have also broadened the understanding of the spectrum of degenerative mitral valve disease through

characterization of mitral annular disjunction, which is frequently associated with MVP and an increased risk of ventricular arrhythmias and sudden cardiac death (SCD) in selected patient subgroups.^{595,596} Other less common etiologies include infective endocarditis, congenital abnormalities of the mitral apparatus, inherited connective tissue disorders, MAC, and lesions related to mediastinal radiation therapy.⁵⁷⁴

Determining the etiology has important prognostic and therapeutic implications, influencing the likelihood of successful valve repair, the anatomical complexity of the intervention, and long-term clinical outcomes.⁵⁸⁰

8.1.3.2. Assessment

The assessment of chronic primary MR should integrate clinical and functional data to identify symptoms, detect early consequences of the disease, and recognize patients at greater risk of progression. Although many patients remain asymptomatic for prolonged periods, the natural history of severe chronic primary MR is not benign. Among initially

asymptomatic patients, the combined annual incidence of symptoms, AF, HF, or need for intervention ranges from 5% to 7% per year.^{584,597,598}

The presence of symptoms remains one of the major prognostic markers of the disease. Exertional dyspnea, fatigue, reduced exercise tolerance, palpitations, AF, congestive symptoms, and thromboembolic events should be systematically investigated. However, clinical assessment alone may underestimate the functional impact of chronic primary MR, particularly in older or sedentary patients. Studies have shown that 20%–40% of patients considered asymptomatic have objectively demonstrable functional limitations on exercise testing, characterizing the so-called falsely asymptomatic patient.^{584,599,600}

Physical examination remains important for initial diagnostic suspicion. The classic finding is a holosystolic apical murmur radiating to axilla, which may be accompanied by a third heart sound in cases of severe MR. However, murmur intensity does not consistently correlate with the severity of MR, making complementary imaging assessment essential.^{574,583}

The development of AF, pulmonary hypertension, or clinical signs of HF represents an important milestone in disease progression. These findings reflect significant hemodynamic consequences of MR and are associated with greater cardiovascular morbidity, a higher risk of hospitalization for HF, and worse clinical outcomes during follow-up.^{574,578,584,597}

ECG and chest radiography provide relevant complementary information, including the presence of AF, left-sided chamber enlargement, cardiomegaly, and pulmonary congestion, thereby contributing to the overall assessment of the patient and identification of associated cardiovascular consequences.⁵⁷⁴ Objective functional assessment plays an important role in apparently asymptomatic patients or when there is discordance between reported symptoms and clinical suspicion. Cardiopulmonary exercise testing allows objective quantification of functional capacity and more accurate assessment of the cardiovascular response to exercise.^{584,599,600}

Following the initial clinical and functional assessment, echocardiography remains the primary modality for anatomical characterization of the mitral valve, quantification of MR, and identification of the structural consequences of the disease.

8.1.4. Echocardiography and Right Heart Catheterization

8.1.4.1. Echocardiography

Echocardiography is the imaging modality of choice for the diagnosis, quantification, and prognostic stratification of chronic primary MR. The assessment should establish the etiology and mechanism of MR, quantify its severity, and characterize its impact on the cardiac chambers using an integrated multiparametric approach encompassing anatomical, quantitative, and functional parameters.^{583,597} The main echocardiographic criteria used in clinical practice are summarized in Table 8.3.^{583,593,597}

Recent evidence reinforces the role of 3D echocardiography in the assessment of chronic primary MR, particularly in the presence of eccentric jets or complex anatomy, by

reducing the inherent limitations of the two-dimensional proximal isovelocity surface area technique and providing better correlation with reference methods, including CMR.⁶⁰¹⁻⁶⁰⁵ Similarly, myocardial deformation parameters, particularly GLS, may identify subclinical ventricular dysfunction before a reduction in ejection fraction and provide incremental prognostic information in apparently asymptomatic patients.^{600,604,605}

The use of artificial intelligence for automated quantification of regurgitation, multiparametric analysis, and risk stratification is an area of active investigation. Although initial results are promising, artificial intelligence tools do not yet have an established role in routine clinical decision-making.^{604,605}

8.1.4.2. Right Heart Catheterization

Right heart catheterization is not routinely recommended for the assessment of chronic primary MR and is currently reserved for situations involving discrepancies between symptoms and echocardiographic findings, suspected significant pulmonary hypertension, or when invasive hemodynamic assessment may influence the therapeutic strategy.^{574,583,605-611}

In these settings, right heart catheterization enables direct characterization of filling pressures and the pulmonary circulation. In patients with advanced MR, increased pulmonary capillary wedge pressure and pulmonary artery systolic pressure (PASP), as well as the presence of a prominent V wave (> 30 mm Hg), reflect backward transmission of left atrial volume overload to the pulmonary circulation and are associated with greater hemodynamic burden and worse prognosis. Increased pulmonary vascular resistance suggests more advanced pulmonary vascular remodeling and potentially irreversible hemodynamic abnormalities (Table 8.4). Post-capillary pulmonary hypertension related to MR is defined by a mean pulmonary artery pressure > 20 mm Hg in conjunction with a pulmonary capillary wedge pressure > 15 mm Hg. Although no validated invasive hemodynamic criteria are available to define the anatomical severity of MR, parameters obtained by right heart catheterization provide complementary information on the physiological consequences of MR and its impact on the pulmonary circulation.⁶⁰⁶⁻⁶¹¹

8.1.4.3. Biomarkers

Biomarkers are not used to define the anatomical severity of chronic primary MR but may complement prognostic stratification, particularly in apparently asymptomatic patients or those with borderline clinical and echocardiographic findings.^{584,612}

Natriuretic peptides, particularly BNP and NT-proBNP, are the most extensively studied biomarkers in chronic primary MR and correlate with cardiac chamber enlargement, increased filling pressures, and ventricular remodeling. Even in asymptomatic patients with significant MR and preserved ejection fraction, elevated BNP levels are an independent predictor of cardiovascular events and an early marker of hemodynamic deterioration, being associated with the

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Table 8.3 – Main echocardiographic parameters in chronic primary mitral regurgitation

Domain	Parameter	Value/definition	Clinical relevance
MR quantification	EROA	$\geq 40 \text{ mm}^2$	Consistent with severe MR; associated with increased cardiovascular mortality and HF
MR quantification	Regurgitant volume	$\geq 60 \text{ mL}$	Consistent with severe MR
MR quantification	Regurgitant fraction	$\geq 50\%$	Consistent with severe MR
Ventricular remodeling	LVEF	Serial assessment	Progressive reduction is associated with worse prognosis
Ventricular remodeling	Indexed LV volumes	Serial assessment	Greater prognostic value than isolated linear measurements
Atrial remodeling	LA volume	Serial assessment	Reflects chronic volume overload and disease progression
PH	PSAP	Serial assessment	Marker of advanced hemodynamic consequences
Subclinical ventricular function	GLS	Less negative than approximately -20%	May identify ventricular dysfunction before a reduction in LVEF
Valve anatomy	3D echocardiography	Whenever available	Improved anatomical characterization and treatment planning
Advanced quantification	3D echocardiography	Particularly useful for eccentric or complex jets	Reduces the limitations of 2D proximal isovelocity surface area technique
Arrhythmic phenotype	MAD	Systematic assessment in degenerative MVP	Associated with a higher risk of ventricular arrhythmias
Treatment planning	TEE	Selected cases	Essential for surgical or transcatheter repair

2D: two-dimensional; 3D: three-dimensional; EROA: effective regurgitant orifice area; GLS: global longitudinal strain; HF: heart failure; LA: left atrial; LV: left ventricular; LVEF: left ventricular ejection fraction; MAD: mitral annular disjunction; MR: mitral regurgitation; MVP: mitral valve prolapse; PH: pulmonary hypertension; PSAP: pulmonary artery systolic pressure; TEE: transesophageal echocardiography.

development of symptoms, AF, HF, and the future need for valve intervention. Accordingly, elevated BNP levels may warrant more frequent clinical and echocardiographic follow-up.^{584,612}

Other biomarkers, including high-sensitivity cardiac troponin, soluble suppression of tumorigenicity 2, and galectin-3, have been investigated as markers of myocardial remodeling, fibrosis, and subclinical injury. Recent evidence suggests that integrating these biomarkers with advanced imaging parameters, including GLS and myocardial fibrosis detected by CMR, may improve prognostic stratification. However, this approach remains investigational and has no established role in routine therapeutic decision-making in chronic primary MR.⁵⁹³⁻⁵⁹⁵ The main biomarkers studied in chronic primary MR and their respective clinical applications are summarized in Table 8.5.⁶¹²⁻⁶¹⁵

8.1.4.4. Cardiac Magnetic Resonance Imaging and Computed Tomography

CMR is the primary complementary imaging modality when clinical and echocardiographic findings are discordant;

its main contribution is the reproducible quantification of ventricular volumes, regurgitant volume, and regurgitant fraction, irrespective of regurgitant jet geometry.^{592,602-605}

Studies have shown that a CMR-derived regurgitant volume $\geq 55\text{--}60 \text{ mL}$ and regurgitant fraction $\geq 40\%\text{--}50\%$ are associated with a higher risk of clinical progression, development of symptoms, and future need for valve intervention.^{464,584} More recent evidence also suggests that a reduced CMR-derived left atrial emptying fraction, particularly values $< 30\%$, may identify patients with primary MR who are at higher risk of clinical events.⁶¹⁶

In addition to quantifying regurgitation, CMR enables tissue characterization using late gadolinium enhancement and parametric mapping. The presence of myocardial fibrosis is associated with more advanced ventricular remodeling, a higher risk of ventricular arrhythmias, and worse prognosis, particularly in patients with MVP and MA.^{595,596,613,614}

Cardiac CT plays a predominantly anatomical role and is used primarily for planning structural interventions. The technique enables detailed characterization of the mitral annulus, quantification of valvular and annular

Table 8.4 – Behavior of the main hemodynamic parameters according to the severity of chronic primary MR

Hemodynamic parameter	Mild MR	Moderate MR	Severe MR	Reference value	Clinical application
RAP	Normal	Normal or mildly elevated	Frequently elevated	2–8 mm Hg	Assessment of systemic congestion and RV function
mPAP	< 20 mm Hg	20–25 mm Hg	> 25 mm Hg	< 20 mm Hg	Diagnosis and quantification of PH
PCWP	≤ 15 mm Hg	15–18 mm Hg	> 18–20 mm Hg	≤ 15 mm Hg	Estimation of LA pressure and filling pressures
PCWP V wave	Small (< 15 mm Hg)	15–30 mm Hg	> 30 mm Hg	Variable	Marker of the hemodynamic consequences of MR
PVR	Normal	Usually normal	May be elevated	< 2 WU	Differentiation between post-capillary and pre-capillary components
Cardiac output	Normal	Normal	May be reduced	4–8 L/min	Assessment of overall circulatory function
Cardiac index	Normal	Usually preserved	May be reduced	≥ 2.2 L/min/m ²	Assessment of hemodynamic reserve
SvO ₂	Normal	Usually preserved	May be reduced	60%–80%	Balance between oxygen delivery and consumption
PASP	< 35 mm Hg	35–50 mm Hg	> 50 mm Hg	< 35 mm Hg	Quantification of the pulmonary hemodynamic consequences of the disease

LA: left atrial; mPAP: mean pulmonary artery pressure; MR: mitral regurgitation; PASP: pulmonary artery systolic pressure; PCWP: pulmonary capillary wedge pressure; PH: pulmonary hypertension; PVR: pulmonary vascular resistance; RAP: right atrial pressure; RV: right ventricular; SvO₂: mixed venous oxygen saturation; WU: Wood units.

calcification, 3D measurements, and assessment of anatomical relationships with adjacent structures relevant to transcatheter procedures.^{593,604}

8.1.4.5. Genetic Evaluation

Most cases of degenerative chronic primary MR occur sporadically and do not require routine genetic testing. However, familial forms of MVP and inherited connective tissue disorders may be associated with early myxomatous degeneration and more complex clinical presentations.^{574,594-596,617}

Genetic evaluation should be considered in patients with early-onset disease (< 50 years), extensive myxomatous degeneration, a family history of MVP, mitral valve surgery, or SCD in first-degree relatives, as well as in the presence of features suggestive of connective tissue disorders, including Marfan, Loeys-Dietz, and Ehlers-Danlos syndromes.^{574,595,596,617}

In patients with an arrhythmic phenotype, particularly in the presence of mitral annular disjunction, myocardial fibrosis, or a family history of SCD, genetic evaluation may

aid counseling and family screening, although its role in therapeutic decision-making remains limited.^{595,596,618,619}

8.1.4.6. Medical Therapy

No pharmacological treatment can correct or halt the progression of primary MR resulting from an anatomical valvular lesion. To date, no pharmacological therapy has consistently been shown to reduce the severity of regurgitation, delay the need for intervention, or modify the natural history of the disease in patients with preserved ventricular function.^{574,583} Accordingly, medical therapy is aimed at controlling symptoms, managing comorbidities, and monitoring disease progression. Strict control of hypertension is recommended, while AF, HF, and other associated cardiovascular conditions should be managed in accordance with their respective guidelines.⁵⁷⁴

Diuretics may be used to relieve congestion and symptoms of HF but do not replace valve intervention when criteria for intervention are met. Vasodilators, renin-angiotensin-aldosterone system inhibitors, ARNIs, and SGLT2i are not

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Table 8.5 – Main biomarkers in chronic primary MR

Biomarker	Biological significance	Potential clinical application	Current limitations
BNP	Ventricular wall stress and volume overload	Complementary prognostic stratification	No validated cutoff for indicating intervention
NT-proBNP	Myocardial stress and increased filling pressures	Complementary prognostic stratification and longitudinal follow-up	Influenced by age, kidney function, and AF
High-sensitivity cardiac troponin	Subclinical myocardial injury	Potential complementary prognostic marker	Insufficient evidence for routine use
sST2	Myocardial remodeling and fibrosis	Potential complementary prognostic marker	Predominantly investigational use
Galectin-3	Myocardial fibrosis and inflammation	Potential complementary prognostic marker	Predominantly investigational use
Integration of biomarkers and advanced imaging	Combined assessment of remodeling, fibrosis, and ventricular function	Emerging strategy for research and prognostic stratification	No prospective validation for clinical decision-making

AF: atrial fibrillation; BNP: B-type natriuretic peptide; NT-proBNP: N-terminal pro-B-type natriuretic peptide; sST2: soluble suppression of tumorigenicity 2. Note: currently, there are no universally accepted cutoff values for BNP, NT-proBNP, or other biomarkers that can independently define the severity of MR or indicate the need for valve intervention.^{584,612-615}

routinely indicated for the treatment of primary MR in the absence of other established clinical indications.^{574,583,620}

In patients who develop left ventricular dysfunction or HF, pharmacological therapy should follow current guideline recommendations for HF, in parallel with periodic reassessment of the severity of MR and the need for valve intervention.⁵⁷⁴

8.1.4.7. Indications for Intervention

Intervention in chronic primary MR is aimed at preventing left ventricular systolic dysfunction, AF, pulmonary hypertension, and VHD-related death. Because disease progression may occur before the onset of symptoms, early identification of markers of clinical and structural deterioration is essential to determine the optimal timing of intervention.^{597,598,606}

Therapeutic decision-making should integrate symptoms, regurgitation severity, cardiac consequences, valve anatomy, individual risk, and the likelihood of durable repair. In patients with a flail leaflet, an early surgery strategy has been associated with better long-term outcomes compared with initial observation, reinforcing the importance of intervention before the development of irreversible cardiac remodeling.⁵⁹⁸

Whenever technically feasible, surgical mitral valve repair should be preferred over valve replacement because it is associated with lower operative mortality, better preservation of ventricular function, and greater long-term survival.^{580,619} At specialized centers, repair rates exceeding 95% and operative mortality rates below 1% can be achieved in patients with degenerative MVP. This concept has been reinforced in contemporary recommendations, which emphasize early intervention in asymptomatic patients with severe primary MR, repairable anatomy, and objective markers of increased risk, provided that the procedure is performed at centers

with extensive expertise in mitral valve repair.^{619,620} In addition, minimally invasive surgical techniques have shown outcomes comparable to those of conventional sternotomy at experienced centers, expanding therapeutic options for patients who are candidates for mitral valve repair.⁶²¹

Transcatheter therapies have expanded treatment options for patients with severe MR and high or prohibitive surgical risk. TEER is currently the main established alternative in this setting, whereas transcatheter mitral valve replacement (TMVR) using dedicated prostheses represents an emerging strategy for selected patients with anatomy unfavorable for repair and high surgical complexity.^{589,590,593,596,621} Contemporary studies have demonstrated high procedural success rates, low rates of residual MR, and consistent clinical outcomes across different TEER platforms, further supporting the established role of this strategy in appropriately selected patients.^{589,622}

Complex cases should be evaluated by a specialized Heart Team, considering valve reparability, eligibility for transcatheter therapies, expected treatment durability, frailty, comorbidities, and surgical risk. In patients with MVP associated with an arrhythmic phenotype, the presence of mitral annular disjunction, myocardial fibrosis, or complex ventricular arrhythmias may contribute to risk stratification, although these findings alone do not currently constitute an indication for valve intervention.^{595,596,617,618}

Volumetric parameters, myocardial fibrosis, and advanced markers of remodeling may complement traditional measures in identifying patients who may benefit from early intervention, but their use should remain integrated with established clinical, echocardiographic, and anatomical criteria.^{603-605,613,614} The main indications for surgical and transcatheter intervention in chronic primary MR are summarized in Table 8.6.

Table 8.6 – Main indications for intervention in chronic primary MR

Clinical scenario	Strength of recommendation	Certainty of evidence	Recommended intervention	Targets
Primary MR				
Symptomatic severe MR with acceptable operative risk ^{597,598,606,619,620}	STRONG	MODERATE	Mitral valve intervention, preferably surgical repair. Gold standard; consistent benefit.	
Symptomatic severe MR with favorable anatomy and high or prohibitive surgical risk ^{589,590}	STRONG	MODERATE	TEER favored. Validated alternative.	
Asymptomatic severe MR with LVEF ≤ 60% or LVESD ≥ 40 mm ^{597,598}	STRONG	MODERATE	Mitral valve intervention, preferably surgical repair. Established indication for early intervention.	
Severe MR when intervention is indicated and degenerative anatomy is suitable for repair ^{580,619,620}	STRONG	MODERATE	Surgical mitral valve repair preferred over surgical valve replacement.	
Asymptomatic severe MR with recent-onset AF attributable to MR ^{597,598}	STRONG	MODERATE	Surgery favored. Depends on local expertise.	
Asymptomatic severe MR with PH (PASP > 50 mm Hg at rest) ^{597,598,607,610,611}	STRONG	MODERATE	Surgery favored. Depends on local expertise.	
Asymptomatic severe MR with a high likelihood of durable repair (> 95%) and low operative mortality at a specialized center ^{598,600,619}	CONDITIONAL	MODERATE	Consider early intervention, preferably surgical repair. Experienced center is essential.	
Symptomatic severe MR with anatomy unsuitable for TEER and high or prohibitive surgical risk ^{593,605,621}	CONDITIONAL	LOW	Consider TMVR with a dedicated prosthesis at a specialized center.	
Ventricular secondary MR				
Symptomatic despite optimized medical therapy	STRONG	MODERATE	TEER favored.	COAP-like
Need for concomitant cardiac surgery	STRONG	LOW	Surgery favored.	Clinical consensus.
High surgical risk	STRONG	MODERATE	TEER favored.	Individualize.
Atrial secondary MR				
Preserved LVEF with atrial dilatation	CONDITIONAL	LOW	Surgery favored	Emerging phenotype
High surgical risk	WEAK	LOW	TEER favored	Limited evidence
Moderate MR with another concomitant cardiac surgery	CONDITIONAL	LOW	Concomitant mitral valve intervention favored	Individualize
Severe MR with surgery for another valve disease	STRONG	LOW	Concomitant mitral valve intervention favored	Integrated approach
Patients not eligible for intervention because of frailty or limited life expectancy	STRONG	LOW	Medical/palliative management favored	Focus on quality of life

AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; MR: mitral regurgitation; PASP: pulmonary artery systolic pressure; PH: pulmonary hypertension; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve replacement.

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8.1.4.8. Follow-Up

The frequency of follow-up should be individualized according to the presence of symptoms, stability of echocardiographic findings, functional capacity, occurrence of AF, left ventricular function, ventricular volumes, left atrium size, PASP, and parameters of severity of MR.^{597,603-606} Suggested intervals for clinical and echocardiographic follow-up are summarized in Table 8.7.

The development of symptoms, new-onset AF, pulmonary hypertension, or deterioration of ventricular function should prompt reassessment of the therapeutic strategy. Similarly, evidence of progressive cardiac remodeling may warrant earlier intervention even in asymptomatic patients.^{597,598}

Following surgical or transcatheter intervention, periodic clinical and echocardiographic follow-up is recommended to assess ventricular function, procedural durability, recurrence of MR, and potential treatment-related complications.^{589,590,619,620}

8.1.4.9. Mandatory Update Table

Although the fundamental principles underlying the diagnosis and treatment of chronic primary MR have been established for decades, recent advances have substantially expanded our understanding of the natural history of the disease, mechanisms of progression, risk stratification, and available therapeutic options. Major developments incorporated into the 2026 update include the consolidation of transcatheter therapies, development of TMVR, increasing use of advanced multimodality imaging, recognition of the arrhythmic phenotype associated with MVP, advances in the genetics of degenerative mitral valve disease, and the growing importance of specialized mitral valve repair centers, as presented in Table 8.8.

8.1.5. Secondary Mitral Regurgitation

8.1.5.1. Prevalence and Etiology

Secondary MR is the most common form of MR in patients with HF and left ventricular dysfunction.

Observational studies have reported a prevalence of moderate or severe MR of approximately 20%–35% amongst patients with HF, with an associated increase in hospitalizations and cardiovascular mortality.⁵⁸⁶⁻⁵⁸⁸ The main etiologies of secondary MR include ischemic heart disease, which accounts for approximately 40%–50% of cases, nonischemic dilated cardiomyopathy (30%–40%), and AF associated with atrial functional MR (AFMR [10%–20%]), the clinical importance of which has been increasingly recognized in recent years.^{575,585}

8.1.5.2. Pathophysiology of Secondary Mitral Regurgitation

Unlike primary MR, secondary MR results from ventricular or atrial remodeling in the presence of structurally normal mitral leaflets.^{574,585-588} The main etiologies include ischemic heart disease, nonischemic dilated cardiomyopathy, and chronic AF. Secondary MR is currently recognized as a heterogeneous syndrome encompassing ventricular and atrial functional phenotypes with distinct pathophysiological mechanisms, prognoses, and therapeutic strategies.^{585-588,624}

In the ventricular functional form, considered the classic and historically most extensively studied presentation of secondary MR, regurgitation results from eccentric left ventricular remodeling associated with ischemic heart disease or dilated cardiomyopathy. In contemporary series, ischemic heart disease accounts for approximately 40%–50% of secondary MR cases, whereas nonischemic cardiomyopathies account for approximately 30%–40%.⁵⁸⁵⁻⁵⁸⁸ Eccentric ventricular dilatation leads to apical and lateral displacement of the papillary muscles, increased tethering forces, restricted leaflet coaptation, and the development of progressive MR. This mechanism predominantly corresponds to Carpentier functional type IIIB and establishes a feedback loop between MR, ventricular remodeling, and HF.⁵⁸⁶⁻⁵⁸⁸

Over the past 2 decades, this phenotype has become the principal pathophysiological model of secondary MR, underpinning much of the evidence from observational

Table 8.7 – Suggested follow-up intervals for chronic primary mitral regurgitation

Severity of MR	Clinical assessment	Echocardiography
Mild	Every 3–5 years	Every 3–5 years
Moderate	Annually	Every 1–2 years
Asymptomatic severe MR (LVEF > 60% and LVESD < 40 mm)	Every 6–12 months	Every 6–12 months
Severe MR approaching the threshold for intervention*	Every 3–6 months	Every 3–6 months
After surgical or transcatheter intervention	Individualized	According to the type of intervention and follow-up findings

LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; MR: mitral regurgitation; PH: pulmonary hypertension. *Patients with progressive ventricular enlargement, declining LVEF, new-onset atrial fibrillation, pulmonary hypertension, or other markers of clinical progression.

Table 8.8 – Key evidence incorporated into the update on chronic primary mitral regurgitation

Trial/area	Population	Main finding	Impact on SBC 2026
UK Mini Mitral Trial ⁵⁹¹	Degenerative MR with an indication for surgery	Minithoracotomy yielded clinical outcomes comparable to conventional sternotomy	Strengthened role of minimally invasive surgery at experienced centers
EXPAND Registry ⁵⁸⁹	Patients undergoing TEER	High procedural success rates and low residual MR in contemporary clinical practice	Consolidation of TEER in appropriately selected patients
CLASP IID ⁶²²	Degenerative MR eligible for TEER	Consistent clinical and echocardiographic outcomes across contemporary edge-to-edge repair platforms	Consolidation of edge-to-edge therapies
Advanced multimodality imaging (3D echocardiography, CMR, and cardiac CT) ^{593,606}	Degenerative MR	Improved anatomical characterization, quantification of regurgitation, and treatment planning	Greater role of multimodality imaging in clinical decision-making
Arrhythmic phenotype of MVP ^{595,596,617,618}	MVP	Association of MAD and myocardial fibrosis with ventricular arrhythmias	More refined risk stratification in selected patients
Genetics of degenerative mitral valve disease ⁶²³	Myxomatous disease and MVP	Improved understanding of the genetic basis of myxomatous degeneration and MVP	Inclusion of genetic evaluation in selected settings
TMVR with dedicated prostheses ⁶²¹	Severe MR with high surgical risk	Promising initial outcomes in patients unsuitable for repair	Inclusion of TMVR as an emerging therapy for selected patients
Specialized mitral valve repair centers ^{619,620}	Degenerative MR with repairable anatomy	Repair rates > 95% and operative mortality < 1% at experienced centers	Greater emphasis on centralization of complex cases and Heart Team assessment

3D: three-dimensional; CMR: cardiac magnetic resonance; CT: computed tomography; MAD: mitral annular disjunction; MR: mitral regurgitation; MVP: mitral valve prolapse; SBC: Brazilian Society of Cardiology; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve replacement.

studies, RCTs, and contemporary transcatheter therapies, including COAPT, MITRA-FR, and RESHAPE-HF2.⁵⁸⁶⁻⁵⁸⁸

In AFMR, left atrial and mitral annular dilatation may produce significant MR even in the absence of relevant ventricular remodeling. In this condition, regurgitation results predominantly from annular dilatation and reduced leaflet coaptation surface, without significant papillary muscle displacement or ventricular tethering. Initially described in patients with chronic AF and isolated annular dilatation, this condition has come to be recognized as a distinct secondary MR phenotype.⁶²⁴⁻⁶²⁶ In contemporary series of severe AFMR, approximately 90% of patients had AF and more than 80% had significant left atrial dilatation, reinforcing the close association between atrial remodeling and the development of this phenotype (Table 8.9).^{685,625,626}

8.1.5.3. Diagnostic Assessment

The diagnostic assessment of secondary MR uses the same modalities employed for primary MR, including TTE, transesophageal echocardiography (TEE), 3D echocardiography, CMR, cardiac CT, biomarkers, and invasive hemodynamic assessment in selected situations. Unlike primary MR, however, interpretation of these modalities should emphasize characterization of the underlying ventricular or atrial remodeling, myocardial function, and the interaction between regurgitation severity and the underlying cardiac disease. The main differences in the application and interpretation of diagnostic modalities between primary and secondary MR are summarized in Table 8.10.^{582,583,593,605}

Echocardiography remains the central modality for identifying the mechanism of regurgitation, differentiating

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Table 8.9 – Evolution of the recognition of atrial functional mitral regurgitation as a distinct phenotype of secondary mitral regurgitation

Study	Scientific Question	Main Contribution	Impact on the Field
Otsuji et al. (2002) ⁶²⁴	Can isolated annular dilatation cause functional MR in the absence of ventricular disease?	Demonstrated that annular dilatation associated with AF can cause functional MR in the absence of significant ventricular remodeling	Introduction of the concept of AFMR
Deferm et al. (2019) ⁶²⁵	What are the characteristics and clinical course of patients with AFMR?	Described the prevalence, clinical characteristics, and outcomes associated with the atrial phenotype	Consolidation of the clinical entity
Machino-Ohtsuka et al. (2016) ⁶²⁶	What are the anatomical and echocardiographic markers of AFMR?	Characterized atrial remodeling, annular dilatation, and specific echocardiographic patterns	Anatomical and echocardiographic definition of the phenotype
Contemporary studies (2020–2025) ^{585,624-626}	Does AFMR represent an entity distinct from ventricular functional MR?	Confirmation of distinct pathophysiological mechanisms, prognosis, and potential therapeutic strategies	Formal recognition of AFMR as a distinct phenotype within secondary MR

AF: atrial fibrillation; AFMR: atrial functional mitral regurgitation; MR: mitral regurgitation.

Table 8.10 – Main differences in the interpretation of diagnostic modalities between primary and secondary MR

Diagnostic modality	Chronic primary MR	Secondary MR
Transthoracic echocardiography	Assessment of valve anatomy and quantification of MR	Quantification of MR and characterization of ventricular or atrial remodeling
Transesophageal echocardiography	Definition of the degenerative mechanism and surgical/transcatheter planning	TEER/TMVR planning and advanced anatomical assessment
3D echocardiography	Anatomical characterization of the leaflets and mitral annulus	Assessment of tethering and annular geometry and structural intervention planning
Cardiac magnetic resonance imaging	Quantification of regurgitation, ventricular volumes, and fibrosis	Quantification of regurgitation, myocardial characterization, and assessment of ventricular remodeling
Cardiac computed tomography	Complementary anatomical assessment	Planning of structural procedures, particularly TMVR
Biomarkers (BNP/NT-proBNP)	Complementary markers of hemodynamic consequences	Key prognostic markers associated with heart failure
Right heart catheterization	Selected cases and diagnostic discrepancies	Assessment of hemodynamic consequences and pulmonary hypertension

BNP: B-type natriuretic peptide; MR: mitral regurgitation; NT-proBNP: N-terminal pro-BNP; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve replacement.

ventricular and atrial phenotypes, and quantifying the underlying cardiac remodeling.^{582,583,585} Unlike primary MR, echocardiographic findings in secondary MR should be interpreted in conjunction with the degree of cardiac remodeling. This relationship was highlighted by the MITRA-FR and COAPT trials, in which patients with apparently similar secondary MR had different clinical outcomes following transcatheter intervention, reinforcing the importance of

an integrated assessment of regurgitation severity and the extent of underlying myocardial disease.^{627,628} Grayburn et al. subsequently proposed the concepts of proportionate and disproportionate MR, providing a pathophysiological framework for interpreting the interaction between ventricular remodeling and severity of MR.⁵⁸¹

Quantification of secondary MR should be multiparametric. An effective regurgitant orifice area (EROA) ≥ 0.20 cm²,

regurgitant volume ≥ 30 mL, and regurgitant fraction $\geq 50\%$ are consistent with severe secondary MR and should always be interpreted in the clinical context and in relation to the extent of cardiac remodeling and severity of the underlying myocardial disease.⁵⁸²⁻⁵⁸⁵ No single parameter should be used in isolation to determine the severity of secondary MR.

In ventricular functional MR, the predominant features are ventricular dilatation, papillary muscle displacement, tethering, and systolic leaflet restriction (Carpentier type IIIb). In AFMR, left atrial and mitral annular dilatation predominate, generally with preserved ejection fraction.^{585,624-626}

Lancellotti et al. demonstrated that secondary MR is dynamic and may increase significantly during exercise, with such an increase being associated with worse prognosis. This finding supports the role of stress echocardiography in patients whose symptoms are disproportionate to findings at rest.⁶²⁹

More recently, 3D echocardiography has assumed an increasing role in the assessment of valve geometry, degree of tethering, annular anatomy and in the planning of transcatheter therapies, particularly TEER and TMVR.^{589,590,593} In addition to echocardiography, CMR, cardiac CT, and invasive hemodynamic assessment may provide complementary information for risk stratification and treatment planning in selected cases, particularly when clinical and echocardiographic findings are discordant or when transcatheter intervention is being considered.^{605,693}

8.1.5.4. Severity and Risk Stratification

Secondary MR is associated with increased HF hospitalizations, cardiovascular mortality, and all-cause mortality. Observational studies have demonstrated that moderate-to-severe MR is an independent prognostic marker

of adverse events and is associated with an approximately 40%–70% increase in mortality risk compared with the absence of significant MR, even after adjustment for the severity of left ventricular dysfunction.^{584,611} Unlike chronic primary MR, however, prognosis depends not only on the severity of MR but also on the interaction between MR, ventricular remodeling, and the underlying myocardial disease.^{582,611} This concept was reinforced by the MITRA-FR and COAPT trials, which yielded different outcomes for transcatheter mitral repair in patients with apparently similar secondary MR.^{627,628} To explain these differences, Grayburn et al. proposed the concepts of proportionate and disproportionate MR, according to which the magnitude of MR should be interpreted in relation to the degree of ventricular dilatation rather than in isolation.⁵⁸¹

EROA ≥ 0.20 cm², regurgitant volume ≥ 30 mL, and MR fraction $\geq 50\%$ are consistent with severe secondary MR and are associated with worse clinical outcomes.⁵⁸²⁻⁵⁸⁵ Right ventricle dysfunction and pulmonary hypertension are independent markers of worse clinical outcomes and mortality, reflecting more advanced stages of the underlying CVD.^{610,611}

Although most prognostic evidence derives from ventricular secondary MR, recent studies suggest that AFMR is also associated with increased HF hospitalizations, recurrent AF, and mortality, reinforcing the need for appropriate risk stratification in these patients.^{585,625,626}

There is currently no universally validated prognostic score for secondary MR. In candidates for valve intervention, the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) and the EuroSCORE II may complement the Heart Team's assessment of procedural risk, although neither was developed specifically for prognostic stratification in secondary MR. The main components of contemporary risk stratification are summarized in Table 8.11.

Table 8.11 – Markers associated with worse prognosis in secondary MR

Domain	Marker	Prognostic association
Severity of MR	EROA ≥ 0.20 cm ²	↑ HF hospitalization; ↑ mortality
	Regurgitant volume ≥ 30 mL	↑ cardiovascular events
	Regurgitant fraction $\geq 50\%$	↑ clinical progression
Left ventricular remodeling	Increased LVESV/LVEDV	↑ mortality
	Reduced LVEF	↑ mortality and HF
RV	RV dysfunction	Strong adverse prognostic marker
Pulmonary circulation	Pulmonary hypertension	↑ mortality and worse therapeutic response
Hemodynamics	Elevated PCWP/prominent V wave	Greater hemodynamic burden
Biomarkers	Elevated BNP/NT-proBNP	↑ hospitalization and mortality
AFMR	Significant atrial dilatation	↑ recurrent atrial fibrillation and HF
Stress echocardiography	Increased MR during exercise	↑ symptoms and worse prognosis

AFMR: atrial functional mitral regurgitation; BNP: B-type natriuretic peptide; EROA: effective regurgitant orifice area; HF: heart failure; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; MR: mitral regurgitation; NT-proBNP: N-terminal pro-BNP; PCWP: pulmonary capillary wedge pressure; RV: right ventricular.

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8.1.5.5. Medical Management of Secondary Mitral Regurgitation

Unlike chronic primary MR, in which valve correction is the cornerstone of treatment, the management of secondary MR is based on optimal treatment of HF and the underlying cardiac disease. Reduction of ventricular remodeling through GDMT, CRT, and, when indicated, myocardial revascularization may reduce the severity of MR and modify its clinical course.^{582,586-588}

Optimization of medical therapy should precede any decision regarding intervention. Contemporary GDMT includes ARNIs, beta-blockers, MRAs, and SGLT2i, therapies associated with reductions in mortality, HF hospitalizations, and adverse ventricular remodeling.^{236,629-632} The incorporation of SGLT2i has further established the concept of maximally optimized medical therapy before consideration of advanced valve therapies.^{236,632}

CRT should be considered in eligible patients and may promote reverse remodeling, improve mechanical synchrony, and reduce functional MR. Studies have demonstrated significant reductions in MR and reverse ventricular remodeling in a substantial proportion of patients undergoing CRT, associated with improved clinical outcomes and prognosis.^{633,634}

In MR secondary to AF, management of AF, optimization of HF therapy when appropriate, and reduction of atrial volume overload are important components of the initial therapeutic strategy. Although the evidence is less robust than that available for ventricular secondary MR, contemporary studies suggest that treatment of the arrhythmia and atrial remodeling may favorably influence the clinical course of these patients.^{585,624-626,590,635,636}

In patients with ischemic heart disease, assessment of myocardial viability and the need for revascularization remains a fundamental component of the therapeutic strategy. In selected cases, revascularization alone may reduce the severity of MR by improving regional and global ventricular function.⁵⁸⁶⁻⁵⁸⁸

The severity of MR may decrease following optimization of medical therapy and ventricular remodeling, supporting systematic reassessment before advanced valve therapies are indicated.^{582,586-588}

After optimization and stabilization of HF treatment, clinical and echocardiographic reassessment is recommended to determine the persistence of MR, its hemodynamic consequences, and the need for additional therapies. Symptomatic patients with persistent, hemodynamically significant secondary MR despite optimized GDMT should be evaluated by a multidisciplinary team involving HF specialists, cardiovascular imaging specialists, interventional cardiologists, and cardiac surgeons.⁵⁸⁶⁻⁵⁹⁰

Recommendations for the medical management of secondary MR	Strength of recommendation	Certainty of Evidence
Optimized GDMT for HF is recommended as initial treatment for patients with secondary MR associated with left ventricular dysfunction. ^{236,630-632}	STRONG	HIGH

Clinical and echocardiographic reassessment after optimization of GDMT is recommended before surgical or transcatheter valve therapies are considered. ^{582,586-590}	STRONG	LOW
Cardiac resynchronization therapy is recommended for eligible patients according to HF guidelines. ^{633,634}	STRONG	HIGH
Assessment of myocardial viability and the need for revascularization should be considered in patients with ischemic heart disease and secondary MR. ⁵⁸⁶⁻⁵⁸⁸	STRONG	LOW
Management of AF and associated conditions should be considered in patients with MR secondary to AF. ^{585,624-626,636}	CONDITIONAL	LOW
Patients with persistent symptomatic secondary MR despite optimized GDMT should be evaluated by the Heart Team to determine the therapeutic strategy. ⁵⁸⁶⁻⁵⁹⁰	STRONG	LOW

AF: atrial fibrillation; CRT: cardiac resynchronization therapy; GDMT: guideline-directed medical therapy; HF: heart failure; MR: mitral regurgitation.

8.1.5.6. Transcatheter and Surgical Therapies

Despite optimization of medical therapy, some patients remain symptomatic with significant secondary MR. In these cases, surgical or transcatheter valve therapies may be considered after evaluation by a specialized Heart Team.⁵⁸⁶⁻⁵⁹⁰ Contemporary recommendations for surgical and transcatheter therapies in secondary MR are summarized in Table 8.12.

The development of TEER has substantially changed the treatment of secondary MR. The MITRA-FR trial randomly assigned 304 patients with severe secondary MR to either TEER or medical therapy alone and found no significant reduction in the composite endpoint of death or hospitalization for HF at 12 months compared with medical therapy alone (54.6% vs. 51.3%, respectively; $p = 0.53$).⁶²⁷ The enrolled population had more dilated ventricles (mean [SD] indexed left ventricular end-diastolic volume of 135 [35] mL/m²) and relatively less severe regurgitation (mean EROA, 31 mm²), suggesting a predominant prognostic impact of the underlying cardiomyopathy.⁶²⁷

In contrast, the COAPT trial randomized 614 patients with persistent secondary MR despite optimized GDMT and demonstrated a significant reduction in HF hospitalizations at 24 months (35.8% vs. 67.9%; HR 0.53; 95%CI 0.40–0.70; $p < 0.001$) as well as a reduction in all-cause mortality (29.1% vs. 46.1%; HR 0.62; 95%CI 0.46–0.82; $p < 0.001$).⁶²⁸ Patients had more severe MR (mean EROA, 41 mm²) and less advanced ventricular remodeling (mean [SD] indexed left ventricular end-diastolic volume of 101 [34] mL/m²), reinforcing the importance of appropriate patient selection for intervention.⁶²⁸

To explain these apparently divergent results, Grayburn et al. proposed the concepts of proportionate and disproportionate MR, suggesting that patients with regurgitation disproportionate to the degree of ventricular remodeling are more likely to benefit from valve intervention, whereas those with very advanced ventricular dilatation have a prognosis driven predominantly by the underlying cardiomyopathy.⁵⁸¹

More recently, the RESHAPE-HF2 trial randomly assigned 505 patients with persistent secondary MR despite optimized GDMT to either TEER or medical therapy alone and demonstrated a reduction in the composite outcome of HF hospitalization and cardiovascular mortality (37.0 vs. 58.9 events per 100 patient-years; RR 0.64; 95%CI 0.48–0.85; $p = 0.002$).⁵⁸⁷ This trial became the second major positive RCT after COAPT, further supporting the consistency of the benefit of TEER in appropriately selected patients.

Contemporary registries have reinforced the applicability of these findings in clinical practice. In the EXPAND Registry, which included more than 1,000 patients treated with MitraClip, procedural success exceeded 95%, with MR $\leq 2+$ in approximately 90% of patients after the procedure and sustained improvement in functional class.⁵⁸⁹ Similar findings were observed in the COAPT Post-Approval Study,

demonstrating the reproducibility of RCT results in real-world populations.⁵⁹⁰ In addition, the 5-year follow-up of COAPT confirmed the durability of the clinical benefit of TEER, with sustained reductions in HF hospitalizations and mortality.⁶³⁵

More recently, the MATTERHORN trial directly compared TEER with surgery in patients with secondary MR. The study demonstrated noninferiority of TEER for the composite endpoint of death, HF hospitalization, need for mechanical circulatory support, or valve reintervention, as well as a lower incidence of perioperative complications.⁵⁸⁸

TMVR represents an emerging alternative for patients with anatomy unsuitable for repair or high surgical complexity. Contemporary studies using dedicated platforms have demonstrated high technical success rates, near-complete elimination of MR, and sustained functional improvement, although the technology remains in a phase of clinical expansion and investigation.^{593,621} Recent 5-year follow-up data with the Intrepid system have further supported the feasibility of this strategy in appropriately selected patients.⁶³⁷

In parallel, emerging evidence suggests that AFMR represents a distinct phenotype from secondary MR caused by ventricular dysfunction. Contemporary observational data have shown an association between TEER and reductions in death or HF hospitalization among patients with moderate-to-severe AFMR, increasing interest in therapeutic strategies specifically targeted to this population.⁶³⁶⁻⁶³⁸

TMVR with the SAPIEN M3 system has emerged as a potential alternative for patients with significant symptomatic MR who are considered unsuitable for conventional surgery or TEER. The main evidence currently available derives from the ENCIRCLE study,⁶³⁹ a prospective multicenter single-arm trial that demonstrated a high procedural success rate, consistent reduction of MR to $\leq 1+$, and significant improvements in functional class and quality of life. Adverse event rates were considered acceptable in a population at high surgical risk. The system incorporates a dedicated anchoring mechanism (mitral dock), allowing transseptal implantation and reducing the risk of complications such as prosthesis embolization and left ventricular outflow tract (LVOT) obstruction. However, because the available data derive from nonrandomized studies without direct comparison with other therapeutic strategies, this approach may be considered conditionally in favor of use, with low certainty of evidence, and its indication should be individualized within the context of an experienced Heart Team.

Table 8.12 – Recommendations for surgical and transcatheter therapies in secondary MR

Clinical scenario	Strength of recommendation	Certainty of evidence	Recommended intervention
Persistent symptomatic severe secondary MR despite optimized GDMT, favorable anatomy, and Heart Team evaluation. ^{586,587,589,590}	STRONG	MODERATE	Mitral repair (TEER)
Severe secondary MR in patients undergoing CABG or other concomitant cardiac surgery. ^{586,597}	STRONG	MODERATE	Surgical correction of MR during the primary procedure

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Symptomatic severe secondary MR despite optimized GDMT and eligible for intervention. ^{586,587,589,590}	WEAK	MODERATE	Consider TEER to reduce HF hospitalizations and improve prognosis
Severe secondary MR with anatomy unsuitable for TEER and acceptable surgical risk. ^{586,597}	WEAK	LOW	Consider mitral valve surgery in selected patients
Severe secondary MR with anatomy unsuitable for TEER and high or prohibitive surgical risk. ^{583,605,621}	WEAK	LOW	Consider TMVR with dedicated prostheses at specialized centers
Severe secondary MR associated with advanced HF and candidacy for advanced therapies. ^{586,597}	WEAK	LOW	Individualize the therapeutic strategy at specialized centers
Persistent symptomatic atrial secondary MR despite optimized medical therapy. ⁶³⁶	WEAK	MODERATE	Consider TEER in selected patients after Heart Team evaluation

CABG: coronary artery bypass grafting; GDMT: guideline-directed medical therapy; HF: heart failure; MR: mitral regurgitation; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve replacement.

8.1.5.7. Clinical and Echocardiographic Follow-Up

Clinical and echocardiographic follow-up is an essential component of the management of MR. Its main objectives are to monitor disease progression, identify cardiac structural consequences at an early stage, detect the onset of symptoms or associated complications, and determine the most appropriate timing for intervention. Serial monitoring enables recognition of the transition from compensated to decompensated disease and may prevent therapeutic delay potentially associated with irreversible cardiac damage.^{597,598} Suggested intervals for clinical and echocardiographic follow-up of MR are summarized in Table 8.13.

In primary MR, follow-up should focus on the early identification of prognostic markers associated with disease progression. In addition to periodic clinical assessment, serial echocardiography allows monitoring of regurgitation severity, LVEF, left ventricular end-systolic diameter, left atrial remodeling, and PASP. Particular attention should be paid to the development of new-onset AF, pulmonary hypertension, and changes in left ventricular function, as these findings are associated with worse prognosis and may constitute criteria for intervention even in the absence of symptoms.^{597,598,607,610,611}

In secondary MR, follow-up should encompass not only the course of MR but also progression of the underlying cardiac disease. In these patients, longitudinal assessment of left ventricular function, the degree of ventricular remodeling, clinical stability of HF, and occurrence of hospitalizations is integral to risk stratification. Unlike primary MR, there are no universally established follow-up intervals for secondary MR; therefore, the frequency of assessments should be individualized according to the course of HF, response to medical therapy, and therapeutic strategy adopted, including TEER, surgery, or TMVR.^{586,587,597}

TTE remains the primary imaging modality for longitudinal follow-up of MR, allowing monitoring of severity of MR, ventricular function, cardiac remodeling, and associated hemodynamic consequences. In selected situations, particularly when there is a discrepancy between symptoms and findings at rest, stress echocardiography, CMR, or cardiac CT may provide complementary information for prognostic stratification and clinical decision-making.^{597,598,614}

Following valve intervention, clinical and echocardiographic follow-up remains essential to document the baseline procedural result, monitor the durability of the correction achieved, and detect complications or disease recurrence at an early stage. In patients undergoing TEER, follow-up should include systematic assessment of residual or recurrent MR, transmitral gradient, cardiac remodeling, and functional status. In patients treated with TMVR, prosthetic valve function, transvalvular gradients, valve thrombosis, and the need for reintervention should also be monitored.^{586,588-590,621}

Table 8.13 – Suggested intervals for clinical and echocardiographic follow-up of mitral regurgitation

Severity of MR	Clinical assessment	Echocardiography
Mild	Every 3–5 years	Every 3–5 years
Moderate	Annually	Every 1–2 years
Asymptomatic severe MR (LVEF > 60% and LVESD < 40 mm)	Every 6–12 months	Every 6–12 months
Severe MR approaching the threshold for intervention*	Every 3–6 months	Every 3–6 months
After surgical repair or TEER	Individualized	Baseline post-procedure and periodic follow-up
After surgical valve replacement or TMVR	Individualized	Baseline post-procedure and periodic follow-up

*LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; MR: mitral regurgitation; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve replacement. *Patients with progressive ventricular enlargement, declining LVEF, new-onset atrial fibrillation, pulmonary hypertension, increasing regurgitation severity, or other markers of clinical progression.*

8.1.5.8. Mandatory Update Table

Although current recommendations for secondary MR are based primarily on pivotal studies that established the role of TEER and surgical strategies, more recent evidence continues to refine patient selection, assessment of durability, the role of emerging technologies, and incorporation of specific disease phenotypes. The main contemporary advances with potential impact on future Brazilian guidelines for secondary MR are summarized in Table 8.14.

8.1.5.9. Final Comparative Table

Primary MR is predominantly a valvular disease in which therapeutic decision-making is guided by the severity of MR and the optimal timing of intervention. In contrast, secondary MR represents a complex syndrome resulting from the interaction among MR, cardiac remodeling, and the underlying myocardial disease. The main pathophysiological, diagnostic, prognostic, and therapeutic differences between these two entities are summarized in Table 8.15.

Table 8.14 – Contemporary evidence with potential impact on future Brazilian guidelines for secondary mitral regurgitation

Study/topic	Year	Type of evidence	Population	Main finding	Potential impact in 2026
COAPT Post-Approval Study ⁵⁹⁰	2023	Real-world registry	Secondary MR treated with TEER	Reproduced the benefits observed in COAPT in an unselected population	External validation of TEER outcomes
COAPT – 5-year follow-up ⁶³⁵	2023	RCT follow-up	Severe secondary MR and symptomatic HF	Sustained benefit of TEER with reductions in HF hospitalizations and mortality	Consolidates TEER as a disease-modifying therapy
RESHAPE-HF ⁵⁸⁷	2024	RCT	Symptomatic HF with moderate-to-severe secondary MR	Significant reduction in HF hospitalizations and cardiovascular mortality	Strengthens the recommendation in favor of TEER
MATTERHORN ⁵⁸⁸	2024	RCT	Severe secondary MR eligible for surgery	TEER was noninferior to surgery for composite clinical outcomes	Potential expansion of TEER indications in selected surgical candidates
ENCIRCLE ⁶³⁹	2025	Multicenter observational study	MR ≥ 3+, severe MS, or MAC	TMVR with the SAPIEN M3 prosthesis	Therapeutic frontier for patients unsuitable for surgery and TEER
AFMR/TEER (REVEAL-AFMR/OCEAN-Mitral) ⁶³⁶	2026	Multicenter observational study	Moderate-to-severe AFMR	TEER associated with a reduction in death or HF hospitalization compared with medical therapy	Potential incorporation of AFMR as a specific therapeutic phenotype
TMVR – Intrepid (5-year follow-up) ⁶³⁷	2026	Prospective follow-up	Significant MR and high surgical risk	Sustained elimination of MR, low transvalvular gradients, and durable functional improvement among survivors	Strengthens TMVR as an alternative for anatomy unsuitable for surgery and TEER
TMVR – Contemporary platforms (SUMMIT, APOLLO, Tendyne) ^{593,621,637}	2024–2026	Prospective studies and registries	Patients with significant MR and complex anatomy	High technical success rates and near-complete correction of MR	Major therapeutic frontier for patients unsuitable for transcatheter mitral repair

AFMR: atrial functional mitral regurgitation; HF: heart failure; MAC: mitral annular calcification; MR: mitral regurgitation; MS: mitral stenosis; RCT: randomized controlled trial; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve replacement.

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Table 8.15 – Main differences between primary and secondary MR

Domain	Primary MR	Secondary MR
Disease mechanism	Structural abnormality of the mitral valve	Ventricular and/or atrial remodeling with a structurally normal valve
Predominant substrate	MVP, myxomatous degeneration, chordal rupture (flail leaflet), rheumatic disease	Ischemic or nonischemic cardiomyopathy, LV remodeling, AF
Carpentier classification	Predominantly type II (excessive leaflet motion)	Predominantly type IIIb (systolic restriction)
Main prognostic determinant	Severity of the valvular lesion	Severity of the underlying myocardial disease
Natural history	Progression of valvular disease	Progression of HF and ventricular remodeling
Main therapeutic goal	Correct the valvular lesion	Treat ventricular disease and reduce residual regurgitation
Goal of intervention	Definitive correction of the valvular lesion	Reduction of hemodynamic burden and improvement in clinical outcomes
Initial treatment	Assessment of valve repair or replacement	Optimized GDMT for HF
Role of surgery	Reference strategy when indicated	More selective and dependent on the clinical context
Role of TEER	Alternative for patients at high surgical risk	Central therapy in selected patients after optimized GDMT
Role of TMVR	Emerging strategy for complex or nonrepairable anatomy	Emerging strategy with potential future expansion
Role of imaging	Anatomical definition and assessment of valve reparability	Quantification of regurgitation, assessment of remodeling, and treatment selection
Risk markers	Symptoms, LVEF, LVESD, PH, and AF	LVEF, ventricular volumes, remodeling, HF hospitalizations, and mortality
Follow-up	Based on progression of regurgitation and development of criteria for intervention	Based on progression of HF, cardiac remodeling, and response to treatment
Heart Team	Definition of the valve intervention strategy	Integration of HF, cardiovascular imaging, structural intervention, and cardiac surgery

AF: atrial fibrillation; GDMT: guideline-directed medical therapy; HF: heart failure; LV: left ventricular; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; MR: mitral regurgitation; MVP: mitral valve prolapse; PH: pulmonary hypertension; TEER: transcatheter edge-to-edge repair; TMVR: transcatheter mitral valve replacement.

8.2. Mitral Stenosis

The main etiology of MS is RHD, which remains more prevalent in developing countries such as Brazil. However, population aging, including in Brazil, has led to an increasing number of cases of degenerative MS.

8.2.1. Rheumatic Mitral Stenosis

MS is the most common rheumatic valvular lesion and results from the sequelae of one or more episodes of rheumatic fever. It is characterized by thickening of the valve leaflets, which classically exhibit doming and commissural fusion, together with varying degrees of subvalvular involvement, leading to progressive reduction in mitral valve area (MVA), increased left atrial pressure, and consequent pulmonary congestion. Although this condition usually affects younger individuals, patients with rheumatic MS are not uncommonly

encountered among older adults. MS is considered clinically significant when MVA is $\leq 1.5 \text{ cm}^2$.^{640,641}

In patients with an MVA $\leq 1.5 \text{ cm}^2$ associated with symptoms or complicating features, including pulmonary hypertension (PASP $> 50 \text{ mm Hg}$) or new-onset AF, valve intervention is indicated.⁵⁷⁴

Medical therapy in this setting is useful primarily to improve symptoms before intervention, unless the patient has a contraindication to intervention, such as limited life expectancy, frailty, or severe comorbidities.

The medications used in this setting include loop diuretics, particularly furosemide, to relieve congestive symptoms, and beta-blockers. In patients with AF and contraindications to beta-blockers, nondihydropyridine CCBs or digoxin may be used to maintain a heart rate of approximately 50–60 beats per minute. Anticoagulation is indicated in the presence of

paroxysmal, persistent, or permanent AF because of the high incidence of cardioembolic events; in this setting, warfarin has been shown to be superior to DOACs.⁶⁴²

Available interventional strategies include percutaneous mitral balloon commissurotomy (PMBC) and open surgery.

PMBC is the preferred approach because it is less invasive, requires a shorter hospital stay, and is as effective as open surgical commissurotomy in appropriately selected patients. For PMBC to be the preferred procedure, the following criteria should be met:

- Absence of left atrial appendage thrombus, confirmed by TEE;
- Absence of greater-than-mild concomitant MR;
- Favorable valve morphology:
 - Block score ≤ 8 ;
 - Absence of commissural calcification.

PMBC is suggested in severely symptomatic patients (NYHA functional class III-IV) with severe MS, suboptimal valve anatomy for the procedure, and who are not candidates for surgery or are at high surgical risk.

CONDITIONAL

LOW

MS: mitral stenosis; MVA: mitral valve area; NYHA: New York Heart Association; PASP: pulmonary artery systolic pressure; PMBC: percutaneous mitral balloon commissurotomy.

8.2.1.1. Percutaneous Mitral Balloon Commissurotomy

8.2.1.2. Open Valve Surgery

Recommendation (GRADE)	Strength of recommendation	Certainty of evidence
PMBC is recommended in symptomatic patients (NYHA functional class II-IV) with severe MS (MVA ≤ 1.5 cm ²) who meet the eligibility criteria for the procedure.	STRONG	MODERATE
PMBC is suggested in asymptomatic patients with severe MS (MVA ≤ 1.5 cm ²) who are eligible for the procedure and have PASP > 50 mm Hg.	CONDITIONAL	MODERATE
PMBC is suggested in asymptomatic patients with severe MS (MVA ≤ 1.5 cm ²) who are eligible for the procedure and have new-onset atrial fibrillation.	CONDITIONAL	LOW

Recommendation	Strength of recommendation	Certainty of evidence
Surgical treatment is recommended in severely symptomatic patients (NYHA functional class III-IV) with severe MS who are not candidates for PMBC.	STRONG	MODERATE
Surgical treatment is recommended in severely symptomatic patients (NYHA functional class III-IV) with severe MS after prior failed PMBC.	STRONG	MODERATE
Surgical treatment is recommended in severely symptomatic patients (NYHA functional class III-IV) with severe MS who require another concomitant cardiac surgical procedure.	STRONG	MODERATE

MS: mitral stenosis; NYHA: New York Heart Association; PMBC: percutaneous mitral balloon commissurotomy.

Guidelines

8.2.1.3. Special Consideration

Patients with concomitant moderate-to-severe functional tricuspid regurgitation should also undergo treatment of the tricuspid lesion, either percutaneously or surgically.

8.2.2. Degenerative Mitral Stenosis

Unlike rheumatic MS, degenerative MS is not characterized by commissural fusion. Obstruction results primarily from MAC extending into the base of the valve leaflets, impairing diastolic flow and creating a tubular geometry of the stenotic valve.⁶⁴³ These patients frequently have multiple associated comorbidities, particularly atherosclerotic conditions.⁶⁴⁴ The prevalence of MAC ranges from 8% to 15% but may exceed 40% among older adults, although only a minority develop hemodynamically significant MS.⁶⁴⁵

Because of advanced age and the presence of significant comorbidities, these patients have high mortality rates, reaching 22% at 1 year and 56% at 5 years.⁶⁴⁶ Progression of MS is highly variable in this population, and the degree of annular calcification does not predict progression of the valvular lesion.⁶⁴³

Severity parameters for degenerative MS are the same as those used for rheumatic MS. The same applies to medical therapy. The major difference lies in the indications for valve intervention. Because commissural fusion is absent in this form of MS, PMBC is not indicated.⁶⁴⁷

As degenerative MS predominantly affects very old patients with substantial comorbidity and PMBC is not indicated, indications for intervention are limited. Accordingly, medical therapy has a central role, and valve intervention is generally reserved for refractory cases.

8.2.3. Current Recommendations

American College of Cardiology/American Heart Association 2020: Class IIb (low level of evidence)

- In severely symptomatic patients (NYHA functional class III/IV) with severe degenerative MS, valve intervention may be considered only after Heart Team discussion and shared decision-making with the patient and family;
- Conventional surgery is technically highly complex because of the risk of mitral annular rupture and difficulties in securing the valve prosthesis to a heavily calcified annulus;
- A transcatheter approach using valve-in-MAC consists of implantation of a transcatheter bioprosthesis anchored by the annular calcification;
- 1-year mortality is approximately 34.5%.⁶⁴⁸

Recommendation	Strength of recommendation	Certainty of evidence
Valve intervention in carefully selected patients with severe symptoms	CONDITIONAL IN FAVOR	LOW

8.3. Aortic Stenosis

8.3.1. Prevalence and Etiology

Degenerative calcific AS is the most prevalent VHD among older adults and represents a major challenge in cardiogeriatrics because of its progressive, often insidious course and its association with high morbidity and mortality. In the absence of treatment, symptomatic severe AS carries a poor prognosis, with mortality reaching up to 50% within 1–2 years after symptom onset.⁶⁴⁹

The global prevalence of calcific AS is estimated at approximately 13.6 million cases, accounting for approximately 150,000 deaths annually. The disease is more common in high-income countries, primarily reflecting differences in population age structure and access to diagnostic methods.

Its prevalence is estimated at 1%–2% among individuals older than 65 years and increases progressively with age, reaching 3%–8% among those aged 75 years or older. In this age group, more than 5% have severe forms of the disease.^{575,650}

Although AS is currently the leading VHD referred for intervention in Europe and North America,^{574,651} underdiagnosis and undertreatment remain relevant issues in contemporary clinical practice.⁶⁴⁹

In Brazil, population aging has been accompanied by a progressive increase in the prevalence of AS. Approximately 3% of the roughly 35 million older adults in the country have degenerative calcific AS, corresponding to approximately 1 million cases.

Morbidity and mortality remain high among untreated individuals, partly reflecting underuse of interventional therapies. Contributing factors include structural limitations of the health care system, logistical barriers, and restricted access to advanced therapies such as TAVI.⁶⁵¹

8.3.2. Echocardiography

TTE is the first-line method for diagnosis, severity stratification, and follow-up of patients with AS. It enables characterization of valve anatomy, including identification of the etiology, as well as qualitative assessment of leaflet mobility and degree of calcification. In addition, it allows assessment of the hemodynamic consequences of valvular obstruction on left ventricular function and cardiac geometry and identification of associated valvular or aortic disease.

TTE enables measurement of the main hemodynamic parameters used to classify AS severity, including peak transvalvular jet velocity (Vmax), mean transvalvular gradient derived from the Bernoulli equation, and effective aortic valve area (AVA), calculated using the continuity equation. Although the effective AVA is conceptually the most appropriate parameter for assessing the anatomical severity of stenosis, its estimation is subject to technical limitations, particularly those related to measurement of the LVOT diameter and the assumptions underlying the hemodynamic model.

Echocardiographic assessment should also include evaluation of the structural consequences of the disease,

such as left ventricular hypertrophy, diastolic dysfunction, and pulmonary hypertension. More recently, a staging classification based on the extent of extravalvular cardiac damage associated with AS has been proposed and has shown incremental prognostic value.⁶⁴⁹

8.3.3. Echocardiographic Criteria for Severity

Classification of AS severity is based on the integration of multiple echocardiographic parameters. Findings may be categorized as concordant or discordant according to the consistency among mean gradient, Vmax, and effective AVA.^{647,652-654}

8.3.4. Concordant Criteria

- High-gradient AS: defined by a mean transvalvular gradient ≥ 40 mm Hg, Vmax ≥ 4.0 m/s, and AVA ≤ 1.0 cm² (or ≤ 0.6 cm²/m²);
- In this setting, AS is considered severe regardless of LVEF or flow conditions.

8.3.5. Discordant Criteria

In some patients, effective AVA ≤ 1.0 cm² is associated with gradients below the threshold for severe disease. In these cases, assessment of systolic flow status is essential and is estimated using the stroke volume index (SVI), defined as stroke volume indexed to body surface area.

- Low flow: SVI ≤ 35 mL/m²;
- Normal flow: SVI > 35 mL/m².

Based on the combination of gradient, flow status, and left ventricular function, the main hemodynamic phenotypes of discordant AS include:

- Low-flow, low-gradient AS with reduced LVEF: mean gradient < 40 mm Hg, effective AVA ≤ 1.0 cm², SVI ≤ 35 mL/m², and LVEF $< 50\%$;
- Low-flow, low-gradient AS with preserved LVEF (paradoxical low flow): mean gradient < 40 mm Hg, effective AVA ≤ 1.0 cm², SVI ≤ 35 mL/m², and LVEF $\geq 50\%$;
- Normal-flow, low-gradient AS with preserved LVEF: mean gradient < 40 mm Hg, effective AVA ≤ 1.0 cm², SVI > 35 mL/m², and LVEF $\geq 50\%$;
- Discordant high-gradient AS: mean gradient ≥ 40 mm Hg associated with effective AVA > 1.0 cm².

In patients with low-flow, low-gradient AS and reduced LVEF, it is essential to distinguish true severe AS with left ventricular systolic dysfunction secondary to afterload mismatch from primary myocardial dysfunction associated with only moderate AS (pseudo-severe stenosis). Dobutamine stress echocardiography may be useful, with assessment of Vmax or mean gradient and valve area under baseline and increased-flow conditions, using dobutamine doses up to 20 μ g/kg/min under appropriate clinical and hemodynamic monitoring.

True severe AS is characterized by a fixed valve area, resulting in an increase in Vmax to ≥ 4 m/s or mean gradient to ≥ 40 mm Hg at any flow level, while valve area remains ≤ 1.0 cm². In contrast, in patients with moderate AS and primary left ventricular dysfunction, valve area increases as flow rises, resulting in only a modest increase in Vmax or transaortic gradient. Some patients do not demonstrate an increase in stroke volume $\geq 20\%$ with dobutamine; this condition is termed absence of contractile reserve or absence of flow reserve.⁶⁵⁵⁻⁶⁵⁹

Some guidelines also define very severe AS as a Vmax ≥ 5.0 m/s or a mean gradient ≥ 60 mm Hg.

8.3.6. Additional Echocardiographic Parameters

The ratio of the velocity-time integrals, also referred to as the dimensionless index or velocity ratio, obtained between the LVOT and the aortic valve jet, eliminates the need to calculate LVOT area and may be particularly useful when other parameters are inconclusive. Because it is independent of body surface area, this index reduces potential errors in valve area estimation related to measurement of LVOT diameter or area. A ratio close to 1.0 is considered normal, whereas values ≤ 0.25 correspond to approximately 25% of the normal valve area for the patient, are consistent with severe AS, and are associated with the development of symptoms and worse clinical outcomes.⁶⁶⁰

Assessment of GLS may be useful for risk stratification and early detection of left ventricular dysfunction. An absolute value below 15% (eg, $> -15\%$) is associated with a worse prognosis and may identify patients with asymptomatic severe AS who are at greater risk of clinical deterioration or mortality.⁶⁶¹⁻⁶⁶³

TEE allows more detailed assessment of valve morphology, planimetry of the effective AVA, investigation of subvalvular obstruction, and evaluation of concomitant VHD. TEE also plays an important role in periprocedural settings and in cases with limitations of TTE. In selected situations, valve area may be measured directly using 3D techniques.⁶⁶⁴

Measurements of AS severity obtained while the patient is hypertensive may underestimate – or less commonly overestimate – the severity of AS. Hypertension imposes a second pressure load on the left ventricle in addition to valvular obstruction, resulting in lower forward stroke volume and a lower transaortic gradient compared with normotensive conditions. Therefore, Doppler velocity data and invasive pressure measurements should ideally be obtained when the patient is normotensive (Table 8.16).⁶⁵²

8.3.7. Cardiac Computed Tomography Angiography

The use of CT has expanded rapidly in the assessment of patients with calcific AS. CT is widely used to quantify valvular calcification and to assist in determining stenosis severity, particularly when echocardiographic parameters are discordant, such as in low-flow, low-gradient AS, for which its use is consistently recommended.

Aortic valve calcium scores $> 2,000$ AU in men and $> 1,200$ AU in women are strongly indicative of severe

Guidelines

Table 8.16 – Main hemodynamic phenotypes of AS based on echocardiographic parameters

Hemodynamic phenotype	Mean gradient	Effective AVA	SVI	LVEF	Main characteristics
High-gradient AS (classic)	≥ 40 mmHg	≤ 1.0 cm ²	Usually normal	Preserved or reduced	Typical form of severe AS; straightforward diagnosis when parameters are concordant
Low-flow, low-gradient AS with reduced LVEF	< 40 mmHg	≤ 1.0 cm ²	≤ 35 mL/m ²	$< 50\%$	May represent true severe stenosis or pseudo-stenosis; dobutamine stress echocardiography is useful
Low-flow, low-gradient AS with preserved LVEF (paradoxical low flow)	< 40 mmHg	≤ 1.0 cm ²	≤ 35 mL/m ²	$\geq 50\%$	Associated with concentric remodeling and a small ventricular cavity
Normal-flow, low-gradient AS	< 40 mmHg	≤ 1.0 cm ²	> 35 mL/m ²	$\geq 50\%$	Frequently represents moderate stenosis or measurement error
Discordant high-gradient AS	≥ 40 mmHg	> 1.0 cm ²	Variable	Variable	Usually indicates severe AS; assess for potentially reversible high-flow states

AS: aortic stenosis; AVA: aortic valve area; LVEF: left ventricular ejection fraction; SVI: stroke volume index.

AS, with high diagnostic accuracy.^{665,666} Higher thresholds ($> 3,000$ AU in men and $> 1,600$ AU in women) increase diagnostic specificity, whereas values $< 1,600$ AU in men and < 800 AU in women make severe stenosis unlikely.⁶⁶⁷

These values should be interpreted cautiously in settings in which severe AS may occur in the absence of substantial calcification, such as in patients with bicuspid aortic valve, concomitant cardiac amyloidosis, or predominantly fibrotic stenosis, including post-rheumatic, radiation-induced, or inflammatory etiologies.⁶⁶⁸⁻⁶⁷¹

Recent evidence suggests that contrast-enhanced CT may enable assessment of the extent of valve leaflet fibrosis, providing a complementary measure of anatomical severity and disease phenotype. This approach may be particularly relevant in women, who frequently have a lower burden of valvular calcification than men.^{665,666}

CT also plays a central role in the assessment of the thoracic aorta in patients with suspected or established aortic root disease, particularly in the presence of a bicuspid aortic valve. Systematic measurement of aortic dimensions – including the sinuses of Valsalva, sinotubular junction, and ascending aorta – is recommended and has direct implications for clinical decision-making and surgical planning.

CT also complements echocardiography in characterizing valve morphology and defining the distribution and extent of calcification, contributing to the choice between surgical aortic valve replacement (SAVR) or TAVI and, when a transcatheter approach is indicated, to selection of prosthesis type and size.^{672,673}

In contemporary clinical practice, CT is an integral component of the preprocedural assessment of patients undergoing SAVR or TAVI, and is routinely recommended for procedural planning, including assessment of the valve annulus, aorta, and vascular access. The method is

particularly useful for identifying porcelain aorta, accurate prosthesis sizing, and assessment of peripheral arterial anatomy for vascular access feasibility.

Finally, with advances in image quality and spatial resolution, electrocardiographically gated coronary CT angiography – combined, when available, with CT-derived fractional flow reserve – may be used to assess the presence and extent of CAD as an alternative to invasive coronary angiography in selected patients undergoing evaluation before valve intervention

Recommendation	Strength of recommendation	Certainty of evidence
CT is recommended for quantification of valvular calcification and confirmation of AS severity in patients with discordant echocardiographic parameters, particularly those with low-flow, low-gradient AS.	STRONG	HIGH
CT-derived aortic valve calcium scores are recommended as a complementary tool for defining the severity of calcific AS, using sex-specific thresholds.	STRONG	HIGH

Aortic valve calcium scores should be interpreted with caution in patients in whom severe AS may occur with a low calcific burden, such as those with bicuspid aortic valve, cardiac amyloidosis, or predominantly fibrotic stenosis (post-rheumatic, radiation-induced, or inflammatory).	STRONG	MODERATE	CT is recommended as part of the preprocedural assessment of patients undergoing surgical or TAVI, including evaluation of the valve annulus, aorta, and vascular access for procedural planning.	STRONG	HIGH
Contrast-enhanced CT is suggested for assessment of valve leaflet fibrosis as a complementary measure of the anatomical severity of AS, particularly in women or when clinical and imaging findings are discordant.	CONDITIONAL	MODERATE	Electrocardiographically gated coronary CT angiography, combined with FFR-CT when available, is suggested as an alternative to invasive coronary angiography for assessment of CAD in selected patients undergoing preparation for valve intervention.	CONDITIONAL	MODERATE
CT is recommended for systematic assessment of the aortic root and thoracic aorta in patients with suspected or established aortic disease, particularly in those with bicuspid aortic valve, including measurement of the sinuses of Valsalva, sinotubular junction, and ascending aorta.	STRONG	MODERATE			
CT is recommended as a complementary method to echocardiography for characterization of valve morphology, distribution of calcification, and planning of the intervention strategy, including prosthesis selection and choice of surgical or transcatheter treatment.	STRONG	MODERATE			

AS: aortic stenosis; CAD: coronary artery disease; CT: computed tomography; FFR-CT: CT-derived fractional flow reserve; TAVI: transcatheter aortic valve implantation.

8.3.8. Exercise Testing

Recommendation	Strength of recommendation	Certainty of evidence
Exercise testing is recommended for risk stratification in patients with apparently asymptomatic severe AS or nonspecific symptoms, with the aim of identifying unrecognized symptoms, reduced functional capacity, and an abnormal BP response to exercise. ⁶⁷⁴	STRONG	MODERATE
Aortic valve replacement is recommended in patients with severe AS who develop symptoms clearly attributable to VHD during exercise testing.	STRONG	MODERATE

Guidelines

Aortic valve replacement is suggested in apparently asymptomatic patients with severe AS who demonstrate an abnormal BP response (a decrease in systolic BP > 20 mm Hg) or poor exercise tolerance during exercise testing.

Pharmacological stress echocardiography, for example with dobutamine, is suggested in patients with AS who are unable to perform exercise testing, to assess hemodynamic response, LV function, and development of symptoms.

Cardiopulmonary exercise testing is suggested as a complementary method to distinguish functional limitation of cardiac, pulmonary, or deconditioning origin and to refine risk stratification in patients with AS.

CONDITIONAL

MODERATE

CONDITIONAL

MODERATE

CONDITIONAL

LOW

AS: aortic stenosis; CAD: coronary artery disease; CT: computed tomography; FFR-CT: CT-derived fractional flow reserve; TAVI: transcatheter aortic valve implantation.

8.3.9. Cardiac Magnetic Resonance Imaging

Recommendation	Strength of recommendation	Certainty of evidence
CMR is recommended in patients with AS when echocardiography does not adequately characterize cardiac structure and function, for assessment of ventricular volumes, systolic function, and ventricular mass.	STRONG	MODERATE

CMR assessment of myocardial fibrosis, particularly using late gadolinium enhancement, is suggested as a complementary tool for risk stratification and clinical decision-making in selected patients with severe AS.^{663,675-678}

CMR is recommended for serial assessment of thoracic aortic dimensions, particularly in patients with bicuspid aortic valve, as an alternative to imaging modalities involving cumulative ionizing radiation exposure.

CMR is suggested as an alternative to CT for planning transcatheter intervention in selected patients, particularly when iodinated contrast or radiation exposure is contraindicated.

CMR is not recommended for quantification of AS severity because of its lower accuracy in estimating transvalvular velocities compared with Doppler echocardiography.

CONDITIONAL

MODERATE

STRONG

MODERATE

CONDITIONAL

MODERATE

STRONG

MODERATE

AS: aortic stenosis; CT: computed tomography; MRI: magnetic resonance imaging.

8.3.10. Cardiac Catheterization

In most patients, echocardiography provides the hemodynamic information required for management. Currently, cardiac catheterization is recommended only when noninvasive tests are inconclusive, when clinical and echocardiographic findings are discordant, and for coronary angiography before SAVR.

8.3.11. Additional Diagnostic Parameters

8.3.11.1. Natriuretic Peptides

Recommendation	Strength of recommendation	Certainty of evidence
Measurement of natriuretic peptides (BNP or NT-proBNP) is suggested in the assessment of patients with AS, particularly those with symptoms of uncertain etiology or multiple comorbidities, to assist in differentiating the origin of symptoms and in prognostic stratification.	CONDITIONAL	MODERATE
Early aortic valve replacement may be considered in asymptomatic patients with severe AS who have persistently elevated natriuretic peptide levels, particularly levels > 3 times the age- and sex-adjusted upper reference limit, in the absence of other causes for the elevation.	CONDITIONAL	MODERATE

AS: aortic stenosis; BNP: B-type natriuretic peptide; NT-proBNP: N-terminal pro-BNP.

Rationale for the evidence: BNP and NT-proBNP are released in response to increased wall stress and stretching of ventricular and atrial cardiomyocytes.⁶⁷⁹ These biomarkers have established prognostic value in HF and AS. Their levels correlate with disease severity, including AVA,⁶⁷⁹ Vmax, and pressure gradients, while also reflecting hemodynamic burden and ventricular remodeling. Persistently elevated levels are associated with a higher risk of progression to symptoms, need for intervention, and mortality. Although the evidence supports their prognostic value and role in risk stratification, an indication for intervention based predominantly on elevated natriuretic peptide levels should be integrated with clinical and echocardiographic data, supporting a conditional recommendation based on moderate-certainty evidence.

8.3.11.2. Cardiac Amyloidosis

ATTR-CA is increasingly recognized as a condition frequently associated with AS in older patients, particularly those with low-flow and/or low-gradient phenotypes. Observational studies indicate that approximately 10%–16% of patients undergoing TAVI have concomitant ATTR-CA.^{680–683}

Recommendation	Strength of recommendation	Certainty of evidence
Investigation for ATTR-CA may be considered in patients with severe AS, particularly in the presence of low-flow and/or low-gradient phenotypes or suggestive clinical and echocardiographic findings, because its identification may contribute to a better understanding of the pathophysiology, risk stratification, and treatment planning.	CONDITIONAL	MODERATE
The presence of ATTR-CA alone should not be considered a contraindication to valve intervention in patients with severe AS. It is suggested that the choice between TAVI and SAVR be individualized, preferably through multidisciplinary discussion, considering functional status, frailty, comorbidities, expected clinical benefit, and patient preferences.	CONDITIONAL	MODERATE

AS: aortic stenosis; ATTR-CA: transthyretin amyloid cardiomyopathy; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

Although cardiac amyloidosis is associated with a worse long-term prognosis, observational studies indicate that patients with severe AS and ATTR-CA may experience symptomatic and functional improvement after valve intervention, including TAVI, despite overall survival remaining lower than that observed in patients without amyloidosis.⁶⁸⁴

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8.3.12. Medical Therapy

To date, no pharmacological therapy has been shown to modify the natural history of AS. Concomitant hypertension should be treated to avoid a further increase in afterload, preferably with renin-angiotensin system blockers, although careful dose titration is required to prevent symptomatic hypotension. In patients with symptomatic severe AS and HF, initiation of medical therapy or temporary improvement in symptoms should not delay intervention. There is no evidence supporting the use of statins to prevent the progression of AS.⁶⁵²⁻⁶⁵⁴

8.3.13. Indications for Aortic Valve Replacement

The choice of the type of aortic valve replacement should be individualized, taking into account age, life expectancy,

expected prosthetic valve durability, patient preferences, comorbidities, and anatomical and clinical characteristics that influence the choice between a surgical or transcatheter approach (Figure 8.1).

In contemporary practice, most patients with AS undergoing valve replacement in Europe and North America receive bioprosthetic valves, either surgically or transcatheter. Bioprosthetic valves do not require long-term oral anticoagulation; however, they have limited durability, which varies according to device type and is inversely related to patient age.^{654,685}

In contrast, mechanical prostheses have high durability but require continuous oral anticoagulation, which is associated with an increased risk of thromboembolic and bleeding events.⁶⁸⁶

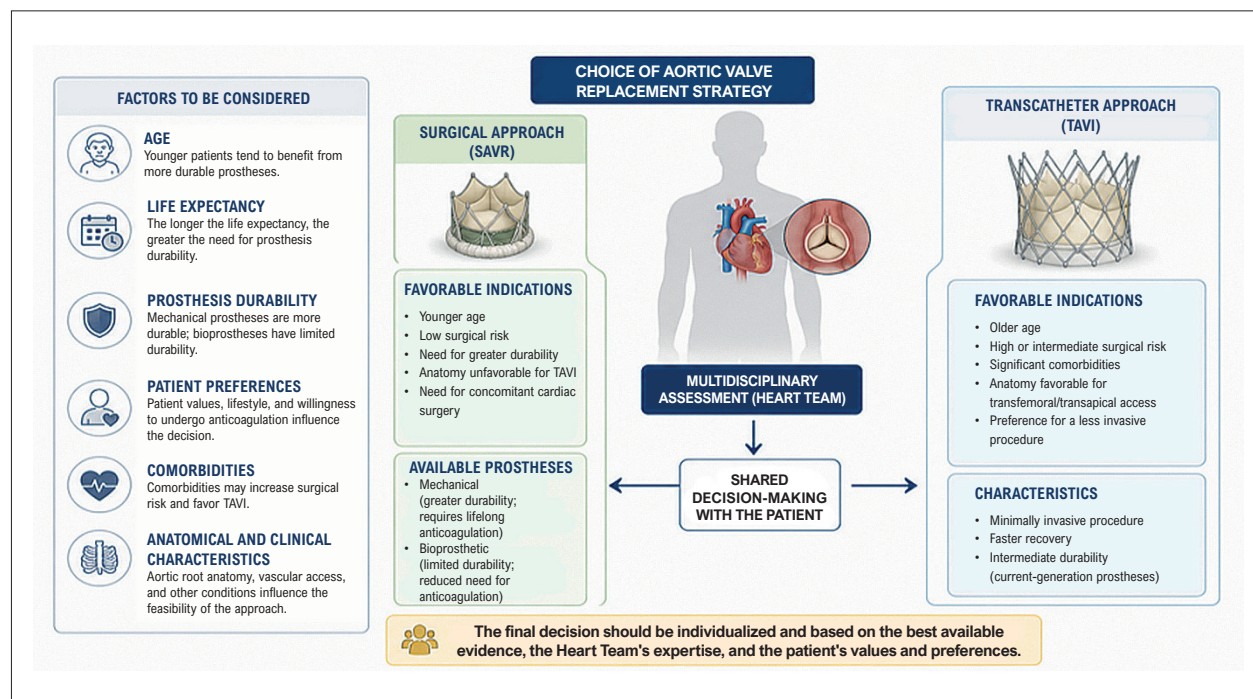


Figure 8.1 – Factors involved in the choice between surgical (SAVR) and transcatheter (TAVI) aortic valve replacement. SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

Recommendation	Strength of recommendation	Certainty of evidence
The use of a mechanical prosthesis is recommended in younger patients, typically those younger than 60 years, because of its greater durability.	STRONG	MODERATE
The use of a bioprosthesis is recommended in patients older than 65 years, in whom its durability tends to be sufficient over their expected lifetime while avoiding the need for chronic oral anticoagulation.	STRONG	MODERATE
It is suggested that the choice between a mechanical prosthesis and a bioprosthesis in patients aged 60–65 years be individualized through shared decision-making between the healthcare team and the patient, considering life expectancy, risk of reintervention, bleeding risk, the need for and ability to maintain anticoagulation, comorbidities, lifestyle, and patient preferences.	CONDITIONAL	MODERATE

8.4. Symptomatic Severe Aortic Stenosis

Recommendation	Strength of recommendation	Certainty of evidence
Early valve intervention is recommended in patients with symptomatic severe AS, a life expectancy of more than 1 year, and a reasonable likelihood of functional recovery. ⁶⁸⁷	STRONG	HIGH
Aortic valve replacement is recommended in all eligible symptomatic patients with severe high-gradient AS (mean gradient ≥ 40 mm Hg, $V_{max} \geq 4.0$ m/s, and effective valve area ≤ 1.0 cm ² or ≤ 0.6 cm ² /m ²).	STRONG	HIGH
Valve replacement is recommended in patients with low-flow, low-gradient AS and reduced LVEF after confirmation of truly severe AS by dobutamine stress echocardiography and/or cardiac CT for quantification of valvular calcium. ^{468,688-690}	STRONG	MODERATE
Optimized medical therapy without valve intervention is recommended in patients with pseudo-severe AS.	STRONG	HIGH
Valve replacement is suggested in patients with low-flow, low-gradient AS and preserved LVEF (paradoxical low flow), after confirmation of stenosis severity by multimodality assessment and of a causal relationship between symptoms and valvular disease. ^{691,692}	CONDITIONAL	MODERATE

Periodic clinical and echocardiographic follow-up is recommended in patients with normal-flow, low-gradient AS and preserved LVEF when multimodality assessment does not confirm truly severe AS.^{652,654,693}

STRONG

MODERATE

AS: aortic stenosis; CT: computed tomography; LVEF: left ventricular ejection fraction; V_{max} : peak transvalvular jet velocity.

8.5. Asymptomatic Severe Aortic Stenosis

A considerable proportion of patients with severe AS are asymptomatic at the time of initial diagnosis. Although valve morphological characteristics, exercise testing, stress imaging methods, and biomarkers aid in risk stratification and in identifying patients who may benefit from early intervention, the optimal management of this population remains uncertain and controversial.

Recommendation	Strength of recommendation	Certainty of evidence
Valve intervention is recommended in asymptomatic patients with severe AS and LVEF $< 50\%$, in the absence of another identifiable cause of ventricular dysfunction. ^{652,694-697}	STRONG	HIGH
Aortic valve replacement is suggested in asymptomatic patients with severe AS and adverse prognostic markers, including very high V_{max} (≥ 5.0 – 5.5 m/s), significantly elevated natriuretic peptide levels, marked valvular calcification, or rapid progression of stenosis. ^{652,665,698-703}	CONDITIONAL	MODERATE

Guidelines

Close clinical and echocardiographic surveillance is recommended in asymptomatic patients with severe AS who do not have ventricular dysfunction or adverse prognostic markers warranting early intervention.

STRONG

MODERATE

AS: aortic stenosis; LVEF: left ventricular ejection fraction; Vmax: peak transvalvular jet velocity.

Recent evidence from RCTs has reassessed the role of early intervention in low-risk patients with asymptomatic severe AS. In the EARLY TAVR trial,⁷⁰⁴ which randomized 901 patients to early TAVI versus clinical surveillance, the interventional strategy significantly reduced the composite endpoint of all-cause mortality, stroke, and unplanned cardiovascular hospitalization over 5 years of follow-up. In contrast, in the EVOLVED trial,⁷⁰⁵ which included patients with evidence of myocardial fibrosis on CMR, early intervention did not result in a significant reduction in mortality or AS-related hospitalizations compared with the conservative strategy.

Prior smaller trials also support the potential benefit of early intervention. In the RECOVERY trial,⁷⁰⁶ asymptomatic patients with very severe AS had a lower risk of cardiovascular mortality with early surgery during long-term follow-up. Similarly, the AVATAR trial⁷⁰⁷ demonstrated a reduction in composite outcomes, including HF hospitalizations and mortality, with sustained benefit during extended follow-up.

A recent meta-analysis including such RCTs demonstrated that early intervention is associated with reductions in cardiovascular hospitalizations, HF events, and cerebrovascular events, without a significant impact on overall or cardiovascular mortality.⁷⁰⁸ However, heterogeneity among the studies represents an important limitation when interpreting these findings.

Accordingly, early intervention may be considered in selected patients with asymptomatic severe AS and low surgical risk, particularly in the presence of high-risk markers, with the decision individualized within the context of the Heart Team. Ongoing studies should provide additional evidence and contribute to further refinement of management strategies in this population.

8.6. Moderate Aortic Stenosis

Aortic valve replacement in patients with moderate AS is generally not indicated as an isolated procedure. It may be considered when performed concomitantly with CABG, intervention on the ascending aorta, or procedures for the treatment of other VHDs.⁷⁰⁹

Observational studies have demonstrated an association between moderate AS and adverse clinical outcomes in patients both with and without HFrEF.⁷¹⁰⁻⁷¹² However, it remains

uncertain whether this association is causal or reflects the high burden of comorbidities frequently observed in this population.

The role of valve intervention in patients with moderate AS and left ventricular dysfunction has been investigated in recent clinical trials. In the TAVR UNLOAD trial,⁷¹³ which included patients with moderate AS and HFrEF, a TAVI strategy did not result in a significant reduction in major clinical outcomes compared with clinical surveillance (moderate-certainty evidence). However, a significant improvement in quality of life was observed in the intervention group.

Therefore, in the absence of other concomitant surgical indications, valve replacement in patients with moderate AS is not routinely recommended. The decision should be individualized in selected cases, particularly in the setting of advanced HF, considering the clinical profile, life expectancy, and Heart Team assessment.

8.6.1. Treatment Options

Recommendation	Strength of recommendation	Certainty of evidence
The choice between SAVR and TAVI should be made through shared decision-making within the Heart Team, considering age, life expectancy, prosthesis durability, comorbidities, valvular and vascular anatomy, and patient preferences.	STRONG	MODERATE
TAVI is suggested as the preferred approach in older patients or those at increased surgical risk, whereas SAVR remains preferable in younger patients with low surgical risk, longer life expectancy, or anatomy unfavorable for the transcatheter procedure.	CONDITIONAL	MODERATE
The choice of surgical prosthesis type (biological or mechanical) should be individualized, considering life expectancy, anticoagulation risk, likelihood of reintervention, and patient preferences.	STRONG	LOW

A bioprosthesis is recommended in patients with a contraindication to, poor adherence to, or refusal of oral anticoagulation.	STRONG	LOW	Balloon aortic valvuloplasty may be considered in specific situations, such as a bridge to TAVI or surgery in patients with decompensated severe AS or in patients requiring urgent high-risk noncardiac surgery.	CONDITIONAL	LOW						
Mechanical prostheses are suggested as the preferred option in younger patients (typically < 60 years) without contraindications to anticoagulation, considering their greater durability.	CONDITIONAL	MODERATE	AS: aortic stenosis; SAVR: surgical aortic valve implantation; TAVI: transcatheter aortic valve implantation.								
Is it suggested that the choice between a mechanical prosthesis and a bioprosthesis in patients aged 50–65 years be individualized according to patient preferences and individual risk profile.	CONDITIONAL	MODERATE	Over recent decades, there has been a substantial increase in the number of patients undergoing aortic valve replacement, driven by the introduction of TAVI, improvements in diagnostic methods, and expansion of therapeutic indications. Nevertheless, significant inequalities in access to TAVI persist worldwide, mainly because of device costs, resource availability, and differences among healthcare systems. In addition, data from contemporary registries suggest that late referral and undertreatment remain common, with a negative impact on clinical outcomes.								
Bioprostheses are suggested as the preferred option in patients older than 65 years, considering their expected durability and the possibility of avoiding chronic oral anticoagulation.	CONDITIONAL	MODERATE	8.7. Choice between a Mechanical Prosthesis and a Bioprosthesis for Surgical Aortic Valve Replacement								
The Ross procedure may be considered in selected young patients, particularly when anticoagulation is undesirable or contraindicated, provided that the procedure is performed at centers experienced in the technique.	CONDITIONAL	MODERATE	The choice between a mechanical prosthesis and a bioprosthesis for SAVR should be based on a shared decision-making process, considering the patient's values and preferences, life expectancy, the risks and implications of oral anticoagulation, and the likelihood and impact of reinterventions over time.								
			<table><tr><th>Recommendation</th><th>Strength of recommendation</th><th>Certainty of evidence</th></tr><tr><td>The choice between a mechanical prosthesis and a bioprosthesis for surgical aortic valve replacement should be based on shared decision-making, considering patient values and preferences, life expectancy, the risks and implications of oral anticoagulation, and the likelihood and impact of reinterventions over time.</td><td>STRONG</td><td>LOW</td></tr></table>			Recommendation	Strength of recommendation	Certainty of evidence	The choice between a mechanical prosthesis and a bioprosthesis for surgical aortic valve replacement should be based on shared decision-making, considering patient values and preferences, life expectancy, the risks and implications of oral anticoagulation, and the likelihood and impact of reinterventions over time.	STRONG	LOW
Recommendation	Strength of recommendation	Certainty of evidence									
The choice between a mechanical prosthesis and a bioprosthesis for surgical aortic valve replacement should be based on shared decision-making, considering patient values and preferences, life expectancy, the risks and implications of oral anticoagulation, and the likelihood and impact of reinterventions over time.	STRONG	LOW									

Guidelines

A bioprosthesis is recommended in patients of any age with a contraindication to oral anticoagulants, difficulty managing anticoagulation, or refusal to use these medications.	STRONG	LOW
A mechanical prosthesis is suggested as the preferred option in patients younger than 50 years, in the absence of a contraindication to oral anticoagulation, because of its greater durability.	CONDITIONAL	MODERATE
It is suggested that the choice between a mechanical prosthesis and a bioprosthesis be individualized in patients aged 50–65 years, considering clinical factors, bleeding risk, lifestyle, life expectancy, and patient preferences.	CONDITIONAL	MODERATE
A bioprosthesis is suggested as the preferred option in patients older than 65 years, considering the lower likelihood of requiring reintervention during their lifetime and the possibility of avoiding chronic oral anticoagulation.	CONDITIONAL	MODERATE

8.7.1. Valve Replacement Modality: Transcatheter Versus Surgical

The emergence and rapid expansion of TAVI represent one of the most important paradigm shifts in the contemporary management of aortic valve disease. TAVI is currently the predominant strategy across different surgical risk profiles among patients with tricuspid AS in North America and Europe, decisively influencing clinical guidelines and clinical practice. This advance is supported by a robust body of

evidence from RCTs demonstrating the noninferiority – and, for selected outcomes, possible superiority – of TAVI compared with SAVR. Most of these studies included patients aged 70–85 years, with limited representation of individuals younger than 70 years, thereby reducing the robustness of the evidence in this population.^{652,654}

Despite current recommendations, the number of TAVI procedures performed in patients younger than 65 years has increased significantly,⁷¹⁴ whereas, in this population, transcatheter intervention may be associated with a higher risk of 5-year mortality compared with surgery.⁷¹⁴⁻⁷¹⁷

Recommendation	Strength of recommendation	Certainty of evidence
An age of 70 years is suggested as a practical reference to assist in the choice between TAVI and SAVR, always integrated into a comprehensive clinical assessment.	CONDITIONAL	MODERATE
The decision between TAVI and SAVR should be individualized within the Heart Team, considering life expectancy, comorbidities, frailty, anatomical characteristics, and implications for lifetime management.	STRONG	MODERATE
CT angiography is recommended for procedural planning and definition of the therapeutic strategy in patients who are candidates for aortic valve intervention.	STRONG	MODERATE
SAVR is recommended in patients in whom transfemoral access for TAVI is not feasible.	STRONG	MODERATE
Alternative access routes for TAVI may be considered in selected patients in whom transfemoral access is not feasible, recognizing that the available evidence is predominantly observational. ^{652,654,718-720}	CONDITIONAL	LOW

SAVR is recommended as the preferred approach in patients with anatomical features unfavorable for TAVI, including an aortic annulus incompatible with available devices, extensive calcification of the aortic annulus or LV outflow tract (with an increased risk of paravalvular regurgitation or rupture), and a high risk of coronary obstruction. ^{673,721,722}	STRONG	MODERATE	The use of validated instruments for frailty assessment is suggested, including the Fried criteria, Clinical Frailty Scale, Essential Frailty Toolset, and multidimensional indices incorporating physical performance, cognition, functional status, and nutritional status. ⁷²⁵⁻⁷²⁷	CONDITIONAL	LOW
TAVI may be considered in patients with conditions that increase surgical risk, such as porcelain aorta, significant chest wall deformities, or prior coronary artery bypass grafting with patent grafts, when technically appropriate. ^{66,723}	CONDITIONAL	LOW	Use of the Essential Frailty Toolset, when available, is suggested because of its greater discriminative ability compared with other frailty scales. ⁷²⁸	CONDITIONAL	MODERATE
CT: computed tomography; LV: left ventricular; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.			TAVI may be considered in patients with moderate-to-severe frailty when intervention is indicated, because of its lower physiological burden and potential for faster recovery compared with surgery. ^{729,730}	CONDITIONAL	LOW
8.7.2. Frailty Status			In patients with advanced frailty, particularly when associated with significant functional dependence or severe comorbidities, a patient-centered approach is suggested, considering the limited expected benefit of intervention and the possibility of palliative care when appropriate.	CONDITIONAL	LOW
Frailty is a key clinical determinant in the assessment of older patients with AS and is consistently associated with higher mortality and worse outcomes after intervention, independently of traditional surgical risk scores. ⁷²⁴ In patients undergoing evaluation for aortic valve replacement, frailty is associated with increased mortality, a higher incidence of periprocedural complications, prolonged hospitalization, and poorer functional recovery.					
Recommendation	Strength of recommendation	Certainty of evidence			
Systematic assessment of frailty is recommended as part of decision-making between TAVI and SAVR, particularly in the context of geriatric cardiology.	STRONG	MODERATE			
			SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.		

Guidelines

In a contemporary multicenter registry of patients undergoing TAVI,⁷³¹ although 5-year mortality was higher among nonagenarians, this excess mortality was predominantly attributable to noncardiovascular causes, whereas cardiovascular mortality was similar across age groups. Notably, age ≥ 90 years was not an independent predictor of mortality, whereas frailty and malnutrition emerged as the main prognostic determinants. Subgroups of patients without these conditions had favorable survival, reinforcing the role of geriatric assessment in the selection of candidates for intervention.

Therefore, therapeutic decision-making should integrate frailty assessment with other clinical, anatomical, and functional factors within a multidisciplinary Heart Team approach, with emphasis on estimating clinical benefit, quality of life, and alignment with the patient's values and preferences.

8.7.3. Bicuspid Aortic Valve

In patients with a bicuspid aortic valve, severe AS tends to occur earlier than in those with a tricuspid aortic valve and is frequently associated with aortopathy.⁷³²⁻⁷³⁴

TAVI has expanded into low-risk populations, with evidence of noninferiority compared with SAVR in selected patients.^{718,720} However, a substantial proportion of younger patients at low surgical risk have bicuspid aortic valve stenosis, a setting in which the equivalence between TAVI and SAVR remains uncertain.⁷³⁵ Recent studies have yielded heterogeneous results. An analysis of low-risk patients from the NOTION-2 trial demonstrated a higher incidence of composite adverse outcomes with TAVI compared with SAVR in patients with bicuspid aortic valves. In contrast, the BIVOLUTX registry showed favorable early outcomes with TAVI in this anatomy, although comparative long-term data remain limited.⁷³¹

To date, no RCTs have been specifically designed to compare TAVI and SAVR in patients with bicuspid aortic valves. The available evidence is based predominantly on observational studies and risk-adjusted analyses. In a recent meta-analysis of five comparative studies (TAVI: 5,901 patients; SAVR: 12,427 patients), TAVI was associated with a higher risk of composite adverse events, including death, stroke, and rehospitalization, at 2-year follow-up.⁷³¹

Consistently, a meta-analysis of 15 studies ($n = 22,085$) demonstrated better long-term survival with SAVR beyond 6 months in patients with bicuspid aortic valves.⁷³⁶ In addition, analysis of the Medicare database showed that TAVI was associated with higher mortality and a higher incidence of stroke at 5 years, despite lower periprocedural mortality.⁷³⁷ Despite the limitations of the available evidence, TAVI is widely used in younger patients. In the United States, approximately half of individuals younger than 65 years with severe AS are treated by a transcatheter approach, although long-term outcomes in this population remain uncertain.⁷³⁸

Recommendation	Strength of recommendation	Certainty of evidence
Surgical aortic valve replacement is recommended as the preferred strategy for treatment of aortic stenosis in bicuspid aortic valve, particularly in younger patients, in the presence of associated aortopathy, or when valve morphology is unfavorable.	STRONG	MODERATE
Transcatheter aortic valve implantation may be considered in patients with bicuspid aortic valve stenosis and high or prohibitive surgical risk, provided that the anatomy is favorable and after individualized Heart Team assessment.	CONDITIONAL	LOW

8.7.4. Complications

Rates of vascular complications and paravalvular regurgitation remain higher after TAVI despite advances in transcatheter prosthesis design, whereas major bleeding, acute kidney injury, and new-onset AF are more frequently observed after SAVR.^{650,739,740} Although paravalvular regurgitation is associated with adverse clinical outcomes,^{741,742} its presence does not appear to significantly affect the overall comparison of outcomes between TAVI and SAVR in available RCTs.⁷³⁹⁻⁷⁴³

The need for permanent pacemaker implantation is more frequent after TAVI, particularly with self-expanding prostheses. In contrast, patients undergoing TAVI experience faster recovery, shorter hospital stays, and earlier improvement in quality of life compared with those treated with SAVR.^{718,739,743}

Infective endocarditis after TAVI is a rare but potentially fatal complication. Its incidence ranges from 0.3 to 2.0 cases per 100 patient-years,⁷⁴⁴ similar to that reported after SAVR.^{744,745}

Although post-TAVI infective endocarditis is recognized as a subtype of prosthetic valve endocarditis, it represents a particularly challenging condition because of its distinctive clinical and microbiological profile, high incidence of complications, the still uncertain role of cardiac surgery, and poor prognosis in most affected patients. The number of TAVI procedures is expected to increase exponentially in the coming years, substantially increasing the population at risk for this complication. Post-TAVI infective endocarditis is associated with high in-hospital mortality, and patients who

survive the index episode have poor long-term outcomes, with approximately two-thirds dying within 5 years of follow-up.⁷⁴⁶

8.7.5. Durability of Bioprostheses and Need for Reintervention

Currently available data do not demonstrate systematic differences in durability between surgical and transcatheter prostheses. RCTs and observational studies have reported comparable rates of bioprosthetic valve dysfunction, particularly structural valve deterioration, during follow-up of up to 10 years.^{654,739,740,743}

However, direct comparison between these modalities remains limited by heterogeneity in the definitions of structural valve dysfunction, relatively short follow-up periods, competing mortality risk, and the use of different types of prostheses in the surgical arms of the studies.^{739,743}

Transcatheter valve implantation within a prior prosthesis, whether a surgical bioprosthesis (TAV-in-SAV) or a degenerated transcatheter prosthesis (TAV-in-TAV), is associated with lower periprocedural risk compared with surgical reoperation (redo SAVR).⁷⁴⁷⁻⁷⁵⁰ However, valve-in-valve procedures, particularly TAV-in-SAV, are associated with a higher risk of severe prosthesis-patient mismatch, a condition associated with worse clinical outcomes in observational studies.⁷⁵¹

In addition, valve-in-valve implantation may result in immobilization of the leaflets of the degenerated prosthesis in the open position, forming a tubular structure (neo-skirt), which may lead to direct coronary obstruction, particularly in patients with narrow sinuses of Valsalva, or indirect obstruction through sinus sequestration when the ascending aorta is narrow and the neo-skirt reaches the sinotubular junction.⁷⁵²⁻⁷⁵⁶ The risk of coronary obstruction varies according to the type of index prosthesis and is particularly high in the presence of stentless surgical bioprostheses or prostheses with externally mounted leaflets.⁷⁵² In the context of TAV-in-TAV, the risk of sinus sequestration is greater with supra-annular prostheses with a high neo-skirt.⁷⁵⁴ Even when coronary flow is preserved, coronary access may become difficult or impossible in a substantial proportion of patients after valve-in-valve procedures, particularly after TAV-in-TAV.⁷⁵⁶ Finally, surgical explantation of a degenerated TAVI prosthesis is technically challenging and is associated with mortality exceeding 10% in most retrospective studies.⁷⁵⁷⁻⁷⁵⁹

Recommendation	Strength of recommendation	Certainty of evidence
SAVR is recommended as the preferred strategy in patients younger than 70 years at low surgical risk, considering lifetime management issues and the limited availability of RCT data in this population.	STRONG	MODERATE

TAVI is recommended as the preferred modality in patients aged 70 years or older with tricuspid AS, provided that anatomy is favorable and transfemoral access is feasible, aiming to reduce early complications and promote faster recovery.

The choice between TAVI and SAVR in patients who are candidates for an aortic bioprosthesis should be individualized within the Heart Team, considering procedural risk, including anatomy and comorbidities, life expectancy, lifetime management implications, the feasibility and complexity of future reinterventions, and patient preferences.

STRONG

HIGH

STRONG

MODERATE

AS: aortic stenosis; RCT: randomized controlled trial; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

8.7.6. Summary of recommendations

Recommendations for diagnostic testing in patients with aortic stenosis	Strength of recommendation	Certainty of evidence
In patients with signs or symptoms of AS or with a bicuspid aortic valve, TTE is indicated for accurate diagnosis of etiology, assessment of hemodynamic severity, LV systolic function, prognosis, and optimal timing of valve intervention.	STRONG	HIGH

Guidelines

In patients with suspected severe low-flow, low-gradient AS and preserved LV ejection fraction, optimization of BP control is recommended before assessment of stenosis severity by TTE, TEE, cardiac catheterization, or CMR.	STRONG	LOW	In patients with suspected severe low-flow, low-gradient AS and normal or reduced LVEF, measurement of the aortic valve calcium score by CT is reasonable to better define stenosis severity.	WEAK	LOW
In patients with suspected severe low-flow, low-gradient AS and reduced LV ejection fraction, low-dose dobutamine stress testing combined with echocardiographic or invasive hemodynamic assessment is reasonable to better define stenosis severity and assess contractile reserve.	WEAK	LOW	In asymptomatic patients with severe AS, exercise testing is reasonable to assess physiological responses to exercise and confirm symptoms.	WEAK	LOW
In patients with suspected severe low-flow, low-gradient AS and normal or reduced LVEF, calculation of the ratio between LVOT velocity and transaortic velocity is reasonable to better define stenosis severity.	WEAK	LOW	In symptomatic patients with severe AS, exercise testing should not be performed to assess physiological responses to exercise or confirm symptoms.	WEAK	LOW

AS: aortic stenosis; BP: blood pressure; CT: computed tomography; LV: left ventricular; LVEF: left ventricular ejection fraction; LVOT: left ventricular outflow tract; MRI: magnetic resonance imaging; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography.

8.7.7. Indications for Intervention in Symptomatic and asymptomatic Severe Aortic Stenosis and Recommended Mode of Intervention

The following recommendations adapt those from the 2020 SBC guidelines and the most recent international guidelines (Recommendations Table) to the GRADE system, prioritizing older patients within Brazilian cardiogeriatrics. The strength of recommendation (Strong or Weak) and certainty of evidence (High, Moderate, Low, or Very Low) are based on evidence from RCTs and meta-analyses, considering frailty, life expectancy > 1 year, and shared decision-making by the Heart Team. The rationales include original citations for consistency.

Recommendation	Strength of recommendation	Certainty of evidence
Symptomatic patients with severe AS		
Valve replacement in symptomatic patients with severe high-gradient AS (mean gradient ≥ 40 mm Hg, $V_{max} \geq 4.0$ m/s, effective AVA ≤ 1.0 cm ² or ≤ 0.6 cm ² /m ²).	STRONG	MODERATE

Valve replacement in symptomatic patients with low-flow AS (SVI ≤ 35 mL/m ²), low gradient (< 40 mm Hg), and reduced LVEF (< 50%) after confirmation of stenosis severity.	STRONG	MODERATE
Valve replacement in symptomatic patients with low-flow AS (SVI ≤ 35 mL/m ²), low gradient (< 40 mm Hg), and preserved LVEF ($\geq 50\%$) after confirmation of stenosis severity.	WEAK	MODERATE
Asymptomatic patients with severe AS		
Valve replacement in asymptomatic patients with severe AS and LVEF < 50% without another identifiable cause.	STRONG	MODERATE
Valve replacement in asymptomatic patients with severe high-gradient AS and LVEF $\geq 50\%$, confirmed as asymptomatic by a normal exercise test when feasible, as an alternative to active surveillance.	WEAK	HIGH
Valve replacement in asymptomatic patients with severe AS and LVEF $\geq 50\%$ when procedural risk is low and at least one adverse marker is present (eg, Vmax > 5 m/s, severe calcification on CT plus Vmax progression ≥ 0.3 m/s/year, BNP/NT-proBNP > 3 times normal, or LVEF < 55% without another cause).	WEAK	MODERATE
Valve replacement in asymptomatic patients with severe AS and a sustained decrease in BP (> 20 mm Hg) during exercise testing.	WEAK	LOW
Mode of treatment		
Valve replacement is recommended at specialized VHD centers that regularly report clinical outcomes and have interventional cardiology and cardiac surgery programs as well as a structured collaborative Heart Team.	STRONG	LOW
The mode of valve replacement should be based on Heart Team assessment of clinical, anatomical, and procedural characteristics, incorporating lifetime management and life expectancy.	STRONG	LOW
TAVI in patients aged ≥ 70 years with tricuspid aortic valve stenosis, if anatomy is suitable.	STRONG	HIGH
SAVR in patients aged < 70 years, if surgical risk is low.	STRONG	MODERATE
SAVR or TAVI for the remaining candidates for aortic valve replacement, according to Heart Team assessment.	STRONG	MODERATE
Nontransfemoral TAVI may be considered in patients unsuitable for surgery and without appropriate transfemoral access.	WEAK	MODERATE
TAVI may be considered for the treatment of severe bicuspid aortic valve stenosis in patients at increased surgical risk, if anatomy is suitable.	WEAK	MODERATE
Balloon aortic valvuloplasty may be considered as a bridge to SAVR or TAVI in hemodynamically unstable patients or in those with severe AS requiring urgent high-risk noncardiac surgery.	WEAK	VERY LOW
SAVR is recommended in symptomatic and asymptomatic patients with severe AS undergoing CABG or surgical intervention on the ascending aorta.	STRONG	VERY LOW
SAVR may be considered in symptomatic and asymptomatic patients with moderate AS undergoing CABG or surgical intervention on the ascending aorta.	WEAK	VERY LOW

AS: aortic stenosis; AVA: aortic valve area; BNP: B-type natriuretic peptide; BP: blood pressure; CABG: coronary artery bypass grafting; CT: computed tomography; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-BNP; SAVR: surgical aortic valve replacement; SVI: stroke volume index; TAVI: transcatheter aortic valve implantation; VHD: valvular heart disease; Vmax: maximum transvalvular velocity.

8.8. Frailty and Degenerative Valvular Heart Disease in Older Adults

Frailty and degenerative VHD have an important pathophysiological and clinical interaction, sharing mechanisms related to aging, inflammaging, oxidative stress, mitochondrial dysfunction, and alterations in mineral metabolism. This relationship is bidirectional: VHD may contribute to hypoperfusion and functional decline, while frailty reduces

physiological reserve and tolerance to hemodynamic changes.⁷⁶⁰⁻⁷⁶⁹

Risk assessment should go beyond chronological age and traditional scores, such as EuroSCORE II and STS, and incorporate measures of frailty, functional status, and nutritional status. Tools such as FRAIL, the Modified Frailty Index, and the Essential Frailty Toolset may contribute to prognostic stratification.^{730,761-763,768-771}

Frailty is a dynamic and potentially modifiable condition. Early identification allows prehabilitation interventions, including exercise, nutritional support, and clinical optimization, with the potential to improve functional capacity and recovery after procedures.^{763-765,725,772,780,772-783}

The decision regarding valvular intervention should be individualized by the Heart Team, taking into account anatomy, procedural risk, frailty, functional status, life expectancy, and patient preferences and goals. Transcatheter techniques may be particularly useful in patients at higher surgical risk, but frailty remains associated with adverse outcomes regardless of the strategy adopted.^{763,767}

In the post-procedural period, early mobilization, cardiac rehabilitation, nutritional support, and prevention of delirium and other complications are essential to reduce functional decline.^{730,765,771} Frailty is also an independent predictor of mortality and cardiovascular events, while functional reserve and nutritional status may be more important determinants of prognosis than chronological age alone.^{730,780,782}

Thus, the frailty assessment should be integrated into the care of older adults with VHD, enabling better risk stratification, identification of modifiable factors, and individualized intervention, with a focus not only on survival but also on preserving independence and quality of life.

9. Cardiac Arrhythmias

Cardiac arrhythmias represent a major public health problem, particularly among older adults, because of their high prevalence, impact on morbidity and mortality, and association with reduced functional capacity and quality of life. Aging promotes structural and electrophysiological changes in the cardiovascular system, including myocardial fibrosis, degeneration of the cardiac conduction system, increased cardiac stiffness, and a greater burden of comorbidities, thereby favoring the development of both bradyarrhythmias and tachyarrhythmias. Among these, AF, supraventricular tachycardias (SVTs), and ventricular arrhythmias are particularly relevant, whereas sinus node dysfunction and atrioventricular block are frequent causes of clinically significant bradyarrhythmias. In addition, syncope is a common manifestation in this age group and is frequently associated with arrhythmias, orthostatic hypotension, neurally mediated reflexes, or structural heart disease. It is associated with an increased risk of falls, hospitalization, loss of functional independence, and mortality. The management of these conditions in older adults poses specific challenges related to frailty, multimorbidity, polypharmacy, pharmacokinetic and pharmacodynamic changes, and the need for individualized therapy based on life expectancy, functional status, and patient preferences. This section addresses the main aspects of the diagnostic assessment, risk stratification, and management of cardiac arrhythmias and syncope in older adults, with emphasis on the particular characteristics of this age group and the best available evidence for clinical practice.

9.1. Syncope in Older Adults

Syncope in older adults represents a major clinical challenge, not only because of its high frequency but also

because of its prognostic, functional, and socioeconomic impact. The incidence of syncope increases progressively with age. Population-based studies have demonstrated an annual incidence exceeding 2% among individuals older than 80 years, making syncope one of the most frequent causes of emergency department admission in this age group.⁷⁸⁴ In addition, up to 40% of the population experiences at least one syncopal episode during their lifetime.⁷⁸⁵ Among institutionalized older adults, the annual incidence of syncope approaches 6% to 7%, with an estimated prevalence of approximately 23%.⁷⁸⁶ Population aging, combined with a high burden of comorbidities, frailty, and polypharmacy, has increased the relevance of syncope as a cause of emergency department visits and hospitalization, particularly among the oldest patients, in whom hospitalization rates may exceed 50%.⁷⁸⁷ Recurrence is common, occurring in approximately 25%–35% of patients within 2 years after the first episode. In addition to the risk of recurrent events, syncope is associated with potentially serious consequences, including falls, trauma, fractures, loss of functional independence, and institutionalization.⁷⁸⁸

Mortality after a syncopal episode is not negligible, particularly in the presence of CVD. Studies have demonstrated mortality rates of approximately 1%–2% within the first 30 days and 7%–10% within the first year after the index event.⁷⁸⁹ In addition, patients with structural heart disease, ECG abnormalities, or suspected arrhythmic etiology have a significantly higher risk of cardiovascular events and mortality than those with reflex syncope or orthostatic hypotension.^{787,788}

The multiplicity of contributing factors, including polypharmacy, cardiovascular and neurological comorbidities, and age-related autonomic changes, makes diagnostic assessment particularly complex. In this context, a systematic and individualized approach is essential to identify high-risk patients, appropriately direct the diagnostic workup, and implement strategies capable of reducing recurrence, adverse events, and health care-related costs.

9.1.1. Definition and Differential Diagnosis

Syncope is defined as a transient and complete loss of consciousness secondary to global cerebral hypoperfusion and is characterized by sudden onset, short duration, and complete spontaneous recovery. Importantly, the mechanism responsible for loss of consciousness must necessarily be global cerebral hypoperfusion for the event to be classified as syncope. This is particularly important in older adults because several conditions may mimic syncope, complicating diagnostic assessment and appropriate management.

The most common mimics include epileptic seizures, particularly focal seizures or those with brief tonic-clonic manifestations, which may be mistaken for transient loss of consciousness. Features such as prolonged postictal confusion, tongue biting, or sphincter release may help distinguish them from syncope. Temporal lobe epilepsies, also referred to as ictal seizures, are rarer conditions that may trigger significant bradyarrhythmias, including atrioventricular block or prolonged sinus pauses, and may therefore present clinically as syncope.⁷⁹⁰ Other conditions that may mimic syncope include

cerebrovascular events, which may present with sudden collapse, weakness, or imbalance, with focal neurological deficits being critical for the differential diagnosis; metabolic disturbances, such as hypoglycemia and hyponatremia, which may also cause dizziness, confusion, and sudden falls; and psychogenic conditions, panic attacks, and psychogenic pseudosyncope, which, although less frequent, should be considered, particularly in patients with a psychiatric history.

However, the greatest diagnostic challenge in older adults is distinguishing syncope from falls. Studies have shown that approximately 45% of nonaccidental falls in older adults may have been caused by unrecognized syncope.⁷⁹¹ This clinical overlap occurs because older adults frequently have peri-event amnesia for loss of consciousness, lack of witnesses, atypical or absent prodromes, and multiple concurrent risk factors for falls, such as gait disorders, peripheral neuropathy, vestibular abnormalities, and muscle weakness.

Accordingly, differentiating true syncope from conditions that mimic syncope requires a detailed clinical assessment, complete physical examination, and often targeted complementary testing. Table 9.1 shows the main conditions that may mimic syncope in older adults.

Table 9.1 – Differential diagnosis of syncope in older adults

Condition	Characteristics and distinguishing features
Epileptic seizures	Distinguished from syncope by features such as prolonged postictal confusion, tongue biting, or urinary incontinence 1.
Stroke/transient ischemic attack	May present with sudden collapse or weakness; the presence of focal neurological deficits is the key determinant for diagnosis 1.
Metabolic abnormalities	Include hypoglycemia and hyponatremia, which may cause dizziness and confusion. Laboratory testing is required 1.
Psychogenic causes	Include panic attacks and psychogenic pseudosyncope. These should be suspected when syncopal episodes are very frequent and in patients with a history of psychiatric disorders 1.
Unexplained falls	In the absence of an evident mechanical cause, any unexplained fall in an older adult should prompt evaluation for syncope, particularly when associated with amnesia for the event, facial trauma, structural heart disease, orthostatic hypotension, or electrocardiographic abnormalities 1.

9.1.2. Etiological Classification

Although syncope in older adults frequently results from the interaction of multiple mechanisms, its etiological classification comprises three main categories: reflex syncope, syncope secondary to orthostatic hypotension, and cardiac syncope.⁷⁸⁷ The etiological distribution differs substantially from that observed in younger adults, with a higher prevalence of orthostatic hypotension and carotid sinus hypersensitivity, as well as frequent simultaneous involvement of more than one causal mechanism in the same syncopal episode.

Reflex syncope is one of the most common causes of transient loss of consciousness in this population. It results from inappropriate activation of cardiovascular reflexes that cause vasodilation and/or bradycardia, leading to transient reduction in cerebral perfusion. It includes classic vasovagal syncope, triggered by pain, emotional stress, or prolonged standing, as well as situational forms associated with urination, defecation, coughing, swallowing, and exercise. Carotid sinus hypersensitivity, which is particularly prevalent in older adults, is also included in this group. Reflex syncope generally presents with autonomic prodromes such as nausea, sweating, pallor, dizziness, and visual dimming and is usually associated with a favorable prognosis.⁷⁸⁷

Cardiac syncope is the etiology of greatest prognostic concern and is associated with a higher risk of major cardiovascular events and mortality. It may result from arrhythmias, including sinus node dysfunction, advanced atrioventricular block, SVTs, or ventricular tachycardias (VTs), as well as structural heart diseases capable of limiting cardiac output or impairing the cardiovascular response to exercise. Major causes include AS, hypertrophic cardiomyopathy, HF, ischemic heart disease, and pulmonary embolism. Cardiac syncope is characteristically sudden in onset, frequently without prodromal symptoms, and may occur during exercise or at rest.⁷⁸⁷

Syncope secondary to orthostatic hypotension results from failure of cardiovascular compensatory mechanisms to maintain adequate BP and cerebral perfusion upon assuming the upright position. This condition is particularly prevalent among older adults because of physiological changes associated with aging, the high burden of comorbidities, and polypharmacy. Causes include hypovolemia; use of diuretics, antihypertensive agents, vasodilators, or medications affecting the autonomic nervous system; and primary or secondary autonomic dysfunction (Figure 9.1).⁷⁸⁷

Early recognition of autonomic failure in patients with syncope and/or orthostatic hypotension is essential because of its important diagnostic, prognostic, and therapeutic implications. Autonomic failure may be classified as primary (degenerative), including multiple system atrophy, Parkinson disease, dementia with Lewy bodies, and pure autonomic failure; or secondary, resulting from peripheral autonomic neuropathies associated with DM, amyloidosis, autoimmune diseases, hereditary sensory-autonomic neuropathies, vitamin B12 deficiency, exposure to neurotoxins, HIV, and other infections.⁷⁹²

Once autonomic failure has been documented, a systematic investigation should be undertaken to define the underlying

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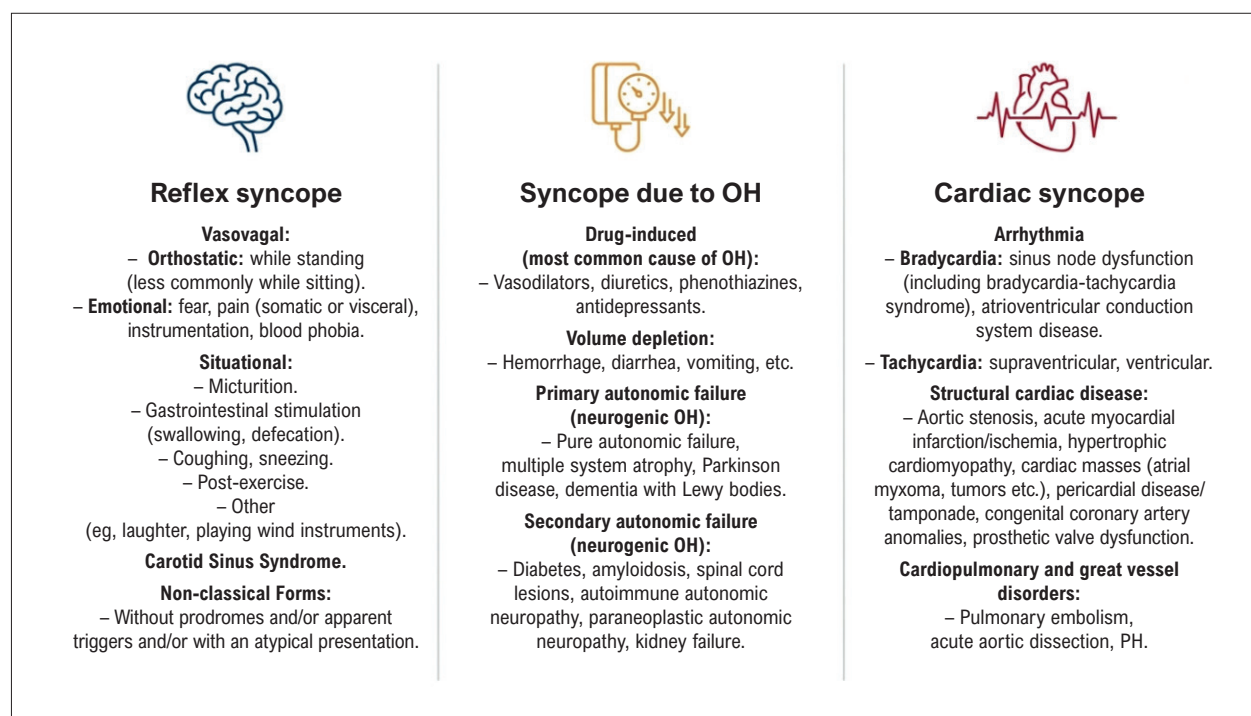


Figure 9.1 – Classification of syncope in older adults. OH: orthostatic hypotension; PH: pulmonary hypertension.

cause, because the specific etiological diagnosis directly influences prognosis and therapeutic strategies.⁷⁹³ Specialized autonomic assessment may include cardiovascular autonomic tests such as the Valsalva maneuver, deep breathing, tilt-table testing, measurement of plasma norepinephrine in the supine and upright positions, and detailed neurological assessment to identify signs of parkinsonism, peripheral neuropathy, or other manifestations of central nervous system involvement.⁷⁹³ In complex cases, particularly those involving multiple comorbidities, progressive autonomic symptoms, or conflicting results, referral to specialized autonomic assessment centers is recommended. Management requires a multidisciplinary approach involving neurologists, cardiologists, geriatricians, and other appropriately trained specialists, allowing optimization of treatment and prevention of complications.

9.1.3. Diagnostic Assessment

The diagnostic assessment of syncope in older adults is based on a detailed medical history and complete physical examination, both of which are mandatory in all cases and form the basis for establishing the diagnosis and guiding the rational use of complementary tests. Studies have shown that in approximately 64% of patients with syncope, the etiology can be determined with certainty (24%) or high probability (40%) based exclusively on the medical history, physical examination, and ECG.⁷⁹⁴ In addition, medical history, physical examination, and ECG play a fundamental role in risk stratification. Risk assessment aims to identify patients at greater likelihood of serious adverse outcomes in the short and long term, thereby guiding decisions regarding hospitalization, additional investigation, and urgent therapeutic interventions.

It should be performed in all patients presenting with loss of consciousness (Table 9.1).

9.1.3.1. Medical History and Physical Examination

The medical history should characterize the circumstances of the event, including body position, relationship with meals, physical activity, and precipitating factors; prodromal symptoms, with autonomic symptoms suggesting reflex syncope and palpitations or absence of a prodrome suggesting an arrhythmic cause; duration of the prodrome; witness accounts; and the recovery period. Past medical history should assess structural heart disease, arrhythmias, comorbidities associated with autonomic dysfunction, and a detailed medication review, which is particularly important in older adults because of polypharmacy.

The physical examination should include a complete cardiovascular assessment, including pulse palpation and cardiac auscultation to identify arrhythmias, murmurs, gallops, or friction rubs; a basic neurological examination; and mandatory measurement of orthostatic vital signs. BP and heart rate should be measured after at least 5 minutes in the supine position, immediately after standing (within 1 minute), and again after 3 minutes of standing. A decrease in SBP ≥ 20 mm Hg or DBP ≥ 10 mm Hg is diagnostic of orthostatic hypotension, regardless of a compensatory increase in heart rate.

9.1.3.2. Electrocardiogram

A 12-lead ECG is an integral part of the mandatory initial assessment of every patient with syncope. ECG abnormalities may suggest an arrhythmic etiology or underlying structural heart

disease and guide the need for additional investigation. High-risk findings include second- or third-degree atrioventricular block, bifascicular bundle branch block, persistent sinus bradycardia (< 50 bpm), sustained or nonsustained tachyarrhythmias, prolonged or shortened QT interval, pathological Q waves suggestive of prior MI, and ventricular pre-excitation. Table 9.2 shows the main features of the medical history, physical examination, and 12-lead ECG associated with increased short-term risk. Recommendations for the initial assessment of older patients with syncope are presented in Table 9.2.

9.1.4. Additional Tests

The use of complementary tests in the evaluation of syncope should be individualized and guided by findings from the medical history, physical examination, and initial ECG. Indiscriminate diagnostic testing is costly and frequently ineffective and should therefore be avoided. Rational selection of additional tests should be based on diagnostic suspicion, risk stratification, and a clear understanding of the diagnostic and prognostic value of each examination.

Table 9.2 – Short-term risk predictors in older patients with syncope or presyncope

Category	High-risk predictors
Clinical history	• Advanced age (> 60 years) • Male sex • History of structural or ischemic heart disease • Prior arrhythmias • Left ventricular dysfunction • Brief or absent prodrome • Syncope during physical exertion or while supine • Associated chest pain or dyspnea • Family history of premature SCD (< 50 years) • Known congenital heart disease
Physical examination	• Systolic BP < 90 mm Hg • Abnormal cardiac examination findings (murmurs, gallop rhythm, signs of HF) • Signs of bleeding or anemia • Focal neurological deficits • Sarcopenia • Dehydration
Electrocardiogram	• Changes suggestive of acute ischemia • Mobitz type II second-degree or third-degree atrioventricular block • Persistent sinus bradycardia (< 50 bpm) or sinus pauses ≥ 3 seconds • Ventricular or supraventricular tachyarrhythmias • Complete left bundle branch block • First-degree atrioventricular block (PR > 200 ms) • Non-sinus rhythm or multiple premature ventricular complex-es • Short PR interval with delta wave (Wolff-Parkinson-White syndrome) • Brugada syndrome (ST-segment elevation in V1-V2 with T-wave inversion) • Prolonged QT interval (QTc > 470 ms in men or > 480 ms in women) • Pathological Q waves

BP: blood pressure; HF: heart failure; PR: PR interval; QT: QT interval; QTc: corrected QT interval; SCD: sudden cardiac death; ST: ST segment.

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Recommendation for the initial assessment of older patients with syncope	Strength of recommendation	Certainty of evidence
A detailed medical history and complete physical examination should be performed in all patients with syncope.	STRONG	MODERATE
A 12-lead electrocardiogram should be performed as part of the initial assessment of all patients with syncope.	STRONG	MODERATE
Orthostatic BP and heart rate measurements should be performed in all patients with syncope.	STRONG	MODERATE
Assessment of the cause and risk stratification for short- and long-term morbidity and mortality are recommended in all patients with syncope.	STRONG	MODERATE
The medical history should include characterization of the circumstances of the event, prodromal symptoms, witness accounts, recovery period, past medical history, medication review, and family history.	STRONG	MODERATE
The physical examination should include a complete cardiovascular assessment (pulse palpation and cardiac auscultation), basic neurological examination, and measurement of orthostatic vital signs.	STRONG	MODERATE
Orthostatic BP and heart rate should be measured after at least 5 minutes in the supine position, immediately after standing (within 1 minute), and again after 3 minutes of standing.	STRONG	MODERATE
A decrease in systolic BP ≥ 20 mm Hg or diastolic BP ≥ 10 mm Hg upon standing is diagnostic of orthostatic hypotension.	STRONG	MODERATE
Low-risk patients with clinically suspected reflex syncope or orthostatic hypotension may be managed in the outpatient setting.	STRONG	MODERATE
High-risk patients with clinically suspected cardiac syncope or an undetermined cause should be managed in the hospital setting.	STRONG	MODERATE

BP: blood pressure; ECG: electrocardiogram.

9.1.4.1. Transthoracic Echocardiography

TTE is indicated in patients with suspected structural heart disease based on the initial assessment. It can identify AS, hypertrophic cardiomyopathy, left ventricular dysfunction, VHD, pericardial tamponade, aortic dissection, and acute right ventricular overload suggestive of pulmonary embolism. Studies have shown that among patients with a medical history, physical examination, or ECG suggestive of heart disease, echocardiography may suggest a diagnosis of cardiac syncope in approximately 48% of cases.⁷⁹⁵ Although echocardiography may not establish the immediate cause of syncope, it provides information on the underlying disease substrate and prognosis. However, routine echocardiography as a screening test in patients without clinical evidence of heart disease has a low diagnostic yield.

9.1.4.2. Prolonged Electrocardiographic Monitoring

Prolonged ECG monitoring has proven utility for diagnosing arrhythmias as the cause of syncope. The duration of monitoring should be individualized according to the frequency of syncopal episodes and the likelihood of an arrhythmic etiology. Available options include 24- to 48-hour Holter monitoring, external event monitors, either patient-activated or with automatic detection, and implantable loop recorders.

Implantable loop recorders are particularly useful in patients with recurrent syncope of uncertain origin, no high-risk criteria, and a high likelihood of recurrence, as well as in patients with high-risk criteria in whom comprehensive assessment has failed to identify a cause or lead to specific treatment. Despite their high diagnostic accuracy and recommendation in international guidelines, implantable loop recorders remain underused in our setting. Studies have shown that these devices can establish a diagnosis in up to 55% of cases of unexplained syncope, compared with only 19% with conventional strategies. They are particularly useful in older adults, in whom the clinical presentation is often atypical, with absent prodromes, amnesia for the event, and difficulty establishing a clinical-ECG correlation.⁷⁹⁶

9.1.4.3. Tilt-table Testing

Tilt-table testing can confirm the diagnosis of reflex vasovagal syncope and distinguish subtypes of orthostatic hypotension. When performed in patients with other possible causes of syncope, it may reveal susceptibility to hypotension and the coexistence of different etiological mechanisms. It should be considered when the initial evaluation does not provide a clear diagnosis of reflex syncope, orthostatic hypotension, postural orthostatic tachycardia syndrome, or psychogenic pseudosyncope.

When the diagnosis of reflex syncope is highly likely based on the medical history and physical examination, tilt-table testing may be useful for patient education regarding recognition of prodromal symptoms and learning physical counterpressure maneuvers. In addition, it may assist in differentiating syncope accompanied by abnormal movements from epileptic seizures and help patients recognize prodromal symptoms and learn physical counterpressure maneuvers.

Carotid sinus massage may be performed during tilt-table testing, increasing diagnostic accuracy, particularly in older adults with suspected carotid sinus hypersensitivity. The procedure is safe in patients without significant carotid stenosis and without stroke or transient ischemic attack within the prior 3 months.

Exercise testing is indicated in patients with syncope occurring during or immediately after physical exertion. Syncope during exercise suggests a cardiac etiology, whereas post-exertional syncope may be cardiac or reflex in origin. Electrophysiological study may be useful in patients with suspected arrhythmic etiology, particularly those with prior MI, myocardial scar, or bifascicular block when syncope

remains unexplained after noninvasive assessment. It is not recommended in patients with a normal ECG and normal cardiac function.

Laboratory tests should be ordered according to specific clinical findings, including hemoglobin when bleeding is suspected, D-dimer when pulmonary embolism is suspected, BNP and troponin when a cardiac etiology is suspected, and a basic metabolic panel in cases of dehydration or electrolyte abnormalities. CT or MRI of the brain has an extremely low diagnostic yield (< 0.1%) and should be requested only when intracranial disease or head trauma is suspected.

Carotid ultrasonography and electroencephalography are not recommended in the routine evaluation of syncope and are appropriate only when symptomatic carotid stenosis or epileptic seizure, respectively, is specifically suspected. Transcranial Doppler ultrasonography is useful when vertebrobasilar insufficiency is suspected and for assessing abnormalities in microcirculatory resistance and cerebrovascular autoregulation that may reduce flow velocity and compromise cerebral perfusion even in the absence of critical decreases in BP.

Recommendations for complementary tests for syncope evaluation in older adults	Strength of recommendation	Certainty of evidence
An implantable loop recorder should be considered in patients with recurrent unexplained syncope after a complete initial evaluation and exclusion of causes requiring immediate intervention, particularly when intermittent arrhythmia is suspected.	STRONG	MODERATE
Exercise testing should be recommended in patients with syncope during or immediately after exertion.	STRONG	MODERATE
Tilt-table testing should be considered in patients with syncope and suspected delayed orthostatic hypotension.	STRONG	MODERATE
Transthoracic echocardiography should be recommended in patients with suspected structural heart disease.	STRONG	MODERATE
Prolonged electrocardiographic monitoring may be requested in patients with suspected arrhythmia as the cause of syncope.	STRONG	MODERATE
Tilt-table testing should be considered in patients with unexplained syncope after the initial evaluation when reflex syncope is suspected.	STRONG	MODERATE
Carotid sinus massage should be considered in patients with syncope of undetermined etiology compatible with a reflex mechanism, in the absence of critical carotid stenosis or a recent cerebrovascular event.	STRONG	MODERATE
Electrophysiological study should be considered in patients with prior myocardial infarction, myocardial scar, or bifascicular block when syncope remains unexplained after noninvasive assessment.	STRONG	MODERATE
Laboratory tests should be ordered based on specific clinical findings, including hemoglobin, D-dimer, B-type natriuretic peptide, troponin, and electrolytes.	STRONG	LOW
Computed tomography or magnetic resonance imaging of the brain should not be routinely requested and is appropriate only when intracranial disease or head trauma is suspected.	STRONG	MODERATE
Carotid ultrasonography should not be requested in the absence of physical examination findings consistent with symptomatic carotid stenosis.	STRONG	MODERATE
Electroencephalography should not be requested as part of the basic evaluation of syncope and is appropriate only when an epileptic seizure is suspected.	STRONG	MODERATE

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9.1.5. Risk Stratification

Risk stratification in older patients with syncope is essential for defining short- and long-term management, guiding immediate decisions regarding the need for hospitalization as well as the management of underlying comorbidities that determine long-term prognosis. Short-term prognosis is primarily related to the cause of syncope and the acute reversibility of the underlying condition and is therefore fundamental for decision-making in the acute setting, whereas long-term prognosis is determined by treatment effectiveness and the severity and progression of underlying diseases, particularly cardiac conditions. Several risk stratification scores have been developed to assist in this assessment. Although the Canadian Syncope Risk Score is considered the most accurate, the FAINTE score was specifically developed in an older population (≥ 60 years) to identify patients at low risk of serious cardiac outcomes within 30 days.⁷⁹⁷ The FAINTE acronym represents five clinical and laboratory variables: F (Failure), history of HF; A (Arrhythmia), history of cardiac arrhythmia; I (Initial ECG abnormal); N (NT-proBNP), elevated NT-proBNP; and T (Troponin), elevated high-sensitivity troponin T (Figure 9.2). Each variable present contributes 1 point, and a FAINTE score of 0 (absence of all five variables) identifies patients at low risk of serious cardiac outcomes. The score demonstrated robust performance in the original derivation study involving 3,177 older adults (mean age, 73 years), with a sensitivity of 96.7% (95%CI 92.9%–98.8%) and specificity of 22.2% (95%CI 20.7%–23.8%) for a score of 0 versus ≥ 1 . The most recent prospective multicenter validation confirmed the excellent performance of the FAINTE score in 1,263 patients aged ≥ 40 years, demonstrating a sensitivity of 96.7% (95%CI 92.4%–100%) and a negative predictive value of 98.8% (95%CI 98.0%–99.7%) for serious cardiac outcomes (Figure 9.2).⁷⁹⁸

However, it is essential to recognize that structured clinical judgment incorporates nuances of the individual clinical context, complex comorbidities, frailty, and specific features of the presentation that are not fully captured by standardized scores. Algorithms should therefore be used as complementary tools that support, but do not replace, clinical decision-making.

FAINTE Score

- F** Failure (heart failure) 
- A** Arrhythmia (history of arrhythmia) 
- I** Initial abnormal ECG 
- N** Elevated NT-proBNP 
- T** Elevated troponin 

Figure 9.2 – FAINTE score for risk stratification of syncope and presyncope in older adults. ECG: electrocardiogram; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Recommendations for risk stratification of older adults with syncope or presyncope	Strength of recommendation	Certainty of evidence
Risk stratification should be performed in all older adults presenting with syncope or presyncope.	STRONG	MODERATE
Low-risk patients with clinically suspected reflex syncope or orthostatic hypotension may be managed in the outpatient setting.	STRONG	MODERATE
Hospitalization is indicated for older patients with syncope potentially related to a cardiac cause or when a serious medical condition is identified during the initial assessment.	STRONG	HIGH

9.1.6. Considerations Regarding the Treatment of Syncope

Treatment of syncope and presyncope in older adults should be directed toward the underlying cause identified during the initial assessment. In all cases, potentially contributing factors such as dehydration, polypharmacy, fluid and electrolyte disturbances, and associated comorbidities should be reviewed. Whenever possible, medications associated with orthostatic hypotension should be reduced or replaced, particularly those with vasodilatory effects or those that interfere with autonomic compensatory mechanisms. The main medications implicated include nitrates, CCBs, alpha-blockers, agents with combined alpha- and beta-blocking activity, and diuretics. In addition, several centrally acting medications may increase the risk of syncope, falls, and orthostatic hypotension, including tricyclic antidepressants, SSRIs, antipsychotics, phenothiazines, and levodopa. Therefore, periodic medication review, with deprescribing when appropriate, represents one of the main strategies for preventing recurrent syncope and related events in older adults.

9.1.6.1. Reflex Syncope and Orthostatic Hypotension in Older Adults

Nonpharmacological measures constitute the cornerstone of treatment for reflex syncope and orthostatic hypotension

in older adults, although their effectiveness varies and adherence is often limited in this population. Maintaining adequate hydration and liberalizing sodium intake, in the absence of contraindications, may help reduce symptoms related to hypotension. Physical counterpressure maneuvers, such as leg crossing, isometric contraction of the lower-limb muscles, and squatting, can increase BP and prevent syncopal episodes in patients with a sufficiently long prodrome and preserved functional capacity. Elastic compression stockings, ideally thigh-high or combined with abdominal compression, may also improve orthostatic symptoms and attenuate the decrease in BP.⁷⁹⁵

Structured physical exercise, also referred to as autonomic rehabilitation, represents a promising nonpharmacological therapeutic strategy for the management of syncope in older adults by modulating cardiovascular autonomic function and improving orthostatic tolerance. Studies have demonstrated that supervised training improves baroreflex sensitivity.⁷⁹⁹ Lower-limb muscle strengthening is particularly beneficial in older adults with orthostatic hypotension because it increases plasma volume, improves venous return, and enhances the effectiveness of physical counterpressure maneuvers.⁸⁰⁰ Passive postural training (tilt training) alone has limitations related to the heterogeneity of the available evidence and poor long-term adherence. However, supervised programs combining orthostatic training with aerobic exercise have demonstrated better results in reducing syncope recurrence, particularly in motivated individuals.⁸⁰¹

Behavioral measures, such as avoiding large meals, exposure to very hot environments, and abrupt postural changes, particularly after meals, may also reduce the occurrence of postprandial hypotension.

Regarding pharmacological treatment, the available evidence in older adults remains limited. Fludrocortisone may be considered in selected cases refractory to nonpharmacological treatment, particularly in the presence of orthostatic hypotension, by promoting volume expansion and symptom improvement. However, it should be used cautiously because of the higher frequency of adverse effects, including edema, hypokalemia, metabolic alkalosis, weight gain, and supine hypertension.⁷⁹⁵ Although

unavailable in Brazil, midodrine, a peripheral alpha-1 adrenergic agonist, may be used in patients with symptomatic orthostatic hypotension, particularly when nonpharmacological measures alone are insufficient. Its primary mechanism of action is to increase peripheral vascular resistance and standing BP, thereby reducing symptoms such as dizziness, presyncope, and syncope. Droxidopa represents another therapeutic option for neurogenic orthostatic hypotension, particularly in patients with Parkinson disease, pure autonomic failure, or multiple system atrophy.⁷⁹⁵ However, these medications require careful monitoring because of the risk of adverse effects, particularly supine hypertension.⁷⁹⁵ Elevating the head of the bed by 10 degrees, allowing the patient to sleep with the head elevated, is useful for minimizing the effects of nocturnal hypertension. In cases of severe supine hypertension (BP > 180/110 mm Hg), a short-acting vasodilator administered at bedtime is recommended.

In patients with recurrent reflex syncope associated with a documented cardioinhibitory response, particularly older patients with unpredictable episodes and a high risk of trauma, pacemaker implantation may be considered to reduce recurrence. This strategy yields the best results in individuals with documented spontaneous asystole (symptomatic pauses > 3 seconds or asymptomatic pauses > 6 seconds) during prolonged monitoring with an implantable loop recorder.⁸⁰² More recently, cardioneuroablation has emerged as a therapeutic alternative for selected patients with recurrent cardioinhibitory reflex syncope through modulation of the atrial autonomic ganglionated plexi. Although initial results are promising, experience in older adults remains limited, and the available evidence is insufficient to recommend its routine use in this population. Its indication should therefore be individualized and restricted to centers with expertise in the procedure.^{803,804}

Given the high prevalence of frailty, multimorbidity, and age-related physiological changes, the therapeutic approach should be individualized, aiming not only to reduce recurrence but also to minimize the risk of falls, trauma, functional decline, hospitalization, and impaired quality of life.

Recommendations for the treatment of syncope and presyncope in older adults	Strength of recommendation	Certainty of evidence
Systematic review of pharmacotherapy and identification of medications potentially associated with orthostatic hypotension, presyncope, and syncope should be performed in all older adults with syncopal episodes.	STRONG	MODERATE
Reduction or substitution of medications associated with orthostatic hypotension should be considered whenever clinically feasible.	STRONG	MODERATE
Nonpharmacological measures, including adequate hydration, liberalization of sodium intake (in the absence of contraindications), and behavioral guidance, should constitute the first step in the treatment of reflex syncope and orthostatic hypotension.	STRONG	MODERATE
Physical counterpressure maneuvers may be recommended in patients with reflex syncope who have recognizable prodromal symptoms and preserved functional capacity.	STRONG	MODERATE

Guidelines

Elastic compression stockings and/or abdominal compression may be considered in patients with symptomatic orthostatic hypotension.	WEAK	MODERATE
Structured physical exercise and autonomic rehabilitation programs may be considered to improve orthostatic tolerance and reduce symptoms.	WEAK	MODERATE
Passive postural training (tilt training) may be considered in selected and motivated patients.	WEAK	LOW
Fludrocortisone may be considered in patients with recurrent reflex syncope or symptomatic orthostatic hypotension refractory to nonpharmacological measures.	WEAK	MODERATE
Midodrine may be considered in patients with persistent symptomatic orthostatic hypotension despite nonpharmacological measures.	WEAK	MODERATE
Droxidopa may be considered in patients with neurogenic orthostatic hypotension, particularly when associated with neurodegenerative diseases.	WEAK	MODERATE
Patients receiving fludrocortisone, midodrine, or droxidopa may be monitored for the development of supine hypertension and other treatment-related adverse effects.	WEAK	MODERATE
Pacemaker implantation may be considered in selected older patients with recurrent cardioinhibitory reflex syncope and spontaneous asystole documented during prolonged monitoring.	WEAK	MODERATE
Cardioneuroablation may be considered in selected cases of recurrent cardioinhibitory reflex syncope, preferably at centers with expertise in the procedure.	WEAK	LOW

9.2. Bradyarrhythmias in Older Adults

Bradycardias are of considerable epidemiological importance in older adults and are more commonly identified in this age group because physiological aging is associated with progressive fibrosis of the sinus nodal tissue, atrial myocardium, and specialized conduction system.⁸⁰⁵ Data from the large Atherosclerosis Risk in Communities (ARIC) and CHS cohort studies, as well as permanent pacemaker registries, demonstrate that sinus node dysfunction and atrioventricular block are more prevalent among individuals in their seventh and eighth decades of life.⁸⁰⁵ Patients aged 75 years or more account for 64% of all cases of pacemaker implantation, reflecting the magnitude of the problem in this age range.

The clinical manifestation of bradycardias in older adults is heterogenous and often dramatic, with syncope being the most relevant symptom.⁸⁰⁵ Other symptoms include palpitations, particularly in bradycardia-tachycardia syndrome, reduced exercise tolerance, muscle fatigue, angina, and, in severe cases, signs of systemic hypoperfusion such as oliguria. Chronotropic incompetence, present in approximately 50% of patients with sinus node dysfunction, manifests as an inability to achieve an adequate heart rate during physical exertion, significantly limiting functional capacity in older adults.

Degeneration of the cardiac conduction system generally follows a slow, progressive course; consequently, symptoms of bradycardia often develop insidiously and may be mistakenly attributed to aging itself, frailty, or other comorbidities, making recognition particularly challenging in older adults. Furthermore, bradycardias in this population frequently coexist with multiple cardiovascular comorbidities, including CAD, HF, VHD, cerebrovascular disease, and AF, further increasing

clinical complexity and making therapeutic management more challenging.⁸⁰⁵

9.2.1. Classification of Bradycardias

Bradycardias are classically divided into intrinsic and extrinsic causes to guide the therapeutic approach. The most relevant intrinsic causes include degenerative fibrosis of the conduction system (Lev-Lenègre disease), ischemic or nonischemic cardiomyopathy, and infiltrative disorders such as amyloidosis and sarcoidosis. Extrinsic causes of greatest clinical importance include medications (beta-blockers, nondihydropyridine CCBs, digoxin, and antiarrhythmic drugs), metabolic disorders (hyperkalemia, hypothyroidism, and hypoxia), and autonomic dysfunction. Identification and treatment of reversible causes are essential before definitive pacemaker therapy is considered, particularly in older adults, among whom polypharmacy and metabolic abnormalities are prevalent. The etiological classification of bradycardias is presented in detail in Table 9.3.

9.2.2. Diagnostic Investigation

The diagnosis of bradycardia can be established using different ECG monitoring modalities, the choice of which should be based on the frequency and nature of symptoms. A 12-lead ECG constitutes the fundamental initial assessment. For patients with daily symptoms, 24- to 48-hour Holter monitoring is appropriate to establish a correlation between symptoms and cardiac rhythm abnormalities and may also identify chronotropic incompetence in physically active individuals. External event monitors (portable loop recorders) provide greater diagnostic accuracy because of their longer

Table 9.3 – Etiological classification of bradycardias

Intrinsic causes	Details
Degenerative fibrosis	Lev-Lenègre disease
Cardiomyopathy	Ischemic or nonischemic
Congenital heart disease	Congenital structural defects
Ischemia/Infarction	Acute myocardial infarction, chronic ischemia
Infection/Inflammation	Chagas disease, diphtheria, infective endocarditis, Lyme disease, myocarditis, sarcoidosis, toxoplasmosis
Infiltrative diseases	Amyloidosis, hemochromatosis, lymphoma
Rheumatologic diseases	Rheumatoid arthritis, scleroderma, systemic lupus erythematosus
Surgical/procedural trauma	Catheter ablation, congenital heart surgery, septal myectomy, valve surgery (including transcatheter aortic valve implantation)
Extrinsic causes	Details
Autonomic disturbance	Carotid sinus hypersensitivity, neurally mediated syncope/presyncope, physical conditioning, situational syncope (coughing, defecation, urination, vomiting, glottic stimulation, medical procedures), sleep (with or without sleep apnea)
Medications	Beta-blockers, nondihydropyridine calcium channel blockers (verapamil, diltiazem), digoxin, antiarrhythmic drugs, lithium, nutraceuticals
Metabolic disorders	Acidosis, hyperkalemia, hypokalemia, hypothermia, hypothyroidism, hypoxia
Endocrine disorders	Thyroid disorders (hypothyroidism and hyperthyroidism), adrenal disorders (pheochromocytoma, hypoadosteronism)
Intoxication	Mercury, cyanide, carbon monoxide, “mad honey,” nicotine, marijuana

monitoring period (up to 2–6 weeks) and are indicated for less frequent but recurrent symptoms. An implantable loop recorder is indicated for patients with infrequent symptoms (> 30 days between episodes) when the initial noninvasive assessment is inconclusive, allowing prolonged monitoring for up to 3 years. In cases of exercise-induced symptoms, exercise testing may clarify suspected chronotropic incompetence or advanced atrioventricular block. Electrophysiological study has a limited role in the evaluation of bradycardia and is reserved for selected cases of recurrent unexplained syncope after a

complete and inconclusive noninvasive evaluation, particularly in patients with bundle branch block or myocardial scar detected on CMR.^{795,806}

Recommendations for the Diagnostic Investigation of Bradycardias	Strength of recommendation	Certainty of evidence
A 12-lead ECG should be performed in all patients with suspected bradyarrhythmia.	STRONG	LOW
Reversible causes (negative chronotropic medications, electrolyte abnormalities, and hypothyroidism) should be investigated in all patients with bradycardia.	STRONG	LOW
Ambulatory ECG monitoring should be performed to establish a correlation between symptoms and bradyarrhythmia, with the type of monitor selected according to the frequency and nature of symptoms.	STRONG	MODERATE
A 24- to 48-hour Holter monitor should be used in patients with daily symptoms (presyncope, syncope, palpitations, exertional dyspnea, or disproportionate fatigue).	STRONG	LOW
A 24- to 48-hour Holter monitor may be used in asymptomatic patients with sinus bradycardia and/or atrioventricular block.	WEAK	LOW

Guidelines

Prolonged event monitoring (external loop recorder or 7-day Holter monitoring) may be considered for patients with weekly to monthly symptoms.	WEAK	MODERATE
An implantable loop recorder may be considered in patients with infrequent symptoms (> 30 days between events), suspected bradyarrhythmia, and an inconclusive noninvasive assessment.	WEAK	LOW
Exercise testing may be considered in patients with exertional symptoms and suspected chronotropic incompetence or exercise-induced atrioventricular block.	WEAK	LOW
Electrophysiological study may be considered in selected patients with suspected bradyarrhythmia and inconclusive noninvasive tests when the result is expected to alter management.	WEAK	LOW

ECG: electrocardiogram.

9.2.3. Considerations Regarding the Treatment of Bradyarrhythmias

Permanent pacemaker implantation is the treatment of choice for symptomatic bradycardia in older adults. In patients with second-degree Mobitz II atrioventricular block or complete atrioventricular block, observational studies have demonstrated significant improvements in survival and reductions in recurrent symptoms, including syncope and HF, compared with patients not treated with a pacemaker.⁸⁰⁵

In general, indications for permanent pacemaker implantation in older patients do not differ substantially from those in general guidelines and should be considered in the absence of reversible causes such as medications, inferior AMI, or electrolyte disturbances.

Dual-chamber pacing is the most widely used modality and is indicated whenever syncope correlates with symptomatic bradyarrhythmias, both in sinus node dysfunction and atrioventricular block. In the absence of symptom-rhythm correlation, the indication remains Class I in cases of advanced atrioventricular block (Mobitz II or complete AV block) and in patients with bundle branch block in whom electrophysiological study demonstrates a prolonged His-ventricular interval ≥ 70 ms. In patients with sinus node dysfunction and preserved atrioventricular conduction, atrial or dual-chamber pacing is preferable to isolated ventricular pacing because it preserves atrioventricular synchrony and reduces the risk of AF and HF.

In cases of cardioinhibitory reflex syncope eligible for cardiac pacing therapy (recommendations for the treatment of syncope and presyncope in older adults), systems using closed loop stimulation technology, which assess changes in myocardial contractility through bioimpedance, may be useful for physiologically increasing heart rate and preventing recurrent syncopal events. This technology allows dynamic adjustment of the pacing rate according to the patient's hemodynamic requirements and may be particularly beneficial in older adults with associated dysautonomia.^{807,808}

Leadless pacemakers represent a particularly attractive therapeutic option for older and frail patients. These capsule-shaped devices are implanted in the right ventricle through the femoral vein and require neither transvenous leads nor a pectoral generator pocket, thereby eliminating complications related to the generator and leads. Although current guidelines already include recommendations for their use in patients with complications related to conventional devices (eg, lead fracture or after device extraction because of infection) and in the presence of critical venous obstruction, age alone requires additional evidence before it can be formally incorporated as an indication in clinical guidelines.⁸⁰⁹ Studies have shown that leadless pacemakers are associated with lower complication rates than conventional transvenous pacemakers, with a mean age of approximately 75–76 years among the patients studied.⁸¹⁰ More recently, dual-chamber leadless systems have been introduced and may provide adequate chronotropic support while preserving atrioventricular synchrony, thereby potentially expanding the indications for these devices.⁸¹¹

Indications for CRT are the same across age groups. Available evidence supports that age should not be a limiting factor for appropriately indicated implantation in older patients with HF, left ventricular systolic dysfunction, and left bundle branch block. Although frail patients are at greater risk of complications after implantation of cardiac implantable electronic devices, the presence of comorbidities is an even stronger predictor of adverse outcomes. Therefore, frailty should not contraindicate the procedure but should be incorporated into an individualized risk-benefit assessment.⁸¹² The decision to implant a pacemaker in an older patient should consider not only technical indications but also life expectancy, comorbidities, frailty, and the patient's goals of care, recognizing that chronological age alone should not be an exclusion criterion for therapies with established benefit.

Recommendations for the treatment of bradyarrhythmias in older adults	Strength of recommendation	Certainty of evidence
Potentially reversible causes of bradycardia, including negative chronotropic drugs, fluid and electrolyte disturbances, and myocardial ischemia, should be investigated and corrected before permanent pacemaker implantation.	STRONG	HIGH
Permanent pacemaker implantation is indicated in older patients with second-degree Mobitz II atrioventricular block, high-grade AV block, or complete AV block not attributable to reversible causes, regardless of symptoms.	STRONG	HIGH
Permanent pacemaker implantation is indicated in older patients with symptomatic sinus node dysfunction (syncope, presyncope, dizziness, or fatigue) with documented ECG correlation with bradycardia, in the absence of reversible causes.	STRONG	MODERATE
Dual-chamber pacing is preferable to isolated ventricular pacing in older patients with advanced AV block or sinus node dysfunction to preserve atrioventricular synchrony.	STRONG	MODERATE
In older patients with BBB and an His-ventricular interval ≥ 70 ms on electrophysiological study, permanent pacemaker implantation is recommended.	STRONG	MODERATE

CRT should be considered in older patients according to the same indications applied to the general population (HF, reduced ejection fraction, and left BBB), and age should not be a limiting factor.	STRONG	MODERATE
Chronological age alone should not be an exclusion criterion for pacemaker implantation in older patients with a well-established indication.	STRONG	MODERATE
Frailty should be considered in the individualized risk-benefit assessment but should not, in isolation, contraindicate pacemaker implantation when there is a clear indication and an expected clinical benefit.	STRONG	MODERATE

AV: atrioventricular; BBB: bundle branch block; CRT: cardiac resynchronization therapy; ECG: electrocardiogram; HF: heart failure.

9.3. Tachyarrhythmias in Older Adults

Both supraventricular and ventricular tachyarrhythmias represent a growing clinical challenge in older adults, with substantial epidemiological and prognostic impact. AF is the most common arrhythmia and will be addressed in a dedicated section of these Guidelines.

9.3.1. Supraventricular Tachycardias

The prevalence of supraventricular arrhythmias increases significantly with age, and individuals older than 65 years have a fivefold higher risk of developing paroxysmal SVT compared with younger individuals.⁸¹³ Premature atrial contractions are extremely prevalent among older adults and are observed in approximately 86% of patients aged 60 to 85 years during prolonged monitoring.⁸¹⁴ Although historically regarded as benign findings, recent evidence indicates that frequent premature atrial contractions are associated with significant adverse clinical outcomes. Meta-analyses have shown that frequent atrial contractions are associated with AF, stroke (adjusted HR 1.41; 95%CI 1.25–1.60), and all-cause mortality

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(adjusted HR 1.26; 95%CI 1.13–1.41). These associations remain significant even after adjustment for confounding factors, suggesting that frequent premature atrial contractions may reflect underlying structural and functional atrial abnormalities, a concept known as atrial cardiomyopathy.^{815,816}

The occurrence of atrial tachycardia increases progressively with aging, accounting for 23% of SVTs in patients older than 70 years.⁸¹⁷ Studies using prolonged monitoring in older adults have demonstrated a high prevalence of SVT episodes, observed in 84.4% of participants with a mean age of 77 years, although only 13.5% reported associated symptoms.⁸¹⁷

Clinical manifestations of supraventricular tachyarrhythmias in older adults range from mild symptoms to severe presentations. The most common symptoms include palpitations, dizziness, awareness of pulsations in the neck, and dyspnea. Older patients with SVT are more prone to syncope or presyncope than younger patients, although they paradoxically exhibit slower heart rates during episodes.⁸¹⁷ This greater susceptibility is related to more pronounced hemodynamic changes, with an abrupt decrease in BP during the first 10–30 seconds after arrhythmia onset.⁸¹⁷ Dyspnea, chest pain, and syncope may occasionally occur, particularly in patients with sustained acute arrhythmias, significant diastolic dysfunction, severe AS, HF, or CAD. The higher the heart rate, the lower the tolerance to the arrhythmia because of reduced cardiac output, resulting in manifestations of cerebral and myocardial ischemia, arterial hypotension, and pulmonary congestion.⁸¹⁸ The forms of SVT in older adults are displayed in Figure 9.3.

9.3.2. Ventricular Tachyarrhythmias

Ventricular arrhythmias represent an important clinical challenge in older adults, with increasing prevalence and complexity with aging. Premature ventricular contractions (PVCs) are found in 70%–80% of individuals older than 60 years and, in most cases, are asymptomatic except when very frequent.⁸¹⁴ When symptomatic, manifestations range from palpitations perceived as repetitive beats or a sensation that the “heart is going to stop” because of compensatory pauses to presyncope, syncope, pulmonary congestion, and disorientation.

The clinical significance of ventricular arrhythmias in older adults depends fundamentally on the presence or absence of structural heart disease. In patients with structural heart disease, complex ventricular arrhythmias may be associated with major coronary events and SCD.⁸¹⁹ Left ventricular hypertrophy is an important determinant of ventricular arrhythmias, and the presence of HF dramatically increases the incidence of VT from 2%–4% in patients without HF to 20%–80%.⁸²⁰ Recent studies have shown that a high PVC burden is associated with left ventricular systolic dysfunction, incident HF, and mortality, with specificity exceeding 90% for predicting the risk of HF over 15 years when the PVC burden is $\geq 10\%$.⁸²¹ Multifocal PVCs and nonsustained VT have also been associated with an increased risk of death and nonfatal adverse cardiovascular events, including stroke.

In contrast, ventricular arrhythmias in older adults without structural heart disease do not appear to carry an adverse

prognostic implication compared with the general population. Therefore, patients with left ventricular dysfunction or hypertrophy and complex ventricular arrhythmias should be considered at high risk of SCD, even when asymptomatic, whereas those without documented structural heart disease generally have a favorable prognosis.

9.3.3. Diagnostic Assessment

The diagnostic assessment of supraventricular and ventricular tachyarrhythmias in older adults should be individualized according to symptom frequency, severity of clinical manifestations, and the presence of structural heart disease. A 12-lead ECG is the fundamental initial examination and should ideally be obtained during the arrhythmic episode to identify the tachycardia mechanism. ECG documentation of the arrhythmia during symptoms provides the strongest evidence of causality and helps distinguish arrhythmic from nonarrhythmic palpitations, although its diagnostic yield is limited when obtained outside the event (3%–26%).⁸¹³

TTE is recommended to assess structural heart disease in patients with documented tachyarrhythmias, particularly those with abnormal physical examination findings, ECG abnormalities, a history of syncope or presyncope, or a family history of cardiomyopathy or SCD.⁸¹³ Similar to the evaluation of syncope, ambulatory ECG monitoring should be selected according to symptom frequency. A 24-hour Holter monitor is appropriate when symptoms occur daily, whereas external event monitors or 7-day Holter monitoring are appropriate for more sporadic symptoms. An implantable loop recorder is indicated in selected cases with infrequent symptoms associated with hemodynamic instability or recurrent unexplained syncope.

CMR should be considered for evaluation of structural heart disease, particularly when arrhythmogenic cardiomyopathy, infiltrative disease, myocarditis, or other conditions not adequately characterized by echocardiography are suspected. Electrophysiological study is indicated when ambulatory monitoring remains nondiagnostic despite a high clinical suspicion of tachyarrhythmia, particularly in patients with syncope preceded by palpitations or those with wide-complex tachycardia of uncertain origin.

Recommendations for the diagnostic assessment of tachyarrhythmias in older adults	Strength of recommendation	Certainty of evidence
A 12-lead ECG should be performed in all older patients with suspected tachyarrhythmia, ideally during the arrhythmic episode and after cardioversion.	STRONG	HIGH

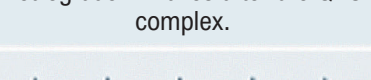
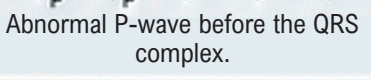
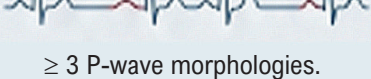
ARRHYTHMIA	VISUAL/TECHNICAL REPRESENTATION (ECG)	BRIEF DESCRIPTION
AF	 Irregular rhythm without P-waves.	Irregular rhythm with absent P-waves.
Atrial flutter	 Sawtooth F waves.	Sawtooth F waves, usually with 2:1, 3:1, or variable AV conduction.
AVNRT	 Narrow QRS complexes with hidden P-waves or pseudo-S/pseudo-R waves.	Regular narrow-QRS tachycardia. P-waves are often hidden within the QRS complexes.
AVRT	 Retrograde P-waves after the QRS complex.	Regular narrow-QRS tachycardia with retrograde P-waves following the QRS complexes.
Focal atrial tachycardia	 Abnormal P-wave before the QRS complex.	Abnormal P-wave preceding each QRS complex, with a generally regular rhythm.
Multifocal atrial tachycardia	 ≥ 3 P-wave morphologies.	At least three distinct P-wave morphologies with a heart rate > 100 bpm.
Junctional tachycardia	 Narrow QRS complexes with AV dissociation.	Regular tachycardia originating from the AV junction.
Premature atrial contractions	 Premature beat with a noncompensatory pause.	Premature beat preceded by a P-wave with a different morphology, followed by a noncompensatory pause.

Figure 9.3 – Differential diagnosis of narrow-QRS tachycardias in older adults. AF: atrial fibrillation; AV: atrioventricular; AVNRT: atrioventricular nodal reentrant tachycardia; AVRT: atrioventricular reentrant tachycardia; ECG: electrocardiogram.

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TTE should be performed in patients with documented tachyarrhythmia to assess structural heart disease.	STRONG	MODERATE
A 24- or 48-hour Holter monitor is indicated in patients with frequent symptoms to establish ECG correlation.	STRONG	MODERATE
A 7-day Holter monitor, external event monitor, or wearable device is indicated in patients with less frequent symptoms.	STRONG	MODERATE
An implantable loop recorder should be considered in patients with infrequent symptoms when an arrhythmic cause is suspected but has not been identified by noninvasive assessment.	STRONG	MODERATE
Exercise testing should be considered in patients with tachyarrhythmias clearly triggered by physical exertion.	STRONG	LOW
CMR should be considered in patients with VT to assess structural heart disease and myocardial fibrosis.	STRONG	MODERATE
Electrophysiological study is indicated in cases of recurrent tachyarrhythmia with inconclusive noninvasive monitoring or when catheter ablation is being considered for therapeutic planning.	STRONG	MODERATE

ECG: electrocardiogram; MRI: magnetic resonance imaging
TTE: transthoracic echocardiography; VT: ventricular tachycardia.

9.3.4. Considerations Regarding the Treatment of Tachyarrhythmias

The principles of tachyarrhythmia treatment in older adults are similar to those applied to younger patients, although they are frequently influenced by underlying structural heart disease, multimorbidity, and polypharmacy. Therapeutic decisions should be individualized, taking into account not only chronological age but also comorbidities, functional status, cognitive status, patient preferences, and symptom severity, with the aim of balancing the potential risks and benefits of each intervention.

9.3.4.1. Supraventricular Tachycardia

Nonsustained atrial tachycardias generally do not require specific treatment. Initial management should prioritize treatment of the underlying condition, when present, and elimination of potential triggers, including excessive caffeine intake, smoking, and use of short-acting β -adrenergic agonists. When pharmacological treatment is required for symptom control, nondihydropyridine CCBs may be used in patients with COPD without significant ventricular dysfunction, whereas low-dose cardioselective beta-blockers are an alternative for patients without contraindications.⁸²²

In sustained, hemodynamically stable paroxysmal SVT, vagal maneuvers should be used as the initial strategy, with the modified Valsalva maneuver being preferred. Carotid sinus massage may be considered in selected cases, provided that it is performed by a trained healthcare professional after exclusion of significant carotid stenosis or a recent cerebrovascular event. If the arrhythmia does not terminate, adenosine is the first-line pharmacological treatment and should be administered under continuous ECG monitoring.⁸²²

When adenosine is ineffective or contraindicated, nondihydropyridine CCBs (verapamil or diltiazem) or beta-blockers may be used in hemodynamically stable patients, taking into account the specific contraindications of each drug class. In patients with hemodynamic instability, hypotension, angina, acute HF, or altered level of consciousness, synchronized electrical cardioversion is indicated, generally using an initial energy of 50–100 J.⁸²² In older adults, particular caution should be exercised with verapamil, diltiazem, and beta-blockers because of the greater risk of hypotension, atrioventricular block, and decompensation of previously undiagnosed sinus node dysfunction.⁸²³

Catheter ablation is considered a first-line therapy for patients with recurrent symptomatic paroxysmal SVT, with success rates exceeding 95% and efficacy comparable between older and younger patients.⁸²² In particular, catheter ablation of atrioventricular nodal reentrant tachycardia has demonstrated high efficacy and safety in patients older than 75 years, with a single-procedure success rate of 94.3% (95%CI 91.2%–97.4%). Although older adults have a greater burden of comorbidities and a theoretically higher risk of procedure-related complications, major adverse events occur in fewer than 3% of cases, and advanced age is not associated with significantly lower acute success or higher recurrence rates.⁸²⁴ Therefore, age alone should not be considered a contraindication to ablation.

The procedure should be considered in patients with recurrent symptomatic episodes, substantial impairment of quality of life, contraindication, failure, or intolerance of pharmacological therapy, as well as in those who wish to avoid chronic antiarrhythmic drug therapy. Atrioventricular nodal reentrant tachycardia episodes are relatively common in older adults because of slowing of conduction through both the fast and slow nodal pathways, which may result in slower, recurrent, and sometimes incessant tachycardias. In these cases, catheter ablation is recommended given the limitations of pharmacological treatment (Figure 9.4).⁸²⁵

9.3.4.2. Ventricular Tachycardia

PVCs and nonsustained VT in patients without structural heart disease generally do not require specific antiarrhythmic therapy. Identification and correction of precipitating factors, such as fluid and electrolyte disturbances, myocardial ischemia, hypoxemia, hyperthyroidism, and stimulant use, should be prioritized.⁸¹⁹

When symptomatic or associated with structural heart disease, beta-blockers are the first-line pharmacological therapy in the absence of contraindications. In sustained VT with hemodynamic instability, immediate synchronized electrical cardioversion is indicated.⁸¹⁹ In hemodynamically stable patients with structural heart disease, amiodarone

and sotalol represent the main therapeutic options, with amiodarone generally preferred in the presence of significant left ventricular dysfunction or HF.⁸²⁵

The choice of antiarrhythmic drug should consider age-related pharmacokinetic changes, including reduced kidney and liver function, greater susceptibility to proarrhythmic effects, and potential drug interactions. Lower starting doses with gradual titration are therefore recommended.⁸²⁵

An ICD is indicated for secondary prevention of SCD in patients with sustained VT or ventricular fibrillation not attributable to reversible causes and is appropriate in older adults with a life expectancy of more than 1 year and functional status compatible with meaningful clinical benefit.^{806,826}

Catheter ablation should be considered in patients with recurrent VT, electrical storm, or intolerance to pharmacological therapy. Success rates are similar to those observed in younger patients, although the risk of complications is higher because of the greater burden of comorbidities and the complexity of the arrhythmic substrate.⁸²⁷

The main antiarrhythmic drugs, their dosing, and considerations for use in older adults are summarized in Table 9.4.

9.4. Atrial Fibrillation

AF is the most prevalent arrhythmia in the geriatric population, with an exponential increase associated with aging. AF affects 6.4% of individuals aged 65–69 years and rises to 28.5% among those aged ≥ 85 years.⁸²⁸ Longitudinal analyses from the Framingham Heart Study demonstrated a substantial increase over 5 decades (1958–2007), with age-adjusted incidence increasing from 3.7 to 13.4 per 1,000 person-years in men and from 2.5 to 8.6 in women.⁸²⁹ Globally, the prevalence of AF doubled between 1990 and 2019, reaching 59.7 million cases, with projections indicating a 2.5-fold increase in the United States by 2050, when more than 50% of patients will be aged ≥ 80 years.⁸³⁰

In recent years, epidemiological studies have demonstrated substantial coexistence between AF and frailty syndrome, with a prevalence of frailty of 39.7% among patients with AF.⁸³¹ Recent longitudinal studies indicate that AF is associated with accelerated progression of frailty over time and that frailty frequently coexists with cognitive impairment and functional dependence in this population.⁸³²

9.4.1. Definition, Classification, and Diagnosis

AF is defined as an atrial arrhythmia characterized by complete disorganization of atrial electrical activity and consequent loss of effective atrial contraction. On the ECG, AF is characterized by irregular R-R intervals, provided that atrioventricular conduction is preserved, absence of well-defined sequential P-waves, and their replacement by fibrillatory waves (f waves) on the ECG baseline.

AF should initially be classified according to its presentation as clinical or subclinical.⁸³³ Clinical AF refers to symptomatic or asymptomatic arrhythmia documented on a 12-lead ECG or single-lead rhythm ECG for at least 30 seconds and validated by a qualified physician. Subclinical AF occurs in patients

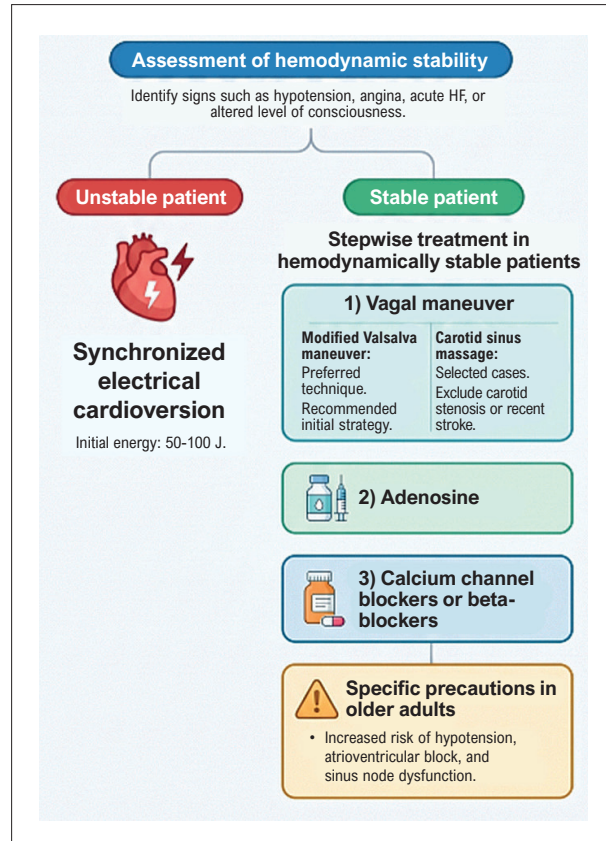


Figure 9.4 – Algorithm for the acute management of supraventricular tachycardias. HF: heart failure.

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Table 9.4 – Medications commonly used for the treatment of tachyarrhythmias in older adults: main indications, dosing, adverse effects, and considerations for use

Medication	Usual dosage	Main indications	Main precautions and adverse effects
Metoprolol	12.5–25 mg/day, titrated up to 200 mg/day	Rate control in AF, PSVT, and symptomatic ectopy	Bradycardia, hypotension, fatigue, and bronchospasm. Start at low doses and titrate slowly.
Bisoprolol	1.25–2.5 mg/day, titrated up to 10 mg/day	Rate control in AF and PSVT	Bradycardia, hypotension, and fatigue. Lower bronchoconstriction potential.
Verapamil	40–80 mg every 8 hours or 120–240 mg/day (extended release)	PSVT and rate control in AF	Hypotension, constipation, peripheral edema, bradycardia, and AV block. Avoid in HFrEF.
Diltiazem	120–360 mg/day	PSVT and rate control in AF	Hypotension, peripheral edema, and bradycardia. Generally better tolerated than verapamil.
Propafenone	150–300 mg every 8 hours	Paroxysmal AF without structural heart disease and recurrent PSVT	Proarrhythmia, bradycardia, dizziness, metallic taste, and conduction disturbances. Contraindicated in CAD or significant structural heart disease.
Sotalol	40–80 mg every 12 hours, adjusted according to kidney function	Recurrent AF and selected VTs	Bradycardia, hypotension, QT prolongation, and torsades de pointes. Requires QT monitoring and dose adjustment according to kidney function.
Amiodarone	Loading: 400–600 mg/day; maintenance: 100–200 mg/day	AF, atrial flutter, VTs, and patients with structural heart disease	Thyroid dysfunction, pulmonary toxicity, hepatotoxicity, neuropathy, photosensitivity, and ocular abnormalities. Requires periodic monitoring.
Adenosine	6 mg IV rapid bolus; if necessary, 12 mg followed by another 12 mg	Acute termination of reentrant PSVT	Flushing, transient dyspnea, chest pain, transient asystole, and bronchospasm. Administer under continuous monitoring and avoid in patients with second- or third-degree atrioventricular block, sick sinus syndrome, known bronchoconstrictive or bronchospastic lung disease, or known hypersensitivity to adenosine.

AF: atrial fibrillation; AV: atrioventricular; CAD: coronary artery disease; HFrEF: heart failure with reduced ejection fraction; IV: intravenous; PSVT: paroxysmal supraventricular tachycardia; QT: QT interval; VT: ventricular tachycardia.

without symptoms attributable to AF who have accelerated atrial rhythm recorded through the atrial lead of cardiac implantable electronic devices or recordings suggestive of AF on implantable loop recorders or wearable devices lasting less than 30 seconds.

The distinction between clinical and subclinical AF is fundamental in clinical practice because patients with subclinical AF were not included in the major clinical trials that form the basis of current AF treatment. These cases should therefore be managed cautiously and assessed individually.⁸¹³

According to duration, AF is classified as paroxysmal (< 7 days), persistent (> 7 days and < 1 year), long-standing persistent (> 1 year with a rhythm-control strategy), permanent (when the physician and patient decide not to pursue restoration of sinus rhythm), and post-ablation (patients who have undergone ablation without arrhythmia recurrence) (Figure 9.5).

Diagnosis is often challenging because AF may be asymptomatic and intermittent. When clinically suspected, prolonged ambulatory monitoring using available technologies

is recommended, including 1- to 7-day Holter monitoring, external loop event monitors for 1–4 weeks, wearable devices such as smartwatches and smartphone applications, and cardiac implantable electronic devices, including implantable loop recorders and pacemakers, to enable documentation of clinical AF with an ECG recording of at least 30 seconds validated by a physician.

9.4.2. Predisposing Factors

Predisposing factors for AF include intrinsic and modifiable factors that contribute to formation of the atrial arrhythmogenic substrate. Among intrinsic factors, advanced age, male sex, and genetic polymorphisms involving connexins, ion channels, and transcription factors are particularly relevant, with more than 160 mutations already implicated in the pathogenesis of AF.⁸³⁴

The most relevant comorbidities include hypertension, HF (which increases the risk four- to sixfold), DM, gastroesophageal reflux disease, hyperthyroidism, and systemic infections.⁸³³

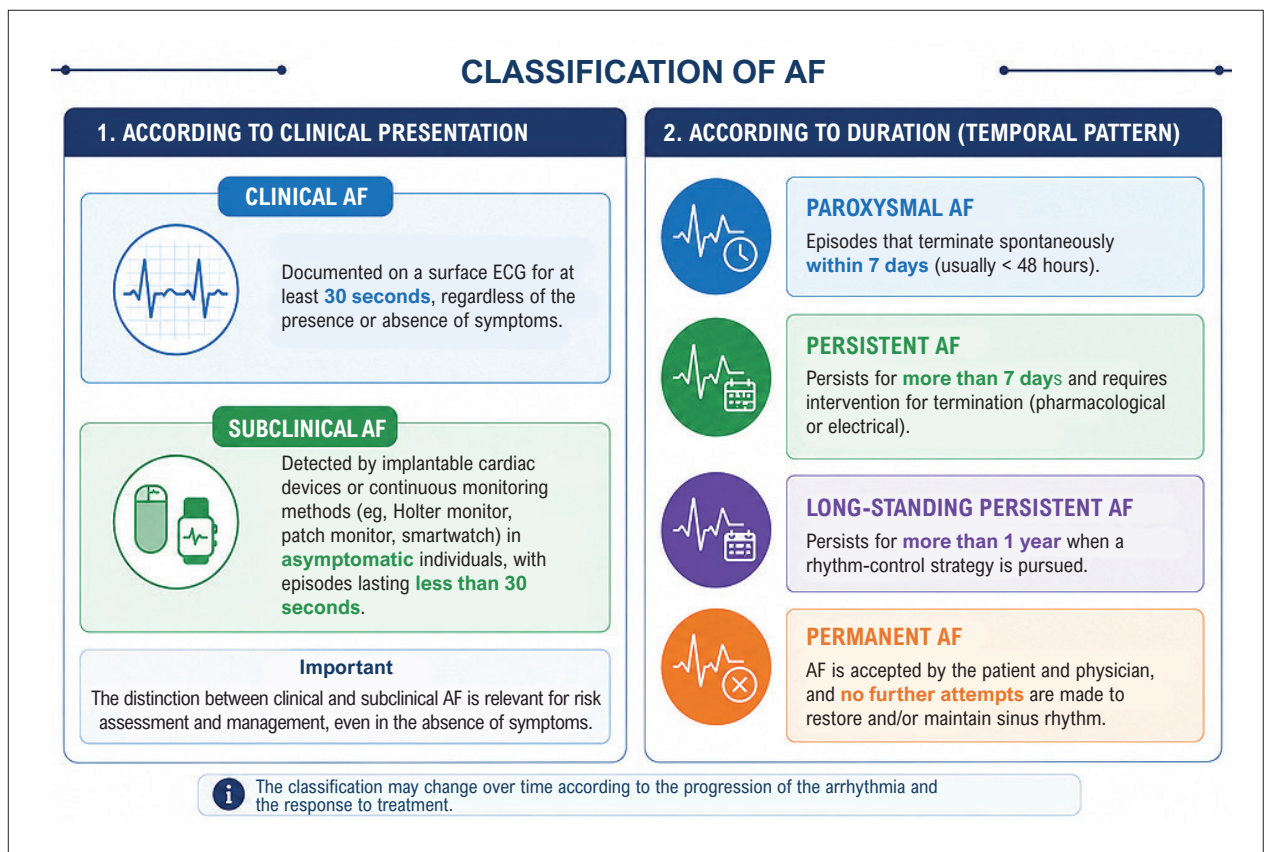


Figure 9.5 – Classification of AF according to clinical presentation and temporal pattern. AF: atrial fibrillation; ECG: electrocardiogram.

Modifiable lifestyle factors play a fundamental role and include obesity, physical inactivity, poor sleep quality (particularly obstructive sleep apnea), alcohol consumption, and smoking. Contrary to what might be expected, moderate caffeine consumption has not been shown to be harmful.⁸³³

The diagnosis of AF in older adults is initially based on medical history, physical examination, and a 12-lead ECG. Clinical manifestations are often atypical or absent, in contrast to younger populations. Approximately 10% to 40% of patients with AF are asymptomatic, and this presentation is significantly more common among older adults.⁸²⁹ In patients older than 80 years, palpitations are present in only 1 in 10 patients.⁸¹⁴ Nonspecific noncardiac symptoms such as fatigue, dyspnea, and dizziness predominate in older adults rather than palpitations or awareness of an irregular heartbeat. However, it is not uncommon for the initial presentation to be a complication of the arrhythmia, such as stroke, systemic thromboembolism, or HF.⁸²⁹

9.4.3. Screening for Atrial Fibrillation in Older Adults and the Role of Prolonged Electrocardiographic Monitoring

Active screening for AF in older adults has gained increasing importance in clinical practice because of the high prevalence of asymptomatic AF in this population and the potential for prevention of ischemic stroke through anticoagulation.

The STROKESTOP trial, which randomized 28,768 Swedish individuals aged 75–76 years to systematic screening versus usual care, demonstrated that screening significantly increased AF detection and resulted in a small but significant reduction in the composite outcome of ischemic stroke, hemorrhagic stroke, systemic embolism, bleeding requiring hospitalization, and all-cause mortality.⁸³⁵ The LOOP trial, which used implantable loop recorders in 6,004 patients aged 70–90 years with stroke risk factors, substantially increased AF detection (HR 3.17; 95%CI 2.81–3.59) over a mean follow-up of 64.5 months, although it did not demonstrate a significant reduction in stroke.⁸³⁶

More recently, the GUARD-AF trial evaluated 11,905 participants aged ≥ 70 years randomized to screening with a 14-day ECG patch versus usual care, identifying AF in 5% of the screening group versus 3.3% of the control group, but without demonstrating a reduction in stroke hospitalizations, possibly because the trial was terminated prematurely during the COVID-19 pandemic.⁸³⁷ Despite still inconclusive evidence regarding the impact of screening on hard clinical outcomes, Brazilian, European, and Canadian guidelines recommend opportunistic screening in patients aged ≥ 65 years, with consideration of systematic screening in those aged ≥ 75 years or at high risk of stroke.

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Several strategies are available for AF screening in older adults, varying in diagnostic accuracy and detection effectiveness. Radial pulse palpation is the simplest and most accessible method, with a sensitivity of 87%–100% but lower specificity. A 12-lead ECG remains the diagnostic gold standard. Single-lead ECG devices have demonstrated sensitivity of 88%–99% and specificity of 76%–100%.⁸³⁸

Detection effectiveness increases with monitoring duration. A 24-hour Holter monitor detects only approximately 2.2% of AF cases, whereas external event monitors detect 7.4% within 1 week and 14.8% within 4 weeks. Implantable loop recorders provide the highest sensitivity, detecting AF in 30%–32% of patients over 3 years compared with 3%–12% with usual care. Wearable devices, including smartwatches, have demonstrated sensitivity of approximately 94% and specificity of 93%–96%, but findings require physician confirmation.⁸³⁹

There are no specific recommendations for AF screening in frail older adults. The decision to screen should be individualized according to life expectancy, bleeding risk associated with anticoagulation, ability to adhere to treatment, and patient preferences. In very frail older adults or those with limited life expectancy, screening may not be appropriate when the risks of anticoagulation are expected to outweigh its potential benefits.

Recommendations for the diagnosis and screening of AF in older adults	Strength of recommendation	Certainty of evidence
Opportunistic screening for AF by pulse palpation or 12-lead ECG is recommended in individuals aged ≥ 65 years.	STRONG	MODERATE
Surface ECG and ECG monitoring with 24- to 72-hour Holter monitoring may be performed in patients with ischemic stroke or systemic embolism who have risk factors for AF.	STRONG	MODERATE
The strategy for systematic screening for AF should be individualized according to clinical suspicion and the patient's cardiovascular risk profile.	STRONG	MODERATE

Prolonged ECG monitoring with an external event monitor (2–4 weeks) or an implantable device may be used in patients with cryptogenic ischemic stroke.	STRONG	MODERATE
An implantable cardiac monitor may be considered in patients with cryptogenic ischemic stroke when prolonged external monitoring is inconclusive.	WEAK	MODERATE
In frail older adults, the decision regarding AF screening should be individualized, considering life expectancy, bleeding risk, ability to adhere to treatment, and patient preferences.	STRONG	LOW

AF: atrial fibrillation; ECG: electrocardiogram.

9.4.4. Prevention of Thromboembolic Events in Older Adults

9.4.4.1. Anticoagulation

Oral anticoagulation is the main strategy for stroke prevention in older adults with AF and should be indicated based on thromboembolic risk rather than chronological age alone. Recent guidelines emphasize that advanced age, frailty, or risk of falls alone are not contraindications to anticoagulation, as the benefit in reducing embolic events generally outweighs the bleeding risk. DOACs are preferred in most eligible older adults because of their better safety profile, particularly the lower incidence of intracranial hemorrhage. Therapeutic decisions should be individualized, considering functional and cognitive status, bleeding risk, life expectancy, and patient preferences.

Risk stratification in older adults with AF uses the same scores validated in the general population, although important limitations should be considered in this age group. The CHA₂DS₂-VA score remains the most extensively validated tool for assessing thromboembolic risk and is recommended by current guidelines.⁸⁴⁰ Patients aged ≥ 75 years automatically receive 2 points for age alone, meaning that virtually all patients in this age group have an indication for anticoagulation. More recent models, such as GARFIELD-AF, have been used to refine prognostic stratification in patients with AF, particularly older adults and individuals with multimorbidity.⁸⁴¹ This score

incorporates a broader range of clinical variables, including age, history of bleeding, kidney failure, HF, smoking, and anticoagulant use, allowing simultaneous estimation of the risks of stroke, bleeding, and mortality. In older adults, this model may provide a more comprehensive assessment of overall risk. Although CHA₂DS₂-VA remains the primary tool recommended by guidelines for determining the indication for anticoagulation, GARFIELD-AF may assist in individualizing therapy and assessing overall risk in more complex older patients.⁸⁴² Both scores are shown in Figure 9.6.

Regarding bleeding risk assessment, HAS-BLED remains recommended by major international guidelines for bleeding risk stratification in older patients with AF and has been extensively validated and widely used in clinical practice, although its accuracy is modest in older adults.⁸⁴³ More recently, scores specifically developed for older adults have become available. The A4C score was developed specifically for patients older than 80 years receiving DOACs and demonstrated better performance than conventional scores.⁸⁴⁴ A4C assesses five components: age ≥ 85 years, anemia, low albumin, amiodarone use, and reduced creatinine clearance, with an A4C ≥ 2 identifying patients at high risk of bleeding (Figure 9.7). Alternatively, the DOAC Score, although not specific to very old patients, incorporates detailed age stratification and performs better than HAS-BLED in patients receiving DOACs. Importantly, no validated score formally incorporates frailty as a variable.⁸⁴⁵

A high bleeding risk score should not be used to contraindicate anticoagulation. Its clinical purpose is to identify higher-risk patients who may benefit from closer follow-up, with reassessments at approximately 4 weeks rather than the usual intervals of 4–6 months. It also helps prioritize potentially modifiable factors, such as adequate BP control, kidney function monitoring, discontinuation of NSAIDs, and reduction of alcohol consumption.

DOACs are recommended as first-line therapy over warfarin for stroke prevention in older patients with nonvalvular AF, based on robust evidence of superior or equivalent efficacy and safety. A meta-analysis including 147,067 octogenarians demonstrated that DOACs significantly reduced the risk of stroke (RR 0.72; 95%CI 0.63–0.82), all-cause mortality (RR 0.82; 95%CI 0.70–0.96), and intracranial hemorrhage (RR 0.47; 95%CI 0.36–0.60) compared with warfarin, with no significant difference in major or gastrointestinal bleeding.⁸⁴⁶ The COMBINE-AF study, which analyzed frail, older (≥ 75 years) patients previously receiving warfarin, demonstrated that switching to standard-dose DOACs resulted in significant reductions in stroke or systemic embolism, fatal and intracranial bleeding, and death, although gastrointestinal bleeding was increased (HR 1.83; 95%CI 1.42–2.36). Although the net clinical outcome was similar between DOACs and warfarin in this specific subgroup, DOACs reduced the most severe types of bleeding (Figure 9.7).⁸⁴⁷

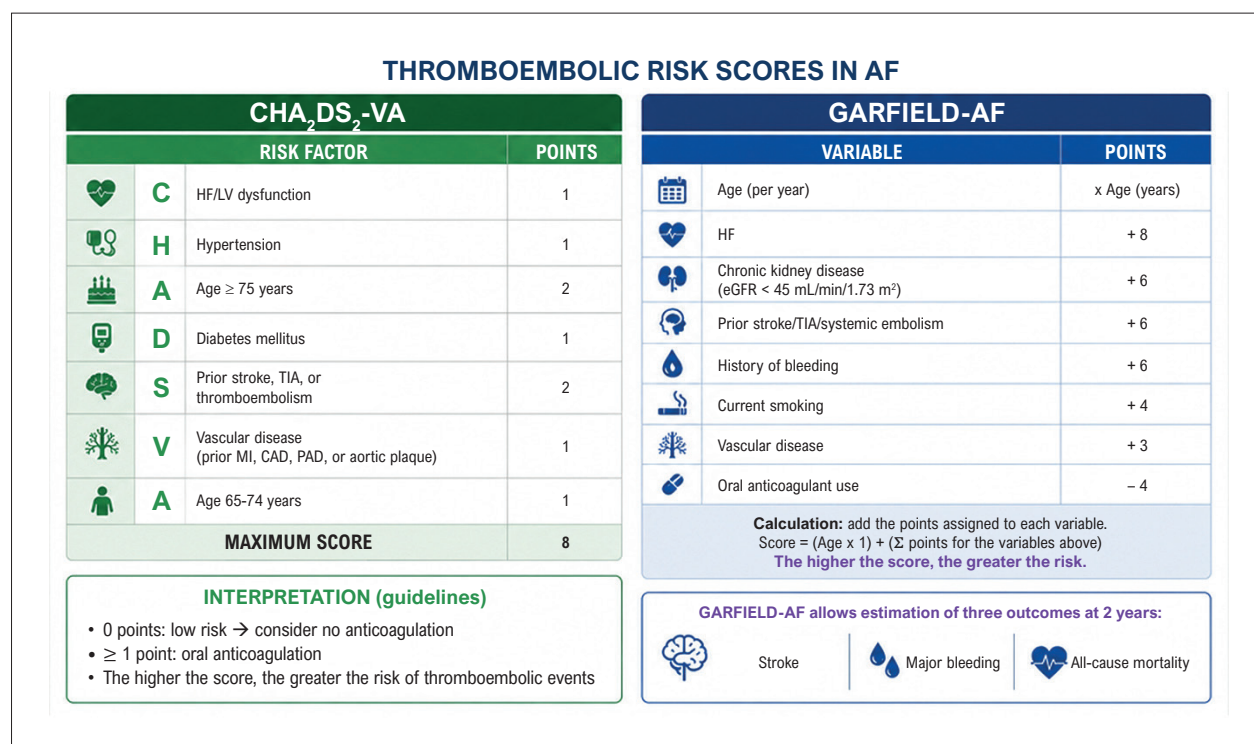


Figure 9.6 – Risk scores used to assess thromboembolic risk in patients with AF. AF: atrial fibrillation; CAD: coronary artery disease; eGFR: estimated glomerular filtration rate; HF: heart failure; LV: left ventricular; MI: myocardial infarction; PAD: peripheral artery disease; TIA: transient ischemic attack. CHA₂DS₂-VA: score recommended by guidelines to guide anticoagulation decisions in AF. GARFIELD-AF: prognostic model that incorporates additional clinical variables and simultaneously estimates the risks of stroke, bleeding, and mortality.

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BLEEDING RISK SCORES IN ANTICOAGULATED OLDER ADULTS

Components and scoring system

HAS-BLED		A4C SCORE (4 criteria beginning with "A" and 1 with "C")		DOAC SCORE (specific to DOAC users)	
COMPONENTS	POINTS	COMPONENTS	POINTS	COMPONENTS	POINTS
H Hypertension Systolic BP > 160 mmHg	1	1. Age • < 85 years • 85–95 years • ≥ 95 years	0 1 3	Age ≥ 75 years	1
A Abnormal kidney or liver function Chronic kidney disease (dialysis, transplantation, or creatinine ≥ 2.26 mg/dL) or chronic liver disease (cirrhosis or bilirubin > 2× ULN, AST/ALT/ALP > 3× ULN)	1	2. Anemia • Hemoglobin < 11 g/dL	2	Reduced kidney function (eGFR < 60 mL/min/1.73 m ²)	1
S Prior stroke	1	3. Low Albumin • Albumin < 3.5 g/dL	1	Anemia (hemoglobin < 12 g/dL)	1
B Prior bleeding or bleeding predisposition History of major bleeding or bleeding predisposition	1	4. Amiodarone use • Amiodarone use	1	Low body weight (≤ 60 kg)	1
L Labile INR TTR < 60%	1	5. Low Creatinine clearance • ≥ 50 mL/min/1.73m ² • 30–50 mL/min/1.73m ² • < 30 mL/min/1.73m ²	0 1 2	Prior bleeding (history of major bleeding)	1
E Age > 65 years (Elderly)	1	Total score: 0–9 points The higher the score, the greater the risk of bleeding.		Total score: 0–5 points The higher the score, the greater the risk of bleeding.	
D Drugs/alcohol Use of NSAIDs/antiplatelet agents or alcohol ≥ 8 units/week	1	A4C = four criteria beginning with the letter "A" + one criterion beginning with the letter "C"			

Figure 9.7 – Scores used to assess bleeding risk in patients with AF. ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BP: blood pressure; DOAC: direct oral anticoagulant; eGFR: estimated glomerular filtration rate; INR: international normalized ratio; NSAIDs: nonsteroidal anti-inflammatory drugs; TTR: time in therapeutic range; ULN: upper limit of normal.

Apixaban demonstrated superiority over warfarin in both efficacy and safety, irrespective of age, including in patients aged ≥ 80 years, with a lower risk of intracranial and extracranial hemorrhage.⁸⁴⁸ For very old patients (≥ 80 years) with contraindications to standard-dose anticoagulation because of a high bleeding risk, the ELDERCARE-AF trial demonstrated that edoxaban 15 mg/day was superior to placebo for preventing stroke or systemic embolism (2.3% vs 6.7%; HR 0.34; 95%CI 0.19–0.61), without a statistically significant increase in major bleeding, with consistent benefit irrespective of frailty status.⁸⁴⁹ Population-based studies have shown that rivaroxaban is associated with a 60% higher risk of gastrointestinal and intracranial bleeding than apixaban in older adults with AF as well as a higher risk of serious ischemic or hemorrhagic events.⁸⁵⁰ Based on this more recent evidence, rivaroxaban should be avoided as the first choice in this population.

Kidney function is a critical determinant of anticoagulant selection, particularly in older adults, and specific dose adjustments or contraindications according to creatinine clearance should be considered. Treatment adherence and patient understanding are fundamental to therapeutic success, making shared decision-making essential in this population. Recommendations for the prevention of thromboembolic events in older patients with AF are presented below.

Recommendations for the prevention of thromboembolic events in older patients with atrial fibrillation	Strength of recommendation	Certainty of evidence
Oral anticoagulation is recommended in older patients with AF and a CHA ₂ DS ₂ -VA score ≥ 2 for the prevention of stroke and systemic thromboembolism.	STRONG	HIGH
DOACs are preferred over warfarin in older adults without moderate/severe MS or a mechanical prosthetic valve because of reductions in mortality, stroke, and intracranial hemorrhage.	STRONG	HIGH

Apixaban has demonstrated a superior efficacy and safety profile in patients aged ≥ 80 years, with reductions in stroke/systemic embolism and major bleeding compared with warfarin.	STRONG	HIGH
The decision to anticoagulate frail older patients should be individualized through comprehensive geriatric assessment, considering the risk-benefit balance; however, frailty alone is not a contraindication to anticoagulation.	STRONG	MODERATE
Bleeding risk scores such as HAS-BLED, A4C, or the DOAC score may be used to identify modifiable risk factors and determine the frequency of clinical reassessment, but should not be used to contraindicate anticoagulation.	STRONG	MODERATE
Rivaroxaban should be avoided in adults aged ≥ 65 years with AF because of higher bleeding rates compared with other DOACs, except when once-daily dosing may improve adherence.	STRONG	HIGH
Edoxaban 15 mg/day may be considered in very old patients (≥ 80 years) for whom standard anticoagulation is contraindicated.	WEAK	MODERATE
Aspirin alone or in combination with clopidogrel is not recommended as an alternative to anticoagulation in older patients with AF.	STRONG	HIGH

AF: atrial fibrillation; DOAC: direct oral anticoagulant; MS: mitral stenosis.

9.4.4.2. Left Atrial Appendage Occlusion

In patients with AF and an absolute contraindication to oral anticoagulation, particularly those with a history of intracranial hemorrhage or recurrent major bleeding, left atrial appendage occlusion (LAAO) represents a therapeutic alternative for stroke prevention since approximately 90% of cardioembolic thrombi in nonvalvular AF originate from this structure.⁸⁵¹ LAAO may be performed percutaneously or surgically during concomitant cardiac procedures.

Studies in older patients have demonstrated that LAAO is feasible and safe, with high procedural success rates in patients aged ≥ 75 years and no significant difference in adverse event rates compared with younger patients (12%–13%).⁸⁵² However, a recent RCT failed to demonstrate the noninferiority of LAAO to best medical therapy, including anticoagulation when appropriate, in patients at high risk of stroke and bleeding, with no reduction in major bleeding in the intervention group.⁸⁵³ Therefore, LAAO should be reserved for selected patients with a genuine contraindication to long-term anticoagulation, with the decision individualized through multidisciplinary assessment considering procedural risks, comorbidities, and life expectancy.

9.4.5. Rhythm Control Versus Rate Control in Older Adults with Atrial Fibrillation

The choice between rhythm-control and rate-control strategies in AF has remained a subject of debate for more than two decades, particularly in the management of older patients, in whom multimorbidity, frailty, and greater susceptibility to adverse events make therapeutic decisions more complex. Landmark studies did not demonstrate superiority of rhythm control over rate control in terms of mortality or major cardiovascular events, establishing ventricular rate control as a reasonable initial strategy for many patients and reserving rhythm control for those with persistent symptoms.^{854,855}

More recent evidence, however, has changed this paradigm. A meta-analysis of 18 RCTs involving 17,536 patients demonstrated that a rhythm-control strategy was associated with reductions in cardiovascular death, stroke, and hospitalization for HF compared with rate control. These benefits were observed primarily in contemporary studies incorporating catheter ablation as part of the rhythm-control strategy.⁸⁵⁶ Consistently, the EAST-AFNET 4 trial demonstrated that early rhythm control reduced the risk of cardiovascular death, stroke, and hospitalization for HF or ACS in patients with recently diagnosed AF.⁸⁵⁷ Thus, rhythm control should not be viewed solely as a strategy for symptom relief but also as a potential disease-modifying intervention in appropriately selected patients.

Accordingly, even in older patients, rhythm control should be considered in symptomatic individuals, those with recently diagnosed AF or associated HF, or when the objective is to reduce arrhythmia progression and its cardiovascular complications. Chronological age alone should not be used to exclude rhythm-control strategies, including catheter ablation. Therapeutic decisions should

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instead be based on functional status, frailty, comorbidity burden, life expectancy, and patient preferences.

9.4.5.1. Rate Control

Beta-blockers and nondihydropyridine CCBs (diltiazem and verapamil) are first-line therapeutic options, with the choice individualized according to the patient's comorbidities and clinical characteristics.⁸³³ Beta-blockers are particularly useful in patients with CAD or HFrEF, whereas diltiazem and verapamil may be preferred in individuals with COPD without significant ventricular dysfunction, provided that LVEF is > 40%.

Digoxin may be used as adjunctive therapy when adequate rate control cannot be achieved with other agents or when these agents are contraindicated, particularly in patients with HF. However, its efficacy is limited during physical exertion, and its use requires caution in older adults because of the greater risk of toxicity associated with reduced kidney function and drug interactions.

Overall, a lenient rate-control strategy, targeting a resting ventricular rate < 100–110 bpm, is appropriate for asymptomatic patients with preserved ventricular function. More stringent rate-control targets (< 80 bpm at rest) may be considered in patients with persistent symptoms, deterioration of left ventricular function, or suspected tachycardia-induced cardiomyopathy. In cases refractory to optimized pharmacological treatment, atrioventricular node ablation combined with pacemaker implantation represents an effective alternative for symptom control and improvement in quality of life.⁸³³

9.4.5.2. Rhythm Control

Rhythm control in older adults with AF may be achieved with antiarrhythmic drugs or catheter ablation. Amiodarone is the most commonly used antiarrhythmic drug in this population because of its efficacy and lower negative inotropic effect and is preferred in patients with left ventricular dysfunction or HF. Other options include sotalol and propafenone, with the choice guided by comorbidities, heart, kidney, and liver function, and the risk of proarrhythmic effects.

Catheter ablation is more effective than antiarrhythmic medications for maintaining sinus rhythm (AF recurrence: 49.9% vs 69.5%; HR 0.52; $p < 0.001$) and significantly reduces death or cardiovascular hospitalization (HR 0.83; $p = 0.001$), although it did not demonstrate a significant reduction in mortality alone in the intention-to-treat analysis of the CABANA trial.⁸⁵⁸

Although RCTs have predominantly included younger patients, observational studies and subgroup analyses indicate that ablation can be performed safely and effectively in carefully selected older adults, providing significant improvements in quality of life. A recent analysis involving patients aged ≥ 65 years demonstrated that catheter ablation reduced the risk of atrial arrhythmia recurrence by 24% compared with antiarrhythmic drug therapy and also reduced electrical cardioversion, hospitalization for HF, and ischemic stroke, with an overall complication rate of 5.9%.⁸⁵⁹

Although the available results are encouraging, very old and frail patients remain underrepresented in RCTs, reinforcing the need to individualize therapeutic decisions in this population.

Recommendations for choosing between rhythm-control and rate-control strategies in the management of older patients with AF	Strength of recommendation	Certainty of evidence
Early rhythm control (within 1 year of diagnosis) should be considered in symptomatic older patients with recently diagnosed AF to reduce cardiovascular death, stroke, and hospitalization for HF or acute coronary syndrome.	STRONG	MODERATE
Rate control is appropriate as an initial strategy in asymptomatic or minimally symptomatic older patients, those with multiple comorbidities, or those with limited life expectancy.	STRONG	MODERATE
The choice between rhythm and rate control should be individualized according to symptoms, comorbidities, functional status, frailty, life expectancy, and patient preferences.	STRONG	MODERATE
Chronological age alone should not be used to exclude rhythm-control strategies, including catheter ablation.	STRONG	MODERATE

AF: atrial fibrillation; HF: heart failure.

Recommendations for the treatment of AF using a rate-control strategy	Strength of recommendation	Certainty of evidence
Beta-blockers or nondihydropyridine calcium channel blockers (diltiazem or verapamil) are recommended as first-line therapy for rate control.	STRONG	HIGH
A lenient heart rate target (resting heart rate 100–110 bpm) is appropriate for asymptomatic patients with preserved ventricular function.	STRONG	HIGH
A more stringent rate-control target (resting heart rate < 80 bpm) may be considered in patients with persistent symptoms, deterioration of ventricular function, or suspected tachycardia-induced cardiomyopathy.	STRONG	MODERATE

Digoxin may be used as adjunctive therapy when adequate rate control cannot be achieved with other agents, particularly in patients with HF, but caution is required because of the risk of toxicity.	WEAK	MODERATE
Atrioventricular node ablation with pacemaker implantation should be considered in cases refractory to optimized pharmacological therapy.	STRONG	MODERATE

AF: atrial fibrillation; bpm: beats per minute; HF: heart failure.

Recommendations for the treatment of AF using a rhythm-control strategy	Strength of recommendation	Certainty of evidence
Amiodarone is preferred in patients with left ventricular dysfunction or HF because of its efficacy and lower negative inotropic effect.	STRONG	MODERATE
Sotalol and propafenone may be considered in selected patients, considering contraindications and heart, kidney, and liver function.	WEAK	MODERATE
Antiarrhythmic drugs should be initiated at lower doses and gradually titrated in older adults because of age-related pharmacokinetic changes, reduced kidney/liver function, and greater proarrhythmic risk.	STRONG	MODERATE
Catheter ablation should be considered in symptomatic older patients with recurrent AF, impaired quality of life, or failure or intolerance of pharmacological therapy.	STRONG	HIGH
Catheter ablation can be performed with reasonable safety in selected older adults, with improved quality of life and reductions in AF recurrence, electrical cardioversion, HF hospitalization, and ischemic stroke.	STRONG	MODERATE
The decision to perform ablation in older adults should consider frailty, functional status, comorbidity burden, life expectancy, and goals of care rather than chronological age alone.	STRONG	MODERATE
Catheter ablation should not be performed in patients with advanced infiltrative cardiomyopathies (amyloidosis), severe mitral stenosis or regurgitation, or cor pulmonale because of the low likelihood of success.	STRONG (AGAINST)	MODERATE

AF: atrial fibrillation; HF: heart failure.

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