

Brazilian Guideline for Valvular Heart Disease – 2026

Produced by: Brazilian Society of Cardiology (in Portuguese: Sociedade Brasileira de Cardiologia – SBC), Brazilian Society of Hemodynamics and Interventional Cardiology (in Portuguese: Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista – SBHCI), Brazilian Society of Cardiovascular Surgery (In Portuguese: Sociedade Brasileira de Cirurgia Cardiovascular – SBCCV)

Guideline authors: Flavio Tarasoutchi,¹ João Ricardo Cordeiro Fernandes,¹ Vitor Emer Egypto Rosa,¹ Roney Orismar Sampaio,¹ Diana Patricia Lamprea Sepulveda,^{2,3} Auristela Isabel de Oliveira Ramos,⁴ Carlos Augusto Homem de Magalhães Campos,¹ Fernando Ribeiro de Moraes Neto,^{3,5} Alberto Rodolpho Hüning,¹ Alberto Takeshi Kiyose,^{6,7,8} Alexandre Abizaid,^{1,9} Alexandre Siciliano Colafranceschi,^{10,11} Ana Paula Tagliari,^{12,13,14} Antonio De Santis,¹ Carlos Manuel de Almeida Brandão,¹ Clara Weksler,¹⁵ Daniella Nazzetta,¹ David Costa de Souza Le Bihan,^{1,16} David Provenziale Titingier,¹ Deborah Christina Nercolini,^{17,18} Dorival Julio Della Togna,⁴ Eduardo França Pessoa de Melo,^{2,19} Eduardo Keller Saadi,^{13,14,20,21} Fabio Antonio Gaiotto,⁷ Fabio Biscegli Jatene,¹ Fábio Sândoli de Brito Junior,^{1,22} Fernanda Castiglioni Tessari,^{1,7} Francisco Diniz Affonso da Costa,^{17,23} Francisco Monteiro de Almeida Magalhães,^{1,24} Henrique Barbosa Ribeiro,¹ Heraldo Guedis Lobo Filho,^{25,26} Isabela Sacilotto,²⁷ João Carlos Ferreira Leal,^{28,29} José Airton de Arruda,^{30,31,32} José Albuquerque de Figueiredo Neto,^{33,34} Jose Honório de Almeida Palma da Fonseca,¹ José Luiz Barros Pena,³⁵ Lucas Tachotti Pires,¹ Lynnie Oberg Arouca Bassoli,¹ Marcelo Kirschbaum,^{1,7} Marcelo Luiz Campos Vieira,^{1,7} Marcelo Westerlund Montera,³⁶ Maria Antonieta Albanes A. M. Lopes,³⁷ Mariana Pezzute Lopes,¹ Marianna Deway Andrade Dracoulakis,^{38,39} Milena Ribeiro Paixão,⁷ Murilo Foppa,^{13,20} Pamela Nogueira Cavalcante,^{4,7} Paulo Ricardo Avancini Caramori,⁴⁰ Pedro Alves Lemos Neto,⁷ Ranna Santos Pessoa,⁴¹ Renato D. Lopes,⁴² Renato Paladino Nemoto,¹ Rodrigo Petersen Saadi,^{14,20} Rogerio Eduardo Gomes Sarmiento Leite,^{21,43} Salvador Rassi,⁴⁴ Tarso Augusto Duenhas Accorsi,⁷ Tiago Costa Bignoto,^{7,8} Valdir Ambrósio Moises,⁶ Vinicius Esteves,⁴⁵ Vinicius Daher Vaz,^{46,47} Vinicius Jose da Silva Nina,³³ Walkiria Samuel Avila,¹ William Antonio de Magalhães Esteves,^{48,49,50,51}

Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo,¹ São Paulo, SP – Brazil

Pronto-Socorro Cardiológico Universitário de Pernambuco da Universidade de Pernambuco,² Recife, PE – Brazil

Instituto do Coração de Pernambuco,³ Recife, PE – Brazil

Instituto Dante Pazzanese de Cardiologia,⁴ São Paulo, SP – Brazil

Universidade Federal de Pernambuco,⁵ Recife, PE – Brazil

Universidade Federal de São Paulo,⁶ São Paulo, SP – Brazil

Hospital Israelita Albert Einstein,⁷ São Paulo, SP – Brazil

Hospital do Coração,⁸ São Paulo, SP – Brazil

Faculdade de Medicina da Universidade de São Paulo,⁹ São Paulo, SP – Brazil

Instituto Nacional de Cardiologia,¹⁰ Rio de Janeiro, RJ – Brazil

Universidade Federal do Estado do Rio de Janeiro,¹¹ Rio de Janeiro, RJ – Brazil

Universidade Federal de Ciências da Saúde de Porto Alegre,¹² Porto Alegre, RS – Brazil

Universidade Federal do Rio Grande do Sul,¹³ Porto Alegre, RS – Brazil

Hospital Mãe de Deus,¹⁴ Porto Alegre, RS – Brazil

Instituto Estadual de Cardiologia Aloysio de Castro,¹⁵ Rio de Janeiro, RJ – Brazil

Grupo Fleury,¹⁶ São Paulo, SP – Brazil

Instituto de Neurologia e Cardiologia de Curitiba,¹⁷ Curitiba, PR – Brazil

Hospital São Marcelino Champagnat,¹⁸ Curitiba, PR – Brazil

Rede D'Or São Luiz,¹⁹ Recife, PE – Brazil

Hospital de Clínicas de Porto Alegre,²⁰ Porto Alegre, RS – Brazil

Hospital Moinhos de Vento,²¹ Porto Alegre, RS – Brazil

Hospital Sírio-Libanês,²² São Paulo, SP – Brazil

Santa Casa de Curitiba,²³ Curitiba, PR – Brazil

Rede D'Or São Luiz,²⁴ São Paulo, SP – Brazil

Universidade Federal do Ceará,²⁵ Fortaleza, CE – Brazil

Hospital de Messejana Dr. Carlos Alberto Studart Gomes,²⁶ Fortaleza, CE – Brazil

Universidade Federal do Rio Grande do Norte,²⁷ Natal, RN – Brazil
Faculdade de Medicina de São José do Rio Preto,²⁸ São José do Rio Preto, SP – Brazil
Hospital Beneficência Portuguesa de São José do Rio Preto,²⁹ São José do Rio Preto, SP – Brazil
Hospital Evangélico de Vila Velha,³⁰ Vila Velha, ES – Brazil
Rede Meridional de Saúde,³¹ Vitória, ES – Brazil
Unimed Vitória,³² Vitória, ES – Brazil
Universidade Federal do Maranhão,³³ São Luís, MA – Brazil
Hospital Universitário Presidente Dutra da Universidade Federal do Maranhão,³⁴ São Luís, MA – Brazil
Hospital Felício Rocho,³⁵ Belo Horizonte, MG – Brazil
Hospital Pró-Cardíaco,³⁶ Rio de Janeiro, RJ – Brazil
Real Hospital Português de Beneficência em Pernambuco,³⁷ Recife, PE – Brazil
Hospital Mater Dei Salvador,³⁸ Salvador, BA – Brazil
Escola Bahiana de Medicina e Saúde Pública,³⁹ Salvador, BA – Brazil
Hospital São Lucas da Pontifícia Universidade Católica do Rio Grande do Sul,⁴⁰ Porto Alegre, RS – Brazil
Hospital Universitário Onofre Lopes da Universidade Federal do Rio Grande do Norte,⁴¹ Natal, RN – Brazil
Duke University Medical Center,⁴² Durham, NC – The United States of America
Instituto de Cardiologia do Rio Grande do Sul,⁴³ Porto Alegre, RS – Brazil
Universidade Federal de Goiás,⁴⁴ Goiânia, GO – Brazil
University Hospitals Harrington Heart & Vascular Institute,⁴⁵ Cleveland, OH – The United States of America
Hospital do Coração Anis Rassi,⁴⁶ Goiânia, GO – Brazil
Hospital Israelita Albert Einstein – Unidade Goiânia,⁴⁷ Goiânia, GO – Brazil
Hospital das Clínicas da Universidade Federal de Minas Gerais,⁴⁸ Belo Horizonte, MG – Brazil
Hospital Orizonti,⁴⁹ Belo Horizonte, MG – Brazil
Faculdade Ciências Médicas de Minas Gerais,⁵⁰ Belo Horizonte, MG – Brazil
Universidade de Itaúna,⁵¹ Itaúna, MG – Brazil

Standards and Guidelines Committee: Humberto Graner Moreira (Chair), Félix José Alvarez Ramires, Helena Cramer Veiga Rey, José Augusto Soares Barreto Filho, Nadine Oliveira Clausell.

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Correspondence: Sociedade Brasileira de Cardiologia – Av. Marechal Câmara, 360/330 – Centro – Rio de Janeiro – CEP: 20020-907. E-mail: diretrizes@cardiol.br

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The report below lists the relationships existing or that occurred during the 12-month period preceding the start of the document preparation:

Expert	Type of relationship with industry
Alberto Rodolpho Hüning	Nothing to be declared
Alberto Takeshi Kiyose	Nothing to be declared
Alexandre Abizaid	Nothing to be declared
Alexandre Siciliano Colafranceschi	Nothing to be declared
Ana Paula Tagliari	Financial Disclosure - Meril Life: Educational activities, Proctoring – Transcatheter aortic prosthesis.
Antonio De Santis	Nothing to be declared
Auristela Isabel de Oliveira Ramos	Financial Disclosure - Medtronic: Lectures, Educational activities – Transcatheter valve prosthesis. - P&F: Lectures, Educational activities – Bicaval prosthesis. - Meril: Lectures, Educational activities – Transcatheter prosthesis.
Carlos Augusto Homem de Magalhães Campos	Financial Disclosure - Boston Scientific: Lectures – Interventional cardiology medical devices. - Abbott: Lectures – Interventional cardiology medical devices.
Carlos Manuel de Almeida Brandão	Nothing to be declared
Clara Weksler	Nothing to be declared
Daniella Nazzetta	Nothing to be declared
David Costa de Souza Le Bihan	Financial Disclosure - Edwards Lifesciences: Consulting, Lectures, Proctoring – Cardiac valve prostheses. - AstraZeneca: Educational activities – Forxiga.
David Provenzale Titinger	Nothing to be declared
Deborah Christina Nercolini	Financial Disclosure - Edwards Lifesciences: Lectures, Proctoring – Transcatheter valves. - Meril: Lectures, Proctoring – Transcatheter valves. - Abbott: Lectures, Proctoring – Transcatheter valves.
Diana Patricia Lamprea Sepulveda	Nothing to be declared
Dorival Julio Della Togna	Nothing to be declared
Eduardo França Pessoa de Melo	Financial Disclosure - Medtronic: Proctoring – TAVI. - Edwards Lifesciences: Proctoring – TAVI. - Abbott: Proctoring – TAVI. - Boston Scientific: Educational activities, Sponsored research, Research grant, Continuing medical education, Travel, Congress registration. - Meril: Proctoring – TAVI. - MicroPort: Proctoring – TAVI.
Eduardo Keller Saadi	Financial Disclosure - Edwards: Fees, Consulting, Lectures, Proctoring, Continuing medical education – Surgical and transcatheter prostheses and devices. - Abbott: Fees, Consulting, Lectures, Proctoring, Continuing medical education – Surgical and transcatheter devices. - Medtronic: Fees, Consulting, Lectures, Proctoring, Continuing medical education – Implantable devices.

Fabio Antonio Gaiotto	Nothing to be declared
Fabio Biscegli Jatene	Nothing to be declared
Fábio Sândoli de Brito Júnior	Financial Disclosure - Edwards Lifesciences: Proctoring – Transcatheter intervention for valvular heart disease. - Medtronic: Proctoring – Transcatheter intervention for valvular heart disease. - Abbott: Proctoring – Transcatheter intervention for valvular heart disease.
Fernanda Castiglioni Tessari	Nothing to be declared
Fernando Ribeiro de Moraes Neto	Financial Disclosure - Edwards: Educational activities – Valvular heart disease.
Flavio Tarasoutchi	Financial Disclosure - Edwards: Participation in a sponsored symposium, Educational activities – Bioprostheses.
Francisco Diniz Affonso da Costa	Financial Disclosure - Cardioproteze Ltda: Advisory Board – Bovine pericardial bioprosthetic valve. Other Relationships - Equity ownership in Cardioproteze Ltda (Orthopedic, prosthetic, equipment, or implant industry), with administrative, management, or decision-making authority. - Employment relationship or paid position at Banco Valvas Cardiacas Mackenzie.
Francisco Monteiro de Almeida Magalhães	Financial Disclosure - MedCOF TEC Preparatory Course: Educational activities – TEC Preparatory Course.
Henrique Barbosa Ribeiro	Financial Disclosure - Edwards Lifesciences: Lectures, Educational activities, Proctoring, Research grant – TAVI and TEER. - Medtronic: Research grant – TAVI.
Heraldo Guedis Lobo Filho	Nothing to be declared
Isabela Sacilotto	Financial Disclosure - Bayer: Educational activities – Firalta.
João Carlos Ferreira Leal	Nothing to be declared
João Ricardo Cordeiro Fernandes	Financial Disclosure - Edwards Lifesciences: Educational activities – Implantable medical devices, such as valve prostheses.
José Airton de Arruda	Financial Disclosure - Edwards Proctor: Proctoring – Instructor for TAVI prosthesis implantation. - Boston Scientific Proctor: Lectures, Proctoring – Watchman device. - Abbott Proctor: Proctoring – Navitor, TAVI prosthesis. - Scietech: Educational activities, Sponsored research, Research grant, Continuing medical education.
José Albuquerque de Figueiredo Neto	Financial Disclosure - Daiichi Sankyo Brasil: Lectures, Educational activities – Bempedoic acid + ezetimibe: understanding the new treatment for dyslipidemia. Other Relationships - Government position: President of CRM-MA.
Jose Honório de Almeida Palma da Fonseca	Nothing to be declared
José Luiz Barros Pena	Nothing to be declared
Lucas Tachotti Pires	Nothing to be declared
Lynnie Oberg Arouca Bassoli	Nothing to be declared
Marcelo Kirschbaum	Nothing to be declared
Marcelo Luiz Campos Vieira	Nothing to be declared

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Marcelo Westerlund Montera	Nothing to be declared
Maria Antonieta Albanes A. M. Lopes	Financial Disclosure - Boston Scientific: Speaker - Lectures, teaching, and continuing medical education – left atrial appendage closure. - Medtronic: Lectures, teaching, and continuing medical education – TAVI and stenting.
Mariana Pezzute Lopes	Nothing to be declared
Marianna Deway Andrade Dracoulakis	Nothing to be declared
Milena Ribeiro Paixão	Other Relationships - Employment relationship or paid position at Einstein Hospital Israelita – telemedicine department.
Murilo Foppa	Nothing to be declared
Pamela Nogueira Cavalcante	Nothing to be declared
Paulo Ricardo Avancini Caramori	Financial Disclosure - Amgen: Advisory Board – Repatha. - Medtronic: Lectures, Proctoring – TAVI. - Boston Scientific: Lectures – LAA closure. - Meril: Educational activities, Sponsored research, Research grant, Continuing medical education, Travel, Accommodation. - Novartis: Lectures – Inclisiran. - Scitech: Lectures, Scientific Committee – Intracoronary imaging and coronary intervention. - St. Jude Abbott: Lectures, Proctoring – TAVI.
Pedro Alves Lemos Neto	Financial Disclosure - Edwards Lifesciences: Lectures – Transcatheter therapies. - Novo Nordisk: Sponsored research – Ziltivekimab. - Johnson & Johnson: Lectures – Impella.
Ranna Santos Pessoa	Financial Disclosure - Boehringer Ingelheim: Sponsored research – Principal Investigator in a study of a new drug.
Renato D. Lopes	Financial Disclosure - Pfizer: Consulting, Lectures – Apixaban. - Bristol Myers Squibb: Consulting, Lectures – Apixaban. - Novartis: Consulting, Lectures – Sacubitril/valsartan. - Novo Nordisk: Educational activities, Sponsored research, Research grant, Continuing medical education. Other Relationships - Equity ownership in TRIBE-MD (Health technology or telemedicine companies; companies providing services to the aforementioned segments), with administrative, management, or decision-making authority.
Renato Paladino Nemoto	Financial Disclosure - MedCOF Group: Educational activities – TEC Preparatory Course.
Rodrigo Petersen Saadi	Financial Disclosure - Edwards Lifesciences: Lectures, Proctoring – TAVI, mitral and tricuspid PASCAL. - Medtronic: Lectures, Proctoring – TAVI. - Abbott: Lectures, Proctoring – TAVI, MitraClip, and TriClip. - Meril: Lectures, Sponsored research, Research grants, Continuing medical education.
Rogério Eduardo Gomes Sarmiento Leite	Financial Disclosure - Abbott: Proctoring – Transcatheter aortic valve prosthesis. - Edwards: Proctoring – Transcatheter aortic valve prosthesis. - Medtronic: Proctoring – Transcatheter aortic valve prosthesis. - Meril: Educational activities, Sponsored research, Research grant, Continuing medical education.
Roney Orismar Sampaio	Nothing to be declared

Salvador Rassi	Nothing to be declared
Tarso Augusto Duenhas Accorsi	Financial Disclosure - Boston Scientific Brasil / Boston Scientific: Educational activities – Left atrial appendage occluder, edge-to-edge repair therapy. - Edwards Lifesciences: Educational activities – Surgical valve prostheses, valvular edge-to-edge repair. - Abbott: Educational activities – Valvular edge-to-edge repair therapy.
Tiago Costa Bignoto	Financial Disclosure - Edwards Lifesciences: Consulting, Lectures, Educational activities, Continuing medical education, Travel, Accommodation – Valve prostheses. - P&F: Educational activities – Valve prostheses. - Abbott: Educational activities, Travel, Accommodation – Valve prostheses.
Valdir Ambrósio Moises	Nothing to be declared
Vinicius Daher Vaz	Financial Disclosure - Edwards Lifesciences: Fees, Lectures, Educational activities, Proctoring, Continuing medical education, Travel, Accommodation – Valve prostheses. - Medtronic: Proctoring, Travel, Accommodation – Valve prostheses. - Abbott: Proctoring – Valve prostheses. - Meril: Fees, Educational activities, Sponsored research, Research grant, Continuing medical education – Travel.
Vinicius Esteves	Nothing to be declared
Vinicius Jose da Silva Nina	Nothing to be declared
Vitor Emer Egypto Rosa	Financial Disclosure - Edwards Lifesciences: Consulting – Medical technology company, primarily specializing in structural heart disease.
Walkiria Samuel Avila	Nothing to be declared
William Antonio de Magalhães Esteves	Financial Disclosure - GlaxoSmithKline, AstraZeneca: Lectures – Vaccines, dapagliflozin. - AstraZeneca: Fees – Dapagliflozin. Other Relationships - Equity ownership in Mamocentro – Centro de Diagnóstico por Imagem LTDA (Health technology or telemedicine companies), with administrative, management, or decision-making authority.

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List of abbreviations and acronyms

18F-FDG PET/CT	fluorine-18 fluorodeoxyglucose positron emission tomography/ computed tomography
ACC	American College of Cardiology
ACEI	angiotensin–converting enzyme inhibitor
AF	atrial fibrillation
AHA	American Heart Association
anti-DNase B	anti-deoxyribonuclease B
ARB	angiotensin II receptor blocker
ASO	antistreptolysin O
AU	Agatston units
BAV	balloon aortic valvuloplasty
BNP	B-type natriuretic peptide
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CIED	cardiac implantable electronic device
CMR	cardiac magnetic resonance
CPET	cardiopulmonary exercise testing
CRP	C-reactive protein
CT	computed tomography
DOAC	direct oral anticoagulant
EACTS	European Association for Cardio-Thoracic Surgery
ECG	electrocardiography
EFT	Essential Frailty Toolset
EOA	effective orifice area
EROA	effective regurgitant orifice area
ESC	European Society of Cardiology
ESR	erythrocyte sedimentation rate
EuroSCORE II	European System for Cardiac Operative Risk Evaluation
FFR	fractional flow reserve
GLS	global longitudinal strain
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HALT	hypoattenuated leaflet thickening
HF	heart failure
HFmrEF	heart failure with mildly reduced ejection fraction
HFpEF	heart failure with preserved ejection fraction
HFrfEF	heart failure with reduced ejection fraction
ICD	implantable cardioverter-defibrillator
iECV	indexed extracellular volume
INR	international normalized ratio
LA	left atrium
LGE	late gadolinium enhancement
Lp(a)	lipoprotein(a)

LV	left ventricle
LVEDD	left ventricular end-diastolic diameter
LVEDDi	left ventricular end-diastolic diameter indexed to body surface area
LVEDV	left ventricular end-diastolic volume
LVEDVi	left ventricular end-diastolic volume indexed to body surface area
LVEF	left ventricular ejection fraction
LVEDS	left ventricular end-systolic diameter
LVEDSi	left ventricular end-systolic diameter indexed to body surface area
LVESV	left ventricular end-systolic volume
LVESVi	left ventricular end-systolic volume indexed to body surface area
LVOT	left ventricular outflow tract
MAC	mitral annular calcification
MAD	mitral annular disjunction
MRA	mineralocorticoid receptor antagonist
MS	mitral stenosis
MVA	mitral valve area
NP	natriuretic peptide
NSAID	nonsteroidal anti-inflammatory drug
NT-proBNP	N-terminal pro-B-type natriuretic peptide
NYHA	New York Heart Association
PASP	pulmonary artery systolic pressure
PBMV	percutaneous balloon mitral valvuloplasty
PCI	percutaneous coronary intervention
PHT	pressure half-time
POAF	postoperative atrial fibrillation
PPM	prosthesis–patient mismatch
RAAS	renin–angiotensin–aldosterone system
RVol	regurgitant volume
SBC	Brazilian Society of Cardiology (Sociedade Brasileira de Cardiologia)
SBP	systolic blood pressure
SGLT2	sodium–glucose cotransporter 2
STS	Society of Thoracic Surgeons
SUS	Brazilian Unified Health System (Sistema Único de Saúde)
TAVI	transcatheter aortic valve implantation
TEER	transcatheter edge-to-edge repair
TMVI	transcatheter mitral valve implantation
TTR	time in therapeutic range
ULN	upper limit of normal
VARC-3	Valve Academic Research Consortium 3

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Central Illustration: Brazilian Guideline for Valvular Heart Disease – 2026



8 KEY NEW RECOMMENDATIONS

Brazilian Guidelines for Valvular Heart Disease

1 ASYMPTOMATIC AORTIC STENOSIS
Severe high-gradient aortic stenosis, without complicating factors and with low surgical risk: **EARLY INTERVENTION** in selected patients, after discussion by the Heart Team.

Strength of recommendation:	WEAK
Certainty of evidence:	HIGH

HEART VALVE TEAM
Center of excellence in valvular heart disease

PATIENT AT THE CENTER OF DECISION-MAKING

SHARED AND INDIVIDUALIZED DECISION-MAKING

- RISK-BENEFIT** and cost-effectiveness
- THERAPEUTIC STRATEGY** best suited to the patient's profile
- INTEGRATED CARE** from patient selection through post-intervention follow-up

* High certainty of evidence for edge-to-edge repair/orthotopic implantation; low certainty of evidence for heterotopic implantation.

2 SYMPTOMATIC AORTIC STENOSIS
Low risk < 70 years: **SURGERY** preferred
Low risk 70–80 years: **TAVI = SURGERY**
Low risk > 80 years: **TAVI** preferred

ACCORDING TO AGE GROUP

3 AORTIC REGURGITATION
TAVI for severe symptomatic aortic regurgitation in patients with a life expectancy > 1 year, contraindication to surgery or prohibitive surgical risk, and favorable anatomy, after Heart Team evaluation.

Strength of recommendation:	WEAK
Certainty of evidence:	LOW

4 TRICUSPID REGURGITATION
Severe, symptomatic tricuspid regurgitation refractory to medical therapy, with contraindication to surgery or high surgical risk and favorable anatomy: **TRANSCATHETER EDGE-TO-EDGE REPAIR** or **ORTHOTOPIC/HETEROTOPIC VALVE IMPLANTATION**.

Strength of recommendation:	STRONG
Certainty of evidence:	HIGH / LOW*

5 PRIMARY MITRAL REGURGITATION
Symptomatic non-rheumatic mitral regurgitation, with favorable anatomy and high surgical risk as determined by the Heart Team: **TRANSCATHETER EDGE-TO-EDGE REPAIR**.

Strength of recommendation:	STRONG
Certainty of evidence:	MODERATE

6 SECONDARY MITRAL REGURGITATION
Ventricular secondary mitral regurgitation, with dyspnea (FC ≥ III) despite optimized medical therapy and appropriate anatomy: **TRANSCATHETER EDGE-TO-EDGE REPAIR** to improve symptoms.

Strength of recommendation:	STRONG
Certainty of evidence:	MODERATE

7 BIOPROSTHETIC VALVE DYSFUNCTION
Severe structural dysfunction of a mitral or aortic bioprosthesis in symptomatic patients at high surgical risk or considered inoperable, after Heart Team evaluation: **VALVE-IN-VALVE**.

Strength of recommendation:	STRONG
Certainty of evidence:	HIGH

8 PREVENTION OF INFECTIVE ENDOCARDITIS
ANTIBIOTIC PROPHYLAXIS in patients at high risk of infective endocarditis undergoing dental extraction, oral surgery, or procedures involving manipulation of gingival tissue or the periapical region.

Strength of recommendation:	STRONG
Certainty of evidence:	MODERATE

TAVI: transcatheter aortic valve implantation • FC: functional class

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1. Introduction

According to the most recent epidemiological data, the prevalence of degenerative valvular heart disease is increasing in Brazil, particularly among older adults. Conversely, rheumatic heart disease remains the leading cause of valvular heart disease in the country, especially among users of the Brazilian Unified Health System (Sistema Único de Saúde [SUS]).¹ Thus, Brazil has a distinctive etiologic profile, sharing characteristics with both high-income and low-income countries. This unique profile warrants recommendations specifically tailored to the Brazilian population, as presented in these guidelines.

Another important consideration is the development of diagnostic and therapeutic technologies, which requires frequent updates. Transcatheter and surgical treatments for patients with valvular heart disease are evolving rapidly, reducing morbidity and improving survival. These advances have also introduced new areas of discussion, including lifelong management strategies. The 2026 Brazilian Guideline for Valvular Heart Disease therefore compile current scientific evidence and expert opinion while retaining the framework proposed in the 2017 and 2020 editions. The recommendations are compared with those of the principal international guidelines – the 2020 American College of Cardiology/American Heart

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Association (ACC/AHA) Guideline and the 2025 European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) Guidelines – allowing management to be tailored to the Brazilian population.²⁻⁵ The sequential steps guiding the anatomical, etiologic, and functional diagnosis of valvular heart disease have also been maintained. These steps support management decisions aligned with best practices and the rational use of resources (Figure 1):

- Step 1: Confirm that the valvular heart disease is anatomically significant. If confirmed, proceed to Step 2. If the disease is anatomically mild or moderate, investigate alternative diagnoses in symptomatic patients and monitor disease progression in asymptomatic patients.
- Step 2: Determine the etiology on the basis of clinical history, medical history, and complementary tests.
- Step 3: Assess symptoms attributable to the valvular heart disease – this is essential when determining the need for intervention. Medical therapy is indicated to relieve symptoms until definitive interventional treatment of the valve disease can be performed.
- Step 4: Evaluate anatomical and/or functional adverse prognostic features, particularly pulmonary hypertension, ventricular remodeling, systolic dysfunction, aortic aneurysmal dilatation, and atrial fibrillation (AF). These findings may determine the need for intervention in asymptomatic patients.

- Step 5: Select the mode of intervention – valvular heart disease may be corrected surgically or through a transcatheter procedure. The choice should be individualized according to surgical risk, comorbidities, and the Heart Team's decision.

We emphasize that this stepwise framework should not alter the sequence of the clinical evaluation, which begins with clinical history, followed by physical examination and complementary tests. Rather, it is intended to guide appropriate clinical reasoning and minimize diagnostic and therapeutic errors.

1.1. Strength of Recommendation and Certainty of Evidence

The recommendations in the current guidelines were developed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, which classifies the strength of recommendation (1 = strong or 2 = weak/conditional) and the certainty of evidence (A = high, B = moderate, C = low, or D = very low) (Figure 2).

To facilitate comparison with international guidelines, we retained columns presenting the corresponding classifications according to the traditional grading system, which is based on 2 domains: class of recommendation and level of evidence.^{4,5} The class of recommendation was categorized as follows: Class I, interventions for which there is evidence and/or consensus that they are beneficial, useful, and effective; Class

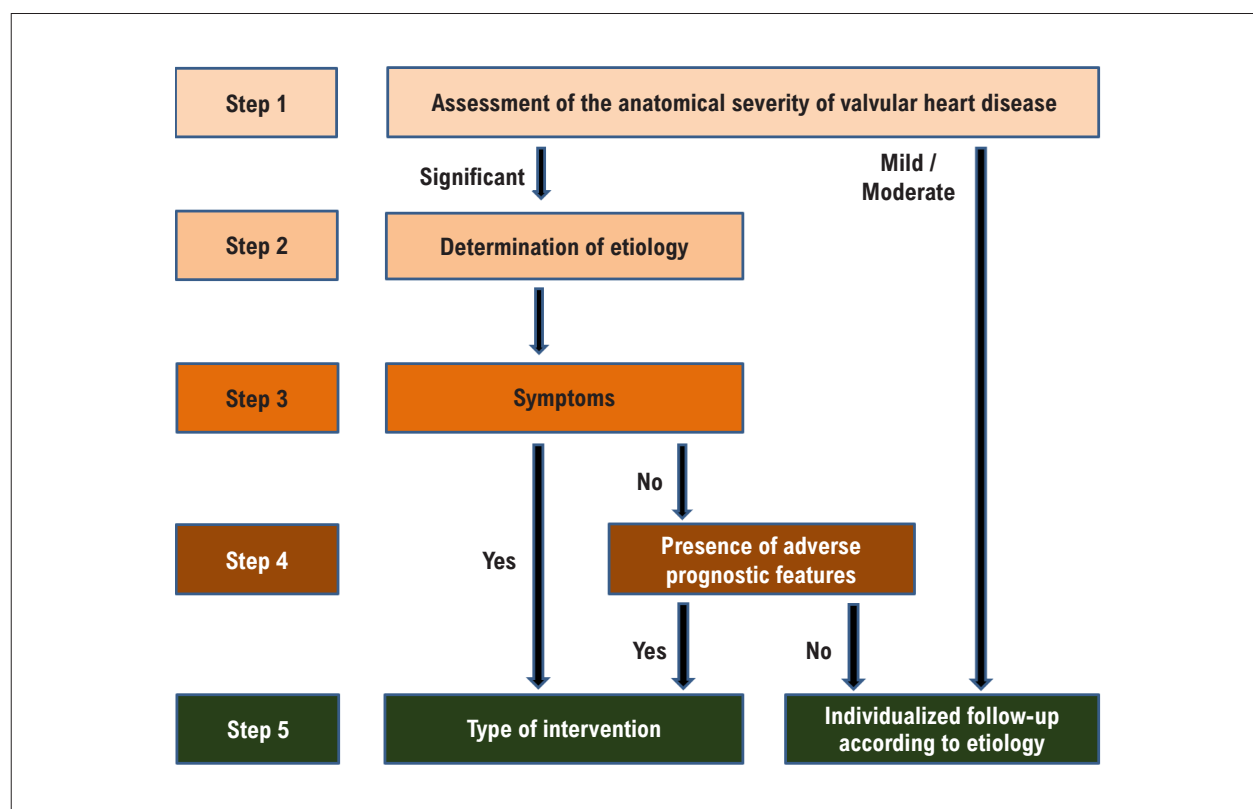


Figure 1 – Algorithm outlining the steps for anatomical, etiologic, and functional diagnosis and subsequent management decisions.

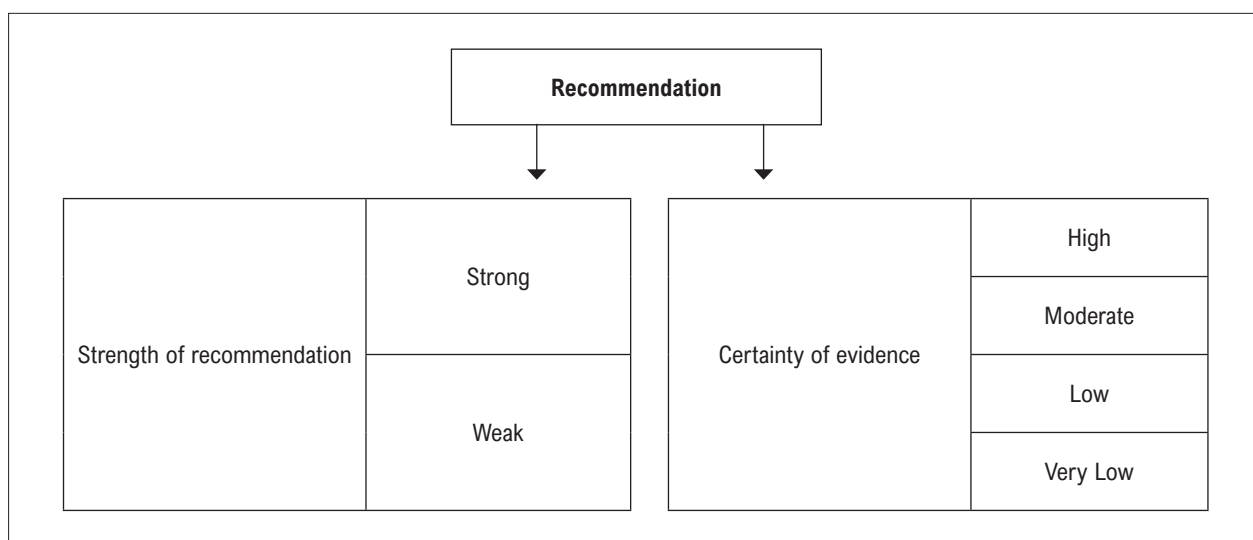


Figure 2 – Strength of recommendation and certainty of evidence according to the GRADE system.

II, interventions for which benefit is likely but less certain, subdivided into Class IIa, when the weight of evidence or opinion favors the intervention, and Class IIb, when usefulness or effectiveness is less well established; and Class III, interventions with no established benefit or that are potentially harmful and therefore should not be recommended. The level of evidence was categorized as follows: Level A, evidence derived from multiple randomized controlled trials or meta-analyses; Level B, data derived from a single randomized controlled trial or large nonrandomized studies; and Level C, recommendations based predominantly on expert consensus, small or retrospective studies, or registries.

1.2. The Heart Team / Heart Valve Team / Heart Valve Center of Excellence

In addition to the rapid advances in transcatheter techniques for treating various forms of valvular heart disease, indications for valvular interventions have become increasingly complex. This is particularly true for asymptomatic individuals, patients with concomitant coronary artery disease (CAD), those with multiple valvular lesions, and patients with several comorbidities that are often not incorporated into preoperative risk scores. Multidisciplinary collaboration through the Heart Valve Team is therefore essential when selecting the optimal therapeutic approach.

The Heart Valve Team is a multidisciplinary group of professionals with expertise in valvular heart disease who share responsibility for determining the most appropriate treatment for each patient. Given the wide range of interventional strategies currently available, the Heart Valve Team is essential for assessing the risk-benefit profile and cost-effectiveness of each strategy and supporting clinical decision-making. The team comprises professionals from several cardiovascular subspecialties, each of whom plays a distinct and essential role at different stages of care. The clinical cardiologist is responsible for patient selection and indication, in addition to pre- and post-intervention follow-up. The cardiac surgeon

and interventional cardiologist perform the procedures recommended by the Heart Valve Team. Cardiovascular imaging specialists analyze imaging data to assess the technical feasibility of each mode of intervention, while echocardiographers, in addition to evaluating preoperative data, may provide intraoperative imaging guidance, contributing to improved procedural outcomes.⁴⁻⁶

1.3. Operative Risk Assessment

The indication for intervention in patients with valvular heart disease should always be based on a comparison between the expected benefit and the estimated risk of the proposed procedure. Online risk calculators are available for this purpose, including the European System for Cardiac Operative Risk Evaluation (EuroSCORE II; <http://www.euroscore.org/calc.html>) and the Society of Thoracic Surgeons (STS) Risk Calculator (<https://acsdiskcalc.research.sts.org/>). These tools have been validated in different populations and can predict 30-day mortality. Patients with an STS score < 4% have conventionally been considered at low surgical risk, whereas those with scores of 4%–8% are considered at intermediate risk and those with scores > 8% at high risk. However, given advances in technology and surgical techniques, a more recent trend is to define low-risk patients as those with an STS score < 2%. For EuroSCORE II, patients with a score < 4% are considered at low risk, whereas those with a score > 4% are considered at increased risk. If the risk estimates provided by the scores are discordant, the higher estimate should be used.⁷⁻¹²

Importantly, risk scores represent only one component of prognostic risk stratification. Factors such as frailty and procedure-specific contraindications, including porcelain aorta, are not incorporated into these scores but are highly relevant to preoperative assessment. Moreover, risk assessment does not replace individualized clinical judgment, and decisions regarding intervention should always be shared with the patient and their family.

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1.4. Key new recommendations of the Brazilian Guideline for Valvular Heart Disease

Notably, the 2026 Guideline presents Table 1, which summarizes the eight key new recommendations proposed in this document, highlighting the most relevant changes for the assessment, decision-making, and management of patients with valvular heart disease.

Table 1 – Key recommendations of the Brazilian Guideline for Valvular Heart Disease – 2026

Clinical scenario	Intervention	Strength of recommendation/ Certainty of evidence
Significant high-gradient aortic stenosis, asymptomatic, without adverse prognostic features, and low surgical risk	Early intervention*	Weak / High
Significant aortic stenosis, symptomatic or with adverse prognostic features	Low risk, age < 70 years	Surgery preferred Strong / High
	Low risk, age 70–80 years	TAVI = surgery Strong / High
	Low risk, age > 80 years	TAVI preferred Strong / Moderate
Significant symptomatic aortic regurgitation with life expectancy > 1 year, contraindication to surgery or prohibitive surgical risk, suitable anatomy, after Heart Team assessment	TAVI	Weak / Low
Significant tricuspid regurgitation refractory to medical therapy, with a contraindication to or high risk for surgery and suitable anatomy	Transcatheter edge-to-edge repair	Strong / High
	Orthotopic implantation	Strong / High
	Heterotopic implantation	Strong / Low
Primary nonrheumatic mitral regurgitation, symptomatic, with suitable anatomy and high surgical risk as determined by the Heart Team	Transcatheter edge-to-edge mitral valve repair	Strong / Moderate
Symptomatic ventricular secondary mitral regurgitation despite optimized medical therapy and with suitable anatomy	Transcatheter edge-to-edge repair	Strong / Moderate

Significant structural dysfunction of a mitral or aortic bioprosthesis in symptomatic patients at high surgical risk or considered inoperable, after Heart Team assessment

Valve-in-valve

Strong / High

Dental extractions, oral surgery, or other procedures requiring manipulation of the gingival or periapical region of the teeth in patients at high risk of infective endocarditis

Antibiotic prophylaxis

Strong / Moderate

*TAVI: transcatheter aortic valve implantation; NYHA: New York Heart Association functional class; BNP: B-type natriuretic peptide; NT-proBNP: N-terminal pro-B-type natriuretic peptide. * Current evidence supporting early intervention is increasing; however, a prognostic benefit in terms of mortality, as observed in other settings in which valvular intervention is indicated, has not yet been demonstrated. Therefore, early intervention may be indicated in selected patients with adverse prognostic markers (late gadolinium enhancement on cardiac magnetic resonance imaging, reduced strain, elevated BNP or NT-proBNP, or a high aortic valve calcium score) after Heart Team discussion.*

2. Frailty

Frailty is a clinical syndrome characterized by diminished physiological reserve, resulting in increased vulnerability and a reduced ability to respond to illness or other stressors.¹³ It is associated with malnutrition, sarcopenia, hormonal disorders, unintentional weight loss, exhaustion, functional decline, and the development of cardiovascular disease.¹⁴ Its prevalence has increased with population aging, contributing to greater dependence in basic activities of daily living, hospitalization, and mortality. Risk factors include cognitive impairment, depression, social isolation, and alcohol consumption. Frailty also imposes a substantial economic burden on both public and private health care systems.¹⁵

In patients with valvular heart disease, frailty should always be investigated and quantified because it is highly relevant to treatment planning, decisions regarding intervention, and the rational use of health care resources.

Distinct profiles of patients with frailty can be identified, including older patients with associated comorbidities, patients who develop frailty because of heart failure (HF) caused by valvular heart disease, and younger patients who develop frailty after undergoing multiple surgical procedures. The latter profile remains relatively common in Brazil because of the substantial prevalence of rheumatic fever.¹⁶

Traditional methods of preoperative risk assessment, including EuroSCORE II and the STS score, cannot accurately

estimate, in patients with frailty, cardiovascular outcomes including in-hospital mortality, acute myocardial infarction, renal failure, and major bleeding.¹⁷ Moreover, isolated subjective assessments such as the eyeball test and gait speed should be avoided because they may provide incomplete or misleading information.⁴

Several instruments are currently available, including the Katz Index, Fried Frailty Scale, Rockwood Clinical Frailty Scale, and Short Physical Performance Battery. These instruments are widely recognized and used in geriatric practice; however, none were developed on the basis of a population-based study specifically involving patients with valvular heart disease.¹⁶

To address this gap, we highlight the Essential Frailty Toolset (EFT) score (Figure 3). The EFT was developed from a prospective, multicenter cohort study conducted at 14 centers in the United States, Canada, and France and involving patients aged > 70 years who underwent aortic valve intervention through surgery or transcatheter aortic valve implantation (TAVI). It is a simple, rapidly administered score with adequate sensitivity that does not

require complex equipment. The EFT assesses 4 domains: ability to stand 5 times from a seated position without using arms; cognitive status, assessed using the Mini-Mental State Examination; serum hemoglobin concentration; and serum albumin concentration. Scores range from 0 to 5, with higher scores indicating greater frailty. The EFT has been validated to predict the risks of 1-year mortality and ventricular dysfunction after aortic valve intervention. An EFT score > 3 indicates a presumed higher risk of developing cardiovascular events after valve intervention; however, this does not imply that proceeding with intervention is inappropriate or harmful to the patient.¹⁸ Once frailty has been identified, a more detailed assessment should be performed using a clinical questionnaire addressing nutritional status over the preceding 6 months, depression, and the ability to perform basic activities of daily living.¹⁵

For patients with frailty, less invasive interventional techniques are preferred. TAVI remains an excellent treatment option for aortic stenosis. In mitral valve disease, transcatheter edge-to-edge repair (TEER) is an option for patients with mitral regurgitation who remain symptomatic

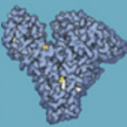
	Five chair rises < 15 seconds	0 points
	Five chair rises > 15 seconds	1 point
	Unable to complete	2 points
	No cognitive impairment	0 points
	Cognitive impairment	1 point
	Serum hemoglobin ≥ 13.0 g/dL = men ≥ 12.0 g/dL = women	0 points
	Serum hemoglobin < 13.0 g/dL = men < 12.0 g/dL = women	1 point
	Serum albumin ≥ 3.5 g/dL	0 points
	Serum albumin < 3.5 g/dL	1 point

Figure 3 – Essential Frailty Toolset (EFT) score for assessing frailty in patients with significant aortic stenosis undergoing valve intervention. Adapted from Afilalo et al.¹⁸

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despite optimal medical therapy. For other primary valve diseases, given the absence of less invasive treatments that improve prognosis, frailty may guide the implementation of preoperative measures intended to reverse the condition completely or partially or may even constitute a contraindication to the procedure. Nevertheless, frailty is a dynamic phenomenon, and treatment of valvular heart disease may improve the patient's clinical status, partially restore functional independence, and reduce disability.

In recent years, health technologies capable of enhancing disease detection have become available, including smartwatches with functions for monitoring heart rate, detecting cardiac arrhythmias, measuring pulse oximetry, and estimating energy expenditure. The data provided by these devices may facilitate the early detection of signs of frailty. Furthermore, the expansion and increasing availability of telemedicine have strengthened interactions among physicians, patients, and their families, enabling improved clinical management and follow-up in the home setting.

3. Mitral stenosis

3.1. Step 1 – Criteria for Determining the Anatomical Severity of Mitral Stenosis

The evaluation of patients with mitral stenosis begins by determining the anatomical severity of the valvular heart disease on the basis of physical examination (Chart 1 and Figure 4). Patients with non-significant mitral stenosis may have an opening snap and a decrescendo mitral diastolic rumble. In patients in sinus rhythm, the murmur exhibits pre-systolic accentuation at the end of diastole. However, physical examination findings are more evident in patients with significant mitral stenosis, in whom electrocardiographic (ECG) and radiographic abnormalities may also be present.

Echocardiography is the primary complementary test for the anatomical assessment of the mitral valve. It is essential for determining disease severity, etiology, hemodynamic consequences, and parameters associated with the likelihood of successful intervention. Each component of the mitral valve

Chart 1 – Step 1: Criteria for determining the anatomical severity of significant mitral stenosis¹⁹⁻²²

Characteristics of significant mitral stenosis	
Physical examination	• Facies mitralis
	• Opening snap
	• Loud S1
	• Loud S2
	• Diastolic rumble with pre-systolic accentuation in patients in sinus rhythm
	• Signs of pulmonary congestion and right heart failure
Electrocardiogram	• Presence of tricuspid regurgitation
	• Left atrial enlargement
	• Right-sided chamber enlargement
Chest radiography	• Atrial fibrillation
	• Normal cardiothoracic ratio
	• Signs of left atrial enlargement:
	• Elevated left main bronchus ("ballerina sign")
	• Double right heart border
	• Fourth arch of the left cardiac silhouette
Echocardiography	• Signs of pulmonary congestion
	• MVA $\leq 1.5 \text{ cm}^2$
	• Mean transmitral diastolic gradient $\geq 10 \text{ mm Hg}$
	• PASP $\geq 50 \text{ mm Hg}$ at rest
Hemodynamic assessment	• PASP $\geq 60 \text{ mm Hg}$ with exertion
	• Indicated when clinical and echocardiographic findings are discordant
	• Transmitral diastolic gradient $\geq 10 \text{ mm Hg}$ (spontaneous or after provocation with atropine and volume loading)
	• PASP $\geq 50 \text{ mm Hg}$

S1: first heart sound; S2: second heart sound; MVA: mitral valve area; PASP: pulmonary artery systolic pressure.

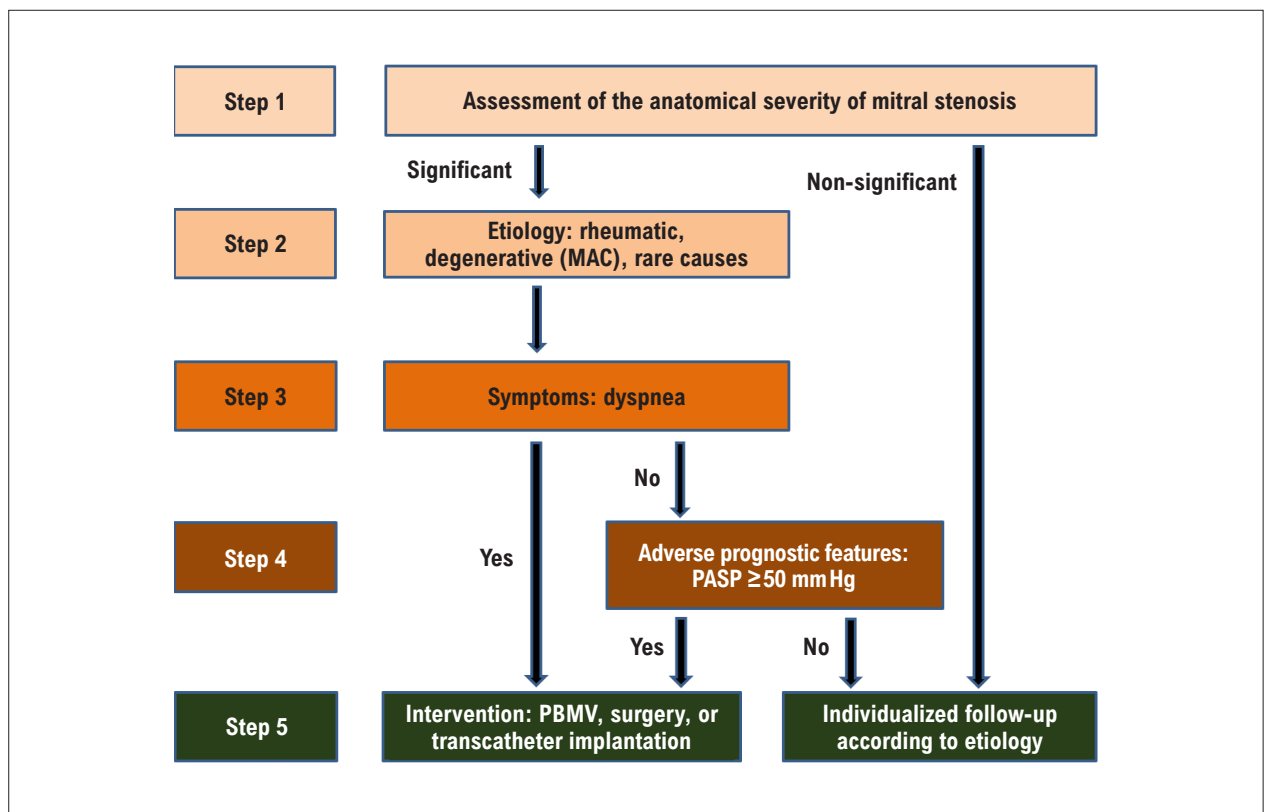


Figure 4 – Algorithm for the assessment of significant mitral stenosis. MAC: mitral annular calcification; PASP: pulmonary artery systolic pressure; AF: atrial fibrillation; PBMV: percutaneous balloon mitral valvuloplasty.

apparatus (the annulus, leaflets, and subvalvular apparatus) should be assessed individually.^{19,20}

The echocardiographic parameters used to classify the severity of mitral stenosis include mitral valve area, which may be measured by planimetry, pressure half-time (PHT) or the continuity equation, and the transmitral diastolic gradient. Because planimetry directly measures the valve orifice, it is less affected by factors such as atrial and ventricular compliance, transvalvular flow, volume status, and diastolic filling time. It is therefore the preferred method for assessing mitral valve area when the echocardiographic window is adequate.²⁰

The importance of 3-dimensional (3D) echocardiography in the detailed assessment of valve anatomy has received increasing emphasis. In mitral stenosis, several studies have demonstrated the important role of this diagnostic method both in assessing rheumatic valvular involvement and in determining the likelihood of success after interventional procedures.²¹ Transesophageal echocardiography also plays an important role, particularly when the acoustic window is limited or further clarification of the etiology of the valvular heart disease is required.²⁰ Moreover, it is the imaging modality of choice for evaluating patients scheduled to undergo percutaneous balloon mitral valvuloplasty (PBMV). It should be performed before the procedure to exclude intracardiac thrombi, the presence of which would contraindicate the intervention.^{20,21}

When clinical and echocardiographic findings are discordant, invasive hemodynamic assessment may be performed to determine the anatomical severity and hemodynamic consequences of mitral stenosis. This assessment includes direct measurement of left atrial pressure – usually inferred from pulmonary capillary wedge pressure – and left ventricular pressure, as well as calculation of the transmitral diastolic gradient, transpulmonary gradient, and pulmonary vascular resistance. In patients without an elevated transmitral gradient, volume loading and intravenous atropine may be used to increase transmitral flow and, consequently, the gradient. A transmitral diastolic gradient ≥ 10 mm Hg, either spontaneous or after provocation, is consistent with significant mitral stenosis.²²

3.2. Step 2 – Assessment of the Etiology of Mitral Stenosis

From an epidemiological perspective, rheumatic fever remains the leading cause of mitral stenosis worldwide, affecting children and young adults, particularly in low- and middle-income countries such as Brazil (Chart 2). In 2020, rheumatic disease affected approximately 40.5 million people worldwide, and its prevalence is projected to increase to 48 million cases by 2030.²³ In high-income countries, its incidence is expected to continue declining over the next decade.^{23,24} Mitral stenosis currently accounts

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Chart 2 – Step 2: Etiology of mitral stenosis

Etiologic characteristics	
Rheumatic fever	• > 90% of cases in low- and middle-income countries • Symptoms between the third and fourth decades of life • Commissural fusion and leaflet thickening • Involvement of the subvalvular apparatus • Doming of the anterior leaflet and reduced posterior leaflet motion • Concomitant mitral and aortic valve involvement
Degenerative (MAC)	• 12%–23% of cases in high-income countries • More common in older adults • May account for up to 60% of cases in patients aged > 75 years • Calcification of the mitral annulus • Absence of commissural fusion • Associated with aortic and coronary calcification
Rare causes	• Congenital • Rheumatologic diseases (systemic lupus erythematosus/rheumatoid arthritis) • Drugs (methysergide/anorectic agents) • Carcinoid syndrome • Fabry disease

MAC: mitral annular calcification.

for approximately 12% of all valvular heart disease in European countries and has a prevalence of 0.1% in the United States.²⁵ In these countries, cases occur predominantly among older adults and young immigrants from less developed regions, including Oceania, Southeast Asia, and sub-Saharan Africa.²⁴

In addition to rheumatic etiology, the proportion of patients with degenerative or calcific mitral stenosis is increasing, particularly among adults aged > 75 years.²⁶ The valvular lesion is caused by mitral annular calcification (MAC), which begins in the posterior portion of the annulus and may extend throughout its circumference to the base of the valve leaflets, restricting leaflet motion and, consequently, atrial emptying. Unlike rheumatic mitral stenosis, the subvalvular apparatus and commissures are not affected by calcification.²⁷ MAC is also a marker of more severe cardiovascular disease and is associated with an increased risk of AF, stroke, and mortality.^{26,28,29} It is more prevalent in women and is associated with comorbidities such as hypertension, diabetes mellitus, and chronic kidney disease; it may also develop after radiotherapy for cancer treatment.^{26,28} MAC affects approximately 23% of older adults, of whom approximately 2%–3% develop mitral stenosis. Mixed mitral valve disease, with concomitant significant mitral regurgitation, is the most common presentation.^{26,28,29}

Other rare causes of mitral stenosis include rheumatic diseases (such as systemic lupus erythematosus and rheumatoid arthritis), storage diseases (such as Fabry disease), Whipple disease, treatment with methysergide or anorectic

agents, carcinoid syndrome, and congenital anatomical abnormalities of the mitral valve (such as a parachute mitral valve or hypoplastic mitral valve).

3.3. Step 3 – Symptoms

In patients with significant mitral stenosis, clinicians should remain alert to the onset of symptoms (Chart 3), the most common of which is dyspnea corresponding to New York Heart Association (NYHA) functional class II–IV. Dyspnea may arise particularly in situations that increase pulmonary venous and capillary pressure, such as physical exertion, pregnancy, and AF. Over time, dyspnea may occur even at rest and may be accompanied by orthopnea. Other symptoms that may develop include palpitations, hemoptysis, dysphonia, dysphagia, cough, and embolic events.

3.4. Step 4 – Adverse Prognostic Features

In parallel with symptom assessment, patient follow-up should include evaluation for potential adverse prognostic features (Chart 4). In significant mitral stenosis, the relevant findings are significant pulmonary hypertension, defined as pulmonary artery systolic pressure (PASP) $\geq$ 50 mm Hg, or AF.

In patients with significant mitral stenosis for whom the presence of symptoms attributable to the valvular disease is uncertain, exercise or pharmacologic stress echocardiography may be performed. An increase in PASP to $\geq$ 60 mm Hg during stress suggests hemodynamic consequences and may indicate the need for intervention.³⁰

Chart 3 – Step 3: Assessment of symptoms in significant mitral stenosis

Symptoms	
Dyspnea (NYHA II–IV)	• Main symptom • Initially occurs in situations that increase pulmonary venous and capillary pressure (physical exertion, atrial fibrillation, and pregnancy) • Dyspnea at rest and paroxysmal nocturnal dyspnea • May be accompanied by palpitations, hemoptysis, dysphonia, dysphagia, and cough • May be accompanied by embolic events involving the cerebral, mesenteric, or peripheral circulation

NYHA: New York Heart Association functional class.

Chart 4 – Step 4: Assessment of adverse prognostic features in significant mitral stenosis

Adverse prognostic features	
Pulmonary hypertension	• PASP ≥ 50 mm Hg at rest • PASP ≥ 60 mm Hg with exertion (exercise stress testing or pharmacologic stress echocardiography)
AF associated with valvular heart disease	• Associated with LA remodeling • Maintain anticoagulation with warfarin, with a target INR of 2.0–3.0

PASP: pulmonary artery systolic pressure; AF: atrial fibrillation; LA: left atrium; INR: international normalized ratio.

Functional echocardiographic parameters such as left atrial strain correlate with left atrial compliance and functional capacity in patients with mitral stenosis.^{31,32} Reduced left atrial strain is associated with the development of symptoms and predicts AF in asymptomatic patients with moderate or significant mitral stenosis.³³ This finding may complement other severity parameters when assessing the need for intervention. However, its use remains limited.

The behavior of biomarkers such as natriuretic peptides (NPs) also correlates with the severity of valvular heart disease and the hemodynamic consequences of mitral stenosis. However, the clinical application of these biomarkers is limited, particularly because of inconsistencies in the cutoff values used.³⁴

3.5. Step 5 – Modes of Intervention

The available modes of intervention and their respective indications are described in Charts 5 and 6.

PBMV remains the treatment of choice for patients with rheumatic mitral stenosis, characterized predominantly by commissural calcification and fusion, provided that they have suitable valve anatomy, as stratified using the Wilkins-Block score (Chart 7), and no contraindications, such as moderate or significant mitral regurgitation or left atrial thrombus. The Wilkins-Block score is based on echocardiographic assessment of the mitral valve, with emphasis on its structural characteristics. Four parameters are considered: leaflet motion, leaflet thickening, degree of calcification, and involvement of the subvalvular apparatus. Each parameter is assigned 1–4 points, resulting in a total score ranging from 4 to 16. Studies have shown that patients with a Wilkins score ≤ 8 have higher procedural success

rates and fewer adverse events after PBMV. Therefore, patients with a Wilkins-Block score ≤ 8 are candidates for PBMV in the absence of contraindications.^{35,36} Even after successful PBMV, approximately 55% of patients may develop restenosis and require repeat intervention. In young patients with suitable anatomy, repeat PBMV is a safe and satisfactory strategy that provides good immediate outcomes in selected cases.³⁷

In patients with anatomy unsuitable for PBMV, defined as a Wilkins score > 10 , or with contraindications to the percutaneous procedure, mitral valve surgery becomes the preferred treatment option. Surgery may consist of mitral commissurotomy or, when valvular involvement is extensive and preservation of the native valve is not feasible, valve replacement with a biological or mechanical prosthesis. PBMV may be considered in selected patients, such as pregnant women or patients at high surgical risk, with a Wilkins score of 9–10, provided that the scores for valvular calcification and subvalvular apparatus involvement do not exceed 2 for either component.

Conversely, in patients with degenerative mitral stenosis, PBMV is not a treatment option because calcification involves the mitral annulus rather than the commissures and may or may not extend to the base of the leaflets. Moreover, these patients are generally older and frequently have multiple comorbidities, resulting in substantially higher surgical risk. Surgery also presents technical challenges that may increase the likelihood of complications, including atrioventricular disruption, coronary sinus injury, circumflex coronary artery injury, and bleeding from the ventricular wall. Initial treatment should therefore be pharmacologic. If this strategy provides adequate symptom control, the patient may remain without an indication for further intervention.²⁸

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Chart 5 – Step 5: Modes of intervention in significant mitral stenosis

Mode	Considerations
Percutaneous balloon mitral valvuloplasty	• Treatment of choice for rheumatic mitral stenosis • Indications: - Symptoms (NYHA II–IV) and/or adverse prognostic features, with a Wilkins-Block echocardiographic score ≤ 8 * (subvalvular apparatus score ≤ 2 and calcification score ≤ 2) - In pregnant women or patients at high operative risk, consider PBMV when the echocardiographic score is 9–10 (subvalvular apparatus score ≤ 2 and calcification score ≤ 2) • Contraindications: - LA thrombus - Moderate or significant mitral regurgitation - Recent embolic event
Surgical treatment (commissurotomy/valve replacement)	• Rheumatic MS with NYHA II–IV symptoms and contraindications to PBMV • Rheumatic MS with adverse prognostic features in patients who are not eligible for PBMV • Degenerative MS refractory to medical therapy
Transcatheter mitral valve implantation (valve-in-MAC)	• Degenerative MS refractory to medical therapy, with a contraindication to or high risk for surgery and suitable anatomy

NYHA: New York Heart Association functional class; PBMV: percutaneous balloon mitral valvuloplasty; LA: left atrium; MS: mitral stenosis; MAC: mitral annular calcification. * Individualize treatment in patients with an echocardiographic score of 9–10. Patients with calcification and subvalvular apparatus scores < 3 have higher PBMV success rates.

Chart 6 – Significant mitral stenosis: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Percutaneous balloon mitral valvuloplasty	• Rheumatic MS with NYHA II–IV symptoms, in the absence of contraindications	Strong / High	I A	I B
	• Asymptomatic rheumatic MS with adverse features, in the absence of contraindications	Strong / Low	IIa B*	IIa C
Surgical treatment (commissurotomy/valve replacement)	• Rheumatic MS with NYHA II–IV symptoms and contraindications to PBMV	Strong / Moderate	I B	I C
	• Asymptomatic rheumatic MS with adverse features in patients who are not eligible for PBMV	Strong / Low	-	-
	• Degenerative MS refractory to medical therapy	Weak / Low**	IIb C	-
	• Asymptomatic rheumatic MS in patients scheduled to undergo another cardiac surgical procedure	Strong / Low	I C	IIa C
Transcatheter mitral valve implantation (valve-in-MAC)	• Degenerative MS refractory to medical therapy, with a contraindication to or high risk for surgery and suitable anatomy	Weak / Low**	IIb C	IIb C

MS: mitral stenosis; MAC: mitral annular calcification; PBMV: percutaneous balloon mitral valvuloplasty; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology. * Class IIa, Level B indication when pulmonary hypertension is present; Class IIb, Level C when AF is present. ** Consider discussion by the Heart Team.

Chart 7 – Wilkins-Block echocardiographic score**Leaflet motion:**

- 1 - Highly mobile valve with only leaflet tips restricted
- 2 - Leaflet mid and base portions have normal motion
- 3 - Valve continues to move forward in diastole, mainly from the base
- 4 - No or minimal forward movement of the leaflets in diastole

Subvalvular thickening:

- 1 - Minimal thickening just below the mitral leaflets
- 2 - Thickening of chordal structures extending to one-third of the chordal length
- 3 - Thickening extended to the distal third of the chords
- 4 - Extensive thickening and shortening of all chordal structures extending down to the papillary muscles

Leaflet thickening:

- 1 - Leaflets near normal in thickness (4–5 mm)
- 2 - Midleaflets normal, considerable thickening of margins (5–8 mm)
- 3 - Thickening extending through the entire leaflet (5–8 mm)
- 4 - Considerable thickening of all leaflet tissue (>8–10 mm)

Valvular calcification:

- 1 - A single area of increased echo brightness
- 2 - Scattered areas of brightness confined to leaflet margins
- 3 - Brightness extending into the mid-portions of the leaflets
- 4 - Extensive brightness throughout much of the leaflet tissue

For patients with symptoms refractory to medical therapy, surgery may be considered when surgical risk is low to moderate, whereas transcatheter mitral valve implantation (TMVI) may be considered for those at prohibitive surgical risk. In these cases, transcatheter implantation uses extensive MAC to anchor the valve prosthesis, and the procedure is commonly referred to as valve-in-MAC.²⁸ Despite advances in interventional cardiology, experience with this procedure remains limited. In clinical studies, it has most frequently been performed through a transeptal or transapical approach. The procedure is also associated with a high rate of complications, including paravalvular leak, left ventricular outflow tract (LVOT) obstruction, and valve embolization, as well as mortality rates as high as 16.7% at 30 days, 34.5% at 12 months, and 67.9% at 5 years.³⁸ However, when successful, it may provide sustained improvement in symptoms attributable to valvular heart disease and improved quality of life at 5 years.³⁸

More recently, the SUMMIT-MAC study, the first prospective trial to evaluate a dedicated transcatheter mitral valve prosthesis in patients with severe MAC, demonstrated substantially superior results, including a technical success rate of 94.2%, 30-day mortality rate of 6.8%, and freedom from all-cause mortality and HF hospitalization rate of 60.4% at 12 months, with significant improvements in functional capacity and quality of life.³⁹ These findings suggest that dedicated devices may improve the safety and

effectiveness of the procedure, although long-term follow-up data remain necessary. The indication should therefore remain individualized and based on multimodality imaging assessment and discussion by an experienced Heart Team. The procedure should be performed at centers with expertise in complex structural heart interventions.

3.6. Individualized Follow-Up

Patients with anatomically mild or moderate valvular heart disease should undergo clinical follow-up with periodic visits and echocardiographic reassessment. For patients with non-significant mitral stenosis, defined as a mitral valve area > 1.5 cm², annual clinical and echocardiographic reassessment is recommended. If symptoms or adverse prognostic features develop before the valvular heart disease becomes anatomically significant, alternative diagnoses that could account for these findings must be considered.

Asymptomatic patients with significant mitral stenosis and no adverse prognostic features should be reassessed at shorter intervals, generally every 6–12 months (Chart 8).

3.7. Medical Therapy

Initial treatment for symptom control consists of reducing heart rate with a beta-blocker, calcium channel blocker, or ivabradine. Ivabradine should be used only in patients in sinus rhythm who cannot tolerate the preceding medications. In

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Chart 8 – Mitral stenosis: Individualized follow-up

Mitral stenosis	Follow-up	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Significant, asymptomatic, and without adverse prognostic features	• Clinical and echocardiographic reassessment	Every 6–12 months	Every 6–12 months	Every year
	• Concomitant intervention in patients undergoing another cardiac surgical procedure (coronary revascularization, ascending aortic surgery, or another valve procedure)	Strong / Low	IIb C	-
Non-significant (MVA 1.5–2.0 cm ² and mean LA–LV diastolic gradient 5–10 mm Hg)	• Clinical and echocardiographic reassessment	Every year	Every 3–5 years	Every 2–3 years
	• Concomitant intervention in patients undergoing another cardiac surgical procedure (coronary revascularization, ascending aortic surgery, or another valve procedure)	Strong / Low	-	-

AHA: American Heart Association; ESC: European Society of Cardiology; LA: left atrium; LV: left ventricle; MVA: mitral valve area; SBC: Brazilian Society of Cardiology.

patients with AF requiring rate control, digoxin or amiodarone may also be used. Heart rate control is intended to prolong ventricular filling time and reduce left atrial pressure, thereby allowing more time for left atrial emptying. The addition of diuretics may further reduce the transmitral gradient by decreasing transmitral flow.

4. Primary Mitral Regurgitation

4.1. Step 1 – Criteria for Determining the Anatomical Severity of Significant Primary Mitral Regurgitation

Significant mitral regurgitation should initially be suspected when cardiac auscultation reveals a regurgitant systolic murmur of grade $\geq 3+/6+$ that radiates toward the axillary line. Other physical examination abnormalities may also be present, as described in Chart 9. An important marker of anatomical severity is diminished intensity of the first heart sound, which may result from ventricular dysfunction or chordal rupture.

When valvular heart disease is suspected, transthoracic echocardiography is the primary examination for diagnosis and confirmation of its anatomical severity (Chart 9).

An important parameter is the effective regurgitant orifice area (EROA), which is associated with all-cause mortality. Compared with the general population, mortality is increased when EROA is ≥ 0.20 cm², with a consistently greater increase at values > 0.40 cm².

When clinical and echocardiographic findings are discordant, transesophageal echocardiography may be used to improve visualization of the leaflets and valvular apparatus, provide more accurate quantification of regurgitation, and better estimate the likelihood of successful surgery. Three-

dimensional echocardiography has proven more accurate than 2-dimensional echocardiography for assessing regurgitant volume. It also provides better anatomical characterization of mitral valve prolapse, with excellent morphological and functional visualization of the affected valve segments, which is useful for surgical planning and transcatheter repair.^{40,41}

Cardiac magnetic resonance (CMR) has been increasingly used to assess mitral regurgitation, including when clinical and echocardiographic findings are discordant. Its main application is the accurate quantification of regurgitant volume and fraction, both of which have prognostic implications. CMR is also important for evaluating myocardial fibrosis and mitral annular disjunction (MAD), which is frequently associated with mitral valve prolapse, ventricular arrhythmias, and sudden cardiac death.⁴²

Computed tomography (CT) is increasingly useful, although its role in quantifying primary mitral regurgitation remains limited. It is particularly valuable for transcatheter procedures because it permits detailed geometric assessment of the mitral leaflets, annulus, and subvalvular apparatus, as well as annular measurements that facilitate the sizing of valve implantation devices.⁴³

Cardiac catheterization is essential for the preoperative assessment of patients with significant mitral regurgitation when concomitant CAD is suspected. During the examination, left ventriculography may be performed by injecting contrast into the left ventricle, allowing direct visualization of blood regurgitation from the left ventricle into the left atrium during systole. Regurgitation is considered significant when graded $> 3+$. Intracardiac pressures may also be measured in conjunction with right heart catheterization to define prognosis and assess the hemodynamic consequences of the disease. Although invasive, cardiac catheterization may be useful in

Chart 9 – Step 1: Criteria for determining the anatomical severity of significant primary mitral regurgitation

Characteristics of significant primary mitral regurgitation	
Physical examination	• Apical impulse displaced to the left and downward • Loud S2 • Regurgitant systolic murmur $\geq 3+/6+$ • Clinical signs of right heart failure (jugular venous distention, hepatomegaly, and lower-extremity edema)
Electrocardiogram	• Signs of left-sided chamber enlargement • Atrial or ventricular arrhythmias
Chest radiography	• Enlarged cardiac silhouette (LA and LV enlargement) • Pulmonary congestion
Echocardiography	• Jet area $\geq 40\%$ of the LA area • Regurgitant fraction $\geq 50\%$ • Regurgitant volume ≥ 60 mL/beat • Vena contracta ≥ 0.7 cm • EROA ≥ 0.40 cm² • E-wave velocity > 1.2 m/s • Systolic flow reversal in the pulmonary veins
Cardiac magnetic resonance	• Assessment of MR severity based on significant regurgitant volume and fraction • Assessment of ventricular function • Assessment of myocardial fibrosis • Assessment of mitral annular disjunction and MVP
Hemodynamic assessment	• Significant regurgitant jet ($> 3+$) during ventriculography • Assessment of intracardiac pressures by right heart catheterization

EROA: effective regurgitant orifice area; LA: left atrium; LV: left ventricle; MR: mitral regurgitation; MVP: mitral valve prolapse; S2: second heart sound.

selected settings because it provides direct visualization of mitral regurgitation and detailed assessment of ventricular function.⁴⁴

Other examinations, including ECG and chest radiography, may also reveal characteristic abnormalities, as shown in Chart 9.

4.2. Step 2 – Assessment of the Etiology of Primary Mitral Regurgitation

Primary mitral regurgitation is associated with an anatomical lesion of the valve leaflet, chordae tendineae, and/or papillary muscle. As with the determination of anatomical severity, transthoracic echocardiography remains the primary tool for establishing the etiology of mitral regurgitation. This step is essential because clinical follow-up and the choice of interventional approach may differ according to disease etiology. MAC may also cause mitral regurgitation; its classification and treatment have been addressed previously (see the Mitral Stenosis chapter).

Rheumatic disease remains the leading and most prevalent cause of primary mitral regurgitation in Brazil, followed by

mitral valve prolapse and associated conditions (flail leaflet and Barlow disease). Within this group, increasing attention has been given to MAD, defined as separation between the mitral annulus and the left ventricular myocardium. MAD is frequently present in arrhythmic mitral valve prolapse. It has been proposed that MAD causes excessive motion of the mitral valve apparatus, which exerts traction on the papillary muscles and the posterobasal left ventricular myocardium, thereby serving as a trigger for ventricular arrhythmias.⁴⁵

The etiologic characteristics and other causes are summarized in Chart 10 and Figure 5.

Importantly, these pathological mechanisms may overlap. Untreated primary mitral regurgitation may lead to left ventricular dysfunction and dilation, resulting in annular dilation and leaflet tethering, which further worsen regurgitation.⁴⁶

4.3. Step 3 – Symptoms

The main symptom in patients with significant disease is dyspnea, which results from pulmonary congestion and typically worsens progressively. This symptom should be

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Chart 10 – Step 2: Etiology of primary mitral regurgitation

Etiologic characteristics	
Rheumatic	• Leaflet thickening and retraction
	• Commissural involvement
	• Concomitant mitral and aortic valve involvement
	• Affects young adults
Mitral valve prolapse and associated conditions (flail leaflet, Barlow disease)	• Leaflet displacement toward the LA ≥ 2 mm
	• Myxomatous degeneration
	• Affects middle-aged and older adults
Other causes	• Infective endocarditis
	• Degenerative (MAC)
	• Marfan syndrome
	• Systemic lupus erythematosus
	• Trauma
	• Congenital lesions

LA: left atrium; MAC: mitral annular calcification.

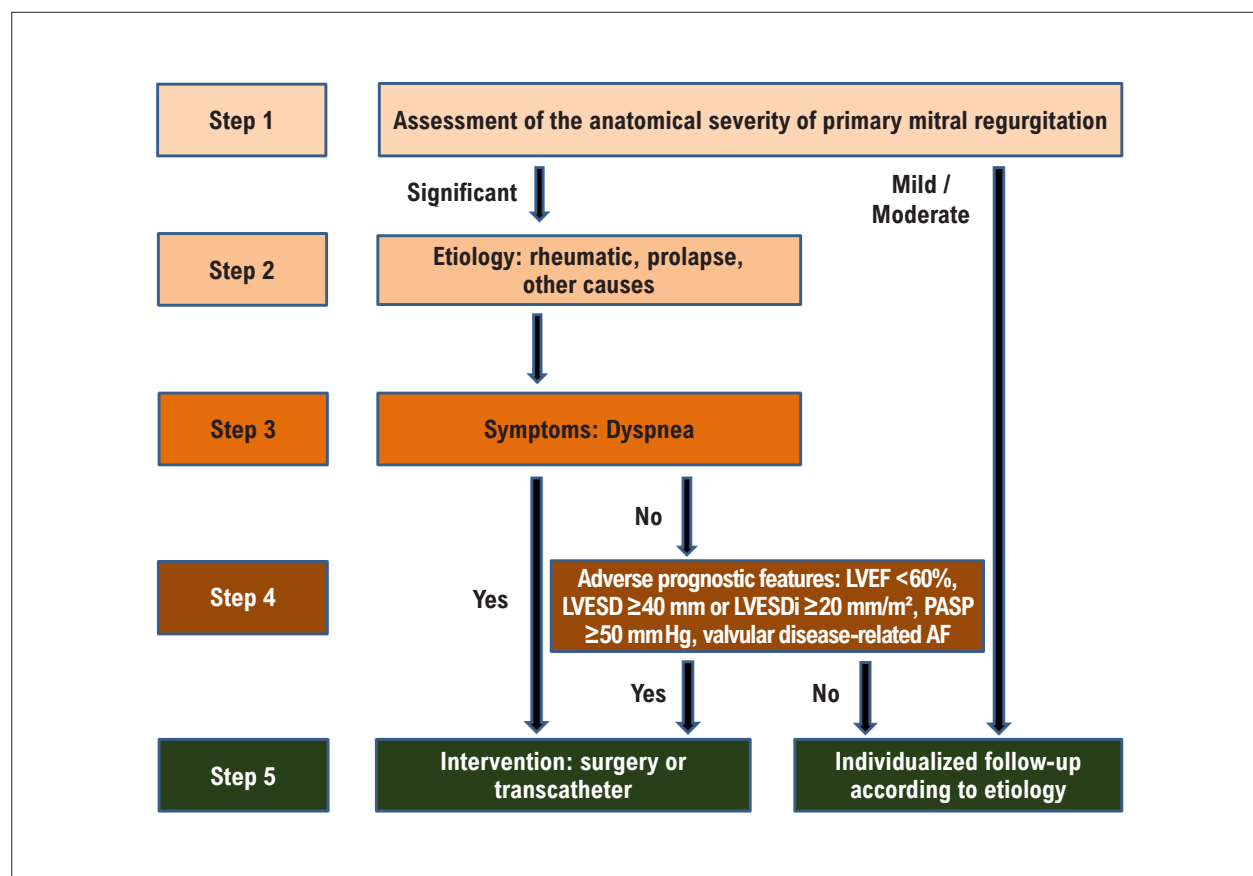


Figure 5 – Algorithm for the assessment of significant primary mitral regurgitation. AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESDi: left ventricular end-systolic diameter indexed to body surface area; PASP: pulmonary artery systolic pressure.

recognized even at early stages, when it occurs only during greater-than-usual exertion (NYHA class II). Dyspnea may be accompanied by other symptoms, as summarized in Chart 11.

Self-reported absence of symptoms may result from unconscious activity restriction in response to fatigue or accommodation of the regurgitant volume in a remodeled left atrium, without sufficient elevation of pressure to cause dyspnea. Therefore, before classifying a patient as asymptomatic, exercise stress testing or cardiopulmonary exercise testing (CPET) may be performed to elucidate symptoms or demonstrate reduced functional capacity. Echocardiographic imaging during functional testing may also demonstrate increased PASP, worsening mitral regurgitation, or deterioration of left ventricular function.⁴⁶

4.4. Step 4 – Adverse Prognostic Features

In truly asymptomatic patients, echocardiographic parameters (left ventricular ejection fraction [LVEF] < 60%, left ventricular end-systolic diameter [LVESD] ≥ 40 mm, and PASP ≥ 50 mm Hg at rest or ≥ 60 mm Hg with exertion) and ECG findings (AF) should be assessed. These findings justify surgical intervention even in the absence of symptoms because, once established, they are associated with worse outcomes and prognosis (Chart 12).

During follow-up of patients without significant disease, a progressive decline in LVEF or progressive left ventricular dilation should prompt consideration of surgical intervention, even before these parameters reach abnormal thresholds.

Global longitudinal strain (GLS) is a sensitive echocardiographic method for detecting early left ventricular dysfunction. It may be particularly useful for determining the optimal timing of intervention in asymptomatic patients by identifying declining left ventricular function before LVEF decreases. Accumulating evidence indicates that GLS has long-term prognostic value in patients with mitral regurgitation who undergo surgery; however, further studies are needed to establish its role in determining the optimal timing of intervention in asymptomatic patients.^{47,48} Its precise role and cutoff values for clinical follow-up remain uncertain.⁴⁹

B-type natriuretic peptide (BNP) is a useful prognostic tool for monitoring patients with mitral regurgitation. Elevated concentrations, particularly > 105 pg/mL, reflect greater disease severity and increased patient risk. Evidence suggests that BNP may be considered alongside abnormalities identified by other examinations when the indication for or optimal timing of surgical intervention remains uncertain. However, its incorporation into clinical practice requires further validation.^{47,50}

4.5. Step 5 – Modes of Intervention

In patients with chronic significant primary mitral regurgitation who have an indication for intervention and suitable anatomy, mitral valve repair is associated with lower mortality, better long-term survival, and superior functional outcomes compared with valve replacement. Therefore,

repair should be the preferred technique whenever there is a high likelihood of achieving complete and durable correction of mitral regurgitation (Charts 13 and 14).⁵¹

The surgical strategy should be individualized according to the etiology of the valvular heart disease, the patient's clinical characteristics, the surgical team's experience, and the anatomical complexity of the valve. In patients with significant degenerative mitral regurgitation, particularly those with mitral valve prolapse, repair should be prioritized whenever technically feasible. Conversely, in patients with advanced rheumatic disease, extensive calcification of the valvular apparatus, or significant involvement of the leaflets and subvalvular apparatus, mitral valve replacement is often the most appropriate strategy because repair is less durable in this setting.

Minimally invasive procedures performed through a right minithoracotomy are increasingly used at specialized centers. However, available data remain insufficient to support their routine use. These procedures should be reserved for selected patients and performed at experienced, high-volume centers with low mortality and durable outcomes after Heart Team discussion.⁴⁶ Robotic mitral valve surgery has also gained some acceptance in selected patients with favorable characteristics, although its indications and use in Brazil remain limited.

Another treatment option is TEER. Because current evidence has not demonstrated a prognostic benefit, this strategy should be restricted to patients with a contraindication to surgery and performed to provide symptomatic benefit.⁵²

TMVI enables treatment of anatomies that are complex or unsuitable for TEER and provides nearly complete elimination of mitral regurgitation. However, TMVI remains limited by high study-exclusion rates, the risk of LVOT obstruction, prosthetic valve thrombosis, the need for detailed CT angiography planning, the absence of medium-term follow-up data, and limited device availability.⁵³

In asymptomatic patients with mitral valve prolapse and no adverse prognostic features, the strategies of early surgery and watchful waiting remain widely debated. The main consequence of mitral regurgitation is volume overload, which progressively impairs left ventricular function and may place the patient in a less favorable condition for surgery. Observational evidence indicates that early intervention is associated with better long-term outcomes when performed under predefined conditions.⁵⁴ Mitral regurgitation must be significant, the procedure must carry low risk, be effective, and provide a durable result; it must also be performed at a center of excellence and must not be considered futile. If the patient does not meet these criteria or if uncertainty remains, early surgery should not be performed, and close individualized follow-up is indicated.⁴⁷

Arrhythmic mitral valve prolapse is a phenotype characterized by the presence of mitral valve prolapse and complex ventricular arrhythmias and is associated with an increased risk of sudden cardiac death, regardless of the anatomical severity of mitral regurgitation and in the

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Chart 11 – Step 3: Assessment of symptoms in significant primary mitral regurgitation

Symptoms

Dyspnea NYHA II–IV	• Main symptom • May be accompanied by palpitations, cough, lower-extremity edema, or thromboembolic events
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NYHA: New York Heart Association functional class.

Chart 12 – Step 4: Assessment of adverse prognostic features in significant primary mitral regurgitation

Adverse prognostic features

Echocardiography	• LVEF < 60% • LVESD ≥ 40 mm (or LVESDi ≥ 20 mm/m²) • PASP ≥ 50 mmHg at rest or ≥ 60 mmHg with exertion
Electrocardiogram	• AF associated with valvular heart disease

AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESDi: left ventricular end-systolic diameter indexed to body surface area; PASP: pulmonary artery systolic pressure.

Chart 13 – Step 5: Modes of intervention for significant primary mitral regurgitation

Modes of intervention Considerations

Mitral valve repair	• First-line procedure in patients with degenerative etiology and suitable anatomy • Patients with rheumatic disease: individualized assessment, less favorable outcomes
Mitral valve replacement	• Anatomy unsuitable for mitral valve repair • Patients with a contraindication to surgery and refractory symptoms • Patients at high surgical risk
Transcatheter edge-to-edge mitral valve repair	• Older patients • Life expectancy > 1 year • Suitable anatomy • Management should be determined by the Heart Team

absence of another cardiac disorder that could account for the arrhythmogenic substrate. The arrhythmias of interest in this context are exclusively ventricular and arise from the mitral apparatus or left ventricle; they do not include atrial arrhythmias or isolated low-risk ventricular ectopy. MAD is part of this spectrum as one component of the arrhythmogenic substrate, although its presence alone does not establish the diagnosis. Markers of increased risk include extensive MAD, bileaflet prolapse, myocardial fibrosis on CMR, frequent ventricular ectopy or nonsustained ventricular tachycardia with adrenergic-dependent behavior, T-wave inversion in the inferior leads, and LVEF < 50%. To date, no validated algorithm can independently predict the risk of sudden cardiac death in these patients. Risk stratification and treatment should therefore be individualized. Symptomatic patients

presenting with palpitations, syncope, or presyncope should undergo further investigation with prolonged ECG monitoring, exercise stress testing, and, when indicated, CMR to permit appropriate arrhythmic risk stratification.

There is currently no evidence supporting the preferential use of a specific antiarrhythmic medication for this phenotype. Beta-blockers may be used for symptom control, whereas other antiarrhythmic agents should be reserved for selected cases after consideration of their efficacy and safety profiles. An implantable cardioverter-defibrillator (ICD) is indicated for secondary prevention after resuscitated cardiac arrest and may be considered for primary prevention in selected cases after multidisciplinary discussion. The role of catheter ablation remains controversial and is reserved primarily for patients with symptomatic or recurrent ventricular arrhythmias.

Chart 14 – Significant primary mitral regurgitation: Recommendations

Modes of intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Mitral valve repair	Rheumatic disease			
	• Symptomatic patients (dyspnea, NYHA ≥ II)	Weak / Low	-	-
	• Asymptomatic patients with adverse prognostic features: ◦ LVEF < 60% and/or LVESD ≥ 40 mm (or LVESDi ≥ 20 mm/m ²)	Weak / Low	-	-
	◦ PASP ≥ 50 mmHg or AF associated with valvular heart disease	Weak / Low	-	-
	Nonrheumatic disease			
	• Symptomatic patients (dyspnea, NYHA ≥ II) with suitable anatomy	Strong / Moderate	I B	I B
	• Asymptomatic patients with adverse prognostic features and suitable anatomy: ◦ LVEF < 60% and/or LVESD ≥ 40 mm (or LVESDi ≥ 20 mm/m ²)	Strong / Moderate	I B	I B
	◦ PASP ≥ 50 mmHg or AF associated with valvular heart disease	Strong / Moderate	-	I B*
	• Asymptomatic patients with MR due to MVP, suitable anatomy, and no adverse prognostic features, treated at experienced centers	Strong / Low	Ila B	Ila B **
	• Arrhythmic MVP and/or MAD in the absence of other indications for intervention	Weak / Very low	-	-
Mitral valve replacement	Rheumatic disease			
	• Symptomatic patients (dyspnea, NYHA ≥ II)	Strong / Moderate	I B	I B
	• Asymptomatic patients with adverse prognostic features: ◦ LVEF < 60% and/or LVESD ≥ 40 mm (or LVESDi ≥ 20 mm/m ²)	Strong / Moderate	I B	I B
	◦ PASP ≥ 50 mmHg or AF associated with valvular heart disease	Strong / Moderate	-	Ila B
	Nonrheumatic disease			
	• Symptomatic patients (dyspnea, NYHA ≥ II) with anatomy unsuitable for mitral valve repair	Strong / Moderate	I B	I B
	• Asymptomatic patients with adverse prognostic features and unsuitable anatomy: ◦ LVEF < 60% and/or LVESD ≥ 40 mm (or LVESDi ≥ 20 mm/m ²)	Strong / Moderate	I B	I B
	◦ PASP ≥ 50 mmHg or AF associated with valvular heart disease	Strong / Moderate	-	Ila B
	• Arrhythmic MVP and/or MAD in the absence of other indications for intervention	Weak / Very low	-	-
Transcatheter edge-to-edge mitral valve repair	Symptomatic nonrheumatic MR with suitable anatomy and high surgical risk, as determined by the Heart Team	Strong / Moderate	Ila B	Ila B

AF: atrial fibrillation; LA: left atrium; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESDi: left ventricular end-systolic diameter indexed to body surface area; MAD: mitral annular disjunction; MR: mitral regurgitation; MVP: mitral valve prolapse; NYHA, New York Heart Association functional class; PASP: pulmonary artery systolic pressure; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology. * If 3 of the following are present: AF, PASP > 50 mmHg, LA dilation, or at least moderate tricuspid regurgitation. ** In the presence of an LA volume > 60 mL/m² or an LA diameter ≥ 55 mm.

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Finally, indications for surgical or transcatheter intervention in patients with arrhythmic mitral valve prolapse and/or MAD should follow the same recommendations applied to other patients with significant mitral regurgitation. A diagnosis of arrhythmic mitral valve prolapse or MAD alone does not constitute an indication for early intervention.

4.6. Individualized Follow-Up

Patients with significant mitral regurgitation who are truly asymptomatic, have no adverse prognostic features, and do not have an indication for early surgery should undergo cardiology follow-up with transthoracic echocardiography every 6–12 months (Chart 15). Additional examinations, including CMR, Holter monitoring, BNP measurement, stress echocardiography, and GLS, may be considered to help determine the optimal timing of surgical intervention.^{43,50}

Patients with moderate mitral regurgitation and preserved ventricular function should undergo annual clinical follow-up, with echocardiography performed at intervals of no more than 2 years. Any onset of symptoms should be reported immediately to the medical team. Follow-up may then be performed earlier than the predefined interval to identify symptoms and/or adverse prognostic features as promptly as possible.

4.7. Medical Therapy

Medical therapy is used in patients with primary mitral regurgitation to relieve symptoms until the procedure can be performed and/or to treat HF resulting from the valvular heart disease. Although surgery is the definitive treatment, medical therapy should be initiated in patients awaiting a procedure and in those who will not undergo interventional treatment. Furosemide is the principal medication used to reduce congestion and consequently relieve dyspnea. Vasodilators may also help control symptoms by reducing afterload, although they provide no prognostic benefit.⁵⁵

5. Secondary Mitral Regurgitation

5.1. Step 1 – Criteria for Determining the Anatomical Severity of Significant Secondary Mitral Regurgitation

Unlike primary mitral regurgitation, which involves structural abnormalities of the mitral valve, secondary (functional) mitral regurgitation is not caused by direct anatomical abnormalities of the valvular apparatus. In these cases, wall-motion abnormalities, apical leaflet tethering, annular dilation, and/or atrial dilation are responsible for regurgitation.⁵⁶ Epidemiological studies indicate that secondary etiology accounts for at least 50% of all cases of mitral regurgitation.⁵⁷

Chart 15 – Primary mitral regurgitation: Individualized follow-up

Primary mitral regurgitation	Follow-up	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Significant, asymptomatic, and without adverse prognostic features	• Clinical and echocardiographic reassessment	Every 6–12 months	Every 6–12 months	Every 6 months
	• Concomitant intervention in patients undergoing another cardiac surgical procedure (coronary revascularization, ascending aortic surgery, or another valve procedure)	Strong / Moderate	I B	-
Moderate (jet area 20%–40% of the LA area, regurgitant fraction 30%–49%, regurgitant volume 30–59 mL/beat, vena contracta area 0.30–0.69 cm, and EROA 0.20–0.39 cm ²)	• Clinical and echocardiographic reassessment	Every 1–2 years	Every 1–2 years	Every 1–2 years
	• Concomitant intervention in patients undergoing another cardiac surgical procedure (coronary revascularization, ascending aortic surgery, or another valve procedure)	Strong / Low	IIa C	-
Mild (jet area <20% of the LA area, regurgitant fraction <30%, regurgitant volume <30 mL/beat, vena contracta <0.30 cm, and EROA <0.20 mm ²)	• Clinical and echocardiographic reassessment	Every 2–3 years	Every 3–5 years	-

EROA: effective regurgitant orifice area; LA: left atrium; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

Significant secondary mitral regurgitation is most prevalent among patients with HF with reduced ejection fraction (HFrEF), affecting 25% of this population. It is present in 10% of patients with HF with mildly reduced ejection fraction (HFmrEF) and 4% of those with HF with preserved ejection fraction (HFpEF).⁵⁸ However, even mild-to-moderate mitral regurgitation is associated with a worse prognosis across the entire HF spectrum.⁵⁹ The prognosis of older patients with secondary mitral regurgitation is particularly poor.⁶⁰

Physical examination is generally unrevealing for the diagnosis of secondary mitral regurgitation; therefore, transthoracic echocardiography is essential.⁶¹

As noted above, adverse outcomes in secondary mitral regurgitation are associated with a smaller calculated EROA. Nevertheless, in accordance with U.S. guidelines, the present document adopts the same quantitative criteria used for primary mitral regurgitation (EROA ≥ 0.40 cm² and regurgitant volume ≥ 60 mL). This decision is based on the findings of the main contemporary studies and on the possibility that regurgitation may be a marker of severe underlying disease, with interventions at earlier stages having limited clinical relevance, low cost-effectiveness, and an unfavorable risk-benefit profile (Chart 16 and Figure 6).⁶²⁻⁶⁴ The most recent European guidelines use different thresholds for quantifying severity in these patients, in the presence of an elliptical regurgitant orifice and under low-flow conditions (EROA ≥ 0.20 cm² and regurgitant volume ≥ 30 mL, respectively).⁶⁵

When clinical and echocardiographic findings are discordant, invasive hemodynamic assessment with left ventriculography, transesophageal echocardiography, or CMR may help determine disease severity.

5.2. Step 2 – Assessment of the Etiology of Secondary Mitral Regurgitation

The mechanisms underlying secondary mitral regurgitation are complex and multifactorial; imaging assessment can be challenging and requires careful analysis.⁵⁶ Three key mechanisms, which frequently coexist, may cause secondary mitral regurgitation: ventricular systolic dysfunction (HFrEF with papillary muscle tethering), annular dilation (atrial functional mitral regurgitation associated with HFpEF and/or AF), and papillary muscle displacement due to ischemic disease (also referred to as ischemic mitral regurgitation) (Chart 17).⁶⁶ Based on analyses of patient profiles and outcomes in the COAPT and MITRA-FR trials, Carabello et al. proposed the concept of tertiary/disproportionate mitral regurgitation, defined as secondary mitral regurgitation that is anatomically more severe than expected for the degree of ventricular dysfunction. Thus, valve intervention may be beneficial in this group.⁶⁷

5.3. Step 3 – Symptoms

The main symptom of secondary mitral regurgitation is dyspnea. Symptoms and signs of right HF may also occur, including lower-extremity edema and jugular venous distention. Patients may additionally experience symptoms associated with specific etiologies, such as chest pain in those with ischemic cardiomyopathy and palpitations in those with atrial functional mitral regurgitation (Chart 18).

5.4. Step 4 – Adverse prognostic features

There are no specific adverse prognostic features unique to patients with secondary mitral regurgitation. However, if structural abnormalities worsen, such as increased PASP, progressive left ventricular dilation, and/or a decline in ejection fraction without another apparent cause, the valvular heart disease may be considered responsible (Chart 19).

5.5. Step 5 – Modes of Intervention

Initial treatment of secondary mitral regurgitation depends on the underlying disease. Patients with left ventricular dysfunction should receive angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), neprilysin inhibitors, beta-blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter 2 (SGLT2) inhibitors, according to current guidelines and the underlying etiology.⁶⁸ Strategies such as cardiac resynchronization therapy and ICD implantation should also be considered.⁶⁸⁻⁷⁰ In patients with chronic coronary syndrome, coronary revascularization – either surgical or percutaneous – should be considered in addition to the aforementioned medical therapy, with the goals of improving symptoms and prognosis.⁷¹

Mortality associated with atrial functional mitral regurgitation is similar to that associated with other mechanisms of secondary mitral regurgitation.⁷² In patients with atrial functional mitral regurgitation, there is insufficient evidence to favor either a rhythm-control or rate-control strategy; however, a reduction in atrial volume with medical therapy is associated with lower mortality in these patients.⁷³ Therefore, whenever feasible, these guidelines suggest a rhythm-control strategy for patients with atrial functional mitral regurgitation and persistent symptoms despite optimal medical therapy, with the aim of promoting reverse atrial remodeling.^{74,75}

Surgical correction of secondary mitral regurgitation is a treatment option for symptom relief in patients who still have dyspnea corresponding to NYHA class III–IV despite optimal medical therapy (Charts 20 and 21).⁷⁶ In patients with ischemic cardiomyopathy, significant secondary mitral regurgitation, and an indication for coronary artery bypass grafting (CABG), concomitant mitral valve repair or replacement during the same procedure is beneficial.^{77,78}

For isolated secondary mitral regurgitation, evidence suggests that TEER may offer advantages over surgery. The MATTERHORN trial, which compared surgical mitral valve repair or replacement with TEER, demonstrated that TEER was noninferior to surgery but significantly safer.⁷⁹

The COAPT and MITRA-FR trials were published in 2018 and evaluated percutaneous TEER in patients with secondary mitral regurgitation, ventricular dysfunction, and optimal medical therapy. Whereas the COAPT trial demonstrated a reduction in mortality and HF hospitalization among patients undergoing TEER, the MITRA-FR trial found no differences in the outcomes assessed. In 2024, the RESHAPE-HF2 trial evaluated the same population and demonstrated that TEER reduced HF hospitalizations and improved symptoms, although it did not reduce mortality.⁸⁰

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Chart 16 – Step 1: Criteria for the determining the anatomical severity of significant secondary mitral regurgitation

Characteristics of significant secondary mitral regurgitation	
Physical examination	• Diminished S1 • Soft, low-pitched holosystolic murmur radiating to the axillary line
Electrocardiogram	• Findings consistent with the underlying disease • Signs of left-sided chamber enlargement
Chest radiography	• Findings consistent with the underlying disease • Increased cardiothoracic ratio in patients with left ventricular dilation • The cardiothoracic ratio may be normal in patients with atrial functional MR; atrial enlargement, left-sided chamber enlargement, and pulmonary congestion may be present
Echocardiography	• Quantification of regurgitation: ◦ Central jet > 40% of the LA ◦ Vena contracta ≥ 0.7 cm ◦ Regurgitant volume ≥ 60 mL/beat ◦ Regurgitant fraction $\geq 50\%$ ◦ EROA ≥ 0.40 cm²
Transesophageal echocardiography	• May be used to confirm the severity and mechanism of MR • Assessment of the feasibility of transcatheter edge-to-edge repair
Hemodynamic assessment	May aid quantification by demonstrating grade 3+/4+ regurgitation on ventriculography
Cardiac magnetic resonance	May aid MR quantification when echocardiographic assessment is limited

S1: first heart sound; EROA: effective regurgitant orifice area; LA: left atrium; MR: mitral regurgitation.

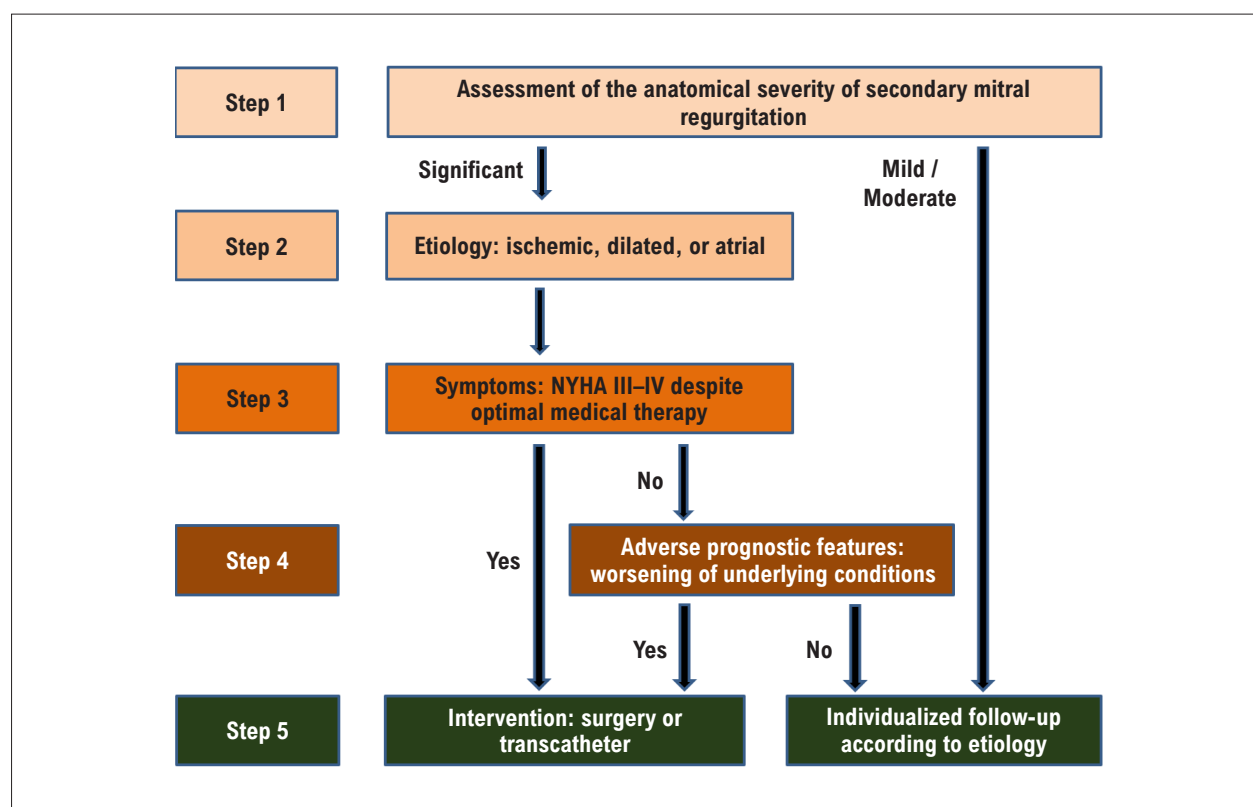


Figure 6 – Algorithm for the assessment of significant secondary mitral regurgitation. NYHA: New York Heart Association functional class.

Chart 17 – Step 2: Etiology of secondary mitral regurgitation

Etiologic characteristics	
Ischemic ventricular	• Regional wall-motion abnormalities • Abnormal positioning of the papillary muscles or valve leaflets (“tenting,” apical tethering, and/or failure of leaflet coaptation) • Mitral annular dilation • Assessment of the coronary arteries by coronary angiography • Assessment of viability and LGE areas by CMR
Dilated ventricular	• Mitral annular dilation – ventricular dilation • Ventricular systolic dysfunction • Abnormal positioning of the papillary muscles or valve leaflets (“tenting,” apical tethering, and/or failure of leaflet coaptation) • Ventricular dyssynchrony • Abnormal atrioventricular mechanical coupling
Atrial functional	• Occurs in patients with AF and dilation of the left atrium and mitral annulus • Absence of ventricular dilation or reduced LVEF • May be associated with HFpEF

LVEF: left ventricular ejection fraction; HFpEF: heart failure with preserved ejection fraction; LGE: late gadolinium enhancement; CMR: cardiac magnetic resonance; AF: atrial fibrillation.

Chart 18 – Step 3: Assessment of symptoms in significant secondary mitral regurgitation

Symptoms	
Dyspnea and fatigue/weakness	• Increased end-diastolic pressure • Pulmonary venous and capillary congestion • May be accompanied by palpitations, cough, ascites, edema, and chest pain • May be accompanied by embolic events

Chart 19 – Step 4: Assessment of adverse prognostic features in significant secondary mitral regurgitation

Adverse prognostic features	
Clinical and echocardiographic assessment	• Worsening of the underlying condition without other attributable causes (increased PASP, increased ventricular dimensions, or decreased LVEF).

LVEF: left ventricular ejection fraction; PASP: pulmonary artery systolic pressure.

Importantly, the 3 trials enrolled patients with different degrees of anatomical severity, as demonstrated by the mean EROA in each trial (COAPT: 0.40 cm², MITRA-FR: 0.31 cm², and RESHAPE-HF2: 0.25 cm²). COAPT tended to enroll patients with tertiary mitral regurgitation – that is, patients with less ventricular dilation.⁸¹

A meta-analysis of the 3 trials suggests that TEER should be indicated to reduce hospitalizations and improve quality of life.⁸² Therefore, these guidelines propose considering mitral TEER in patients with significant ventricular secondary mitral regurgitation refractory to optimal medical therapy,

with the goals of controlling symptoms and reducing HF hospitalizations, after Heart Team discussion.

For patients with significant ventricular secondary mitral regurgitation and refractory symptoms whose anatomy is considered unsuitable for TEER, transcatheter mitral valve replacement is emerging as a feasible and effective strategy. Data from registries such as CHOICE-MI and studies of transseptal systems have demonstrated rates of mitral regurgitation reduction ($\leq 1+$) exceeding 95% at 1 year, with sustained functional improvement.^{83,84} The decision to use this technology should account for comorbidities

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Chart 20 – Step 5: Modes of intervention in significant secondary mitral regurgitation

Mode	Considerations
Optimal medical therapy	- All patients: Provide optimal medical therapy in accordance with current heart failure guidelines - Assess the indication for cardiac resynchronization therapy when appropriate - Atrial functional: Patients with atrial fibrillation may benefit from a rhythm-control strategy
Mitral valve replacement or repair	- Ischemic: mitral valve replacement or repair when myocardial revascularization is indicated - Mitral valve repair when another concomitant valve intervention is indicated
Transcatheter edge-to-edge mitral valve repair	- Assessment by the institutional Heart Team is required - Indicated in patients with persistent symptoms despite medical therapy - Procedural feasibility must be assessed by echocardiography
Transcatheter mitral valve implantation	- Alternative for patients at high surgical risk with anatomy unsuitable for TEER - Remains investigational (off-label)
Surgical left atrial appendage closure	For patients with atrial fibrillation or atrial flutter undergoing cardiac surgery

TEER: transcatheter edge-to-edge repair.

Chart 21 – Significant secondary mitral regurgitation: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Ventricular mitral regurgitation				
	Patients with dyspnea (NYHA ≥ III) despite optimal medical therapy, for symptom improvement	Weak / Low	IIb B	IIb C
Mitral valve replacement or repair	Myocardial revascularization or another concomitant cardiac surgical procedure	Strong / Moderate	IIa B	I B
Atrial mitral regurgitation				
	Patients with dyspnea (NYHA ≥ III) despite optimal medical therapy, for symptom improvement	Weak / Low	-	IIa B
Ventricular mitral regurgitation				
Transcatheter edge-to-edge repair	Symptomatic patients despite optimized medical therapy and with suitable anatomy	Strong / Moderate	IIa B	I A
	Atrial mitral regurgitation Patients with dyspnea despite optimized medical therapy, with contraindication to or high risk for surgery, and with suitable anatomy, for symptom improvement	Weak / Low	-	IIb B
Surgical left atrial appendage closure	Patients with atrial fibrillation or atrial flutter undergoing cardiac surgery, to reduce thromboembolic events	Strong / High	IIa B	-

NYHA: New York Heart Association functional class; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

and ventricular anatomy to mitigate procedural risks. Because this technology remains under development, long-term data on durability and morbidity and mortality outcomes are still lacking.

Mitral valve intervention should be considered in patients with significant atrial secondary mitral regurgitation who remain symptomatic despite optimal medical therapy. Surgical mitral annuloplasty is the preferred technique in most cases because it directly addresses the main pathophysiological mechanism of the disease – mitral annular dilation – and provides favorable durability and control of regurgitation.^{85,86}

For symptomatic patients with significant atrial secondary mitral regurgitation who have a contraindication to surgery or high surgical risk, TEER may be considered after up-titration of medical therapy, provided that the anatomy is suitable for the procedure. Observational studies have demonstrated high technical success rates and significant clinical improvement. However, anatomical features specific to atrial mitral regurgitation, including planar leaflet coaptation, large regurgitant jets, and a relatively small mitral valve area, may predispose patients to the development of elevated transmitral gradients after the procedure, requiring meticulous echocardiographic planning.⁸⁷

Finally, based on the most recent available evidence, the present document recommends concomitant left atrial appendage closure during cardiac surgery in patients with AF or atrial flutter to reduce thromboembolic events.⁸⁸

6. Aortic Stenosis

6.1. Step 1 – Criteria for Determining the Anatomical Severity of Aortic Stenosis

To date, only patients with anatomically significant aortic stenosis derive benefit from intervention. Therefore, determining anatomical severity is essential. Six physical examination findings suggest significant aortic stenosis: a *pulsus parvus et tardus*, a late-peaking systolic ejection murmur, diminished intensity of the second heart sound, diminished intensity of the first heart sound, the Gallavardin phenomenon, and paradoxical splitting or a single second heart sound. Complementary examinations include ECG, chest radiography, echocardiography, CT, and invasive hemodynamic assessment, with echocardiography being the most important modality in the initial evaluation (Chart 22 and Figure 7).^{89,90} Significant aortic stenosis is defined as an aortic valve area ≤ 1.0 cm² and/or an indexed aortic valve area ≤ 0.6 cm²/m² in the presence of a mean left ventricular–aortic gradient ≥ 40 mmHg or a peak aortic jet velocity ≥ 4.0 m/s.

A special subgroup comprises patients with low-flow, low-gradient aortic stenosis, defined as an aortic valve area ≤ 1.0 cm² and a mean left ventricular–aortic gradient < 40 mmHg (Figure 8). Once anatomical severity has been confirmed, intervention is also indicated. In patients with low-flow, low-gradient aortic stenosis and preserved LVEF, potential errors in echocardiographic measurements should first be excluded. The following parameters support a diagnosis of significant aortic stenosis^{91–94}:

- Indexed aortic valve area ≤ 0.6 cm²/m²;
- Elevated aortic valve calcium score on CT (> 1300 Agatston units [AU] in women and > 2000 AU in men);
- Systolic blood pressure (SBP) ≤ 140 mmHg;
- Stroke volume index ≤ 35 mL/m².

Patients who meet the other criteria above but have a normal stroke volume index (> 35 mL/m²) are classified as having normal-flow, low-gradient aortic stenosis. Evidence on this condition is limited and derived primarily from observational studies. Therefore, no consensus exists regarding optimal management; however, valve intervention tends to be considered in symptomatic patients when no other cause of symptoms is identified.^{95,96}

Patients with low-flow, low-gradient aortic stenosis and reduced LVEF (classical low-flow aortic stenosis) should undergo low-dose dobutamine stress echocardiography (20 μ g/kg/min) (Figure 9). The first step is to assess the ventricular contractile response, known as contractile reserve. In the presence of contractile reserve (an increase of $\geq 20\%$ in stroke volume and/or an increase of > 10 mmHg in the mean left ventricular–aortic gradient), patients whose aortic valve area decreases or remains unchanged at peak stress have significant aortic stenosis. An increase in aortic valve area of up to 0.2 cm² is accepted as indicating maintenance of aortic valve area. Patients with an increase in aortic valve area ≥ 0.3 cm² and a final aortic valve area > 1.0 cm² are classified as having moderate aortic stenosis (pseudo-severe aortic stenosis).⁹⁷ In the absence of contractile reserve, aortic valve calcium scoring should also be performed to determine anatomical severity. Patients without contractile reserve likewise derive benefit from surgical or transcatheter intervention.⁹⁸

6.2. Step 2 – Assessment of the Etiology of Aortic Stenosis

The prevalence of degenerative/calcific aortic stenosis has increased markedly with rising life expectancy, reaching up to 5% among individuals aged > 75 years (Chart 23). It is currently the leading cause of aortic stenosis and is associated with the same risk factors as atherosclerosis, affecting up to 4.5% of individuals aged > 75 years in high-income countries.¹ In younger populations, the main etiologies are rheumatic disease and bicuspid aortic valve. Rheumatic aortic stenosis is also characterized by combined mitral and aortic valve involvement and an association with varying degrees of aortic regurgitation. Bicuspid aortic valve affects approximately 2% of the population and is associated with aortopathy in approximately 70% of cases.⁹⁹ Because Brazil has a transitional age structure typical of low- to middle-income countries, aortic stenosis has a bimodal prevalence distribution, with all etiologies encountered across different age groups. Determining the etiology of aortic stenosis is essential for selecting the appropriate treatment. Most patients enrolled in studies of TAVI had degenerative aortic stenosis. Patients with rheumatic or bicuspid aortic stenosis were excluded from nearly all trials.

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Chart 22 – Step 1: Criteria for determining the anatomical severity of significant aortic stenosis

Characteristics of significant aortic stenosis	
Physical examination	• <i>Pulsus parvus et tardus</i>
	• Late-peaking systolic ejection murmur
	• Diminished S2
	• Diminished S1
	• Gallavardin phenomenon
Electrocardiogram	• Paradoxical splitting of S2 or a single S2
	• Left-sided chamber enlargement
Chest radiography	• Ventricular repolarization abnormalities (strain pattern)
	• Cardiothoracic ratio may be normal
Echocardiography	• Signs of pulmonary congestion
	• $AVA \leq 1.0 \text{ cm}^2$
	• Indexed $AVA \leq 0.6 \text{ cm}^2/\text{m}^2$
	• LV–aortic gradient $\geq 40 \text{ mm Hg}$
	• Peak aortic jet velocity $\geq 4.0 \text{ m/s}$
Dobutamine stress echocardiography	• Ratio of the LVOT to aortic jet maximum velocity < 0.25
Multidetector computed tomography of the chest	• Indicated to assess anatomical severity in patients with low-flow, low-gradient AS and reduced LVEF
Hemodynamic assessment	• Aortic valve calcium score $> 1300 \text{ AU}$ in women and $> 2000 \text{ AU}$ in men supports the diagnosis of significant valve heart disease
Special situations	• Peak LV–aortic gradient $\geq 50 \text{ mm Hg}$
	• Low-flow, low-gradient AS with reduced LVEF, defined as $AVA \leq 1.0 \text{ cm}^2$, $LVEF < 50\%$, and mean LV–aortic gradient $< 40 \text{ mm Hg}^*$ - In the presence of contractile reserve (an increase of $\geq 20\%$ in stroke volume and/or an increase of $> 10 \text{ mm Hg}$ in the mean LV–aortic gradient), patients whose AVA decreases or remains unchanged at peak stress have significant AS. An increase in AVA of up to 0.2 cm^2 is accepted as indicating maintenance of AVA. Patients with an increase in AVA $\geq 0.3 \text{ cm}^2$ are classified as having moderate AS (pseudo-severe AS) - In the absence of contractile reserve, anatomical severity should be corroborated by aortic valve calcium scoring on chest CT • Low-flow, low-gradient AS with preserved LVEF (“paradoxical” AS), defined as $AVA \leq 1.0 \text{ cm}^2$, $LVEF > 50\%$, and mean LV–aortic gradient $\leq 40 \text{ mm Hg}^*$. In these cases, the following parameters should be present to establish significant AS: - Elevated aortic valve calcium score - Stroke volume index $\leq 35 \text{ mL/m}^2$ • Patients who meet the other criteria above but have a normal stroke volume index ($> 35 \text{ mL/m}^2$) are classified as having normal-flow, low-gradient AS. This entity has been recently described, evidence remains limited, and these patients appear to benefit from valve intervention when symptomatic.

AS: aortic stenosis; AU: Agatston units; AVA: aortic valve area; LV: left ventricular; LVOT: left ventricular outflow tract; LVEF: left ventricular ejection fraction; CT: computed tomography; S1: first heart sound; S2: second heart sound. *In patients with low-flow, low-gradient AS and either preserved or reduced LVEF, particular attention should be paid to potential errors in echocardiographic measurements.

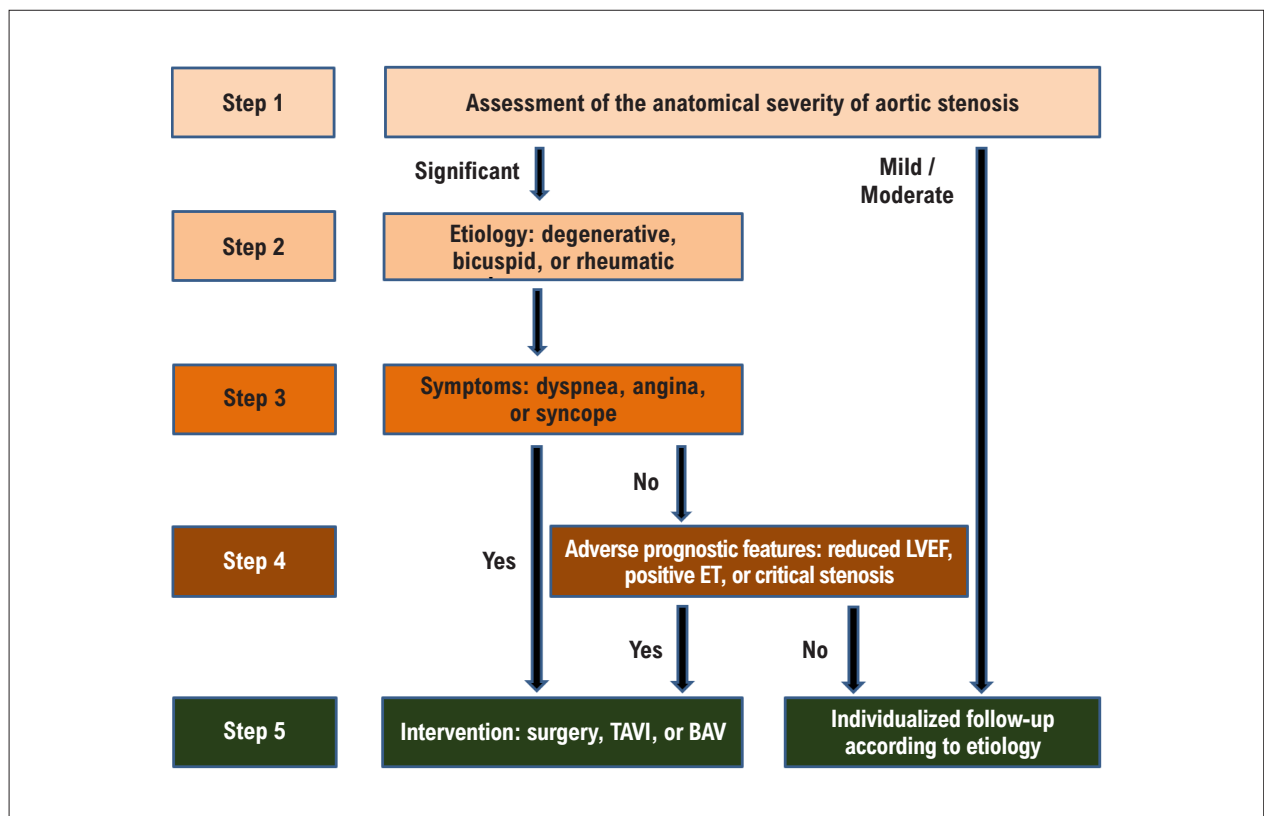


Figure 7 – Algorithm for the assessment of significant aortic stenosis. LVEF: left ventricular ejection fraction; ET: exercise testing; TAVI: transcatheter aortic valve implantation; BAV: balloon aortic valvuloplasty.

6.3. Step 3 – Symptoms

The classic triad of symptoms in patients with aortic stenosis comprises angina, syncope, and dyspnea. Among symptomatic patients, mortality is approximately 50% at 2 years (Chart 24).

Angina results from reduced capillary density and a decreased transmural gradient within the hypertrophied myocardium, leading to an imbalance between oxygen supply and demand. Dyspnea may result from diastolic and/or systolic dysfunction. In diastolic dysfunction, ventricular hypertrophy reduces compliance and shifts the pressure–volume curve upward and to the left, while also increasing filling pressures and causing pulmonary hypertension. In systolic dysfunction, ventricular impairment may occur in the setting of low-flow, low-gradient aortic stenosis or inadequate ventricular adaptation, known as afterload mismatch. Syncope results from the inability to increase cardiac output as required, particularly when peripheral vascular resistance decreases.

Heyde syndrome is the association of significant aortic stenosis with gastrointestinal bleeding due to angiodysplasia and acquired von Willebrand factor deficiency. Evidence supports correction of the valvular heart disease regardless of the presence of symptoms or adverse prognostic features. A recent meta-analysis including 1054 patients found that treatment of aortic stenosis resulted in recovery of von Willebrand factor in 87% of patients and cessation of bleeding

in 73%. Complete recovery occurred within 3 days of surgical valve replacement and within 3–7 days of TAVI.^{100,101}

Patients with significant aortic stenosis and dyspnea, angina, or syncope have an unequivocal indication for intervention. When the presence of symptoms is uncertain, exercise testing may be performed (standard exercise stress testing or CPET).^{102,103}

6.4. Step 4 – Adverse Prognostic Features

In the absence of symptoms, adverse prognostic features should be assessed to determine whether intervention is indicated (Chart 25). The adverse prognostic features currently included in the guidelines are:

- Left ventricular dysfunction on echocardiography (LVEF < 50%): Based on 3 observational studies, each including more than 1000 patients, the European guidelines consider an LVEF < 55% an indication for valve intervention in asymptomatic patients (Class IIa recommendation, Level of Evidence B).^{104–106} Based on 2 studies, the American guidelines report an increased risk with an LVEF < 60%.^{104,107} Furthermore, in asymptomatic patients with a progressive decline in LVEF to < 60%, the guidelines recommend considering intervention after other causes have been excluded.^{105,108,109}
- Exercise stress testing: Contraindicated in symptomatic patients and/or those with left ventricular dysfunction. Criteria for a positive test include:

Guidelines

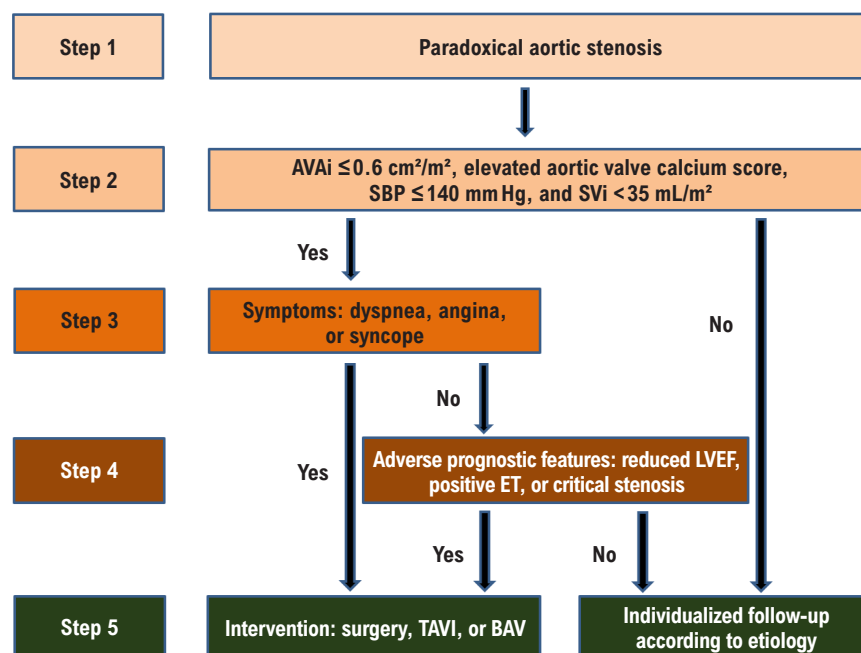


Figure 8 – Algorithm for decision-making in paradoxical aortic stenosis. AVAi; indexed aortic valve area; SBP: systolic blood pressure; SVi: stroke volume index; LVEF: left ventricular ejection fraction; ET: exercise testing; TAVI: transcatheter aortic valve implantation; BAV: balloon aortic valvuloplasty.

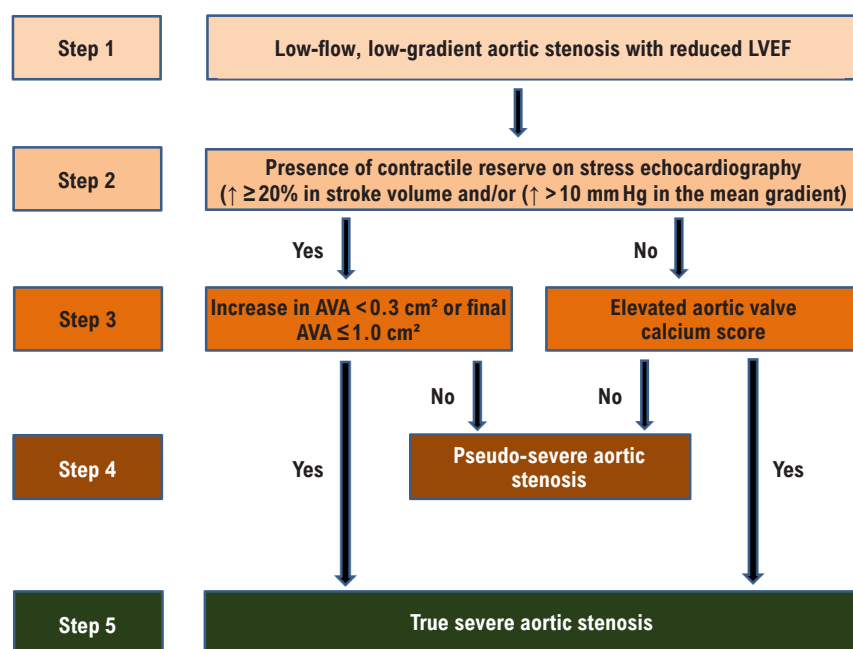


Figure 9 – Algorithm for confirming anatomical severity in low-flow, low-gradient aortic stenosis with reduced ejection fraction. AVA: aortic valve area; LVEF: left ventricular ejection fraction; CT: computed tomography.

Chart 23 – Step 2: Etiology of aortic stenosis

Etiologic characteristics	
Atherosclerotic/ degenerative	• Associated with advanced age • Prevalence: 3%–5% of the population aged >75 years • Associated with aortic valve calcification • Presence of risk factors associated with atherosclerosis
Rheumatic	• Commissural fusion • Concomitant mitral and aortic valve involvement • Occurs in younger age groups • Associated with varying degrees of aortic regurgitation
Bicuspid	• Prevalence: 2% of the population • Associated with aortopathy (approximately 70% of cases) • Lateral-to-lateral orientation of the commissural cleft: predictor of aortic stenosis progression

Chart 24 – Step 3: Assessment of symptoms in significant aortic stenosis

Symptoms	
Dyspnea	• Diastolic dysfunction: left ventricular hypertrophy leads to reduced compliance, an upward and leftward shift of the ventricular pressure–volume curve, elevated filling pressures, and pulmonary venous and capillary hypertension • Systolic dysfunction: occurs with inadequate ventricular adaptation (afterload mismatch) and in low-flow, low-gradient states • Patients with equivocal symptoms (pseudo-asymptomatic) may undergo standard exercise stress testing or cardiopulmonary exercise testing to assess exertional dyspnea
Angina	• Imbalance between oxygen supply and demand in the hypertrophied myocardium • Reduced myocardial perfusion gradient (elevated end-diastolic pressure)
Syncope	• Results from the inability to increase cardiac output during marked reductions in total peripheral resistance • May result from the use of vasodilators (common precipitating agents) • Cardioinhibitory reflex is associated with 50% of cases
Heyde syndrome	• Gastrointestinal bleeding associated with angiodysplasia and von Willebrand factor deficiency • Treatment of aortic stenosis appears to reduce bleeding rates

Chart 25 – Step 4: Assessment of adverse prognostic features in significant aortic stenosis

Adverse prognostic features	
Echocardiography	• LV dysfunction: LVEF <50% • Markers of poor prognosis: AVA <0.7 cm², peak aortic jet velocity ≥5.0 m/s, or mean LV–aortic gradient ≥60 mmHg
Exercise stress testing/ CPET	• Limited functional capacity • Abnormal blood pressure response: an increase in SBP <20 mmHg or a decrease in SBP >10 mmHg • Arrhythmias: ventricular tachycardia or more than 4 consecutive premature ventricular complexes • Horizontal or downsloping ST-segment depression >2 mm • Contraindicated in symptomatic patients and/or those with LV dysfunction

LV: left ventricular; LVEF: left ventricular ejection fraction; AVA: aortic valve area; CPET: cardiopulmonary exercise testing; SBP: systolic blood pressure.

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- Limited functional capacity;
 - Abnormal blood pressure response: an increase in SBP < 20 mmHg or a decrease in SBP > 10 mmHg;
- Arrhythmias: ventricular tachycardia or more than 4 consecutive premature ventricular complexes;
- Horizontal or downsloping ST-segment depression > 2 mm.
 - Critical aortic stenosis: aortic valve area < 0.7 cm², peak aortic jet velocity ≥ 5.0 m/s, or mean left ventricular–aortic gradient ≥ 60 mmHg.

Regarding critical aortic stenosis, 2 multicenter randomized trials compared surgery with medical therapy in asymptomatic patients and demonstrated a benefit of surgical intervention. However, a large proportion of the study populations had critical aortic stenosis, supporting the need for intervention in patients with an aortic valve area < 0.7 cm², peak aortic jet velocity ≥ 5.0 m/s, or mean left ventricular–aortic gradient ≥ 60 mmHg.^{107,110}

Biomarkers such as BNP and N-terminal pro-B-type natriuretic peptide (NT-proBNP) may be useful for diagnostic, disease progression, and prognostic assessment; they also appear to predict mortality in patients with significant aortic stenosis. Some studies suggest that values exceeding 3 times the upper limit of normal may assist in decision-making regarding intervention. However, prospective studies on the topic are lacking.^{111–114}

Other parameters of interest include longitudinal strain and CMR-quantified myocardial fibrosis. Evidence suggests that reduced longitudinal strain is an early marker of impaired ventricular contractility, even when LVEF is preserved, and may help identify asymptomatic patients who require valve intervention. Values < 14.7% have also been associated with a trend toward higher mortality.^{115–117} Regarding interstitial fibrosis, a recent prospective study evaluated 457 patients with asymptomatic moderate or significant aortic stenosis. Increased extracellular volume fraction on CMR, in particular, was independently associated with the composite outcome of death or HF hospitalization.¹¹⁸

Late gadolinium enhancement (LGE) has also been identified as a prognostic marker of myocardial injury that may correlate with future cardiovascular events.^{119–122} EVOLVED was the first prospective randomized trial to evaluate patients with asymptomatic aortic stenosis and myocardial fibrosis identified by LGE on CMR.¹²³

6.5. Step 5 – Modes of Intervention

To determine the most appropriate mode of intervention for each patient, the following should be considered: surgical risk (assessed using scores such as the STS score and EuroSCORE II), frailty, anatomical characteristics, and institutional experience (Charts 26 and 27 and Figure 7).

Chart 26 – Step 5: Modes of intervention in significant aortic stenosis

Mode	Considerations
Surgical aortic valve replacement	• First-line treatment for patients aged < 70 years without a contraindication to surgery and without high surgical risk • May be indicated in patients with frailty or intermediate surgical risk, or for older patients at low surgical risk depending on the decision of the Heart Team and the unavailability of a transcatheter procedure
TAVI	• Assessment by the institutional Heart Team is required • Transfemoral access is preferred • First-line treatment for patients with intermediate, high, or prohibitive surgical risk, contraindications to conventional surgery, or frailty • Increasing evidence supports its use in patients at low surgical risk (STS score < 4%, EuroSCORE II < 4%, or logistic EuroSCORE < 10%) • Data on TAVI in patients aged < 70 years and on valve durability remain limited • Computed tomography angiography of the aorta is the imaging modality of choice for assessing the access site, valve size and type, feasibility of the procedure, and potential complications • Contraindicated in patients with an estimated life expectancy < 12 months • Special considerations apply to bicuspid aortic valve: evidence remains limited
Balloon aortic valvuloplasty	• Bridging strategy to definitive intervention (surgery or TAVI) in patients with hemodynamic instability or advanced symptoms • Palliative treatment for patients with definitive contraindications to conventional surgery and TAVI

TAVI: transcatheter aortic valve implantation; STS: Society of Thoracic Surgeons; EuroSCORE: European System for Cardiac Operative Risk Evaluation.

Chart 27 – Significant aortic stenosis: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Conventional surgery or TAVI*	Symptomatic patients (NYHA ≥ II, syncope, or angina)	Strong / High	I A	I B
	Asymptomatic patients with adverse prognostic features: - LVEF < 50%	Strong / Moderate	I B	I B
	- Positive exercise stress testing	Strong / Moderate	IIa B	IIa C
	Asymptomatic patients with critical valve disease: AVA < 0.7 cm ² , peak aortic jet velocity ≥ 5.0 m/s, or mean LV–aortic gradient ≥ 60 mm Hg	Strong / Moderate	IIa B (If low surgical risk and BNP > 3× ULN or increase in peak velocity ≥ 0.3 m/s/year)	IIa B (Age-adjusted elevated BNP, PASP > 60 mmHg, or peak aortic jet velocity > 5 m/s)
	Progressive decline in LVEF to < 60%	Weak / Low	IIb B	IIa B (LVEF < 55%)
	SPECIAL SITUATIONS			
	Significant low-flow, low-gradient AS with reduced LVEF: - With contractile reserve	Strong / Moderate	I B	I B
	- Without contractile reserve + elevated aortic valve calcium score	Strong / Moderate	I B	I B
	Symptomatic paradoxical significant AS	Strong / Moderate	I B	IIa B
	Heyde syndrome	Strong / Low	-	-
Choice between surgery and TAVI**	Inoperable, prohibitive surgical risk, and/or frailty - TAVI	Strong / High	I A	I A
	- Surgery	Weak / High	-	-
	High surgical risk - TAVI	Strong / High	I A	I A
	- Surgery	Weak / High	-	-
	Intermediate surgical risk - TAVI	Strong / High	I A	I A
	- Surgery	Weak / High	I A	-
	Low surgical risk, age 70–80 years - TAVI	Strong / High	I A	I A
	- Surgery	Strong / High	I A	-
	Low surgical risk, age > 80 years - TAVI	Strong / Moderate	I A	I A
	- Surgery	Weak / Moderate	-	-
	Low surgical risk, age < 70 years - TAVI	Weak / Moderate	-	-
	- Surgery	Strong / High	I A (Age < 65 years)	I B

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Balloon aortic valvuloplasty	Symptomatic, with severe hemodynamic instability and definitive intervention (TAVI or conventional surgery) is not feasible or available; used as a bridging strategy	Strong / Low	IIB C	IIB C
	Palliative treatment for symptomatic patients with contraindications to conventional surgery and/or TAVI	Weak / Low	-	-

*TAVI: transcatheter aortic valve implantation; NYHA: New York Heart Association functional class; LVEF: left ventricular ejection fraction; AVA: aortic valve area; LV: left ventricular; BNP: B-type natriuretic peptide; ULN: upper limit of normal; PASP: pulmonary artery systolic pressure; AS: aortic stenosis; Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology. * Mandatory prerequisite: assessment by the institutional Heart Team, including surgical risk, degree of frailty, anatomical characteristics, and comorbidities. ** Technical feasibility, the risks and benefits of each procedure, patient preference, local expertise, and the availability of procedures should also be considered when selecting the intervention.*

Surgical aortic valve replacement is a well-established technique with steadily improving outcomes. Patients at low predicted risk of mortality are those with STS and EuroSCORE II scores < 4%. However, studies comparing TAVI with surgery in this population have increasingly demonstrated mortality rates below those predicted by these scores.^{124,125}

Transfemoral TAVI is preferred over alternative approaches (transaortic, subclavian, and transapical access) because it is less invasive and associated with fewer complications. These alternative access sites are therefore recommended only when transfemoral access is technically contraindicated.¹²⁶

All current guidelines unequivocally recommend TAVI over surgery for patients who are inoperable, frail, and/or at high surgical risk. The PARTNER 1B trial, which evaluated a balloon-expandable valve in patients at prohibitive surgical risk, demonstrated lower mortality with TAVI than with optimal medical therapy at 1 and 5 years.¹²⁷ PARTNER 1A and the CoreValve U.S. pivotal trial, which evaluated a self-expanding valve, enrolled patients at high surgical risk. In PARTNER 1A, TAVI was noninferior to surgery for all-cause mortality at 1 and 5 years. In the CoreValve trial, after a learning curve, TAVI was superior to surgery at 2 years of follow-up.^{128,129}

The 2020 guideline update already identified transfemoral TAVI as the preferred strategy for patients at intermediate surgical risk, defined as EuroSCORE II and/or STS scores of 4%–8%. PARTNER 2 compared TAVI with surgery in this setting. TAVI was noninferior to surgery for the composite of all-cause mortality or major stroke at 2 and 5 years.¹²⁶ The SURTAVI trial, which evaluated self-expanding valves in patients at intermediate surgical risk, reported a similar outcome at 2 years of follow-up.¹³⁰

In patients at low surgical risk (EuroSCORE II < 4%), the main trials comparing TAVI with surgery found no significant differences in mortality between the 2 approaches. In PARTNER 3, TAVI was associated with a reduction in the composite of all-cause mortality, stroke, or rehospitalization at 1 and 2 years.¹³¹ However, at 5 and 7 years, outcomes were similar between the TAVI and surgery groups, as was the

incidence of bioprosthetic valve failure.^{132,133} The NOTION and Evolut Low Risk trials, which evaluated self-expanding valves, also enrolled patients at low surgical risk. In NOTION, TAVI was noninferior to surgery for the composite of all-cause mortality, stroke, or myocardial infarction.¹³⁴ In Evolut Low Risk, TAVI was noninferior to surgery for all-cause mortality or disabling stroke at 4 years of follow-up.¹³⁵

The DEDICATE trial, published in 2024, evaluated 1414 patients at low or intermediate surgical risk (median STS score, 1.8%), of whom 701 underwent TAVI with unrestricted selection of valve type. A balloon-expandable valve was used in 61.4% of patients. At 1 year, the composite of all-cause mortality or stroke occurred in 5.4% of the TAVI group and 10.0% of the surgery group, once again demonstrating the noninferiority of TAVI to surgery.¹²⁵

NOTION-2 reported results similar to those of previous trials but included 100 patients with a bicuspid aortic valve, an etiology excluded from the other studies. In the bicuspid cohort, the adverse event rate was higher with TAVI (14.3%) than with surgery (3.9%), suggesting that patients with bicuspid aortic stenosis constitute a distinct subgroup requiring specific considerations.¹³⁶

Longer-term analyses of studies involving patients at low surgical risk have shown sustained trends toward outcomes with transfemoral TAVI that are similar or superior to those with surgery, suggesting that TAVI should be the preferred treatment in these patients. However, an important consideration is that the mean age of the study populations was 75.4 years. Therefore, among patients at low surgical risk, and extending to intermediate risk, TAVI should be avoided in those aged < 70 years until robust data on valve durability become available.¹³⁷⁻¹³⁹

The 10-year follow-up of NOTION is the longest available at the time of publication of these guidelines. Despite the use of first-generation valve systems, TAVI was associated with rates of bioprosthetic valve failure and reintervention similar to those observed with surgical bioprostheses, but with less prosthetic valve dysfunction, a lower prevalence of prosthesis–patient mismatch (PPM), and lower transprosthetic

gradients. Importantly, fewer than 40% of patients completed the 10-year follow-up.¹³⁹

Patients with small aortic annulus are at risk of poorer hemodynamic outcomes after valve implantation because of PPM. In this population, a recent study compared transcatheter versus surgical approaches and found no superiority in hemodynamic parameters with either strategy.¹⁴⁰ The study population was predominantly female, and enrollment did not reach the prespecified sample size. Specifically for TAVI, the use of self-expandable supra-annular valves in small aortic annuli tends to be associated with less structural valve deterioration at 12 months than balloon-expandable valves, while remaining noninferior with respect to clinical outcomes.¹⁴¹

Another important aspect, unanimously endorsed by Brazilian and international guidelines, is the need for each case to be evaluated by a Heart Team. Technical feasibility, the risks and benefits of each procedure, patient preference, local expertise, and the availability of procedures should also be considered when selecting the intervention.⁶

For patients with hemodynamic instability or advanced symptoms, balloon aortic valvuloplasty (BAV) may be used as a bridging strategy to provide symptom improvement or

hemodynamic stabilization before definitive intervention. However, its benefits are short-lived. A literature review until 2013, involving 4123 patients, found that BAV was used as a bridge to subsequent TAVI in 23.4% of patients, with mortality and vascular complication rates of 2.9% and 10.2%, respectively.¹⁴²⁻¹⁴⁴

6.6. Individualized Follow-Up

Patients without an indication for intervention should undergo frequent monitoring because of the risk of disease progression (Chart 28).

Patients with significant aortic stenosis who are asymptomatic and have no adverse prognostic features currently have an indication for valve surgery only when undergoing another invasive cardiovascular procedure, such as coronary revascularization, ascending aortic surgery, or another valve procedure. Some studies have evaluated intervention in this population. The highest level of evidence comes from 2 randomized trials comparing surgery with medical therapy. The outcome assessed was all-cause mortality in the first trial and the composite of death, myocardial infarction, stroke, or HF hospitalization in the second trial.^{107,110} Importantly, a substantial proportion of participants had Class IIa adverse

Chart 28 – Aortic stenosis: Individualized follow-up

Aortic stenosis	Follow-up	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Significant, asymptomatic, and without adverse prognostic features	• Clinical and echocardiographic reassessment	Every 6 months	Every 6–12 months	Every 6 months
	• Concomitant intervention in patients undergoing another cardiac surgical procedure (coronary revascularization, ascending aortic surgery, or another valve procedure)	Strong / Low	I B	I C
	• Early intervention in patients with high-gradient aortic stenosis and low surgical risk*	Weak / High	-	IIa A
Moderate (AVA 1.1–1.5 cm ² and mean LV–aortic gradient 25–39 mm Hg)	• Clinical and echocardiographic reassessment	Every year	Every 1–2 years	Every year
	• Concomitant intervention in patients undergoing another cardiac surgical procedure (coronary revascularization, ascending aortic surgery, or another valve procedure)	Weak / Low	IIa C	IIa C
Mild (AVA > 1.5 cm ² and mean LV–aortic gradient < 25 mm Hg)	• Clinical and echocardiographic reassessment	Every 2–3 years	Every 3–5 years	Every 2–3 years

AVA: aortic valve area; BNP: B-type natriuretic peptide; LV: left ventricular; NT-proBNP: N-terminal pro-B-type natriuretic peptide; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

* Current evidence supporting early intervention is increasing; however, a prognostic benefit in terms of mortality, as observed in other settings in which valvular intervention is indicated, has not yet been demonstrated. Therefore, early intervention may be indicated in selected patients with adverse prognostic markers (late gadolinium enhancement on cardiac magnetic resonance imaging, reduced strain, elevated BNP or NT-proBNP, or a high aortic valve calcium score) after Heart Team discussion.¹⁴⁹

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prognostic features (critical aortic stenosis). Therefore, surgery is not yet routinely indicated for asymptomatic patients without adverse prognostic features.

In the EARLY TAVR trial, patients aged > 65 years with significant aortic stenosis and no indication for intervention were randomly assigned to TAVI or clinical surveillance. Most patients performed a treadmill stress test before enrollment.¹⁴⁵ TAVI improved the composite outcome of mortality, stroke, or rehospitalization, although this benefit was driven primarily by unplanned hospitalizations, with no difference in mortality or stroke. Furthermore, hospitalization included patients in the clinical surveillance group who were admitted for TAVI during the first 6 months. Most patients in this group developed symptoms in the first 6 months. Because the trial was unblinded, one possible explanation for this rapid onset of symptoms is that patients in the control group may have reported subjective symptoms to undergo intervention, a statistical phenomenon known as subtraction anxiety.¹⁴⁶

Three recent meta-analyses evaluated asymptomatic aortic stenosis without adverse prognostic features based on 4 trials: AVATAR, RECOVERY, EARLY TAVR, and EVOLVED. In one meta-analysis, early valve intervention was associated with a reduction in cardiovascular or HF hospitalization (this finding remained consistent when studies of surgery and TAVI were analyzed separately) and stroke, with no differences in mortality compared with clinical surveillance.¹⁴⁷ In the other meta-analyses, valve intervention reduced the composite of death, hospitalization, stroke, or myocardial infarction, but did not reduce mortality when assessed separately.^{148,149} Therefore, until additional evidence becomes available, TAVI should not be routinely indicated for asymptomatic patients without adverse prognostic features.¹⁵⁰

Moderate aortic stenosis, defined as an aortic valve area of 1.1–1.5 cm² and a mean left ventricular–aortic gradient of 25–39 mm Hg, has an indication for valve surgery only when the patient is undergoing another invasive cardiovascular procedure, such as coronary revascularization, ascending aortic surgery, or another valve procedure. Patients with moderate aortic stenosis and left ventricular dysfunction may have a higher rate of HF hospitalization than those without aortic stenosis.^{151–153} The TAVR UNLOAD trial evaluated patients with asymptomatic moderate aortic stenosis and HFrEF (LVEF, 20%–50%).¹⁵⁴ A total of 178 patients were randomly assigned to TAVI or clinical surveillance. The primary outcome was a composite of all-cause mortality, disabling stroke, hospitalization for aortic stenosis or HF, and changes in quality of life at 1 year. Mean LVEF was 39%. TAVI was not superior to clinical surveillance, although quality of life improved in the intervention group. An important limitation was that fewer patients were enrolled than originally planned because of the COVID-19 pandemic. Therefore, in selected patients with moderate aortic stenosis and ventricular dysfunction, TAVI may be indicated to improve symptoms in those who remain in NYHA class III or IV despite optimal medical therapy.

Mild aortic stenosis, defined as an aortic valve area > 1.5 cm² and a mean left ventricular–aortic gradient < 25 mm Hg, requires clinical and echocardiographic follow-up only.

6.7. Medical Therapy

Preoperative: To date, no medication has been shown to slow the progression of aortic stenosis or prevent progression to significant disease, much less improve prognosis. Treatment of hypertension, when indicated, reduces afterload and facilitates ventricular ejection. However, excessive blood pressure reduction should be avoided because it may worsen symptoms by reducing cardiac output in the setting of fixed LVOT obstruction. Negative chronotropic agents are indicated only for rate control in patients with tachyarrhythmias. Targeting lower heart rates, as in mitral stenosis, also reduces cardiac output and may be harmful in aortic stenosis. Diuretics are indicated for symptom relief in patients with pulmonary or systemic congestion.

Because statins slow the progression of atherosclerotic plaque, their potential effect on the progression of aortic stenosis has been investigated. However, there is currently no evidence of a direct benefit on valvular heart disease, although management of other risk factors, such as hypercholesterolemia and CAD, remains essential for reducing morbidity. A 2010 trial evaluated simvastatin plus ezetimibe in more than 1800 patients with moderate aortic stenosis. Despite reductions in low-density lipoprotein cholesterol levels and coronary events, the treatment did not reduce the progression of aortic stenosis.¹⁵⁵ Atorvastatin versus placebo likewise did not slow disease progression or improve markers of the anatomical severity of aortic stenosis (76% of participants had mild to moderate disease). Similar findings were reported with rosuvastatin.^{156,157} Denosumab and alendronate have also been evaluated for slowing the progression of aortic stenosis, without success.¹⁵⁸

Pelacarsen, another medication being investigated for this purpose, reduces lipoprotein(a) [Lp(a)] by directly targeting the messenger RNA that encodes apolipoprotein(a). It is currently being evaluated in the ongoing Lp(a)FRONTIERS CAVS trial (NCT05646381).

Postoperative: ACEI therapy after TAVI has been proposed to promote reverse remodeling and reduce concentric hypertrophy; one study also reported lower mortality.¹⁵⁹ A recent meta-analysis including more than 21,000 patients found that the use of ACEIs or ARBs after TAVI or surgery was associated with reductions in all-cause mortality, cardiovascular mortality, and the incidence of AF. However, additional randomized trials are required.¹⁶⁰

7. Aortic Regurgitation

7.1. Step 1 – Criteria for Determining the Anatomical Severity of Significant Aortic Regurgitation

The physical examination findings used to determine the severity of aortic regurgitation (Chart 29 and Figure 10) include a high-pitched, blowing holodiastolic decrescendo murmur associated with diminished intensity of the second heart sound. A midsystolic ejection murmur may also be present because of the increased transaortic flow generated by volume overload. Another possible finding is the Austin Flint murmur, a rumbling mid-diastolic murmur heard at the mitral area that results from restricted diastolic opening of the anterior mitral leaflet caused by the aortic regurgitant jet (functional mitral stenosis).

Chart 29 – Step 1: Criteria for determining the anatomical severity of significant aortic regurgitation

Characteristics of significant aortic regurgitation	
Physical examination	• Diminished S2 • Midsystolic ejection murmur • Austin Flint murmur • Water-hammer (Corrigan) pulse • Widened pulse pressure • Musset, Becker, dancing carotids, Müller, Quincke, Rosenbach, Gerhardt, Traube, Duroziez, Mayne, and Hill signs
Electrocardiogram	• Left-sided chamber enlargement
Chest radiography	• Increased cardiothoracic ratio • Ascending aortic dilation
Echocardiography	• Abnormal valve morphology (thickening, bicuspid valve, or prolapse) and failure of leaflet coaptation • Large regurgitant jets • Ventricular dilation • Holodiastolic flow reversal in the descending aorta • Vena contracta > 0.6 cm • Jet width > 0.65 cm • Jet area ≥ 60% • Regurgitant fraction ≥ 50% • Regurgitant volume ≥ 60 mL/beat • EROA ≥ 0.30 cm²
3D echocardiography	• Assessment of eccentric jets • Improved assessment of valve morphology
Cardiac magnetic resonance	• Regurgitant fraction > 33% • Regurgitant volume ≥ 60 mL/beat • Regurgitant orifice area ≥ 0.48 cm²
Hemodynamic assessment	• Elevated LV end-diastolic pressure • Significant aortic regurgitation on aortography
Computed tomography angiography of the aorta	• Assessment of aortic diameters

EROA: effective regurgitant orifice area; LV: left ventricular; S2: second heart sound.

Other characteristic findings of significant aortic regurgitation include a water-hammer (Corrigan) pulse, characterized by a rapid upstroke and high amplitude, and an increased difference between systolic and diastolic blood pressures. This widened pulse pressure may produce several peripheral signs that are also characteristic of significant aortic regurgitation: Musset sign (involuntary rhythmic head movement synchronous with each heartbeat), Becker sign (retinal artery pulsations observed during fundus examination), dancing carotids (synchronous pulsation of the carotid arteries in the neck caused by increased diastolic blood flow, with arterial dilation followed by contraction), Müller sign (visible systolic pulsation of the uvula), Quincke sign (visible

capillary pulsation in the nail bed, elicited by gently pressing the patient's fingertip under a light source), Rosenbach sign (visible or palpable liver pulsation), Gerhard sign (palpable pulsation in the lumbar region), Traube sign (high-pitched, pistol-shot sounds heard when auscultating over the femoral arteries), Duroziez sign (a double murmur heard over the femoral artery – systolic with proximal compression and diastolic with distal compression), Mayne sign (widened pulse pressure, defined as an increased difference between systolic and diastolic blood pressures).¹⁶¹⁻¹⁶³

Complementary examinations may provide additional information. ECG may show left-sided chamber enlargement, whereas chest radiography may demonstrate an enlarged

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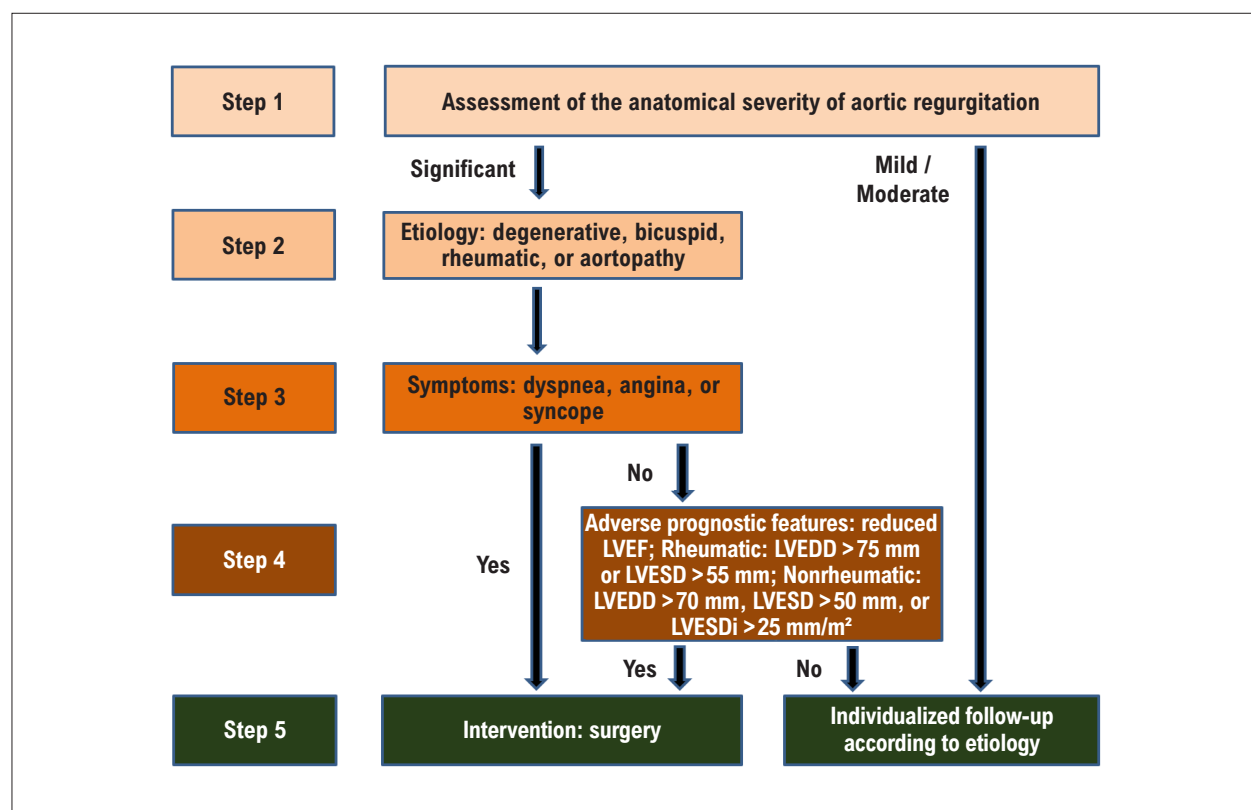


Figure 10 – Algorithm for the assessment of significant aortic regurgitation. LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESDi: left ventricular end-systolic diameter indexed to body surface area.

cardiac silhouette due to left ventricular dilation caused by the volume overload of chronic significant aortic regurgitation and the resulting eccentric hypertrophy. In patients with associated aortopathy, radiographic evidence of aortic dilation may also be present.¹⁶¹⁻¹⁶³

Color Doppler echocardiography is the essential diagnostic tool for confirming the anatomical severity of aortic regurgitation. It also enables assessment of the etiology, the presence or absence of ascending aortic dilation, ventricular dimensions, and ventricular function, all of which are important for clinical decision-making. Regurgitation severity is quantified using qualitative and quantitative criteria.^{164,165} Abnormal valve morphology, failure of leaflet coaptation, large regurgitant jets, ventricular dilation, and holodiastolic flow reversal in the descending aorta suggest anatomically significant valve heart disease. Collectively, the following echocardiographic parameters define significant aortic regurgitation:

- Vena contracta > 0.6 cm
- Jet width $\geq 65\%$ of the LVOT
- Regurgitant fraction $\geq 50\%$
- Regurgitant volume ≥ 60 mL/beat
- EROA ≥ 0.30 cm²
- Holodiastolic flow reversal in the descending aorta

Transesophageal and 3D echocardiography have been increasingly incorporated into clinical practice. These modalities are particularly useful when transthoracic assessment is limited, such as in the presence of eccentric jets, and for detailed anatomical evaluation of the aortic valve, including bicuspid aortic valves.¹⁶⁵⁻¹⁶⁷

In some cases, echocardiography may be inconclusive in determining the anatomical severity of aortic regurgitation. For example, a patient may have a strong clinical suspicion of significant aortic regurgitation without clear echocardiographic criteria of severity. When clinical and echocardiographic findings are discordant, additional diagnostic methods, such as invasive hemodynamic assessment and CMR, are recommended.¹⁶⁷

CMR is considered the gold standard for direct quantification of regurgitant volume and fraction using phase-contrast imaging, which enables direct measurement of antegrade and retrograde flow at the level of the aortic root. Studies have demonstrated that a regurgitant fraction $> 32\%$ – 35% on CMR is associated with adverse outcomes; these thresholds are lower than conventional echocardiographic criteria.¹⁶⁸ CMR also enables precise measurement of ventricular volumes, accurate assessment of ventricular function, and quantification of myocardial fibrosis using LGE and T1 mapping, incorporating additional diagnostic and prognostic markers.^{169,170} Recent studies have demonstrated that a left

ventricular end-systolic volume indexed to body surface area (LVESVi) ≥ 43 – 45 mL/m² and a left ventricular end-diastolic volume indexed to body surface area (LVEDVi) ≥ 109 mL/m² are validated predictors of adverse outcomes and outperform linear dimensions, particularly in patients with preserved ejection fraction.^{166,171}

During invasive hemodynamic assessment, elevated left ventricular end-diastolic pressure and significant aortic regurgitation on aortography support the diagnosis of anatomically significant aortic regurgitation.^{161,162}

When aortic dilation is present, CT angiography is the imaging modality of choice for determining the maximum aortic diameter, which is essential for planning surgical treatment.¹⁷²

7.2. Step 2 – Assessment of the Etiology of Aortic Regurgitation

Aortic regurgitation may result from primary disease of the semilunar cusps and/or aortopathy involving the valve annulus (Chart 30). The main etiologies involving the valve leaflets include rheumatic fever, sequelae of infective endocarditis, degenerative disease, and congenital abnormalities such as bicuspid aortic valve and myxomatous degeneration. Disorders involving the aortic annulus include ascending aortic dissection (generally associated with acute aortic regurgitation), aneurysmal dilation (caused primarily by systemic arterial hypertension and connective tissue disorders such as Marfan and Ehlers–Danlos syndromes), seronegative spondyloarthropathies (ankylosing spondylitis and Reiter syndrome), syphilitic aortitis, and Takayasu arteritis.^{161–163}

In high-income countries, bicuspid and degenerative etiologies predominate, whether due to aortic dilation or leaflet calcification and retraction. In low- to middle-income countries, including Brazil, rheumatic disease still accounts for a substantial proportion of cases, frequently affects young adults, and is commonly associated with mitral valve disease.^{161,166,173}

7.3. Step 3 – Symptoms

Because of progressive ventricular remodeling in chronic aortic regurgitation, patients often remain asymptomatic for many years. Given the high morbidity and mortality associated with symptom onset, this step is critically important because the identification of symptoms prompts referral for surgical intervention (Chart 31).

Dyspnea is the symptom most frequently associated with aortic regurgitation. It results from left ventricular volume overload, with a consequent increase in left ventricular end-diastolic pressure and pulmonary venous and capillary congestion. Initially, it manifests as exercise intolerance; as the disease progresses, however, dyspnea may occur at rest and may be accompanied by orthopnea and paroxysmal nocturnal dyspnea.^{161,162}

Exertional angina is another symptom associated with significant aortic regurgitation. It results from reduced coronary flow reserve secondary to increased ventricular mass and the consequent increase in myocardial oxygen demand, combined with reduced coronary perfusion pressure. Angina may also occur during sleep because a lower heart rate increases regurgitant volume and reduces diastolic blood pressure, with a consequent decrease in diastolic coronary perfusion pressure. Syncopal episodes may occur because of reduced effective cardiac output.^{161–163}

Assessing symptoms in patients with aortic regurgitation may be challenging, particularly in older adults who frequently appear asymptomatic because they have unconsciously limited their activities. In these cases, functional testing with standard exercise stress testing or CPET is recommended to confirm the absence of symptoms.

7.4. Step 4 – Adverse Prognostic Features

The main adverse prognostic features associated with aortic regurgitation is loss of left ventricular function, resulting from increased systolic wall stress and eccentric left ventricular hypertrophy (Chart 32). Studies have shown that an LVEF below 55%, particularly below 50%, is associated with higher

Chart 30 – Step 2: Etiology of aortic regurgitation

Etiology	Characteristics
Rheumatic	• High prevalence in Brazil • Generally associated with mitral valve disease • Common in young adults
Degenerative/calcific	• Generally associated with aortic stenosis • Common in older adults
Bicuspid	• Associated with aortopathies: aortic aneurysm (20%–56%), acute aortic dissection (0.5%–5.6%), and aortic coarctation (5.6%)^{19,24–26} • Common in young adults
Disorders associated with altered aortic annulus geometry	• Systemic arterial hypertension, ascending aortic dissection, Marfan syndrome, ankylosing spondylitis, syphilitic aortitis, osteogenesis imperfecta, Ehlers–Danlos syndrome, Reiter syndrome, and subaortic stenosis
Other	• Infective endocarditis, myxomatous degeneration, traumatic injury, rheumatoid arthritis, and ventricular septal defect with aortic cusp prolapse

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Chart 31 – Step 3: Assessment of symptoms in significant aortic regurgitation

Symptom	Mechanism
Dyspnea	Left ventricular volume overload, with increased left ventricular diastolic pressure and pulmonary venous and capillary congestion
Exertional angina	Reduced coronary flow reserve
Nocturnal angina	Nocturnal bradycardia, increased regurgitant volume, and decreased diastolic blood pressure
Syncope	Reduced effective cardiac output

Chart 32 – Step 4: Assessment of adverse prognostic features in significant aortic regurgitation

Adverse prognostic features	
Echocardiography	• LVEF <50%
	• LVEDD >70 mm (nonrheumatic) and >75 mm (rheumatic)
	• LVESD >50 mm (nonrheumatic) and >55 mm (rheumatic)
	• LVESDi >25 mm/m ²
	• Progressive decline in LVEF and progressive LV dilation
Cardiac magnetic resonance*	• LVESVi ≥43–45 mL/m ²
	• LVEDVi ≥109 mL/m ²
	• iECV ≥24 mL/m ²
	• Late gadolinium enhancement
Biomarkers*	• BNP ≥130 pg/mL

*BNP: B-type natriuretic peptide; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVESDi: left ventricular end-systolic diameter indexed to body surface area; LVESVi: indexed left ventricular end-systolic volume; LVEDVi: indexed left ventricular end-diastolic volume; iECV: indexed extracellular volume. *Cardiac magnetic resonance imaging and BNP findings should be interpreted together with echocardiographic parameters when determining the presence of adverse prognostic features.*

mortality. Furthermore, a decline in LVEF is associated with worse postoperative outcomes, including a substantial increase in mortality.^{174–176}

Although initially compensatory, ventricular remodeling also becomes a marker of poor prognosis during the natural history of the disease, with a particularly negative impact in nonrheumatic aortic regurgitation. Studies have shown that a left ventricular end-diastolic diameter (LVEDD) >75 mm in patients with rheumatic disease and >70 mm in those with nonrheumatic disease, as well as an LVESD >55 mm and >50 mm, respectively, are associated with higher mortality.^{172, 175, 176}

Indexing these diameters to body surface area is currently considered important, particularly in patients with a small body surface area, such as women, and in those with an LVEF between 50% and 55%. An LVESD indexed to body surface area (LVESDi) >25 mm/m² is associated with worse outcomes, including higher mortality, worsening symptoms, and ventricular dysfunction. Recent evidence suggests that even lower LVESDi thresholds (>20–22 mm/m²) may be associated with adverse outcomes and should be considered particularly in patients at low surgical risk.¹⁶⁶

Furthermore, volumetric indices, particularly LVESVi, may be superior to linear dimensions for predicting outcomes. An LVESVi ≥43–45 mL/m² has been validated as a predictor of adverse events in asymptomatic patients with preserved LVEF.^{166,171}

GLS has emerged as a sensitive marker of subclinical myocardial dysfunction, detecting abnormalities before LVEF declines. GLS values worse than –18% to –19% predict higher mortality before and after aortic valve replacement, whereas a value of –15% confers a 2- to 3-fold higher risk of adverse events.^{166,167}

Beyond fixed cutoff values, progressive left ventricular dilation or a progressive decline in LVEF in asymptomatic patients – even when the aforementioned thresholds have not been reached – as well as functional abnormalities such as impaired GLS, should be considered when determining the indication for intervention.

More recently, studies evaluating the role of BNP in aortic regurgitation have shown that elevated levels are associated with greater severity of valvular heart disease.¹⁷⁷ BNP levels >130 pg/mL have been associated with adverse clinical outcomes in asymptomatic patients with significant aortic regurgitation and preserved ventricular function.^{166,177}

Additional information may also be obtained from CMR. The presence of myocardial fibrosis assessed using LGE is associated with worse postoperative outcomes, including persistent symptoms, failure of ventricular function to recover, and higher mortality. An elevated indexed extracellular volume (≥ 24 mL/m²), reflecting interstitial fibrosis, is also associated with higher mortality and a greater need for surgery in asymptomatic patients.^{169,170}

Combining these tools with echocardiographic parameters may improve severity stratification in asymptomatic patients and support decisions regarding the optimal timing of intervention.

7.5. Step 5 – Modes of Intervention

Conventional surgery remains the primary interventional strategy for patients with aortic regurgitation (Chart 33). In most cases, aortic valve replacement with a bioprosthetic or mechanical valve is recommended. Aortic valve repair, with the aim of preserving the native valve, may be considered in selected patients with suitable valve anatomy when performed at specialized centers, particularly in cases involving concomitant aortic surgery. Patients with ascending aortic dilation ≥ 4.5 cm should undergo combined aortic valve replacement and ascending aorta replacement.¹⁷⁸

TAVI has emerged as a treatment option for selected patients with significant aortic regurgitation. Historically, the use of commercially available devices designed for aortic stenosis in patients with pure aortic regurgitation was associated with higher complication rates, including valve embolization, significant paravalvular regurgitation, and mortality, due to the absence of valvular calcification and the presence of annular dilation, which hinder device anchoring.¹⁷⁹

However, recent studies of dedicated devices for aortic regurgitation have reported promising results. The ALIGN-AR study, which evaluated a dedicated device for aortic regurgitation in 700 patients, reported a technical success rate of 95%, 30-day mortality of 1.6%, stroke in 1.7%, and 1-year mortality of 7.7%, with a substantial reduction in regurgitation, favorable valve hemodynamics, and sustained myocardial remodeling for up to 2 years. These findings suggest that TAVI may be a viable option for selected patients with symptomatic significant aortic regurgitation,

high surgical risk, and suitable anatomy, particularly when performed at specialized centers using dedicated devices after discussion by the Heart Team.^{166,179-181}

7.6. Step 6 – Modes of Intervention

Current guidelines recommend surgery for all symptomatic patients with significant aortic regurgitation (Chart 34). In asymptomatic patients, intervention is indicated in the presence of left ventricular dysfunction or significant left ventricular dilation.

Concomitant aortic valve surgery is recommended in patients with significant aortic regurgitation undergoing another cardiac surgical procedure and should be considered in those with moderate aortic regurgitation.^{182,183}

7.7. Individualized Follow-Up

Patients who are asymptomatic and have no adverse prognostic features, as well as those with mild or moderate aortic regurgitation, should undergo individualized follow-up with periodic clinical and echocardiographic reassessment to allow early identification of the need for intervention.

Particular attention should be given to patients with an indication for another surgical procedure, such as CABG, ascending aorta surgery, or intervention on another valve. In these cases, concomitant aortic valve surgery is recommended for patients with significant aortic regurgitation who are asymptomatic and have no adverse prognostic features and should also be considered in those with moderate aortic regurgitation, as shown in Chart 35.^{182,183}

7.8. Medical Therapy

There is no evidence that medical therapy reduces disease severity or alters its natural history in patients with significant aortic regurgitation. However, it may be used to treat concomitant conditions, such as hypertension, and to relieve symptoms while patients await intervention.¹⁶¹

In patients with symptomatic significant aortic regurgitation and/or adverse prognostic features who have prohibitive surgical risk and are not candidates for transcatheter intervention, vasodilators and diuretics may provide symptom relief. In the

Chart 33 – Step 5: Modes of intervention in significant aortic regurgitation

Mode	Considerations
Surgery – Valve replacement	• Treatment of choice for most patients • Patients with ascending aortic dilation ≥ 4.5 cm should undergo combined aortic valve replacement and ascending aorta replacement
Surgery – Valve repair	• May be considered in patients with suitable anatomy when performed at specialized centers, particularly in combination with repair of the ascending aorta
TAVI	• May be considered in patients at high surgical risk or considered inoperable who have suitable anatomy, after Heart Team discussion • Dedicated devices have shown promising results

TAVI: transcatheter aortic valve implantation.

Guidelines

Chart 34 – Aortic regurgitation: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Aortic valve replacement	Symptoms	Strong / Moderate	I B	I B
	LVEF $\leq$ 50%	Strong / Moderate	I B	I B
	Ventricular dilation: • Rheumatic: LVEDD > 75 mm or LVESD > 55 mm	Strong / Moderate	-	-
	• Nonrheumatic: LVEDD > 70 mm, LVESD > 50 mm, or LVESDi > 25 mm/m ²	Strong / Moderate	IIa B	I B
	Concomitant intervention when undergoing ascending aorta surgery (incidental procedure)	Strong / Low	I C	I C
Aortic valve repair	Suitable valve anatomy, at specialized centers	Weak / Moderate	-	IIa B
TAVI	Symptomatic patients with a life expectancy > 1 year, contraindication to surgery or prohibitive surgical risk, and suitable anatomy, after Heart Team discussion	Weak / Low	-	IIb B

LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESDi: left ventricular end-systolic diameter indexed to body surface area; TAVI: transcatheter aortic valve implantation; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

Chart 35 – Aortic regurgitation: Individualized follow-up

Aortic regurgitation	Follow-up	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Significant, asymptomatic, and without adverse prognostic features	Clinical and echocardiographic reassessment	6 months	6–12 months	3–6 months
	Concomitant intervention in patients undergoing another cardiac surgical procedure	Strong / Low	I C	I C
Moderate • VC 0.3–0.6 cm • RF 30%–49% • RVol 30–59 mL • EROA 0.10–0.29 cm ²	Clinical and echocardiographic reassessment	1–2 years	1–2 years	1–2 years
	Concomitant intervention in patients undergoing another cardiac surgical procedure	Strong / Low	IIa C	-
Discrete • VC < 0.3 cm • RF < 30% • RVol < 30 mL • EROA < 0.10 cm ²	Clinical and echocardiographic reassessment	3–5 years	3–5 years	3–5 years

EROA: effective regurgitant orifice area; FR: regurgitant fraction; VC: vena contracta; RVol: regurgitant volume; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

presence of ventricular dysfunction, there is no robust evidence supporting the use of renin–angiotensin–aldosterone system (RAAS) inhibitors, ARBs, or sacubitril-valsartan in accordance with HF guidelines; however, these agents may be considered to improve symptoms through vasodilation.

In patients with concomitant aortopathy, beta-blockers and vasodilators – particularly RAAS antagonists – are recommended to control the rate-pressure product, reduce aortic wall stress, and delay the progression of aortic dilation. Beta-blockers are the preferred first-line drug class, particularly in patients with Marfan syndrome. ARBs may be considered as an alternative in patients intolerant to beta-blockers or may be used in combination with beta-blockers, particularly when additional blood pressure control is required. Although evidence is lacking to support these therapies in patients with bicuspid aortic valve and dilation of the aortic root and/or ascending aorta, a similar treatment approach is recommended by analogy.^{172,184–186}

7.9. Acute Aortic Regurgitation

Acute aortic regurgitation may result from abnormalities of the valvular apparatus, as observed in infective endocarditis or as a complication of transcatheter procedures, or from aortic disease, particularly aortic dissection. It may also occur after chest trauma.

Unlike chronic aortic regurgitation, the volume overload of acute aortic regurgitation affects a nonremodeled left ventricle, resulting in severe pulmonary congestion (acute pulmonary edema) and reduced cardiac output. This may lead to cardiogenic shock and necessitate emergency surgery.^{161,162}

Echocardiography is essential for confirming the diagnosis and assessing the severity and mechanism of aortic regurgitation. Although acute aortic dissection may be suspected on echocardiography, CT angiography of the aorta is the first-line imaging method when dissection is suspected. If it is unavailable, transesophageal echocardiography may be used because it has greater sensitivity and specificity than transthoracic echocardiography.

In the presence of signs of acute pulmonary edema and tissue hypoperfusion, vasodilator therapy may be used to reduce left ventricular volume overload and temporarily stabilize the patient; however, it must not delay surgery. In patients with aortic dissection, beta-blockers are indicated to control the rate-pressure product. However, they should be used cautiously in the presence of aortic regurgitation because they may blunt compensatory tachycardia and precipitate hemodynamic deterioration. Emergency surgery is indicated in all cases.¹⁶¹

8. Tricuspid Regurgitation

8.1. Step 1 – Criteria for Determining the Anatomical Severity of Significant Tricuspid Regurgitation

Tricuspid regurgitation is a complex, multifaceted condition that is frequently underdiagnosed or diagnosed late. It affects up to 0.55% of the general population and approximately 4%–7% of older adults.^{187–189} Tricuspid regurgitation is strongly associated with increased morbidity and mortality and represents a major clinical and therapeutic challenge requiring a comprehensive, multidisciplinary approach to management.^{190–192}

Moderate to significant tricuspid regurgitation requires specific follow-up, particularly to determine the etiology of the valve disease and assess its associated consequences.¹⁸⁷ Given the large and heterogeneous population of patients with tricuspid regurgitation, recent studies have proposed expanding the ‘significant’ grade of tricuspid regurgitation into significant, massive, and torrential categories, which have prognostic implications for HF hospitalization (Chart 36).¹⁹³

8.2. Step 2 – Assessment of the Etiology of Tricuspid Regurgitation

In most cases (> 90%), tricuspid regurgitation is functional and secondary to clinical conditions that cause abnormalities of the tricuspid annulus, right atrium, and/or right ventricle. Atrial secondary tricuspid regurgitation accounts for 10%–25% of cases, is associated with AF, and is characterized by failure of leaflet coaptation in the presence of marked annular and atrial dilation, with normal right ventricular structure and function. Ventricular secondary tricuspid regurgitation is associated with a worse prognosis and is characterized by right ventricular dilation and dysfunction resulting from precapillary or postcapillary pulmonary hypertension, primarily in association with left-sided heart disease (valvular heart disease or cardiomyopathy) and/or pulmonary hypertension. Cardiac implantable electronic device (CIED)–related tricuspid regurgitation is considered a distinct subgroup because it may exhibit features of both primary and secondary tricuspid regurgitation. Primary tricuspid regurgitation is generally related to rheumatic or congenital heart disease. It may also be associated with previous medical interventions, such as repeated endomyocardial biopsies, or may occur as a consequence of infective endocarditis or other more rare causes (Chart 37).^{194,195}

8.3. Step 3 – Symptoms

In patients with significant tricuspid regurgitation, nonspecific symptoms may develop as the duration of significant valvular dysfunction increases. Fatigue is the most common symptom; dyspnea and physical examination findings of systemic venous congestion may also occur. These manifestations have a substantial impact on patients’ quality of life and are important in decision-making regarding the most appropriate treatment strategy (Chart 38).

8.4. Step 4 – Adverse Prognostic Features

Even in asymptomatic patients, the persistent volume overload imposed by tricuspid regurgitation may result in eccentric right ventricular remodeling and may justify valve intervention. Therefore, right ventricular dilation or dysfunction, unless significant, is considered an adverse prognostic feature (Chart 39).

A growing body of evidence has demonstrated the independent prognostic importance of tricuspid regurgitation. Patients with isolated moderate to significant tricuspid regurgitation have higher mortality regardless of the presence or absence of right ventricular dysfunction, pulmonary hypertension, AF, mitral regurgitation, or left ventricular dysfunction. Furthermore, greater tricuspid regurgitation severity is associated with a worse prognosis.¹⁹⁶

Guidelines

Chart 36 – Step 1: Criteria for determining the anatomical severity of significant tricuspid regurgitation

Characteristics of significant tricuspid regurgitation	
Physical examination	• Pathologic jugular venous distention • Loud S2 (pulmonary hypertension) • Regurgitant systolic murmur at the left sternal border with the Rivero-Carvalho sign • Hepatomegaly/ascites • Lower-extremity edema/anasarca
Electrocardiogram	• Right-sided chamber enlargement • Atrial fibrillation
Chest radiography	• Signs of right-sided chamber enlargement • Pulmonary congestion in the presence of concomitant left-sided disease • Straightening/bulging of the pulmonary trunk
Transthoracic echocardiography	• EROA: - Significant: 0.40–0.59 cm² - Massive: 0.60–0.79 cm² - Torrential: ≥0.80 cm² • Reversed flow in the hepatic veins • Regurgitant volume >45 mL/beat • Dense, triangular, early-peaking regurgitant jet on continuous-wave Doppler • Vena contracta: - Significant: 0.7–1.3 cm - Massive: 1.4–2.0 cm - Torrential: ≥2.1 cm • Annulus diameter ≥40 mm • Determine the etiology • RV function and size • Pulmonary artery pressure
Transesophageal echocardiography	• Should be considered when the diagnosis remains uncertain, the TTE window is inadequate, or the patient is a candidate for transcatheter intervention • Leaflet morphology • Valve annulus size • Characteristics of the regurgitant jet(s)
Hemodynamic assessment	• When clinical and echocardiographic findings are discordant • Measure PASP in cases of failure of leaflet coaptation or when echocardiographic measurement is difficult • Assess pulmonary hypertension and vasodilator responsiveness
Cardiac magnetic resonance	• When clinical and echocardiographic findings are discordant, image quality is limited, or echocardiographic findings are inconclusive • Reference method for quantifying RV function and size • Regurgitant volume ≥45 mL and/or tricuspid regurgitant fraction ≥50%
Computed tomography	• Should be considered when the patient is a candidate for transcatheter intervention • Assessment of the valvular apparatus, RV, and right coronary artery • Assessment of vascular access (jugular or femoral) • Assessment of the angles between the venae cavae, right atrium, and valve plane

EROA: effective regurgitant orifice area; PASP: pulmonary artery systolic pressure; RA: right atrium; RV: right ventricle; S2: second heart sound; TTE: transthoracic echocardiography.

Chart 37 – Step 2: Etiology of tricuspid regurgitation

Etiologic characteristics	
Primary	• Leaflet retraction in rheumatic involvement • Prolapse and myxomatous degeneration • Radiation-induced damage (after radiotherapy) • Blunt chest trauma • Infective endocarditis • Repeated endomyocardial biopsies • Carcinoid syndrome • Congenital disease (Ebstein anomaly)
Secondary	• Tricuspid annular dilation (> 40 mm or > 21 mm/m²). • Atrial ◦ Generally associated with atrial fibrillation • Ventricular ◦ RV dysfunction and/or remodeling ◦ Combination of annular dilation and leaflet tethering
CIED-related (caused by interaction with intracardiac leads)	• Leaflet impingement • Entanglement or rupture of the chordae tendineae • Adhesion to the leaflets • Leaflet laceration
Rare causes	• Rheumatologic diseases • Drugs (methysergide/anorectic agents) • Fabry disease

RV: right ventricle; CIED: cardiac implantable electronic device.

Chart 38 – Step 3: Assessment of symptoms in significant tricuspid regurgitation

Symptoms	
Dyspnea (NYHA II–IV)	• In secondary tricuspid regurgitation, results from left-sided heart disease (pulmonary venous and capillary congestion and pulmonary arterial hypertension) • Exertional dyspnea and paroxysmal nocturnal dyspnea
Fatigue	• Main symptom • Associated with lower-extremity pain and edema • More common in right heart failure

NYHA: New York Heart Association functional class.

Chart 39 – Step 4: Assessment of adverse prognostic features in significant tricuspid regurgitation

Adverse prognostic features	
Echocardiography and/or CMR	Primary tricuspid regurgitation: progressive RV dilation or dysfunction
Right heart catheterization	Assessment of significant pulmonary hypertension or elevated PVR in selected cases after echocardiography, particularly in candidates for intervention

CMR: cardiac magnetic resonance; PVR: pulmonary vascular resistance; RV: right ventricular.

Guidelines

8.5. Step 5 – Modes of Intervention

When tricuspid valve intervention is indicated, a fundamental step is assessing the patient's surgical risk based on clinical evaluation, frailty, and surgical risk scores. Of particular relevance is the TRI-SCORE, a simple dedicated risk-prediction model developed to estimate outcomes after isolated tricuspid valve surgery for significant tricuspid regurgitation. It may be used as an ancillary tool to estimate risk and guide the choice between surgical and transcatheter treatment.^{197,198}

When intervention is indicated, tricuspid valve repair with an annuloplasty ring is the preferred surgical treatment, provided the patient's surgical risk is acceptable. This approach reduces the tricuspid annulus diameter, improves leaflet coaptation, and corrects regurgitation. Valve replacement is reserved for patients whose anatomy is unsuitable for repair with a satisfactory result. Isolated tricuspid valve surgery is still infrequently indicated and carries the highest surgical risk among valve procedures, with operative mortality of approximately 10%. Furthermore, no data have yet demonstrated a survival benefit from surgical treatment. Thus, the main goals of surgery in this population remain symptom improvement and the prevention of severe right ventricular dysfunction.¹⁹⁹⁻²⁰¹

Patients with CIED-related tricuspid regurgitation require particular attention and multimodality imaging to determine whether regurgitation is attributable to the intracardiac lead(s) or whether the leads are not directly involved. Strategies such as lead replacement and/or extraction may be considered after weighing the risks and benefits, and decisions should be made by the Heart Team.²⁰²

In recent years, an increasing body of evidence has emerged regarding transcatheter tricuspid valve treatment. However, its true effect on mortality remains uncertain, although some studies have suggested improved survival compared with medical therapy alone.²⁰³ Several devices have been developed. Transcatheter strategies include reducing the tricuspid annulus (annuloplasty), improving leaflet coaptation (transcatheter repair), using spacer

devices, and, more recently, implanting orthotopic prostheses (into the native annulus) or heterotopic prostheses (into the venae cavae) to protect the organs from venous hypertension caused by reverse flow. The first randomized controlled trial comparing transcatheter repair with optimal medical therapy in patients with isolated tricuspid regurgitation (mean age, 78 years) demonstrated a significant reduction in tricuspid regurgitation and consistent improvement in quality of life in the intervention group at 12 months. At 2-year follow-up, these benefits were maintained, and HF hospitalizations were reduced, although mortality was not significantly affected.^{204,205} In parallel, a study comparing orthotopic valve replacement with medical therapy demonstrated that transcatheter tricuspid valve replacement eliminated tricuspid regurgitation or reduced it to mild or none/trivial in most patients, with significant and sustained improvements in functional capacity and quality of life, but no impact on mortality.²⁰⁶

Regardless of the technique used, decisions regarding tricuspid valve intervention should be comprehensively evaluated by the Heart Team. This assessment should incorporate clinical characteristics, risk stratification, anatomy defined by multimodality imaging, access to available technologies, and operator experience to select the most appropriate treatment strategy. Several additional studies evaluating these less invasive techniques are underway and should provide further evidence in the coming years to guide the management of tricuspid regurgitation in patients at high surgical risk who have not responded adequately to optimal medical therapy (Charts 40 and 41 and Figure 11).^{204,205-212}

The TRIC-I-HF trial demonstrated, for the first time, a statistically significant reduction in clinical outcomes with transcatheter intervention in symptomatic patients with severe TR and a high risk of HF events. Transcatheter repair combined with medical therapy improved the hierarchical outcome of death, HF hospitalization, and quality of life at 1 year (WR 2.42; $p < 0.001$), and also reduced the composite outcome of death or HF hospitalization during follow-up of up to 3 years (HR 0.40; 95% CI 0.29–0.55; $p < 0.001$).²¹³

Chart 40 – Step 5: Modes of intervention in significant tricuspid regurgitation

Mode	Considerations
Tricuspid valve repair	• Treatment of choice • Indications: - Surgery for another valve disease in the presence of a tricuspid annulus diameter ≥ 40 mm and/or moderate to significant TR - Isolated TR refractory to medical therapy in patients without contraindications and at low surgical risk • Contraindications: severe RV systolic dysfunction
Surgical valve replacement	• When valve repair is contraindicated • Bioprosthetic valve preferred • Contraindications: severe RV systolic dysfunction and severe pulmonary hypertension
Transcatheter valve intervention	• Symptoms refractory to medical therapy in patients with a contraindication to surgery or at high surgical risk • Contraindications: severe RV systolic dysfunction and severe pulmonary hypertension

TR: tricuspid regurgitation; RV: right ventricular.

Chart 41 – Significant tricuspid regurgitation: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Tricuspid valve repair	• Surgery for another valve disease and significant TR	Strong / Moderate	I B	I B
	• Surgery for another valve disease and tricuspid annulus diameter ≥ 40 mm in the presence of moderate to significant TR	Strong / Moderate	IIa B	IIb B
	• Significant isolated secondary TR refractory to medical therapy	Strong / Moderate	-	IIa B
	• Significant isolated primary TR in an asymptomatic patient with progressive RV dilation or decline in RV function	Strong / Low	IIb C	IIa C
	• Significant isolated primary TR in a symptomatic patient without RV dysfunction	Strong / Low	IIa B	I C
Surgical valve replacement	• TR requiring intervention when valve repair is not feasible	Strong / Moderate	I B	I C
Transcatheter tricuspid valve intervention	• TR refractory to medical therapy in patients with a contraindication to surgery or at high surgical risk and with suitable anatomy:			
	– Edge-to-edge repair for symptomatic benefit and improved clinical outcomes	Strong / High	-	IIa A
	– Orthotopic implantation for symptomatic benefit	Strong / High	-	IIa A
	– Heterotopic implantation for symptomatic benefit	Weak / Low	-	IIa A

TR: tricuspid regurgitation; RV: right ventricular; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

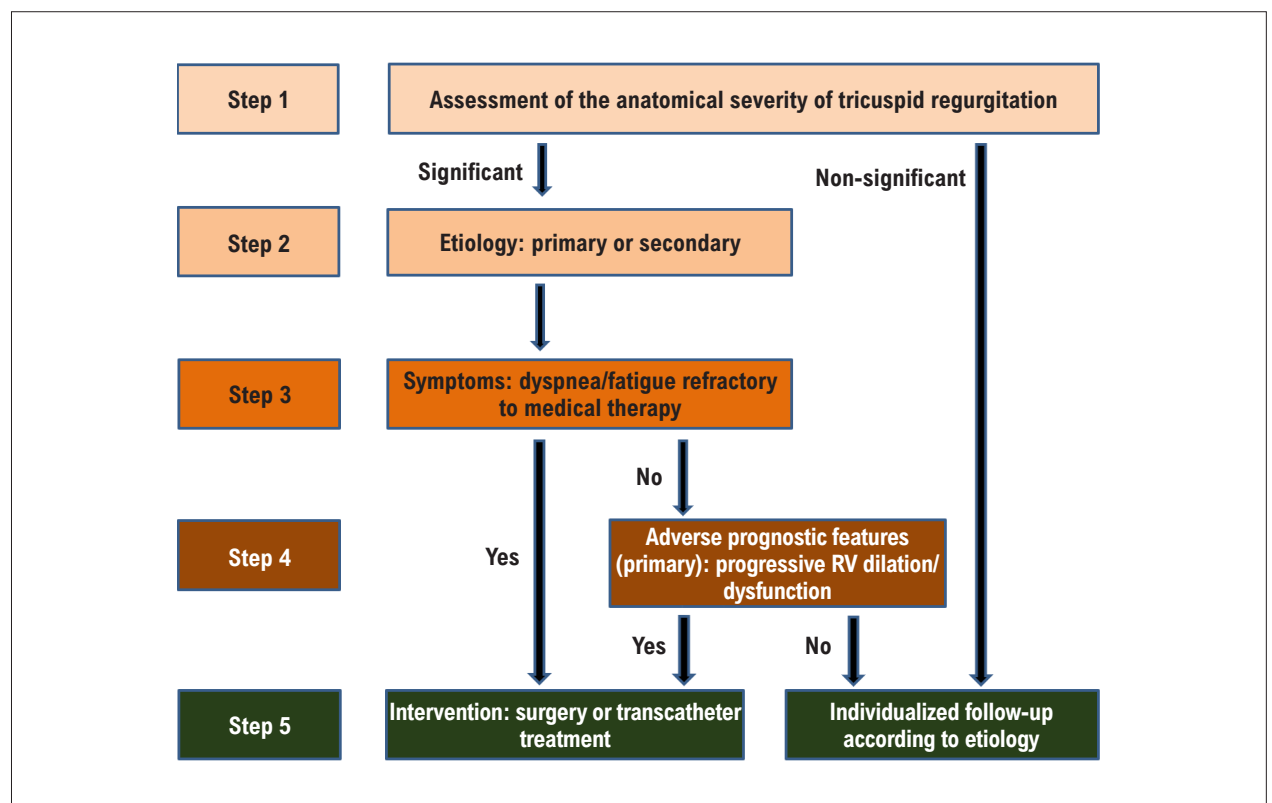


Figure 11 – Algorithm for the assessment of significant tricuspid regurgitation. RV: right ventricular.

Guidelines

8.6. Individualized follow-up

Certain groups of patients should be monitored frequently because of the risk of progression to valve disease requiring intervention (Chart 42). Particular attention should therefore be given to the following groups:

Asymptomatic significant tricuspid regurgitation without adverse prognostic features: At present, valve surgery is indicated only in patients undergoing surgery for another left-sided valve disease.

Asymptomatic moderate tricuspid regurgitation: At present, valve surgery is indicated only in patients undergoing surgery for another left-sided valve disease when the tricuspid annulus diameter is > 40 mm.

8.7. Medical Therapy

Patients with significant tricuspid regurgitation and signs or symptoms of right HF generally require medical therapy to achieve clinical stabilization. Sodium and fluid restriction, together with diuretic therapy, may be used to reduce volume overload. Loop diuretics are often the first-line treatment to relieve systemic congestion. However, in many cases, the diuretic response must be enhanced through combination therapy with MRAs and thiazide diuretics. Because tricuspid regurgitation is secondary in most cases, optimal medical therapy should be provided for concomitant HF. Pulmonary vasodilator therapy should be used when indicated in the setting of pulmonary hypertension, and a rhythm-control strategy should be pursued whenever feasible in patients with concomitant AF.

9. Tricuspid Stenosis

Tricuspid stenosis is a rare valve disease, accounting for less than 1% of all valve lesions.²¹⁴ Echocardiography remains the primary tool for diagnosis, assessment of etiology, and determination of anatomical severity (Chart 43).²¹⁵ Rheumatic disease is the most common cause of tricuspid stenosis, accounting for more than 90% of cases and frequently accompanied by mitral and/or aortic valve involvement. Other potential causes include congenital heart disease, such as Ebstein anomaly, carcinoid syndrome, systemic lupus erythematosus, antiphospholipid antibody syndrome, iatrogenic causes, thrombosis, and infective endocarditis, among others (Chart 44).²¹⁶

Symptoms and physical examination abnormalities may be present in patients with anatomically significant tricuspid stenosis. The most common symptoms are fatigue and presyncope, which may be accompanied by manifestations of right HF (Chart 45). In asymptomatic patients with significant tricuspid stenosis, the presence of adverse prognostic features should be investigated to determine the indication for intervention (Chart 46).

The presence of symptoms secondary to significant tricuspid stenosis indicates the need for surgical or transcatheter intervention, as does the presence of adverse prognostic features in asymptomatic patients.

Medical therapy with diuretics and sodium restriction should be used only as a bridge to intervention. It may relieve symptoms of right-sided congestion but does not alter the natural history of the disease.

Surgical intervention for significant tricuspid stenosis is also indicated in patients undergoing another concomitant cardiac surgical procedure (incidental surgery) (Charts 47 and 48). When feasible, valve repair is the preferred surgical strategy (commissurotomy).²¹⁸ However, surgical valve replacement is frequently required, with a bioprosthetic valve preferred because of the high risk of thrombosis associated with mechanical valves.²¹⁹ Observational studies suggest good durability of bioprosthetic valves, with more than 50% of patients remaining free from reoperation 15 years after surgery. Nevertheless, a mechanical valve may be reasonable in younger patients with good adherence to anticoagulation, although this approach has rarely been used in Brazil.²²⁰⁻²²³

Percutaneous balloon tricuspid valvuloplasty is infrequently performed because tricuspid stenosis is often accompanied by tricuspid regurgitation. Furthermore, the available literature is limited. The procedure may be recommended in selected cases as a bridge to definitive surgical treatment or as a palliative strategy in patients at high surgical risk.²¹⁷

Finally, tricuspid transcatheter valve implantation has recently been investigated, although experience in patients with tricuspid stenosis remains limited.²²⁴

10. Multivalvular Heart Disease

Multivalvular heart disease is defined as the simultaneous involvement of 2 or more native heart valves and may

Chart 42 – Tricuspid regurgitation: Individualized follow-up

Tricuspid regurgitation	Follow-up	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Significant, asymptomatic, and without adverse prognostic features	• Clinical and echocardiographic reassessment	Every 6 months	-	-
	• Concomitant intervention in patients undergoing surgery for another valvular heart disease	Strong / Moderate	I B	I B
Moderate, asymptomatic	• Concomitant intervention in patients undergoing surgery for another valvular heart disease when the tricuspid annulus diameter is > 40 mm	Strong / Moderate	IIa B	IIb B

SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

Chart 43 – Step 1: Criteria for determining the anatomical severity of tricuspid stenosis²¹⁴

Characteristics of significant tricuspid stenosis	
	• Early opening snap • Loud S1
Physical examination	• Diastolic rumble at the left sternal border, with pre-systolic accentuation in patients in sinus rhythm, that increases with inspiration • Signs of systemic congestion: hepatomegaly, ascites, lower-extremity edema, jugular venous distention, and Kussmaul sign
Electrocardiogram	• RA overload • Atrial fibrillation
Chest radiography	• RA enlargement
Echocardiography	• Tricuspid valve area $\leq 1.0 \text{ cm}^2$ • Mean diastolic RA–RV gradient $\geq 5 \text{ mm Hg}$ • Isolated RA enlargement • Tricuspid PHT $\geq 190 \text{ ms}$
Hemodynamic assessment	• When clinical and echocardiographic findings are discordant • Mean diastolic RA–RV gradient $\geq 5 \text{ mm Hg}$
Cardiac magnetic resonance	• When clinical and echocardiographic findings are discordant or echocardiographic image quality is limited

PHT: pressure half-time; RA: right atrium; RV: right ventricle; S1: first heart sound.

Chart 44 – Step 2: Etiology of significant tricuspid stenosis²¹⁴⁻²¹⁷

Etiologic characteristics	
	• Most common cause • Associated with other valve diseases
Rheumatic	• Leaflet thickening and retraction • Commissural fusion • Common in young adults
Other	• Infective endocarditis • Systemic lupus erythematosus • Carcinoid syndrome • Congenital abnormalities • Atrial myxoma • Radiation-induced damage (after radiotherapy) • Storage diseases: amyloidosis and Fabry disease • Whipple disease • Iatrogenic causes

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Chart 45 – Step 3: Assessment of symptoms in significant tricuspid stenosis

Symptoms	
Fatigue	• Main symptom
	• Associated with lower-extremity pain and edema
	• Absence of dyspnea
	• May be associated with palpitations, ascites, and signs of liver dysfunction

Chart 46 – Step 4: Assessment of adverse prognostic features in significant tricuspid stenosis

Adverse prognostic features	
Electrocardiogram	• Atrial fibrillation
Systemic congestion	• Assessment of liver involvement (elevated liver enzymes and abnormal coagulation profile)

Chart 47 – Step 5: Modes of intervention in significant tricuspid stenosis²¹⁶⁻²²²

Mode	Considerations
Percutaneous balloon tricuspid valvuloplasty	• Option as a bridge to definitive surgical treatment • Palliative treatment for patients at high surgical risk
Surgical tricuspid valve replacement	• Preferred, particularly in younger patients
Tricuspid transcatheter valve implantation	• When valve repair is not feasible or in the setting of concomitant cardiac surgery (incidental surgery) • Bioprosthetic valve preferred (individualized assessment)
Transcatheter tricuspid valve implantation	• Limited experience

comprise stenotic and/or regurgitant lesions of primary or secondary origin. It is distinct from mixed valve disease, which refers to the coexistence of stenosis and regurgitation in the same valve.²²⁵⁻²²⁷

An estimated 30%–50% of patients with native left-sided valvular heart disease have concomitant moderate or significant valve lesions, and their prognosis is worse than that of patients with isolated valve disease.²²⁵⁻²²⁷ Although common and complex, multivalvular heart disease is underdiagnosed and undertreated and is not adequately addressed in international guidelines.^{225,227}

10.1 Step 1 – Criteria for Determining the Anatomical Severity of Multivalvular Heart Disease

The diagnosis of multivalvular heart disease depends on the valves involved, the type of lesion (stenosis or regurgitation), and the predominant valve lesion (Chart 49).²²⁵⁻²²⁷

On physical examination, the characteristics of each murmur should be identified according to the valve involved. It is important to distinguish these murmurs from functional murmurs caused by altered hemodynamics. One example is the Austin Flint murmur, which occurs when the regurgitant jet of significant aortic regurgitation impairs mitral valve

opening, producing a murmur of functional mitral stenosis. This distinction is particularly important when determining the predominant valve lesion.^{225,226}

ECG and chest radiography may demonstrate abnormalities secondary to the predominant valve lesion, including evidence of left-sided or right-sided chamber enlargement, AF, and pulmonary congestion.

Echocardiography is essential for diagnosing multivalvular heart disease and determining the anatomical severity of each valve lesion. Diagnostic assessment is particularly challenging because the hemodynamic consequences of one valve lesion may interfere with the functional assessment of another, leading to either underestimation or overestimation of its severity.²²⁵⁻²²⁸ For example, the increased afterload and intraventricular pressure associated with moderate or significant aortic stenosis may result in overestimation of mitral regurgitation severity, whereas concomitant mitral regurgitation may lead to underestimation of the transaortic gradient in aortic stenosis.^{165,225,226}

Therefore, multiple parameters, including valve area, gradients, jet velocities, and EROA, should be integrated with clinical findings to accurately grade the severity of each valve lesion.^{225,226,228}

Chart 48 – Tricuspid stenosis: Recommendations²¹⁶⁻²²²

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA*	ESC
Percutaneous balloon tricuspid valvuloplasty	• Patient at high or prohibitive surgical risk	Weak / Very low	-	-
Tricuspid valve replacement or repair (commissurotomy)	• Symptomatic significant TS or significant TS with adverse prognostic features	Strong / Low	-	I C
	• Significant TS with an indication for mitral and/or aortic valve surgery	Strong / Low	-	I C

AHA: American Heart Association; ESC: European Society of Cardiology; TS: tricuspid stenosis; SBC: Brazilian Society of Cardiology. *Current AHA guidelines do not address tricuspid stenosis.

Chart 49 – Step 1: Criteria for determining the anatomical severity of multivalvular heart disease

Characteristics of multivalvular heart disease	
Physical examination	• Presence of murmurs distinctly characterized as mitral, aortic, and/or tricuspid – regurgitation, stenosis, or mixed valve disease • Exclude murmurs caused by hemodynamic interference (eg, Austin Flint murmur) • Physical examination is particularly important for determining the predominant valve lesion
Electrocardiogram	• Electrocardiographic abnormalities depend on the predominant valve lesion and its consequences
Chest radiography	• Radiographic abnormalities depend on the predominant valve lesion and its consequences
Echocardiography	• Anatomical severity parameters are the same as those used for isolated valve disease • Integrate as many parameters as possible (valve area, gradients, jet velocities, regurgitant orifice area, etc.), because dysfunction of one valve may result in underestimation or overestimation of dysfunction in another valve • Assess the etiology (primary or secondary) of each valve lesion
Hemodynamic assessment	• Indicated when clinical and echocardiographic findings are discordant
Multidetector computed tomography of the chest	• Aortic valve calcium score • Assessment of mitral annular calcification
Cardiac magnetic resonance	• Morphological and functional assessment and quantification of regurgitant lesions using dedicated software

Hemodynamic assessment may be useful in cases of clinical–echocardiographic discordance. CT may likewise provide complementary information, such as the aortic valve calcium score and assessment of MAC, thereby yielding additional data regarding the etiology and anatomical severity of each valve lesion. CMR may provide both morphological and functional information using dedicated software. It can quantify valvular regurgitation when echocardiographic findings are inconclusive and provide information on ventricular function and myocardial fibrosis.^{226,228}

10.2. Step 2 – Assessment of the Etiology of Multivalvular Heart Disease

Primary valve diseases arise from direct involvement of the valvular apparatus and include rheumatic, degenerative,

congenital, and radiation-induced disease, infective endocarditis, and other etiologies. Particular attention should be given to rheumatic fever because primary involvement of multiple valves may occur simultaneously or at different times. Rheumatic disease accounts for most cases of primary multivalvular heart disease in low- to middle-income countries, including Brazil (Chart 50).^{225, 226,229} Degenerative disease is more common in high-income countries, where calcific aortic and mitral stenosis may coexist.²²⁵⁻²²⁷ In patients with aortopathies, such as Marfan and Ehlers–Danlos syndromes, mitral and aortic regurgitation may also coexist.^{225,226}

Secondary valve diseases result from changes in the geometry of the right-sided or left-sided cardiac chambers, leading to tricuspid and mitral regurgitation, respectively. The main causes include ischemic heart disease and dilated cardiomyopathies.²²⁵⁻²²⁷

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Chart 50 – Step 2: Etiology of multivalvular heart disease

Etiologic characteristics	
Atherosclerotic/ degenerative	• Most common etiology in high-income countries • Patients are generally older • Aortic stenosis is frequently present, and secondary mitral regurgitation is common • Mitral annular calcification • Possible association with aortic and coronary calcification
Rheumatic	• Accounts for most cases of primary multivalvular heart disease in low- to middle-income countries, including Brazil • Typical in younger patients, with symptoms developing between 20 and 40 years of age • Commissural fusion, leaflet thickening, and subvalvular apparatus involvement • Mixed valve disease is common • Metachronous progression is common
Infective endocarditis	• Valve regurgitation caused by destruction of the mitral and/or aortic valvular apparatus • Metastatic infection involving the aortic and mitral valves
Connective tissue disorders (Marfan and Ehlers–Danlos syndromes)	• Mitral and aortic regurgitation • Assess for involvement of the ascending aorta

Furthermore, primary and secondary involvement may coexist in multivalvular heart disease, ie, dysfunction of one valve may occur secondary to a primary lesion affecting a downstream valve. Examples include tricuspid regurgitation accompanying primary mitral stenosis and functional mitral regurgitation secondary to aortic stenosis or aortic regurgitation.²²⁵⁻²²⁷

10.3. Step 3 – Symptoms

Symptoms are generally related to the valve lesion with greater anatomical severity. When both lesions are significant, the more proximal valve lesion usually predominates (Chart 51).²²⁵⁻²²⁷ Dyspnea is the most common symptom, particularly exertional intolerance. Chest pain may occur, especially in patients with aortic valve disease, and may also be present in some patients with pulmonary hypertension. Symptoms of low cardiac output and syncope are more common when aortic stenosis and mitral regurgitation coexist because this combination may substantially reduce forward stroke volume. Manifestations of right HF, such as peripheral edema and ascites, may occur in patients with right-sided chamber involvement due to tricuspid regurgitation and/or concomitant pulmonary hypertension.

It is important to recognize that symptoms may occur in patients with moderate disease affecting 2 valves. In these cases, the combined hemodynamic consequences of the individual valve lesions may cause symptoms. A detailed assessment of each valve is therefore recommended to determine the etiology and anatomical severity of each lesion, because echocardiographic parameters may be underestimated depending on the combination of associated valve dysfunctions.^{225,227}

10.4. Step 4 – Adverse Prognostic Features

As in single-valve disease, asymptomatic patients should be assessed for adverse prognostic features to determine whether intervention is indicated. In multivalvular heart disease, these features generally arise from the valve lesion with the greatest anatomical severity (Chart 52). A particular consideration in these patients is that progression of one valve lesion and the development of adverse prognostic features may lead to another associated valve dysfunction. One example is mitral stenosis complicated by pulmonary hypertension and secondary tricuspid regurgitation.²²⁵⁻²²⁷

10.5. Step 5 – Modes of Intervention

Intervention is indicated in the presence of symptoms and/or adverse prognostic features (Charts 53 and 54). In multivalvular heart disease, it is important to identify the predominant valve lesion and determine the etiology of each lesion, ie, whether it is primary or secondary.

In general, surgery is the first-line treatment for all operable patients.²³⁰ When one valve lesion is significant and the other is moderate, concomitant intervention on both valves is indicated, except in patients at high surgical risk.²³¹ The choice between valve repair and replacement depends on the valve involved, the etiology, and valve anatomy. Valve repair is generally preferred for degenerative mitral valve disease, whereas valve replacement is the procedure of choice for aortic valve disease. In the presence of functional mitral or tricuspid valve disease, the surgical technique should be individualized according to the criteria outlined previously.²³⁰

Chart 51 – Step 3: Assessment of symptoms in multivalvular heart disease

Symptoms	
Dyspnea	• Main symptom • Initially triggered by events that increase pulmonary venous and capillary pressure, such as physical exertion • May be accompanied by palpitations, hemoptysis, dysphonia, dysphagia, or cough, depending on the consequences of each valve lesion
Precordial pain	• Particularly in the presence of stenotic or regurgitant aortic valve disease • May be caused by pulmonary hypertension
Low cardiac output/ syncope	• Occurs particularly when aortic stenosis and mitral regurgitation coexist
Right heart failure	• Peripheral edema, ascites, and hepatic congestion and dysfunction • Occurs in patients with tricuspid regurgitation and/or pulmonary hypertension affecting the right ventricle

Chart 52 – Step 4: Assessment of adverse prognostic features in multivalvular heart disease

Adverse prognostic features	
Pulmonary hypertension	• PASP ≥ 50 mm Hg at rest • More common in the presence of concomitant mitral stenosis • Associated with secondary tricuspid regurgitation and symptoms of right heart failure • Associated with increased surgical risk
New-onset atrial fibrillation	• Associated with left atrial remodeling and more common in the presence of mitral valve disease
Ventricular dilation	• More common in regurgitant valve disease • Consider ventricular diameters according to the type of valve dysfunction

PASP: pulmonary artery systolic pressure.

Chart 53 – Step 5: Modes of intervention in multivalvular heart disease

Mode	Considerations
Percutaneous balloon mitral valvuloplasty	• Significant rheumatic mitral stenosis with suitable anatomy and no concomitant significant aortic valve involvement
Surgical treatment	• Mitral valve replacement or repair, depending on the anatomy of the valvular apparatus • Avoid aortic valve repair – valve disease and symptoms frequently recur despite an adequate immediate result • Treat concomitant anatomically moderate valve disease during intervention for the significant valve lesion, except in patients at high surgical risk
Transcatheter treatment – TAVI, mitral or tricuspid TEER, or valve-in-valve implantation	• Significant aortic stenosis and significant primary mitral regurgitation in patients at high surgical risk or considered inoperable (after Heart Team assessment) • Mitral, tricuspid, or aortic bioprosthetic valve dysfunction in symptomatic patients at high surgical risk or considered inoperable (after Heart Team assessment) • When concomitant significant secondary valve disease is present, the primary valve lesion is generally treated first, followed by reassessment

TAVI: transcatheter aortic valve implantation; TEER: transcatheter edge-to-edge repair.

Guidelines

Chart 54 – Significant multivalvular heart disease: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Surgical treatment	• Symptomatic multivalvular heart disease	Strong / Moderate	-	-
	• Multivalvular heart disease with adverse prognostic features	Strong / Low	-	-
	• Intervention for a concomitant moderate valve lesion during treatment of significant valve disease or another cardiac or ascending aortic surgical procedure	Strong / Low	Ila C	Ila C

SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

Transcatheter treatment may be considered in patients at high surgical risk. Transcatheter interventions permit a staged approach, allowing assessment of the effect of correcting the principal valve lesion on the remaining valve disease. Thus, the predominant valve lesion is generally treated first. Particularly when the second valve dysfunction is secondary, the patient can then be reassessed for potential reverse remodeling and improvement in the severity of the untreated valve dysfunction.²³²⁻²³⁵

A common example is a patient with significant aortic stenosis and secondary mitral regurgitation. In these cases, the usual strategy is to perform TAVI and subsequently reassess the mitral regurgitation and the patient's symptoms.^{233,236} In patients with significant aortic stenosis and significant primary mitral regurgitation, treatment of both valves is generally anticipated. TAVI and mitral TEER may be performed during the same procedure or as a staged strategy because persistent mitral regurgitation is associated with higher mortality.²³⁴⁻²³⁶ Discussion by the Heart Team is essential in all these scenarios.

In patients with rheumatic mitral stenosis, PBMV remains the first-line intervention when valve anatomy is suitable and there is no concomitant significant aortic valve involvement.²²⁹

10.6. Medical Therapy

Medical therapy is indicated to relieve symptoms while patients await intervention and for patients with prohibitive surgical risk who are not candidates for transcatheter treatment and therefore remain under clinical management.²²⁴

Treatment should be directed toward the predominant valve lesion. However, the hemodynamic effects of each medication on the other concomitant valve lesion must be considered.^{225, 226} Vasodilators may be beneficial in regurgitant lesions. In mitral stenosis, beta-blockers may be used for heart rate control, as may digoxin in the presence of AF. In patients with aortic stenosis, beta-blockers and vasodilators should be used cautiously because of the risks of worsening cardiac output and severe hypotension, respectively. Beta-blockers also warrant caution in mitral regurgitation because an excessive reduction in heart rate may worsen regurgitation. Diuretics are recommended to

relieve congestive symptoms. If necessary, a loop diuretic may be combined with other drug classes, such as thiazide diuretics and MRAs.

When concomitant ventricular dysfunction is present, guideline-directed medical therapy for HF is recommended, particularly when myocardial dysfunction was not caused by the valve disease; in these cases, robust scientific evidence supporting such therapy is lacking. Nevertheless, the specific precautions associated with each valve lesion should be considered.

Individualized follow-up for asymptomatic patients without adverse prognostic features is described in Chart 55.

11. Prosthetic Valve Dysfunction

After valve replacement surgery, patients should undergo periodic clinical and echocardiographic follow-up. Over time, prosthetic valves may develop structural deterioration, resulting from intrinsic damage to the valve prosthesis, or nonstructural dysfunction, resulting from extrinsic abnormalities such as thrombosis, infective endocarditis, PPM, or paravalvular regurgitation.²³⁸

Structural deterioration occurs more frequently in bioprosthetic than in mechanical valves. An echocardiogram obtained before hospital discharge is an important reference for appropriate longitudinal assessment. Once prosthetic valve dysfunction has been confirmed, the patient should be referred to a heart valve center of excellence.

Complementary imaging studies, including transesophageal echocardiography and cardiac CT, are highly important for confirming the precise mechanism of dysfunction.

The decision to perform surgical or transcatheter reintervention should ideally be made by the Heart Team, considering the anatomical diagnosis and the patient's clinical condition, particularly their surgical risk.

11.1. Step 1 – Criteria for Determining the Anatomical Severity of Prosthetic Valve Dysfunction

In addition to a clinical history of worsening symptoms, particularly exertional dyspnea, the diagnosis should incorporate physical examination and echocardiographic

Chart 55 – Multivalvular heart disease: Individualized follow-up

Multivalvular heart disease	Follow-up	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Significant, asymptomatic, and without adverse prognostic features	• Clinical and echocardiographic reassessment	Every 6 months	Every 6–12 months	Individualized
	• Concomitant intervention in patients undergoing another cardiac surgical procedure (coronary revascularization, ascending aortic surgery, or another valve procedure)	Strong / Low	I B	I C
Moderate	• Clinical and echocardiographic reassessment	Every year	Every 1–2 years	Individualized
	• If symptoms are present, the anatomical severity of each valve lesion should be reassessed using complementary methods, and interventional treatment should be considered	Weak / Low	-	-
Discrete	• Clinical and echocardiographic reassessment	Every 2–3 years	Every 3–5 years	Individualized

SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

findings consistent with the mode of dysfunction. Comparison with previous examinations showing normal prosthetic valve function permits assessment of disease progression.

Transthoracic echocardiography is the first examination indicated when prosthetic valve dysfunction is clinically suspected (Chart 56).²³⁸ However, transesophageal echocardiography and, less frequently, cardiac CT angiography may help confirm the diagnosis and determine anatomical severity.

11.2. Step 2 – Assessment of the Etiology of Prosthetic Valve Dysfunction

Prosthetic valve stenosis: Mechanical valves generally have excellent durability; however, stenosis may develop because of device thrombosis, pannus, or a combination of both (Chart 57). PPM occurs when the effective orifice area (EOA) of the implanted prosthetic valve is inadequate relative to the patient's body surface area, particularly in patients with smaller valve annuli and/or an aortic prosthesis. In this setting, although the prosthesis is structurally normal, its opening area is insufficient. Consequently, an elevated transprosthetic gradient and an indexed EOA $\leq 0.85 \text{ cm}^2/\text{m}^2$ are observed immediately after valve surgery.

Bioprosthetic valves are more susceptible to degeneration over time, and stenosis may result from structural or nonstructural causes. Structural deterioration directly affects the leaflets, which become thickened and/or calcified. In nonstructural dysfunction, the prosthesis is anatomically normal, but PPM or paravalvular regurgitation is present. Particularly in older prostheses, PPM is often accompanied by additional abnormalities that restrict leaflet motion, such as pannus, thrombosis, or even vegetation in the setting of infective endocarditis. Although PPM is uncommon in

the mitral and tricuspid positions because these annuli are naturally larger, it may occur particularly after a valve-in-valve procedure because the transcatheter valve implanted in the previous surgical prosthesis must be smaller. Prosthetic valve stenosis can be distinguished from PPM by restricted leaflet motion and comparison with imaging obtained during the initial postoperative period. Prosthetic valve stenosis involves intrinsic leaflet dysfunction, with progressive worsening of prosthetic stenosis parameters.²³⁸

Prosthetic valve regurgitation: Prosthetic valve regurgitation is classified according to the location of the regurgitant flow as central or paravalvular.

Central dysfunction in a bioprosthetic valve may result from restricted leaflet motion secondary to calcification or from valve degeneration (leaflet perforation or rupture). In mechanical valves, central regurgitation results from impaired disc motion caused by pannus, thrombosis, or vegetation. Paravalvular regurgitation is characterized by regurgitant flow between the prosthetic valve and the native annulus. It is more common with mechanical valves than with bioprosthetic valves and is caused by suture dehiscence of the valve sewing ring. It may occur in the setting of infective endocarditis, annular degeneration, or incomplete expansion of TAVI.

11.3. Step 3 – Symptoms

The most common symptom is dyspnea, resulting from pulmonary venous and capillary congestion secondary to prosthetic valve dysfunction (Chart 58). However, angina and/or syncope may occur in significant stenotic or regurgitant aortic prosthetic valve dysfunction through the same pathophysiologic mechanisms observed in native valve dysfunction.

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Chart 56 – Step 1: Criteria for the determining the anatomical severity of anatomically significant prosthetic valve dysfunction

Characteristics of significant prosthetic valve dysfunction	
Physical examination	Clinical findings according to the predominant type of prosthetic valve dysfunction (stenosis or regurgitation)
Transthoracic echocardiography	- Determine the type of valve dysfunction and confirm its anatomical severity, particularly: – leaflet thickening – leaflet calcification and restricted motion – reduced EOA – valvular or paravalvular regurgitation – increased mean transvalvular gradient (aortic prosthesis: increase ≥ 20 mmHg with a mean gradient ≥ 30 mmHg; mitral prosthesis: increase ≥ 10 mmHg) - Assess worsening ventricular systolic function - Assess progression of cardiac chamber dilation - Assess indirect signs of elevated PASP
Transesophageal echocardiography	- Inadequate transthoracic echocardiographic window, diagnostic uncertainty, or need for improved anatomical assessment - Improved assessment of significant paravalvular regurgitation in patients with anatomy suitable for transcatheter treatment. Three-dimensional imaging is essential for this purpose - Improved assessment of prosthetic valve thrombosis and/or pannus
Hemodynamic assessment with a manometer	Only when clinical and echocardiographic findings are discordant
Cardiac and aortic CT angiography	- Assessment of prosthetic valve thrombosis/pannus and preprocedural planning for valve-in-valve implantation - Assessment of the aorta

CT: computed tomography; EOA: effective orifice area; PASP: pulmonary artery systolic pressure.

Chart 57 – Step 2: Etiology of significant prosthetic valve dysfunction

Etiologic characteristics	
Prosthetic valve stenosis	Mechanical prosthesis: – thrombosis – pannus Bioprosthesis: Structural: – leaflet degeneration – leaflet calcification Nonstructural: – endocarditis – thrombosis – pannus – prosthesis–patient mismatch (indexed EOA ≤ 0.85 cm²/m²) or ≤ 0.70 cm²/m² in patients with obesity), particularly severe when < 0.65 cm²/m² in patients with BMI < 30 kg/m² or < 0.55 cm²/m² in those with BMI > 30 kg/m²
Prosthetic valve regurgitation	Central: – leaflet degeneration (rupture or perforation) – leaflet calcification – thrombosis – pannus – endocarditis Paravalvular: – endocarditis – annular degeneration

BMI: body mass index; EOA: effective orifice area.

Chart 58 – Step 3: Assessment of symptoms in significant prosthetic valve dysfunction

Symptoms	
Dyspnea (NYHA II–IV)	• Pathophysiology varies according to the predominant dysfunction, leading to pulmonary venous and capillary congestion
Angina	• May occur in significant stenotic aortic prosthetic valve dysfunction
Syncope	• May occur in significant stenotic aortic prosthetic valve dysfunction

NYHA: New York Heart Association functional class.

11.4. Step 4 – Adverse Prognostic Features

The assessment of adverse prognostic features in prosthetic valve dysfunction is complex because many patients already have pulmonary hypertension, cardiac chamber dilation, or ventricular dysfunction resulting from the previous valvular heart disease (Chart 59). Therefore, progression of these abnormalities or the emergence of new parameters that were previously absent should be recognized and considered when determining the indication for intervention.

11.5. Step 5 – Modes of Intervention

The risks associated with valve reintervention are higher than those associated with the initial procedure. Factors to consider include advanced age, poor clinical status, ventricular dysfunction, concomitant CAD, pulmonary hypertension, and more challenging surgical access. In addition, comorbidities such as renal dysfunction, malnutrition, obesity, and diabetes increase the risk of reoperation.²³⁸ The choice between surgical intervention and a transcatheter procedure depends on the experience of the medical team, availability of a specialized center, patient- and prosthesis-specific characteristics, and shared decision-making by the Heart Team (Charts 60 and 61).

For prosthetic valve stenosis, the 2 main modes of intervention are redo surgical valve replacement and transcatheter valve-in-valve implantation. Surgery is the only available intervention for patients with a mechanical prosthesis, whereas either a transcatheter approach or redo surgical valve replacement may be considered for patients with bioprosthetic valve stenosis.

Despite its higher intrinsic procedural risk, redo surgical valve replacement is associated with a lower incidence of paravalvular regurgitation and PPM. It has also been associated with greater cumulative survival and lower pressure gradients in patients undergoing redo surgical aortic valve replacement.²³⁹ Therefore, surgery is the preferred mode of intervention whenever feasible.

Compared with surgery, a valve-in-valve procedure is an acceptable alternative for patients with symptomatic bioprosthetic valve stenosis who are at high surgical risk or considered inoperable. The VIVID registry, which analyzed 459 patients who underwent a valve-in-valve procedure, reported a 1-month mortality rate of 7.6%. Survivors experienced significant improvement in functional capacity (NYHA class I–II), and the 1-year overall survival rate was 83.2%.²⁴⁰ The most common complications of a valve-in-valve

procedure in the aortic position are PPM and coronary artery obstruction, whereas LVOT obstruction is the most important risk in the mitral position. Valve migration is another serious but less common complication.

For prosthetic valve regurgitation, the 3 main modes of intervention are redo surgical valve replacement, percutaneous closure of paravalvular regurgitation, and a valve-in-valve procedure for central regurgitation in patients with a bioprosthesis. The choice of strategy should consider surgical risk, whether the anatomy is suitable for the proposed approach, and the expertise of the procedural team.

Surgery is the preferred intervention for significant central or paravalvular prosthetic valve regurgitation in symptomatic patients or those with refractory hemolytic anemia. Although valve reoperation carries a higher risk than the initial surgery, mortality and morbidity rates are acceptable. A cohort study of 3380 patients undergoing redo aortic valve replacement demonstrated an acceptable difference in operative mortality, with rates of 4.6% after reoperation and 2.2% after the initial intervention ($p < 0.0001$), as well as relatively low complication rates.²³⁸ These findings were consistent with those reported by Shah et al. for the surgical repair of paravalvular regurgitation, with a mortality rate of 3% among 495 patients undergoing this procedure.²⁴¹ In patients with a bioprosthesis and significant central regurgitation secondary to leaflet degeneration, the risk of rapid disease progression because of leaflet rupture or perforation is considerable. Therefore, redo surgical valve replacement may be considered even in asymptomatic patients.

In patients with central bioprosthetic valve regurgitation who are at high surgical risk or considered inoperable, a transcatheter valve-in-valve procedure may be considered at a specialized center after individualized assessment and discussion by the Heart Team.

Percutaneous closure of paravalvular regurgitation may be an alternative for selected patients. Those most likely to benefit are symptomatic patients or those with hemolytic anemia refractory to medical therapy who are at high surgical risk or considered inoperable and have suitable anatomy. This approach should be considered at specialized centers after discussion by the Heart Team.

12. Prosthetic Valve Thrombosis

Prosthetic valve thrombosis is an uncommon event that occurs more frequently in mechanical prostheses in the mitral position. Its clinical presentation spans a broad spectrum,

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Chart 59 – Step 4: Assessment of adverse prognostic features in significant prosthetic valve dysfunction

Adverse prognostic features	
Echocardiography	• Development or progression of:
	- Ventricular systolic dysfunction
	- Left ventricular remodeling/pulmonary hypertension
	• Significant bioprosthetic valve calcification
Hemolytic anemia	• Occurs in patients with significant prosthetic valve regurgitation, particularly paravalvular regurgitation

Chart 60 – Step 5: Modes of intervention in significant prosthetic valve dysfunction

Mode	Considerations
Surgery (redo valve replacement)	• Treatment of choice • Indications: significant structural prosthetic valve dysfunction, prosthesis–patient mismatch, or paravalvular regurgitation, with symptoms and/or hemolytic anemia refractory to medical therapy
Transcatheter intervention (valve-in-valve)	• Structural dysfunction of a mitral, tricuspid, or aortic bioprosthesis in symptomatic patients at high surgical risk or considered inoperable (after Heart Team assessment)
Percutaneous closure of paravalvular regurgitation	• Significant paravalvular regurgitation associated with hemolytic anemia or heart failure symptoms (NYHA III–IV) in patients at high surgical risk who have anatomy suitable for the procedure; should be performed at a specialized center

NYHA: New York Heart Association functional class.

Chart 61 – Prosthetic valve dysfunction: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Surgical valve replacement	• Symptomatic significant structural prosthetic valve dysfunction	Strong / Moderate	I B	I C
	• Refractory hemolytic anemia	Strong / Low	I B	I C
	• Asymptomatic significant structural prosthetic valve dysfunction in a patient at low surgical risk	Strong / Low	IIa B	IIa C
Percutaneous closure of paravalvular regurgitation	• Paravalvular regurgitation with hemolysis or refractory heart failure symptoms in a patient with suitable anatomy and high surgical risk (after Heart Team assessment)	Strong / Moderate	IIa B	IIa B
Valve-in-valve	• Significant structural bioprosthetic valve dysfunction in a symptomatic patient at high surgical risk or considered inoperable (after Heart Team assessment)	Strong / High	IIa B	*

SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology. * IIa B: aortic position; IIb B: mitral and tricuspid positions.

ranging from asymptomatic disease to HF and low cardiac output, and is associated with high morbidity and mortality.²⁴²

Mechanical valve thrombosis occurs in 0.1% to 5.7% of patients undergoing surgery. It usually develops within the first 3 months of valve replacement but may occur at any time in the presence of inadequate anticoagulation or associated conditions.²⁴³ Bioprosthetic valves are less thrombogenic than

mechanical valves, with an estimated incidence of thrombosis ranging from 0.03% to 6%. However, its incidence has increased because of the growing number of transcatheter procedures and the use of advanced imaging techniques.²⁴² Bioprosthetic valve thrombosis commonly occurs within the first 3 months of implantation, although cases have been reported more than 5 years after surgery.²⁴⁴

Contemporary studies have also shown that subclinical bioprosthetic valve thrombosis, particularly after TAVI, is more common than previously recognized. It is detected primarily by cardiac CT and may have implications for valve durability.²⁴⁵⁻²⁴⁷ Recent reviews suggest that this phenomenon may represent an early stage in the spectrum of valve thrombosis, without overt hemodynamic consequences but potentially associated with early structural valve deterioration.²⁴⁸

Prosthetic valve thrombosis alters the transvalvular gradient and produces a stenotic valvular lesion. Its clinical consequences span a broad spectrum, from minimal symptoms to cardiogenic shock. Fundamental components of the evaluation include a targeted history addressing chest pain, new-onset dyspnea or worsening NYHA functional class, palpitations, peripheral edema, and signs of low cardiac output, in addition to the assessment of adherence to anticoagulant therapy, regular monitoring of anticoagulation, and measurement of prothrombin time and the international normalized ratio (INR), when indicated (Charts 62, 63, and 64).

Widely available ancillary tests, such as ECG and chest radiography, support clinical assessment, and echocardiography is essential.

Mechanical valve thrombosis should be suspected when transthoracic echocardiography, transesophageal echocardiography, or cardiac CT demonstrates restricted leaflet motion or debris consistent with thrombus adherent to the valve. An increase in the transprosthetic gradient of > 50% from baseline or an absolute increase of ≥ 10 mm Hg across a mechanical aortic prosthesis may also support the diagnosis.²⁴³

Initial assessment and diagnostic confirmation are usually performed with transthoracic echocardiography and may be complemented by transesophageal echocardiography.

When available, 4-dimensional cardiac CT in clinically stable patients and fluoroscopy may help confirm restricted leaflet motion and assist in evaluating differential diagnoses and complications.

In patients with bioprosthetic valve thrombosis without significant hemodynamic compromise (NYHA class I or II) or evidence of prosthetic valve obstruction on ancillary testing, oral anticoagulation and outpatient imaging surveillance are indicated. In patients with a mechanical prosthesis and a large (particularly > 8 mm) and/or mobile thrombus, which therefore carries a high risk of embolization, hospitalization for

Chart 62 – Step 1: Criteria for the determining the anatomical severity of prosthetic valve thrombosis

Characteristics of prosthetic valve thrombosis	
Clinical assessment	• Symptoms and signs suggestive of acute or worsening heart failure (dyspnea, chest pain, low cardiac output, or syncope)
	• Murmur consistent with a stenotic valvular lesion
	• Muffled mechanical valve click
Electrocardiogram	• Clinical history suggesting inadequate anticoagulation (INR outside the therapeutic range)
	• Findings consistent with the underlying disease that prompted valve surgery
Chest radiography	• Acute changes are uncommon
	• Findings consistent with the underlying disease that prompted valve surgery
	• Acute changes in the cardiac silhouette are uncommon
Echocardiography	• Pulmonary congestion may be present
	• Essential for diagnosis
	• Transesophageal echocardiography is preferred
Hemodynamic assessment (fluoroscopy)	• Documentation of thrombus adherent to the valve, including its location and size
	• Restricted leaflet motion

INR: international normalized ratio.

Chart 63 – Step 2: Etiology of prosthetic valve thrombosis

Etiologic characteristics	
Inadequate anticoagulation	• Discontinuation of anticoagulation
	• Drug–food interactions
	• INR below the therapeutic target

INR: international normalized ratio.

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Chart 64 – Step 3: Assessment of symptoms in prosthetic valve thrombosis

Symptoms	
Dyspnea	• Main symptom
	• Mild worsening: NYHA I–II
	• Red flag: NYHA III–IV
Precordial pain	• Possible coronary embolism
Low cardiac output/ syncope	• Suggests significant obstruction

NYHA: New York Heart Association functional class.

intravenous anticoagulation is indicated. If follow-up imaging after 5 to 7 days shows no resolution of the thrombus, or in cases of severe hemodynamic compromise (NYHA class III or IV), fibrinolysis or valve surgery may be indicated (Charts 65 and 66).²⁴⁹

Factors favoring fibrinolysis include high surgical risk, low bleeding risk, right-sided valve involvement, a first episode of valve thrombosis, and a thrombus area < 0.8 cm². Treatment options are alteplase, 10 mg as a bolus followed by 90 mg over 2 hours, or streptokinase, 500,000 IU over 20 minutes followed by 1,500,000 IU over 10 hours. The success rate of echocardiography-guided fibrinolysis exceeds 90%, whereas the rates of systemic embolism and major bleeding are below 2% (Charts 67 and 68).^{249,251}

Factors favoring surgery include a contraindication to fibrinolysis, high bleeding risk, low surgical risk, suspected pannus associated with thrombosis, and the need for other concomitant cardiac surgical procedures (eg, myocardial revascularization).²⁵² The 30-day mortality associated with redo surgical valve replacement is < 5% among patients in NYHA class I or II but may reach 10% to 15% among clinically unstable patients.²⁵³

A multicenter observational study compared thrombolysis with alteplase versus surgery in 158 patients at 8 centers; 70% had signs and symptoms of prosthetic valve thrombosis, and 75% had a prosthesis in the mitral position. Compared with surgery, the 6-hour and 25-hour slow-infusion thrombolytic regimens were associated with lower rates of overall complications (12% vs 62.7%) and thromboembolism (2.4% vs 5.3%), as well as lower rates of total bleeding (8.4% vs 16%) and 3-month mortality (2.4% vs 18.7%). These findings reinforce previous evidence regarding the efficacy and safety of the less invasive approach.²⁵⁴

Discussion by the *Heart Team* is recommended for decision-making in all clinical scenarios, with the risks of fibrinolysis and surgery assessed individually. In the presence of hemodynamic instability, surgery is preferred, except in patients at very high surgical risk.²⁵²

Subclinical thrombosis after TAVI, known as hypoattenuated leaflet thickening (HALT), should also be considered. HALT is characterized by leaflet thickening, with or without restricted leaflet motion, in the absence of corresponding clinical manifestations or criteria for prosthetic valve dysfunction or thrombosis. It is detected

primarily by CT²⁴⁵ and was reported 3 months after TAVI in 12.4% of patients receiving anticoagulation and 32.4% of those receiving dual antiplatelet therapy.²⁵⁵ HALT may be associated with early prosthetic valve degeneration but has not been associated with increased cardiovascular mortality. Initiation or adjustment of oral anticoagulation and serial imaging follow-up are recommended to exclude progression to prosthetic valve thrombosis.

12.1. Lifetime Management

The advent of transcatheter valve interventions has brought lifetime management to the forefront, making it an essential consideration in clinical practice. The first step is to determine whether the patient should undergo conventional surgery or a transcatheter intervention. For patients with an indication for valve surgery, the choice among valve repair, a bioprosthetic valve, and a mechanical prosthesis is fundamental. Both the mode of intervention (surgical or transcatheter) and type of prosthesis should be determined through shared decision-making involving a multidisciplinary evaluation, the Heart Team, the patient, and the patient's family. The Heart Team recommendation regarding the treatment strategy should be based on the available evidence and anatomical considerations, balancing the risks and benefits of the available options.

12.2. Selection of Prosthetic Valve Type

Shared decision-making regarding the type of prosthesis should consider several factors, including age, life expectancy, the patient's values and preferences, expected bioprosthetic valve durability, the risk of PPM, the anticipated need for and feasibility of reintervention, and the risks associated with anticoagulation with vitamin K antagonists after mechanical valve implantation (Chart 69).²⁵⁶

Bioprosthetic valves are generally preferred for patients with limited life expectancy, comorbidities that may require future surgical procedures, or a high risk of bleeding complications. Although bioprosthetic valves in younger patients have higher rates of degeneration and lower durability than those implanted in older patients, concerns about INR monitoring, dietary restrictions, inability to participate in certain physical activities, and drug interactions may lead patients to prefer a bioprosthetic valve over a mechanical prosthesis. Nevertheless, a mechanical prosthesis may be a suitable option for younger

Chart 65 – Step 4: Assessment of adverse prognostic features in prosthetic valve thrombosis

Finding	Interpretation
Thrombus > 8 mm or pedunculated	• High risk of embolization associated with thrombolysis
Pulmonary hypertension	• PASP ≥ 50 mm Hg at rest • Associated with mitral stenosis • Signs of right heart failure • Increased surgical risk
Atrial fibrillation associated with valve thrombosis	• Significant atrial remodeling
Subclinical leaflet thrombosis (TAVI)	• Relatively common after transcatheter procedures • Diagnosed by computed tomography • Adjustment or initiation of oral anticoagulation • Serial imaging follow-up

PASP: pulmonary artery systolic pressure; TAVI: transcatheter aortic valve implantation.

Chart 66 – Step 5: Modes of intervention in prosthetic valve thrombosis

Mode of intervention	Considerations
Thrombolysis	• rt-PA (alteplase), 10 mg as a bolus followed by 90 mg over 2 hours, or streptokinase, 500,000 IU over 20 minutes followed by 1,500,000 IU over 10 hours • Slow infusion*: t-PA (tenecteplase), 25 mg over 6 hours, repeated up to a total dose of 150 mg until valve function is restored
Valve surgery	• Reserved for patients at high risk of hemorrhagic complications or at prohibitive embolic risk

rt-PA: recombinant tissue plasminogen activator; t-PA: tissue plasminogen activator; IU: international unit. *A randomized trial demonstrated that surgery was not more efficacious and resulted in higher mortality than low-dose, slow-infusion t-PA.²⁵⁰

Chart 67 – Prosthetic valve thrombosis: Recommendations

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Thrombolysis	• Right-sided valve thrombosis	Strong / Moderate	Ila B	-
	• Thrombus < 8 mm, NYHA I–III, and persistent thrombus after intravenous anticoagulation	Strong / Moderate	Ila B	I B
Valve surgery	• NYHA IV and left-sided valve thrombosis	Strong / Moderate	I B	I B
	• Large (> 8 mm), mobile thrombus involving a left-sided valve	Strong / Low	Ila C	Ila C (> 1 cm)
Anticoagulation with vitamin K antagonists	• Acute thrombosis in a clinically stable patient	Strong / Moderate	Ila B	I B
	• Subclinical thrombosis after a transcatheter procedure or surgery	Strong / Low	Ila B	Ila B

NYHA: New York Heart Association functional class; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

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Chart 68 – Prosthetic valve thrombosis: Factors favoring surgery or fibrinolysis

Favoring surgery	Favoring fibrinolysis
• Experienced surgical team available	• Surgical team unavailable or inexperienced
• Low surgical risk	• High surgical risk
• High bleeding risk or contraindication to fibrinolytic therapy	• Low bleeding risk and no contraindication to fibrinolytic therapy
• Recurrent thrombosis	• First episode of prosthetic valve thrombosis
• NYHA functional class IV	• NYHA functional class I–III
• Thrombus area $>0.8 \text{ cm}^2$	• Thrombus area $\leq 0.8 \text{ cm}^2$
• Mobile thrombus	• Right-sided valve thrombosis
• Left atrial thrombus	• No left atrial thrombus
• Left-sided valve thrombus in a clinically unstable patient who cannot wait for the effect of heparinization	• Persistent left-sided valve thrombus after heparinization in a clinically stable patient

NYHA: New York Heart Association functional class.

Chart 69 – Factors favoring a mechanical or bioprosthetic valve

Favoring a mechanical prosthesis	Favoring a bioprosthetic valve
• Age <50 years or increased risk of structural valve deterioration (hyperparathyroidism or hemodialysis)	• Age >65 years
• Low risk associated with long-term anticoagulation	• Limited life expectancy
• Adherence to therapy and access to INR monitoring	• High risk of bleeding with long-term anticoagulation
• Another indication for long-term anticoagulation (eg, atrial fibrillation)	• Limited access to or difficulty with INR monitoring
• High risk associated with valve reintervention (porcelain aorta or previous radiation exposure)	• Follow-up at a heart valve center of excellence with favorable outcomes for surgical reinterventions and the capability to perform valve-in-valve procedures
• Small aortic annulus, which may preclude a future valve-in-valve procedure	• Desire for pregnancy in the near future

INR: international normalized ratio.

patients because of its greater durability, particularly when future interventions would carry high surgical risk, such as in patients with previous radiation exposure, a porcelain aorta, or a small aortic annulus.²⁵⁷⁻²⁶¹

The balance between the risk of reintervention for a bioprosthetic valve and that of long-term anticoagulation with warfarin should be discussed thoroughly. Bioprosthetic valve degeneration is more common in younger patients, whereas the risk of anticoagulation-related complications increases with age. Some patients may prefer to accept the risks of anticoagulation to avoid future surgery. In women with a desire for pregnancy, the risks of anticoagulation during pregnancy should be considered. Thromboembolic complications are less frequent among pregnant women with bioprosthetic valves, and pregnancy does not accelerate bioprosthetic valve deterioration.²⁶²

If vitamin K antagonist anticoagulation is contraindicated or the patient declines warfarin therapy, a bioprosthetic valve should be considered because direct oral anticoagulants

(DOACs) are contraindicated in patients with mechanical prostheses.²⁶³

Patients who undergo aortic valve replacement with a bioprosthetic valve before 50 years of age have marked and early structural valve deterioration. The 15-year risk of reoperation varies according to age at the initial surgery: 22% for patients aged 50 years, 30% for those aged 40 years, and 50% for those aged 20 years. Importantly, not all bioprosthetic valves have the same durability.²⁵⁹

For patients aged 50 to 65 years, the optimal choice remains uncertain. The greater durability of newer bioprosthetic valves may favor their use in this age group. Conversely, the risks of bleeding and thrombosis are low among patients with mechanical prostheses who have good adherence to warfarin therapy.^{240,264-266,267} Study findings in patients aged 50 to 65 years have varied. Some studies have shown lower mortality with mechanical aortic prostheses in patients younger than 60 years and with mechanical mitral prostheses in those younger than 65

years,^{268,269} whereas others have found no differences, mainly because of their observational design, limited information regarding prosthesis type, and insufficient statistical power.^{270,271} Large retrospective observational studies have demonstrated similar survival in this age group regardless of the type of prosthesis.²⁷²⁻²⁷⁴ However, studies such as that by Chikwe et al. have shown higher reoperation rates and a lower incidence of stroke among bioprosthetic valve recipients in this age group.²⁵⁸ Systematic reviews and meta-analyses suggest reduced mortality among patients who select mechanical prostheses up to 60 years of age and between 50 and 70 years of age, respectively.^{275,276} Therefore, for patients aged 50 to 65 years, the choice should be made through shared decision-making, with particular consideration given to the risks of thrombosis and bleeding with a mechanical prosthesis and the potential need for future intervention because of structural bioprosthetic valve deterioration.²⁶²

For patients older than 65 years, the risk of structural bioprosthetic valve deterioration decreases to 10% over 15 to 20 years, whereas the risk of warfarin-related bleeding increases. Because the expected durability of a bioprosthetic valve exceeds life expectancy in this age group, bioprosthetic valves are preferred to avoid bleeding risk.²⁵⁸

Aortic valve replacement with the patient's pulmonary autograft combined with homograft pulmonary valve replacement (the Ross procedure) is a complex operation that avoids implantation of an aortic prosthesis and eliminates the risks associated with anticoagulation. David et al. found that, in appropriately selected patients, durability may be comparable to that of mechanical aortic prostheses when the procedure is performed at centers with expertise in aortic root replacement.²⁷⁷ However, other studies have shown that both the pulmonary homograft in the aortic position and the pulmonary valve are at risk of future degeneration, with approximately 50% of patients requiring reintervention within 10 to 20 years. The procedure should therefore be reserved for young patients with suitable anatomy in whom the risks of anticoagulation are undesirable and should be avoided. Given its complexity, the Ross procedure should be performed at a heart valve center of excellence.^{257,278,279}

Strategies for patients with a small aortic annulus include annular enlargement and sutureless or rapid-deployment aortic valve replacement, which may shorten cardiopulmonary bypass time and potentially reduce perioperative complications.

12.3. Transcatheter Therapy (TAVI) Versus Conventional Surgery

Although open surgery has traditionally been the preferred treatment for patients with valvular heart disease, transcatheter therapy has recently emerged as an excellent option that is changing this paradigm. Large randomized controlled trials have shown that TAVI is a viable option for patients aged ≥ 70 years with significant aortic stenosis. It provides a less invasive alternative across a broad spectrum of patients, ranging from those considered inoperable or at very high surgical risk to those at low surgical risk.^{131,280-282}

Although current guidelines recommend a surgical bioprosthetic valve as the preferred option for patients aged < 65 years, TAVI has been increasingly used in younger

patients. Data from the United States show that, in 2021, approximately 50% of patients aged < 65 years with significant aortic stenosis were treated with TAVI.²⁸³ However, most studies of patients at low surgical risk included few individuals aged < 65 years (for example, 6.9% of participants in the PARTNER 3 trial). A U.S. study of 9557 patients undergoing aortic valve replacement that compared TAVI with surgery found a higher 6-year mortality in the TAVI group (23.3% vs 10.5%) and a greater need for permanent pacemaker implantation (10.7% vs 6.2%). No differences were observed in stroke, rehospitalization, or reintervention.²⁸⁴

The durability of TAVI remains incompletely understood. Moreover, challenges involving coronary access, TAV-in-TAV procedures, and surgery for TAV explantation mean that TAVI is not routinely recommended for patients aged < 70 years who are at low surgical risk. These considerations should also inform the choice of surgical bioprosthetic valve implantation or TAVI in patients aged ≥ 70 years.^{285,286}

12.4. Durability

TAVI provides favorable short-term outcomes (at 1 year), with shorter hospitalization and a lower composite risk of death, stroke, or rehospitalization than surgical bioprosthetic valve replacement (8.5% vs 15.1%; $p < 0.001$).¹³¹ However, evidence regarding the long-term durability of transcatheter heart valves remains limited because most early TAVI studies enrolled older patients whose survival was limited to only a few years after the procedure. Additional registries have provided longer follow-up, although they have predominantly included older patients and earlier generations of transcatheter valves. Sathananthan et al. reported a cumulative incidence of structural valve deterioration of 6.5% at 10 years among patients who underwent TAVI between 2005 and 2009.²⁸⁷ In another study, Testa et al. found an incidence of structural valve deterioration of 2.5% at 8 years among patients who underwent TAVI between 2007 and 2011.²⁸⁸ In addition, Holy et al. reported that only 5 of 152 patients required a second procedure during 9 years of follow-up.²⁸⁹

Analyses of randomized controlled trials and propensity score-adjusted studies comparing TAVI with conventional surgery have demonstrated favorable midterm durability of TAVI (7–8 years), comparable or even superior to that of surgical bioprosthetic valves. The incidences of stage 2 or 3 structural valve deterioration according to Valve Academic Research Consortium 3 (VARC-3) criteria were as follows:

- PARTNER 2A and the SAPIEN 3 intermediate-risk registry (S3IR): 9.5% after TAVI with SAPIEN XT, 3.9% with SAPIEN 3, and 3.5% after conventional surgery at 5 years.²⁹⁰
- Pooled analysis of the CoreValve U.S. High Risk Pivotal and SURTAVI trials: 1.82% after TAVI with CoreValve or Evolut (Medtronic) vs 2.67% after conventional surgery at 5 years.²⁹¹
- PARTNER 3: 7.6% after TAVI with SAPIEN 3 vs 7.3% after conventional surgery at 7 years.¹³³
- NOTION: 12.5% after TAVI with CoreValve vs 13.9% after conventional surgery at 10 years.¹³⁹

The rates of all-cause bioprosthetic valve failure were as follows:

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- PARTNER 2A–S3IR: 4.7% after TAVI with SAPIEN XT, 2.6% with SAPIEN 3, and 1.3% after conventional surgery at 5 years.
- PARTNER 3: 6.9% after TAVI with SAPIEN 3 vs 7.5% after conventional surgery at 7 years.
- NOTION: 9.7% after TAVI with CoreValve vs 13.8% after conventional surgery at 10 years.¹³⁹

These data indicate that, except for first-generation balloon-expandable valves, the midterm durability of transcatheter valves is at least equivalent to that of surgical bioprosthetic valves. Regarding clinical data from studies with longer follow-up, the NOTION trial reached the 10-year milestone. However, because mortality was high and only 25% of patients remained alive at 10 years, definitive conclusions regarding the long-term durability of TAVI remain limited.¹³⁹ In the PARTNER 2 trial, 10-year follow-up showed lower survival after TAVI than after surgery among patients at intermediate risk, particularly those who underwent TAVI through nonfemoral access.²⁹² At 6-year follow-up in the Evolut Low Risk trial, no difference was observed between TAVI and surgery in the composite outcome of death or stroke; however, the reintervention rate was higher after TAVI.²⁹²

Furthermore, patients assigned to TAVI in the NOTION trial received first-generation self-expanding valves, whereas 35% of the surgical valves were Trifecta or Mitroflow models, both of which have demonstrated durability concerns.

For patients whose life expectancy exceeds the anticipated durability of the selected prosthesis, detailed CT assessment is essential at the time of the initial valve intervention to anticipate future risks, always incorporating evaluation by the Heart Team.⁵

13. Coronary Artery Disease

CAD frequently coexists in candidates for valve surgery, particularly in the setting of degenerative aortic stenosis, with a prevalence ranging from 40% to 70%.²⁹³⁻²⁹⁵ Defining the coronary anatomy before valve intervention is essential to determine the feasibility of concomitant revascularization, periprocedural risk, and long-term prognosis.

13.1 Assessment of the Pretest Probability of Coronary Artery Disease

The investigation of CAD before valve surgery should be guided by the patient's probability of having CAD and clinical characteristics. Noninvasive assessment with coronary CT angiography may be performed in patients with low or intermediate pretest probability of CAD to exclude significant disease. If the examination reveals moderate to significant or indeterminate lesions, invasive coronary angiography should be performed.²⁹⁵

Invasive coronary assessment is mandatory in patients with a high probability of CAD, including those with atherosclerotic risk factors (eg, diabetes, dyslipidemia, or hypertension), suggestive symptoms, evidence of ischemia on functional testing, or a history of CAD, as well as men

aged > 40 years and postmenopausal women. Invasive coronary angiography should also be performed in patients with left ventricular dysfunction and when evaluating the etiology of secondary mitral regurgitation.²⁹⁵

13.2. Management of Coronary Artery Disease in Patients with an Indication for Valve Surgery

In patients with significant valvular heart disease and concomitant significant CAD (stenosis $\geq 70\%$ or $\geq 50\%$ in the left main coronary artery), the recommended standard approach is combined valve surgery and CABG, regardless of the presence of coronary symptoms, and should be considered as an incidental procedure.²⁹³⁻²⁹⁵ Although combined surgery increases immediate perioperative risk, it reduces the risk of perioperative myocardial infarction and improves long-term survival.²⁹³⁻²⁹⁵ In patients whose risk would increase substantially with combined surgery or whose coronary anatomy is unsuitable for CABG, percutaneous coronary intervention (PCI) guided by fractional flow reserve (FFR), is an option.²⁹³⁻²⁹⁶

Complete revascularization should be pursued whenever possible, and an internal thoracic artery graft should be used for significant lesions of the left anterior descending coronary artery. In patients with stenoses of 50% to 70%, management should be individualized; combined surgery may be considered as an incidental procedure to avoid another cardiac operation in the near future.²⁹³⁻²⁹⁵

13.3. Management of Coronary Artery Disease in Patients with an Indication for Transcatheter Aortic Valve Implantation

Among patients undergoing TAVI, the prevalence of CAD ranges from 44% to 81%, and many have multivessel disease.^{297,298} In this population, PCI should be considered for lesions with FFR ≤ 0.80 or stenosis $\geq 90\%$, taking into account the patient's age, anatomical severity, comorbidities, bleeding risk, and life expectancy (Chart 70).²⁹⁹

Three strategies may be used to manage coronary lesions in patients undergoing TAVI: PCI before, concomitantly with, or after the procedure. The most common strategy is PCI before TAVI because it may improve hemodynamic status before the valve procedure and prevent future complications related to untreated CAD. This approach is safe and feasible, even in patients with left main coronary artery disease.^{300,301} It also avoids potential difficulties with coronary access after TAVI, particularly with supra-annular valves.^{296,299}

Concomitant PCI and TAVI may be an attractive strategy for clinically unstable patients, those with very high aortic gradients, and those at high risk of coronary occlusion, such as patients with ostial lesions, a low left main coronary artery height, or a valve-in-valve procedure. This strategy may also reduce the risks associated with additional vascular access, resulting in fewer bleeding complications and a shorter overall procedure time. However, concomitant PCI may require a larger volume of contrast and increase the risk of renal failure.³⁰²⁻³⁰⁴

Chart 70 – Intervention for coronary artery disease concomitant with valve intervention

Intervention	Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Coronary artery bypass grafting	• Indication for surgical valve intervention and stenosis $\geq 70\%$ in an epicardial coronary artery or $\geq 50\%$ in the left main coronary artery	Strong / Low	Ila C	I C
Percutaneous coronary intervention	• Indication for transcatheter valve intervention and a proximal coronary lesion with FFR ≤ 0.80 or stenosis $\geq 90\%$	Strong / Low	Ila C	Ila B

AHA: American Heart Association; ESC: European Society of Cardiology; SBC: Brazilian Society of Cardiology; FFR: fractional flow reserve.

According to recent meta-analyses, PCI after TAVI may be associated with better short- and long-term clinical outcomes, including lower mortality, than PCI performed before or during TAVI.³⁰⁵

13.4. Management of Coronary Artery Disease in Patients with Moderate Valvular Heart Disease

Concomitant myocardial revascularization and valve surgery during the same operation are indicated in patients with significant valvular heart disease (Chart 70). When valvular heart disease is moderate, surgical management should be individualized with guidance from the Heart Team.^{306,307}

In patients with moderate secondary or ischemic mitral regurgitation, combined surgical treatment remains controversial. Current evidence suggests that adding mitral valve surgery to CABG in patients with moderate ischemic mitral regurgitation does not significantly reduce long-term mortality or improve left ventricular reverse remodeling compared with CABG alone.³⁰⁸⁻³¹⁰ The addition of mitral valve repair has also been associated with longer operative time and adverse neurologic events.^{311,312} Although mitral valve repair may reduce the severity of mitral regurgitation and improve symptoms, it has no significant impact on long-term survival or functional outcomes. Therefore, the decision to perform repair should be individualized with guidance from the Heart Team.^{311,313}

Management also remains controversial in patients with moderate aortic stenosis and concomitant significant CAD.^{306,307} Uncertainty regarding the rate of natural valve disease progression and survival without valve surgery complicates the decision to perform valve replacement at the time of CABG, particularly in older patients. Although concomitant valve replacement may eliminate the risk of reoperation, it exposes the patient to perioperative risks and long-term valve-related complications.³¹⁴

14. Anticoagulant and Antiplatelet Therapy

Anticoagulant and antiplatelet therapy aims to prevent thrombotic events while minimizing the risk of bleeding complications. Recent studies have examined this topic and provided increasingly robust evidence regarding the safety

and efficacy of these therapies across different valvular heart disease settings. Consequently, this has become one of the most rapidly evolving areas since the previous update of this guideline.

14.1. Native Valves

In patients with paroxysmal or permanent AF and rheumatic mitral stenosis, anticoagulation is the preferred strategy for preventing thrombotic events (Chart 71).³¹⁵ In all other cases, the risk of thrombotic events should be calculated using the CHA₂DS₂-VA score, with points assigned as follows: HF (1 point), hypertension (1 point), age ≥ 75 years (2 points), diabetes mellitus (1 point), history of stroke, transient ischemic attack, or thromboembolism (2 points), vascular disease (1 point), and age 65 to 74 years (1 point). Anticoagulation is recommended for a score ≥ 2 and should be considered for a score ≥ 1 .⁷⁶ Female sex is no longer included in the score in light of recent data showing a decline in stroke incidence in recent years and no clinically relevant sex-based difference in this setting.³¹⁶⁻³¹⁸

DOACs were evaluated in a retrospective Korean cohort study that compared their off-label use with warfarin in 2230 patients with mitral stenosis. DOAC use was associated with a lower incidence of the composite outcome of stroke and systemic embolism, with bleeding rates similar to those observed with vitamin K antagonists.³¹⁹ These findings should be interpreted with caution because of important study limitations, including its observational design, the absence of data on time in therapeutic range (TTR) with warfarin, a lack of information on the etiology and anatomical severity of mitral stenosis, and incomplete matching between groups. Although TTR was not reported for this population, another Korean cohort of patients with AF and stroke demonstrated suboptimal anticoagulation control with warfarin: of nearly 34,000 INR measurements, only 44.6% were within the therapeutic range, whereas 41.7% showed an INR < 2.0 .³²⁰

The INVICTUS noninferiority trial enrolled 4531 patients with rheumatic heart disease and AF, predominantly with moderate to significant mitral stenosis, who were randomly assigned to receive warfarin or rivaroxaban (20 mg or 15 mg once daily, adjusted for renal function). The incidence of stroke was numerically higher in the rivaroxaban group (90 vs 65 events), as was mortality (552 vs 442 deaths). The difference

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Chart 71 – Indications for oral anticoagulation

Clinical condition	Medication	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Native valves				
• Rheumatic mitral stenosis with atrial fibrillation and/or left atrial thrombus*	Warfarin	Strong / Moderate	I C	I B
	DOACs when warfarin cannot be used	Weak / Low	-	III B
• Other valvular heart diseases with atrial fibrillation	Warfarin	Strong / Moderate	I A	-
	DOACs	Strong / Moderate	I A	I A
Surgical treatment				
• Concomitant ablation of atrial fibrillation or atrial flutter during valve surgery		Strong / Moderate	Ila B	I A (mitral valve surgery) Ila B (surgery on other valves)
• Concomitant left atrial appendage closure during valve surgery		Strong / Moderate	Ila B	I B
Valve repair				
• Sinus rhythm + mitral valve repair (first 3 months)	Warfarin	Weak / Low	-	-
	DOACs	Weak / Low	-	Ila B
	Aspirin	Weak / Low		Ila B
Bioprosthetic valves				
• Atrial fibrillation (first 3 months)	Warfarin	Strong / Moderate	Ila B	-
	DOACs	Weak / Moderate	-	-
• Atrial fibrillation (long-term)	Warfarin	Strong / High	I A	-
	DOACs	Strong / High	I A	Ila B
• Sinus rhythm – mitral valve (first 3 months)	Warfarin	Weak / Low	Ila B	Ila B
	DOACs	Weak / Low	-	-
	Aspirin	Weak / Low	Ila B	-
• Sinus rhythm – aortic valve (first 3–6 months)	Warfarin	Weak / Low	Ila B	Ila B
	DOACs	Weak / Low	-	-
	Aspirin	Weak / Low	Ila B	Ila B
• Sinus rhythm – aortic or mitral valve (long-term)	Warfarin	Weak / Very low		
	DOACs	Weak / Very low	-	-
	Aspirin	Weak / Low	Ila B	IIb C
TAVI				
• Atrial fibrillation	Warfarin	Strong / High	I A**	I B
	DOACs	Strong / High	I A	I B
	Warfarin	Not indicated	3 months IIb B	III A
• Sinus rhythm	DOACs	Not indicated	III B	III A
	Aspirin or clopidogrel	Strong / Moderate	Ila B	I A (for 1 year) Ila C (after 1 year)

• Sinus rhythm + angioplasty and stenting	Aspirin + clopidogrel for up to 12 months according to stent type	Strong / High	-	-
• Atrial fibrillation + angioplasty and coronary stenting	OAC (warfarin or DOAC) + aspirin + clopidogrel for > 1 week but < 1 month, followed by clopidogrel + OAC (warfarin or DOAC) for 6–12 months according to stent type. Thereafter, OAC (warfarin/DOAC) alone	Strong / Moderate	-	-
Mechanical valves				
	Warfarin	Strong / High	I A***	I B
	DOACs	Not indicated	III B	III A
	Routine warfarin + aspirin	Not indicated	IIb B	IIa B ****
	Warfarin + aspirin after a thromboembolic event despite a therapeutic INR	Strong / Moderate	-	-
• Indication for heparin bridging for procedures with a high bleeding risk	Noncardiac procedures when the INR is in the therapeutic range in patients at high thrombotic risk	Strong / Moderate	IIa C	IIa B

OAC: oral anticoagulation; DOAC: direct oral anticoagulant; TAVI: transcatheter aortic valve implantation; INR: international normalized ratio; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

* Consider warfarin anticoagulation in patients with mitral stenosis and episodes of atrial tachycardia or left atrial enlargement with spontaneous echocardiographic contrast.

** Warfarin in patients with atrial fibrillation: IIa B for the first 3 months after implantation and I A thereafter.

*** For patients with a mechanical aortic valve and additional risk factors for thromboembolism (eg, atrial fibrillation, previous thromboembolism, ventricular dysfunction, hypercoagulable state) or an older-generation prosthesis (eg, ball-in-cage): warfarin with a target INR of 3.0 – I B. For patients with a mechanical bileaflet or aortic tilting disk valve and no thromboembolic risk factors: warfarin with a target INR of 2.5 – I B.

**** In the presence of concomitant atherosclerotic disease and low bleeding risk.

in restricted mean survival time was –72 days (95% CI, –117 to –28), primarily because of a greater number of sudden cardiac deaths and deaths from mechanical valve failure or HF. Consequently, major cardiovascular events occurred more frequently among patients treated with rivaroxaban. Based on these findings, warfarin remains the treatment of choice for patients with AF associated with rheumatic heart disease. The relative benefit of warfarin became more apparent after 12 to 18 months of follow-up, in parallel with progressive improvement in anticoagulation control. At baseline, only 33.2% of participants had an INR between 2.0 and 3.0; this proportion increased to 56.1% at 6 months, 59.0% at 1 year, 65.3% at 2 years, and 64.1% at 4 years. These findings suggest that the greater protection observed with warfarin may be related to the increase in TTR during follow-up, in addition to a potential protective effect of anticoagulation in the setting of rheumatic heart disease.³²¹

Warfarin can be safely initiated at 5 mg/day in patients younger than 65 years and at 2.5 mg/day in those aged 65 years or older. Prothrombin time should be measured on day 3 to assess for an excessive response to treatment and again on day 5, after which the dose should be adjusted as needed. During this phase, testing should be performed at intervals of no more than 5 days until the therapeutic range is achieved. The INR is generally monitored monthly, and monthly monitoring is reasonable in patients receiving a stable long-term dose who have not been exposed to new factors that may interact with warfarin (Chart 72). If the INR is outside the target range, it should be reassessed earlier, within 1 to 2 weeks. Dose adjustments should correspond to a mean of 10% to 15% of the total weekly dose, and the factors responsible for INR variability should be investigated. Point-of-care prothrombin time testing provides rapid and reliable results; however, its availability remains limited because of the high cost of the device and test strips.

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Chart 72 – Warfarin dose adjustment

INR	Dose adjustment
≤ 1.5	Increase the total weekly dose by 15%
1.51–1.99	Increase the total weekly dose by 10%
2.0–3.0*	Maintain the current dose
3.01–4.0	Reduce the total weekly dose by 15%
4.01–4.99	Hold 1 dose and reduce the total weekly dose by 10%
5.0–8.99	Hold until INR is 2.0–3.0, then restart at a total weekly dose reduced by 15%
≥ 9.0	Admit the patient to the hospital; hold warfarin for approximately 4 days; administer oral vitamin K, 1.0–2.5 mg, repeating the dose after 24–48 hours if INR has not decreased to <5.0; and restart anticoagulation when INR approaches the target range (<4.0)

INR: international normalized ratio. * When the target INR range is 2.5–3.5, dose-adjustment thresholds should be increased by 0.5, except when INR is ≥9.0.

In clinical practice, anticoagulation control is frequently poorer than that achieved in clinical trials. Although the optimal protective effect of warfarin is achieved with a TTR > 65%, data from the Brazilian RECALL registry showed that among 4585 patients followed for 1 year, the mean TTR was only 49.5%.^{322,323} Thus, although warfarin remains the treatment of choice, its effectiveness depends directly on the quality of INR control. In strictly exceptional circumstances, DOACs may be considered after all strategies to optimize warfarin therapy have been exhausted, including repeated attempts at dose adjustment and pharmacologic and dietary counseling, if the INR remains extremely labile or regular anticoagulation monitoring is not feasible where the patient lives. In this situation, the patient should be clearly informed that this strategy may provide less protection against thromboembolism than well-controlled warfarin therapy. This counseling, the reasons for the therapeutic choice, and the patient's agreement should be documented in the medical record.

Finally, when valve surgery is indicated in a patient with AF, rhythm control through concomitant surgical ablation should be considered.³²⁴ In addition, left atrial appendage closure in patients with AF reduces embolic events and improves mid- to long-term survival.³²⁵ Maintenance of sinus rhythm is beneficial over the long term; however, anticoagulation should not be discontinued in patients with an established indication, including after left atrial appendage closure, except in selected patients at very high bleeding risk.

In patients without AF, anticoagulation may be considered when mitral stenosis is associated with a previous embolic event, left atrial thrombus or spontaneous echocardiographic contrast, a left atrial diameter ≥ 50 mm or volume ≥ 50 mL/m², or sustained atrial tachycardia.

14.2. Valve Repair

After valve repair surgery in patients in sinus rhythm, evidence supporting the optimal antithrombotic strategy remains limited and is based on observational studies.^{326–330} A prospective multicenter study demonstrated a higher incidence of thromboembolic events during the first 6 weeks

after mitral valve repair in the absence of antithrombotic therapy.³²⁶ After mitral valve repair, antiplatelet therapy with aspirin, 75 to 100 mg/day, may be considered for the first 3 months. A systematic review of 5093 patients found no significant differences between vitamin K antagonists and antiplatelet therapy in thromboembolic events or mortality during this period.³³⁰ Data on DOACs after mitral valve repair remain limited. Observational data suggest efficacy and safety similar to those of warfarin, although randomized controlled trials are still required to confirm these findings.³²⁸

14.3. Bioprosthetic Valves

In patients with a bioprosthetic valve and AF, anticoagulation is indicated regardless of the CHA₂DS₂-VA score. Evidence regarding DOAC use in this setting derives primarily from subgroup analyses of the ARISTOTLE and ENGAGE AF-TIMI 48 trials, the DAWA pilot study, and the Brazilian multicenter randomized RIVER trial.^{331–334} These analyses, which compared DOACs with warfarin in subgroups of patients with bioprosthetic valves, found no significant differences in clinical outcomes.^{331–333}

The RIVER trial enrolled 1005 patients and confirmed the noninferiority of rivaroxaban to warfarin. A subgroup analysis suggested a longer time to the event with rivaroxaban than with warfarin during the first 3 months after surgery.³³⁴ However, because this was a post hoc analysis, caution is recommended when using DOACs during this period. Therefore, vitamin K antagonists are recommended for the first 3 months after bioprosthetic valve implantation in patients with AF. Thereafter, vitamin K antagonist therapy may be continued or the patient may transition to a DOAC. DOAC use during the initial 3-month period may be considered in selected situations, such as in patients with highly labile INR or when regular INR monitoring is not feasible.

In patients with a bioprosthetic valve who do not have AF or another indication for anticoagulation, aspirin or anticoagulation during the first 3 to 6 months after surgery has been considered. However, the available evidence is inconsistent and derived from only a few small randomized studies.^{335–345} Therefore, current

guidelines do not recommend routine aspirin or anticoagulation during the first 3 to 6 months after surgery in patients with a bioprosthetic valve who do not have AF or another indication for anticoagulation. Long-term anticoagulation is not indicated in these patients.^{340,346} Specifically for prostheses in the aortic position, because of lower thrombogenicity, vitamin K antagonists have not demonstrated an additional benefit over aspirin.³⁴⁷ In addition, the randomized ENAVLE trial, which enrolled 218 patients without AF who underwent valve repair or aortic or mitral bioprosthetic valve implantation, demonstrated that edoxaban was noninferior to warfarin during the first 3 months after surgery.³⁴⁸

14.4. Mechanical Prostheses

Mechanical prostheses are associated with a high risk of thrombotic events. In a landmark meta-analysis, the annual incidence of major thrombotic events – including prosthetic valve thrombosis, stroke with permanent neurologic deficit, and peripheral ischemia requiring surgical intervention – was approximately 1% among patients receiving vitamin K antagonist anticoagulation. This risk was 4-fold higher among patients receiving no anticoagulation or antiplatelet therapy alone.³⁴⁹

Oral anticoagulation with a vitamin K antagonist is mandatory and should be continued indefinitely in all patients with a mechanical prosthesis. To date, no DOAC has demonstrated safety or efficacy in this setting. Two randomized controlled trials were terminated early because of increased adverse events in the DOAC groups. The REALIGN trial, which compared dabigatran with warfarin in patients with mechanical prostheses, found higher incidences of bleeding and thromboembolic events with dabigatran, particularly during the early postoperative period.³⁵⁰ Similarly, the PROACT Xa trial, which evaluated apixaban in patients with an On-X mechanical aortic valve beginning 3 months after implantation, was terminated early because of a higher incidence of thrombotic events in the apixaban group, despite concomitant aspirin use by 94% of participants.³⁵¹

For mechanical aortic valves without additional thromboembolic risk factors, the target INR is 2.5, with a therapeutic range of 2.0 to 3.0. For mechanical mitral valves, the target INR is 3.0, with a therapeutic range of 2.5 to 3.5. A higher INR target may also be considered for patients with mechanical aortic valves and concomitant AF, thrombotic events despite an INR within the therapeutic range, or reduced ejection fraction. The ongoing randomized LIMIT trial (NCT03636295), which is in the recruitment phase, aims to evaluate a target INR of 1.5 to 2.5 in patients with bileaflet mechanical heart valves in the aortic position other than On-X. For an On-X aortic valve, the target INR may be reduced to 1.8 (1.5–2.0) in combination with aspirin, 75 to 100 mg/day, based on the randomized PROACT trial.³⁵²

14.5. Transcatheter Aortic Valve Implantation

In patients undergoing TAVI who do not have AF or another formal indication for anticoagulation, single antiplatelet therapy is the recommended strategy for preventing thrombotic events. Historically, dual antiplatelet therapy was

used by extrapolation from post-PCI management. However, the POPular TAVI cohort A trial demonstrated that single antiplatelet therapy provides antithrombotic protection similar to that of dual antiplatelet therapy, with a lower risk of bleeding.³⁵³

Prophylactic anticoagulation after TAVI in patients without a previous indication for anticoagulation has also been investigated following reports of subclinical leaflet thrombosis in this setting. In the GALILEO trial, which compared rivaroxaban with antiplatelet therapy in patients without a previous indication for anticoagulation, rivaroxaban was associated with a higher risk of bleeding without a significant reduction in thromboembolic events.³⁵⁴ Similarly, the ATLANTIS trial demonstrated no benefit of apixaban over antiplatelet therapy in patients undergoing TAVI without an indication for anticoagulation.³⁵⁵ Therefore, prophylactic anticoagulation is not recommended in these patients.

For patients with AF and/or another indication for anticoagulation, anticoagulation alone is the preferred therapy. The POPular TAVI cohort B trial compared anticoagulation alone with anticoagulation plus clopidogrel during the first 3 months after TAVI and found a lower risk of bleeding with anticoagulation alone. Approximately 24% of participants received a DOAC, whereas the remainder received a vitamin K antagonist.³⁵⁶ The ENVISAGE-TAVI AF trial compared edoxaban with warfarin in 1426 patients and demonstrated a similar net clinical benefit with the 2 strategies. However, edoxaban was associated with a higher risk of bleeding, particularly gastrointestinal bleeding.³⁵⁷ Therefore, either a vitamin K antagonist or a DOAC may be used in patients undergoing TAVI who have a formal indication for anticoagulation, with careful monitoring for gastrointestinal bleeding in those receiving a DOAC.

14.6. Bleeding Risk Assessment

The HAS-BLED score is the most widely used tool for estimating bleeding risk in patients receiving oral anticoagulation. The score includes the following factors: uncontrolled hypertension (1 point), renal dysfunction (1 point), hepatic dysfunction (1 point), history of stroke or transient ischemic attack (1 point), history of bleeding (1 point), labile INR (1 point), age > 65 years (1 point), and drug or alcohol use (1 or 2 points). Patients with a score ≥ 3 are considered at high risk of bleeding.³⁵⁸ Because many of these factors are also included in the CHA₂DS₂-VA score, individuals at high bleeding risk frequently also have a high thromboembolic risk.

In the Brazilian RECALL registry, physician judgment was the leading reason anticoagulation was not prescribed to patients with a formal indication, accounting for nearly 25% of cases.³⁵⁹ Fall risk in older adults is commonly considered in this decision. However, one study estimated that approximately 295 falls in 1 year would be required to outweigh the benefits of warfarin anticoagulation in preventing thrombotic events.³⁶⁰ Although this estimate has limitations and was calculated before DOACs became available, fall risk or a subjective perception of frailty should not be used in isolation as a contraindication to anticoagulation.

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Bleeding risk assessment should extend beyond the HAS-BLED score. Additional factors should be considered, including adherence to treatment, a history of major bleeding, comorbidities associated with an increased thrombotic or hemorrhagic risk, and the patient's socioeconomic status. The latter includes the feasibility of INR monitoring for patients receiving warfarin and potential access to DOACs. Identifying these factors permits targeted interventions for modifiable conditions and appropriate patient counseling regarding the management of trauma, bleeding, and drug interactions. A high HAS-BLED score should not be used in isolation to contraindicate anticoagulation but rather to guide strategies for reducing bleeding risk.

14.7. Postoperative Atrial Fibrillation

Postoperative AF (POAF) is common after heart valve surgery, with an incidence of up to 50% to 60%.^{361,362} Major risk factors for POAF include advanced age, male sex, obesity, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, rheumatic heart disease, left atrial enlargement, reduced left ventricular ejection fraction, hypokalemia, hypomagnesemia, dopamine or dobutamine use, and preoperative withdrawal of beta-blockers.^{363,364}

A meta-analysis of 57 studies including 246,340 patients demonstrated that POAF is associated with higher perioperative mortality and greater incidences of stroke, myocardial infarction, and acute kidney injury, as well as longer hospital and intensive care unit stays. In the long term, POAF is also associated with higher mortality, a greater risk of stroke, and an increased likelihood of progression to permanent AF.³⁶² However, it remains unclear whether these associations reflect direct causality or indicate patients at higher risk. Another meta-analysis of 55 studies involving 540,209 patients undergoing heart surgery found that approximately 25% of patients who developed POAF progressed to permanent AF within 5 to 10 years.³⁶⁵

Evidence regarding the specific treatment of POAF, particularly in patients with valvular heart disease, remains limited. In general, beta-blockers should not be initiated routinely solely for prophylaxis before valve surgery because of the risk of clinical decompensation. This strategy may be considered in selected settings, such as mitral stenosis. Patients already receiving beta-blockers preoperatively should continue treatment during the perioperative period.³⁶⁶ For POAF episodes lasting < 24 to 48 hours, restoration of sinus rhythm should be attempted. If AF recurs or an episode lasts > 24 to 48 hours, anticoagulation should be considered unless contraindicated.

14.8. Periprocedural Bridging Anticoagulation

Patients receiving oral anticoagulation who are scheduled to undergo a surgical or invasive procedure should be assessed to determine whether treatment must be temporarily discontinued. In patients receiving a DOAC, management should consider the bleeding risk of the procedure and the elimination time of the drug. Heparin bridging is not recommended in these patients. For procedures with a very low bleeding risk, the DOAC may be continued;

alternatively, the preceding evening dose may be omitted to avoid performing the procedure during the peak drug effect. For low-bleeding-risk interventions, DOAC therapy should be discontinued 24 hours before the procedure. For procedures with a high bleeding risk, DOAC therapy should be discontinued for 48 hours. In patients with low body weight (< 50 kg), renal dysfunction, or concomitant medications that prolong the DOAC effect, an additional 24 hours of interruption should be considered.³⁶⁷

In patients receiving vitamin K antagonists, the decision regarding bridging therapy should balance thromboembolic risk against the bleeding risk of the procedure. For emergency surgery, the anticoagulant effect should be reversed immediately. Before a procedure with a low bleeding risk, the INR should be measured to ensure that it is within the therapeutic range, allowing the procedure to be performed without discontinuing the vitamin K antagonist. When anticoagulation must be interrupted, thromboembolic risk should be carefully assessed to determine whether heparin bridging is required.

The BRIDGE trial included 1884 patients who were randomly assigned to temporary interruption of vitamin K antagonist therapy with or without perioperative heparin bridging. Routine bridging provided no benefit and increased bleeding risk. However, the trial excluded patients at high thrombotic risk, including those with mechanical heart valves or recent thrombotic events.³⁶⁸ Thus, heparin bridging is recommended for patients at high thromboembolic risk, including those with a mechanical prosthesis, rheumatic valvular heart disease, a CHADS₂ score of 5 or 6, stroke or transient ischemic attack in the previous 3 months, recent venous thromboembolism, or severe thrombophilia. Bridging therapy may be considered for patients at intermediate risk, including those with a CHADS₂ score of 3 or 4, venous thromboembolism in the previous 3 to 12 months, mild thrombophilia, or active cancer. In patients at low thromboembolic risk, heparin bridging is not recommended; discontinuation of the vitamin K antagonist alone is sufficient.³⁶⁹

15. Rheumatic Fever and Rheumatic Heart Disease

Rheumatic fever and chronic rheumatic heart disease are fundamentally nonsuppurative complications of pharyngotonsillitis caused by group A beta-hemolytic streptococci (*Streptococcus pyogenes*) and result from a delayed immune response to this infection in genetically predisposed populations. Most cases of rheumatic heart disease occur in low- to middle-income countries, which account for more than 80% of cases identified worldwide.³⁷⁰⁻³⁷²

Rheumatic fever was considered a global health problem for many years. However, during the first half of the 20th century, its incidence declined dramatically in high-income countries following improvements in health care, housing, and education. Treatment of group A streptococcal pharyngotonsillitis within 9 days of symptom onset remains the cornerstone of rheumatic fever control.³⁷³⁻³⁷⁵

Rheumatic fever is underdiagnosed and often recognized only after rheumatic carditis has caused permanent valve

damage, leading to hospitalizations and surgical procedures in young adults. Management of recurrent rheumatic carditis requires a multifaceted approach that includes early diagnosis, appropriate treatment, and robust preventive strategies.^{229,372,376}

15.1. Epidemiology and Pathophysiology

Rheumatic heart disease is estimated to affect approximately 30 to 40 million people worldwide and accounts for 1.0% to 1.5% of all cardiovascular deaths.^{229,376} In Brazil, it remains the leading cause of valvular heart disease, with a prevalence of 3.6 cases per 1000 population.³⁷⁷ Evidence dating from the early 1900s shows that both clinical and subclinical group A streptococcal throat infections precede outbreaks of rheumatic fever, making early treatment of pharyngotonsillitis the cornerstone of primary prevention.³⁷³ Since the early 2000s, it has also been proposed that group A streptococcal skin infection, known as impetigo, may be associated with the development of rheumatic fever activity in Australian Aboriginal populations.^{371,378}

Valvulitis is the predominant manifestation of rheumatic carditis during childhood, whereas myocardial and pericardial involvement occur less frequently during this period. Decompensated HF occurs in only 10% of patients with acute rheumatic fever and has been described mainly during subsequent episodes of reactivation of rheumatic carditis in adulthood. Importantly, after the first episode of rheumatic fever, progression to chronic valvular heart disease may occur in more than half of patients over 10 to 15 years of follow-up. Approximately 16% may develop symptomatic significant aortic and/or mitral valve disease requiring intervention.³⁷⁹⁻³⁸¹

15.2. Diagnosis

The diagnosis of rheumatic fever is based on the Jones criteria, which include major manifestations (arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules) and minor manifestations (fever, polyarthralgia, and elevation of erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP]). A definite initial episode of rheumatic fever requires either 2 major criteria or 1 major and 2 minor criteria, as summarized in Chart 73. The populations of Brazil, Australia, India, Africa, and several low- to middle-income countries are considered at high risk of rheumatic fever. However, in high-income countries, which are considered low-risk settings, certain manifestations classified as major criteria in high-risk populations, such as polyarthralgia or monoarthritis, are considered minor criteria.

The Jones criteria, first described in 1944 and subsequently modified, with the most recent revision published in 2015, remain the gold standard for the diagnosis of a first outbreak of rheumatic fever. Classification into major and minor criteria is based on the specificity rather than the frequency of each manifestation.^{382,383} The diagnosis is primarily clinical, although ancillary tests demonstrating an inflammatory process and evidence of prior streptococcal infection support the diagnosis. ECG and echocardiography are also essential for assessing cardiac involvement and the presence of valvular heart disease.

The probability of rheumatic fever is high when there is evidence of prior streptococcal infection, determined by elevated antistreptolysin O (ASO) and anti-deoxyribonuclease B (anti-DNase B) titers, together with at least 2 major criteria

Chart 73 – Updated criteria for the diagnosis of acute rheumatic fever

Initial episode of rheumatic fever	Evidence of prior group A streptococcal infection + 2 major manifestations, OR 1 major + 2 minor manifestations
Possible rheumatic fever (first episode)	- 1 major or 1 minor manifestation, OR - No evidence of prior group A streptococcal infection
Recurrent episode of rheumatic fever in a patient with documented history of rheumatic fever or rheumatic heart disease	1 major manifestation*
Major manifestations	Minor manifestations
• Carditis (including subclinical evidence of rheumatic valvulitis on echocardiogram) • Migratory polyarthritides or aseptic monoarthritis or polyarthralgia** • Sydenham's chorea • Erythema marginatum • Subcutaneous nodules	• Fever $\geq 38^{\circ}\text{C}$** • Monoarthralgia • ESR ≥ 30 mm/h or CRP ≥ 30 mg/L** • Prolonged PR interval on electrocardiogram

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein. * This modification of the criteria for recurrence is based on evidence from recent studies describing patients with isolated carditis, most without other major or minor criteria, who presented with ventricular dysfunction and improved after corticosteroid therapy.^{389,390} ** In high-income countries considered to be at low risk, polyarthralgia is classified as a minor criterion. In addition, in low-risk populations, fever qualifies as a minor criterion at a temperature $\geq 38.5^{\circ}\text{C}$, and ESR is now ≥ 60 mm/h.

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or 1 major and 2 minor criteria. However, successive revisions have increased the specificity of the diagnostic criteria at the expense of sensitivity, particularly because evidence of prior streptococcal infection is required. Importantly, estimates suggest that approximately 20% of patients with acute rheumatic fever may not have elevated ASO titers.³⁸⁴

Because other causes of chorea are rare, its presence supports a diagnosis of rheumatic fever even in the absence of other criteria or evidence of prior streptococcal infection. Similarly, the initial clinical manifestations of indolent carditis may be subtle; by the time the patient seeks medical attention, cardiac abnormalities may be the only manifestation, and acute phase reactants and anti-streptococcal antibody titers may be normal. Furthermore, in patients with a history of a previous acute episode of rheumatic fever or confirmed chronic rheumatic heart disease, recurrent carditis in adulthood may be diagnosed based on a single major criterion. Recent studies suggest that rheumatic fever reactivation in adults often presents as isolated carditis, frequently as rheumatic myocarditis leading to ventricular dysfunction, without other major or minor criteria.^{385,386} Therefore, once alternative diagnoses have been excluded, chorea, indolent carditis, and recurrent rheumatic carditis represent 3 exceptions in which the Jones criteria should not be applied rigidly. In these cases, the presence of 1 major criterion is sufficient to establish the diagnosis and initiate treatment.

15.3. Major Criteria

Carditis: Carditis is the most severe manifestation of rheumatic fever because it is the only manifestation that may cause permanent sequelae and death. It occurs in 40% to 70% of first episodes, although more recent series using echocardiographic assessment have reported higher prevalences.^{379,387} Carditis tends to develop early, and cardiac involvement is characterized by pancarditis (endocarditis, pericarditis, and myocarditis); however, valve lesions are the main determinants of the clinical presentation and prognosis. Pericardial involvement is uncommon and does not occur in isolation. Large pericardial effusions and cardiac tamponade are rare. During initial outbreaks, myocarditis generally does not cause ventricular dysfunction.

Endocardial involvement is the diagnostic hallmark of rheumatic carditis and most frequently affects the mitral and aortic valves. During the acute phase, mitral regurgitation is the most common lesion, followed by aortic regurgitation. Conversely, valve stenosis develops later, during the chronic phase. Three murmurs are characteristic of the first episode and may not represent permanent valve dysfunction: the systolic murmur of mitral regurgitation, the Carey Coombs murmur (a diastolic rumble related to the increased flow caused by mitral regurgitation), and the diastolic murmur of aortic regurgitation. The absence of a murmur does not exclude cardiac involvement.²²⁹ Mild carditis without other manifestations of the disease may frequently go unnoticed, and the valve lesion may be detected only during routine medical examinations or subsequent outbreaks throughout the patient's life. Depending on the extent of cardiac involvement, the severity of carditis ranges from subclinical to fulminant disease.

Subclinical carditis is characterized by a normal cardiovascular examination with echocardiographic evidence of pathological valvular regurgitation. It should preferably be identified through population-based echocardiographic screening for rheumatic sequelae. Screening should ideally be performed in children and young adults (up to 20 years of age) using portable devices or point-of-care echocardiography performed by trained health care professionals (Chart 74).^{388,389} The frequent inadequate treatment of streptococcal pharyngotonsillitis, including antibiotic courses of insufficient duration or dosage, has reduced the frequency of the acute symptomatic phase of rheumatic fever without reducing its incidence, thereby increasing the frequency of subclinical carditis.³⁹⁰ Furthermore, the early diagnosis of subclinical carditis allows secondary prophylaxis to prevent progression to more severe disease.³⁹¹

- Portable echocardiography has proved effective in identifying mitral and aortic valve abnormalities, such as stenosis and regurgitation, according to the World Heart Federation criteria.³⁹² Portable devices are highly recommended in areas with a high prevalence of rheumatic fever, particularly in low-income countries where access to specialized care may be limited.³⁹³ Point-of-care echocardiography is recommended for screening

Chart 74 – Recommendations on population-based screening for rheumatic fever

Recommendation	Strength of recommendation	Certainty of evidence
• Population-based echocardiographic screening using transthoracic echocardiography or point-of-care echocardiography performed by trained health care professionals		
• Use of the revised World Heart Federation criteria for diagnostic screening for rheumatic fever with point-of-care echocardiography		
• Performance of at least 1 transthoracic or point-of-care echocardiographic examination during the lifetime of individuals aged 7 to 20 years to screen for rheumatic fever, particularly in vulnerable populations	Strong	Moderate
• Performance of comprehensive echocardiography by an echocardiographer when point-of-care echocardiography identifies an abnormality that is suspicious or diagnostic of rheumatic fever		

at-risk populations, such as school-aged children and young adults, among whom subclinical disease may be prevalent. Studies have shown that point-of-care echocardiography can detect up to 10 times as many cases of valvular heart disease as traditional cardiac auscultation, making it a valuable tool in resource-limited settings.^{394,395} In addition, the portability of these devices reduces costs, facilitates mass screening, and enables non-specialist health workers to perform examinations with reasonable accuracy, thus improving the detection of heart disease in primary care.^{388,396}

Recurrent rheumatic carditis in adulthood is discussed in a separate section.

- **Arthritis:** Arthritis is the most common manifestation of rheumatic fever, occurring in 75% of cases. It is self-limited and resolves without sequelae. It is generally very painful despite the absence of marked inflammatory findings on physical examination. Arthritis is often the only major criterion present. When arthritis and carditis coexist, an inverse relationship between the severity of the 2 manifestations has been reported. Rheumatic fever-associated arthritis is asymmetric and migratory and preferentially affects the large joints, particularly those of the lower extremities. Inflammation in each joint rarely persists for more than 1 week, and the overall clinical presentation resolves within 1 month. Atypical patterns are increasingly common and include additive arthritis, monoarthritis, and involvement of small joints and the spine.^{371,372}

- **Sydenham's chorea:** Sydenham's chorea occurs predominantly in female children and adolescents and is rare after 20 years of age. Its reported prevalence ranges from 5% to 36%. Onset is usually insidious and is characterized by emotional lability and muscle weakness, which may hinder diagnosis. This neurologic disorder is characterized by rapid, involuntary, uncoordinated movements that disappear during sleep and are exacerbated by stress and physical exertion. These movements may involve the muscles of the face, lips, eyelids, and tongue and are frequently generalized. Episodes of chorea last an average of 2 to 3 months but may persist for more than 1 year.^{371,372} Because chorea may develop after a prolonged latent period following group A streptococcal infection, the diagnosis of rheumatic fever in this setting does not require the presence of other criteria. Thus, Sydenham's chorea alone establishes the diagnosis of rheumatic fever, although it is frequently associated with clinical or subclinical carditis and, less commonly, with arthritis.³⁹⁷

- **Erythema marginatum:** Erythema marginatum is a very rare manifestation, reported in fewer than 3% of cases. However, it is a highly specific criterion for the diagnosis of acute rheumatic fever. It is characterized by erythematous lesions with well-defined borders, clear centers, and rounded or irregular contours. The lesions are multiple, painless, and non-pruritic and may coalesce, producing a serpiginous appearance. They occur mainly on the trunk, abdomen, and medial aspects of the upper and lower extremities, sparing the face. The lesions are evanescent, may persist for minutes or hours, frequently change shape, and usually appear with exposure to heat. They generally

occur early in the disease course but may persist or recur for months.^{371,372}

- **Subcutaneous nodules:** Subcutaneous nodules are rare, occurring in only 2% of patients, and are strongly associated with severe carditis. They are multiple, rounded, variable in size (0.5–2.0 cm), firm, mobile, and painless and are covered by normal-appearing skin without inflammatory changes. They are located over bony prominences and extensor tendons and are more readily detected by palpation than by inspection. They occur most commonly over the elbows, wrists, knees, ankles, occipital region, Achilles tendon, and spine. Their onset is delayed, usually occurring 1 to 2 weeks after the other manifestations. They regress rapidly after treatment of carditis is initiated and rarely persist for more than 1 month. Although subcutaneous nodules are highly specific, they are not pathognomonic of acute rheumatic fever because similar lesions may occur in other rheumatologic diseases, such as polyarticular juvenile idiopathic arthritis, systemic lupus erythematosus, and mixed connective tissue disease.^{371,372}

15.4. Minor Criteria

Minor criteria encompass nonspecific clinical and laboratory findings that, together with the major manifestations and evidence of prior streptococcal infection, help establish the diagnosis of rheumatic fever.

- **Arthralgia:** Arthralgia differs from arthritis in that joint pain occurs with movement without evidence of swelling or warmth. It is a criterion with low specificity, and differential diagnoses should be considered. Arthralgia with an asymmetric, migratory polyarticular pattern involving the large joints is highly suggestive of rheumatic fever and is frequently associated with carditis; however, monoarthralgia should also be considered. Thus, in high-risk populations, including the Brazilian population, polyarthralgia should be considered a major diagnostic criterion and monoarthralgia a minor criterion. In low-risk populations, generally those in high-income countries, polyarthralgia is considered a minor manifestation. Importantly, when arthritis is included as a major criterion, arthralgia cannot be included as a minor criterion.

- **Fever:** Fever is common at the onset of an acute episode and occurs in nearly all cases of arthritis. It has no characteristic pattern. Fever generally resolves spontaneously within a few days and responds rapidly to nonsteroidal anti-inflammatory drugs (NSAIDs). Patients with carditis without concomitant arthritis may present with low-grade fever, whereas those with pure chorea are generally afebrile. In high-risk populations, defining fever as a temperature $> 38^{\circ}\text{C}$ improves sensitivity for diagnosing acute rheumatic fever. In low-risk populations, however, fever remains defined as a temperature $\geq 38.5^{\circ}\text{C}$.^{371,372}

- **PR interval:** The PR interval may be prolonged in patients with rheumatic fever, even in the absence of carditis, as well as in healthy individuals. ECG should be performed in all patients with suspected rheumatic fever and repeated after 1 to 2 weeks to document normalization. The PR interval is considered prolonged at values > 0.18 seconds in children

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and > 0.20 seconds in adolescents and adults.^{371,372} A prolonged PR interval should not be considered a minor criterion when carditis is present as a major criterion.

- Acute phase reactants: Patients with acute rheumatic fever usually have elevated serum CRP and/or ESR levels. However, the peripheral blood leukocyte count is generally < 15 × 10⁹/L in 75% of patients, making leukocytosis a marker with low sensitivity. Inflammatory markers, or acute phase reactants, are not specific to rheumatic fever but are useful for monitoring inflammation during the acute phase and its subsequent resolution. Acute phase reactant levels generally increase at the beginning of an acute episode and decline by the end of the second or third week. CRP tends to increase and decrease more rapidly, whereas ESR may remain elevated for 3 to 6 months. In high-risk populations, a serum CRP level ≥ 30 mg/L or an ESR ≥ 30 mm/h is recommended as a minor diagnostic criterion. Importantly, any combination of acute phase laboratory tests should be counted as only 1 minor manifestation of rheumatic fever.^{371,372}

15.5. Recurrent Rheumatic Carditis

In acute rheumatic carditis, antibodies cross-react with cardiac tissues and streptococcal antigens. They bind to the valvular endothelium, increasing the expression of adhesion molecules and recruiting inflammatory cells such as neutrophils, macrophages, and T lymphocytes, resulting in inflammation, tissue destruction, and necrosis. Aschoff nodules, which are pathognomonic of the disease, contain macrophage- and monocyte-like cells that present antigens to T cells. Proinflammatory cytokines are produced in these nodules, perpetuating the immune response and activating autoreactive T-cell clones.³⁹⁸⁻⁴⁰⁰

Recurrent rheumatic carditis in adulthood is one of the most severe manifestations of rheumatic fever and may be triggered by several factors, including recurrent streptococcal infections, inadequate adherence to secondary prophylaxis with benzathine penicillin, and genetic and immunologic factors that may predispose individuals to recurrent episodes of rheumatic fever.

Clinical presentation: Approximately 20% of patients with a history of rheumatic fever may experience reactivation of rheumatic carditis within 10 years, and diagnosing a recurrent episode in adults is generally challenging.⁴⁰¹ Unlike the first episode of rheumatic fever, recurrent rheumatic carditis

most often involves the myocardium.^{385,402} Current evidence suggests that myocardial involvement, with or without ventricular dysfunction, may occur regardless of the severity of valve dysfunction in adults with recurrent rheumatic carditis. In a case series of heart transplant recipients with rheumatic valvular heart disease and refractory HF, 27.7% underwent heart transplant because of previously undiagnosed rheumatic myocarditis. The diagnosis was established by the presence of Aschoff nodules on histopathologic analysis, a finding pathognomonic of acute rheumatic fever.³⁸⁶

Diagnosis: Acute rheumatic carditis should be suspected in adults presenting with new-onset cardiac decompensation, generally accompanied by ventricular dysfunction, in the absence of a more likely cause. It is often a diagnosis of exclusion. Symptomatic improvement and reverse cardiac remodeling after specific corticosteroid therapy support the diagnosis, which is frequently challenging and underrecognized in clinical practice. The diagnosis of recurrent rheumatic carditis is based on the presence of signs and symptoms of HF accompanied by evidence of cardiac inflammation. In this setting, the diagnostic approach should include complementary multimodality assessment, centered primarily on transthoracic echocardiography (Chart 75). The role of nuclear imaging in recurrent myocarditis, including gallium-67 scintigraphy and fluorine-18 fluorodeoxyglucose positron emission tomography/CT (18F-FDG PET/CT), remains uncertain. Most previous studies of 18F-FDG PET/CT and scintigraphy included children experiencing a first episode, whereas studies of recurrent carditis in adults are scarce. However, these imaging methods have been used to demonstrate active myocardial inflammation, providing support for the diagnosis.³⁸⁵ CMR may aid the differential diagnosis by excluding other etiologies of HF, such as viral myocarditis and ischemic cardiomyopathy, but is generally normal in patients with rheumatic carditis. Laboratory tests, including inflammatory markers (ESR and CRP), may also be used. However, because rheumatic myocarditis is indolent, usually has a protracted clinical course, and is often diagnosed late, inflammatory marker levels are not infrequently within the reference range.^{371,372}

15.6. Clinical Management of Acute Rheumatic Fever

The goals of treatment of acute rheumatic fever are to suppress inflammation, minimize its clinical effects on the heart, joints, and central nervous system, eradicate group A *Streptococcus* from the oropharynx, and relieve the

Chart 75 – Recommendations for the diagnosis of recurrent rheumatic carditis in adults

Recommendation	Strength of recommendation	Certainty of evidence
• In patients with a history of rheumatic fever, suspect recurrent rheumatic carditis in the presence of heart failure symptoms and/or new-onset ventricular dysfunction not explained by the valvular heart disease, after excluding other more common diagnoses (tachycardia-induced cardiomyopathy and ischemia)	Strong	Very low
• If available, perform gallium-67 scintigraphy or fluorine-18 fluorodeoxyglucose positron emission tomography when reactivation of rheumatic carditis is suspected		

principal symptoms. In patients with suspected rheumatic fever, whether a first or recurrent episode, the need for hospitalization depends on the severity of the clinical presentation. Hospitalization is indicated for moderate to severe carditis, disabling arthritis, and severe chorea. Hospitalization may also shorten the interval between clinical suspicion and diagnosis and allow treatment to be initiated promptly. In addition, it provides an opportunity to educate patients and their families about the disease and the importance of adherence to secondary prophylaxis. The duration of hospitalization depends on symptom control, particularly the control of carditis.^{371, 372, 403}

Pharyngotonsillitis should be treated and streptococci eradicated from the oropharynx whenever rheumatic fever is clinically suspected, regardless of the throat culture result. The goals are to reduce the patient's streptococcal antigen exposure and prevent transmission within the community. In patients experiencing a first episode, the prescribed treatment also marks the initiation of secondary prophylaxis (Chart 76).⁴⁰⁴

Symptomatic treatment should include metamizole (dipyrone) or acetaminophen for fever and NSAIDs for joint pain. Anti-inflammatory therapy generally provides effective control of arthritis, with signs and symptoms resolving within 24 to 48 hours. Aspirin remains the first-line treatment for joint involvement, particularly in children. The recommended dose in adults is 4 to 8 g/day. Naproxen and ibuprofen are effective alternatives to aspirin, offering comparable efficacy, simpler dosing, and better tolerability.^{405,406} Corticosteroids are not routinely indicated for isolated arthritis. When corticosteroid therapy is indicated, as in patients with concomitant carditis, there is no need to continue or initiate an NSAID.

Chorea is a late manifestation of rheumatic fever and has a benign, self-limited course in most patients. For mild or moderate chorea, rest in a quiet environment with minimal external stimulation is recommended. Benzodiazepines, sodium valproate, and carbamazepine may also be used. When anticonvulsant therapy fails, haloperidol or risperidone may be considered to control residual symptoms. Specific corticosteroid therapy is indicated only for severe chorea when the involuntary movements interfere with the patient's usual activities and do not respond to the previously described medications. In patients refractory to these

treatments, including corticosteroid therapy, experimental approaches such as plasmapheresis and intravenous immunoglobulin may be considered, although supporting evidence remains limited.^{371,407,408}

Treatment of carditis is based on controlling inflammation and managing HF and arrhythmias. Corticosteroids and other anti-inflammatory agents for rheumatic carditis have been evaluated in some older meta-analyses; however, these medications have not been shown to reduce long-term progression to valvular heart disease.^{409,410} Importantly, these studies were conducted more than 40 years ago, when echocardiography was not widely available, and had several statistical limitations.³⁷¹ Thus, although there is no clear scientific evidence that corticosteroids reduce valve injury or improve the prognosis of rheumatic carditis, they are recommended in patients with moderate to severe carditis and in those with pericarditis. The principal goals are to accelerate recovery and reduce inflammation.⁴⁰⁹ In patients with mild carditis without HF, no specific medical therapy is recommended, and corticosteroids or salicylates are not indicated.^{403,411}

The corticosteroid of choice for the treatment of carditis is oral prednisone or prednisolone at a dose of 1 to 2 mg/kg/day, up to a maximum of 80 mg/day. Intravenous methylprednisolone may be considered in very severe cases or in patients unable to receive oral medication.^{412,413} Treatment duration varies, although corticosteroid therapy is generally continued for 4 weeks, followed by slow and progressive dose tapering, with a weekly reduction of 20% to 25%. Given the high dose and prolonged duration of corticosteroid therapy, empiric ivermectin therapy is suggested before treatment is initiated to prevent disseminated strongyloidiasis.

Regarding recurrent rheumatic carditis in adulthood, recent studies suggest that systemic corticosteroid therapy is associated with reversal, or at least improvement, of ventricular dysfunction caused by rheumatic myocarditis.³⁸⁵ These patients should be treated similarly to those experiencing a first episode of rheumatic carditis, based on the following 3 major pillars of treatment:

- Treatment of active Lancefield group A streptococcal infection, if present, and prevention of recurrence, preferably with benzathine penicillin G every 21 days.

Chart 76 – Recommendations for the management and treatment of recurrent rheumatic carditis in adults

Recommendation	Strength of recommendation	Certainty of evidence
• Treat active Lancefield group A streptococcal infection and prevent further recurrences, preferably with benzathine penicillin G every 21 days		
• Manage heart failure with diuretics and vasodilators to achieve clinical compensation		
• Prescribe oral prednisone at 1 mg/kg/day for 3–4 weeks in confirmed cases	Strong	Low
• Repeat transthoracic echocardiography after 4 weeks of treatment to reassess ventricular function		
• Prescribe intravenous methylprednisolone to patients with suspected very severe carditis and cardiogenic shock who are unable to receive oral prednisone		

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- Management of HF with diuretics and vasodilators to achieve clinical compensation, together with disease-modifying therapies, particularly ACEIs and MRAs.
- Corticosteroid therapy in patients with severe carditis.

Echocardiography should be repeated after 4 weeks of corticosteroid therapy to reassess ventricular function.

Surgical intervention may be required in patients who have significant and persistent valve damage in addition to ventricular dysfunction. However, valve replacement surgery should preferably be performed after carditis has been treated and myocardial inflammation has been adequately controlled to reduce surgical risk.^{403,414} In patients with acute valve dysfunction and hemodynamic instability refractory to clinical management, emergency surgery is indicated.

15.7. Primary Prevention

Primary prophylaxis is based on recognizing and treating streptococcal infections to prevent a first episode of rheumatic fever by reducing streptococcal exposure and treating pharyngotonsillitis within 9 days of symptom onset.⁴¹⁵ Although reducing exposure is difficult in low- to middle-income countries, treating pharyngotonsillitis is relatively simple and effective. Asymptomatic or minimally symptomatic streptococcal infections and inadequate treatment, whether because bacteriostatic antibiotics are used or therapy is administered for an insufficient duration, represent challenges to the primary prevention of rheumatic fever.

Benzathine penicillin remains the treatment of choice because of the established susceptibility of group A *Streptococcus*, its bactericidal activity, clinical and bacteriologic efficacy, low incidence of adverse effects, good adherence to the prescribed regimen, narrow antimicrobial spectrum, and low cost.⁴¹⁶ Amoxicillin, oral penicillin V, ampicillin, and cephalexin are also treatment options, although none has demonstrated superior efficacy to benzathine penicillin (Chart 77). In patients with a clear history of penicillin-induced anaphylaxis, cephalosporins should preferably be avoided, and azithromycin is an option.⁴¹⁷

All patients with streptococcal pharyngitis should receive appropriate antibiotic treatment, preferably a single intramuscular dose of benzathine penicillin G. This option is preferred because the simple dosing regimen promotes treatment adherence and ensures complete eradication of

Streptococcus pyogenes from the oropharynx, reducing the risk of rheumatic fever.

15.8. Secondary Prevention

Secondary prophylaxis for rheumatic fever requires balancing the risk of recurrence, which is highest during the first year after diagnosis and progressively decreases over 5 to 10 years, against the logistical challenges of administering penicillin. Young patients and those with valve damage are at increased risk of severe complications if recurrence occurs, supporting continued prophylaxis. Even patients whose first episode consisted solely of arthritis or chorea remain at high risk of developing carditis or rheumatic heart disease; secondary prophylaxis is therefore indicated for all patients with a history of acute rheumatic fever.^{371,401,403}

The treatment of choice is benzathine penicillin G at a dose of 600,000 IU for children weighing ≤ 27 kg and 1,200,000 IU for those weighing > 27 kg every 21 days, administered by deep intramuscular injection.^{229,370,371,403,418-421} Measures to reduce pain during benzathine penicillin administration should be considered to improve adherence. The use of 0.25 mL of 2% lidocaine without a vasoconstrictor reduces pain during administration and over the first 24 hours without significantly affecting serum penicillin levels.⁴²² Oral penicillin V at a dose of 250 mg twice daily should be prescribed only in exceptional circumstances because benzathine penicillin G is approximately 10 times more effective than oral therapy in preventing recurrent rheumatic fever. Erythromycin and sulfadiazine are alternatives for patients allergic to penicillin (Chart 78).^{371,391,401,403}

The duration of prophylaxis depends on the patient's age, the interval since the most recent episode, the presence of carditis during the initial episode, the number of recurrences, the patient's socioeconomic status, and the severity of residual rheumatic heart disease. In general, patients without cardiac involvement whose manifestations were limited to arthritis or pure chorea may discontinue prophylaxis at 21 years of age or 5 years after the most recent rheumatic episode, whichever is longer. Patients with late sequelae of cardiac involvement should continue prolonged prophylaxis until at least 40 years of age or lifelong if they have frequent occupational exposure to *Streptococcus pyogenes*. Importantly, adults, including those older than 40 years, may experience recurrent

Chart 77 – Primary prophylaxis for rheumatic fever: Recommendations for the treatment of group A streptococcal pharyngotonsillitis

Medication/Option	Regimen	Duration
Benzathine penicillin G	≤ 27 kg: 600,000 IU > 27 kg: 1,200,000 IU	Single dose
Penicillin V	500 mg every 12 hours	10 days
Amoxicillin	500 mg orally every 8 hours	10 days
Cephalexin (for penicillin hypersensitivity)	500 mg orally every 12 hours	10 days
Azithromycin (for penicillin-induced anaphylaxis)	500 mg orally once daily	5 days
Clindamycin (for penicillin-induced anaphylaxis)	600 mg orally every 8 hours	10 days

Chart 78 – Recommended medications and dosing regimens for secondary prophylaxis of rheumatic fever

Medication	Dose and frequency
Benzathine penicillin G	≤ 27 kg – 600,000 IU
	> 27 kg – 1,200,000 IU
	Every 21 days
Penicillin V	250 mg orally twice daily
Erythromycin* (for patients allergic to penicillin)	250 mg twice daily
Sulfadiazine* (for patients allergic to penicillin)	1 g/day

* May be used until penicillin desensitization is completed.

rheumatic carditis, manifested predominantly as myocarditis. In these cases, secondary prophylaxis should be continued for at least 10 years after reactivation. The recommended duration of secondary prophylaxis, together with the strength of recommendation and certainty of evidence according to the latest scientific evidence, is presented in Chart 79 and summarized in Chart 80.

16. Infective Endocarditis Prophylaxis

Infective endocarditis represents a global public health challenge. In 2019, its estimated incidence was 13.8 cases per 100,000 population per year, resulting in approximately 66,300 deaths worldwide.⁴²³ Given the associated high morbidity and mortality, identifying effective preventive strategies is critically important and has been a major focus of research.⁴²⁴

The development of infective endocarditis generally requires several conditions, including the competence of the host immune response.⁴²⁵ Bacteria and fungi may enter the body through various portals, including infections involving the skin, oral cavity, gastrointestinal tract, or genitourinary tract. In addition, health care exposure, including invasive diagnostic or therapeutic procedures such as transcatheter or surgical interventions, has become an increasingly important predisposing factor for the development of infective endocarditis.⁴²⁶⁻⁴²⁹

The oral cavity is an important portal of entry for pathogens, particularly oral group streptococci. Therefore, procedures that involve manipulation of the gingival or periapical region of the teeth are considered at high risk of causing bacteremia.^{430,431}

Antibiotic prophylaxis before invasive dental procedures, such as extractions and oral surgery, has previously been shown to be associated with a significant reduction in the incidence of infective endocarditis among high-risk individuals.⁴³¹ Based on new studies published after 2015, the recommendation for antibiotic prophylaxis in this setting has been strengthened, with clearer definition of the population at risk and consideration of the advances in transcatheter valve interventions.

16.1. Patients at Risk of Infective Endocarditis

Antibiotic prophylaxis is recommended or should be considered for certain groups of individuals at increased risk of developing infective endocarditis. These include:

- Patients with a history of infective endocarditis⁴³²⁻⁴³⁴;
- Patients with surgical or transcatheter prosthetic valves⁴³⁵⁻⁴⁴¹;
- Patients who have undergone valve repair with prosthetic material;
- Patients with anatomically moderate or significant valvular heart disease;
- Patients with a diagnosis of bicuspid aortic valve;
- Patients with CIEDs, such as pacemakers and defibrillators;
- Patients with congenital heart disease, including untreated cyanotic congenital heart disease, and those whose surgery involves prosthetic material, including valved conduits or systemic to pulmonary shunts^{442,443};
- Patients with ventricular assist devices⁴⁴⁴;
- Recipients of solid organ transplant – the risk of infective endocarditis is highest during the first 6 months after transplant.⁴⁴⁵

Patients with atrial septal defect closure devices, left atrial appendage closure devices, vascular grafts, vena cava filters, or central venous system ventriculoatrial shunts, as well as those who have undergone surgery with non-valve-related prosthetic material, are also considered at high risk of infective endocarditis, but only during the first 6 months after implantation.⁴⁴⁶

16.2. Dental Procedures

Antibiotic prophylaxis is a preventive measure recommended for patients at high risk of infective endocarditis undergoing at-risk dental procedures. These procedures involve substantial manipulation of oral tissues, which may allow bacteria to enter the bloodstream and increase the risk of infective endocarditis.⁴⁴⁷ The main target for antibiotic prophylaxis is oral streptococci, which commonly colonize the oral cavity.

Dental procedures requiring antibiotic prophylaxis in high-risk patients include:

- Dental extractions;
- Oral surgery, including periodontal surgery, implant surgery, and oral biopsies;
- Manipulation of the gingival or periapical region of the teeth, including scaling and root canal procedures;
- Dental implant placement.^{447,448}

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Chart 79 – Recommendations for secondary prophylaxis of rheumatic fever

Recommendation	Strength of recommendation	Certainty of evidence
• Administer benzathine penicillin G every 21 days for secondary prophylaxis of rheumatic fever • Continue benzathine penicillin G until 21 years of age or for 5 years after the most recent episode in patients with rheumatic fever without carditis • Continue benzathine penicillin G until 25 years of age or for 10 years after the most recent episode in patients with rheumatic fever with carditis and only mild residual valvular heart disease • Continue prophylaxis until 40 years of age or for 10 years after the most recent episode (whichever is longer) in patients with rheumatic fever with carditis and moderate to severe residual valvular heart disease or previous cardiac surgery to correct the valve disease • Continue benzathine penicillin G beyond 40 years of age in patients with rheumatic fever with carditis and occupational exposure to <i>Streptococcus pyogenes</i>	Strong	Low
• Use oral antibiotic prophylaxis with penicillin V, erythromycin, or sulfadiazine in patients with rheumatic fever who are not allergic to penicillin	Weak	Low
• Administer benzathine penicillin G every 21 days for secondary prophylaxis of rheumatic fever in patients with recurrent rheumatic carditis during adulthood, for at least 10 years after the most recent episode	Strong	Low

Chart 80 – Duration of secondary prophylaxis for rheumatic fever

Category	Duration
• Rheumatic fever without carditis: isolated arthritis or pure chorea	Until 21 years of age or for 5 years after the most recent episode of rheumatic fever*
• Rheumatic fever with carditis but no sequelae or only very mild residual valve disease (excluding stenotic lesions even if mild)	Until 25 years of age or for 10 years after the most recent episode of rheumatic fever*
• Rheumatic fever with carditis and severe sequelae or previous cardiac surgery	Until at least 40 years of age Lifelong in patients with occupational exposure
• Recurrent rheumatic carditis during adulthood	Until 40 years of age or for 10 years after the most recent episode* Lifelong in patients with occupational exposure

* *Whichever is longer.*

16.3. Antibiotic Prophylaxis Regimens

Chart 81 summarizes the main antibiotic prophylaxis regimens recommended before dental procedures. Amoxicillin is generally the first-line option because of its low risk of adverse events. In patients allergic to penicillin, cephalexin, clarithromycin, or azithromycin are the main alternatives.⁴⁴⁹ The antibiotic should be administered as a single dose 30 to 60 minutes before the procedure.

16.4. Non-Dental Procedures

To minimize the risk of infective endocarditis, an aseptic operational environment should be ensured during all invasive medical procedures. This includes the use of sterile techniques, rigorous hand hygiene by all health care professionals involved, and appropriate disinfection of the surgical site to reduce the bacterial load on the skin or mucous membranes.^{426,427}

Additional recommendations for reducing the risk of infective endocarditis include:

- Antibiotic prophylaxis before CIED implantation;
- Periprocedural antibiotic prophylaxis for patients undergoing transcatheter implantation or surgical placement of a prosthetic valve or endovascular prosthesis;
- Eradication of potential sources of infection (including odontogenic origin) at least 2 weeks before implantation of prosthetic valves or other external devices, except in urgent surgery.

16.5. Gastrointestinal and Genitourinary Tract Procedures

Current evidence supporting routine antibiotic prophylaxis in high-risk patients undergoing non-dental procedures is less robust. The latest ESC guidelines on infective endocarditis recommend highly restricted use of antibiotic prophylaxis before these procedures because of the limitations of the

Chart 81 – Antibiotic prophylaxis regimens for high-risk dental procedures

Situation	Antibiotic	Dose
No allergy to penicillin or ampicillin	Amoxicillin	2 g orally
	Ampicillin	2 g IV or IM
	Cefazolin or ceftriaxone	1 g IV or IM
Allergy to penicillin or ampicillin	Cephalexin	2 g orally
	Azithromycin or clarithromycin	500 mg orally
	Cefazolin or ceftriaxone	1 g IV or IM

IM: intramuscular; IV: intravenous.

available observational data.⁴²⁵ However, considering the severity of infective endocarditis, the economic burden associated with hospitalization, and the clinical consequences for patients, we consider antibiotic prophylaxis before gastrointestinal and genitourinary tract procedures to be justified (Chart 82). These procedures include:

- Procedures involving manipulation of infected mucosa or mucosa suspected of being infected;
- Procedures involving incision or biopsy of the gastrointestinal mucosa (including upper gastrointestinal endoscopy and colonoscopy with biopsy);
- Cystoscopy;
- Urologic surgical procedures.

The suggested antibiotic regimen for these situations is presented in Chart 82. A comparison of the antibiotic prophylaxis recommendations is summarized in Chart 83.

16.6. Patient Education

Preventing infective endocarditis requires several measures other than antibiotic prophylaxis, including education, appropriate oral hygiene, symptom monitoring, and effective communication between patients and health care professionals. Collectively, these measures can substantially reduce the risk of infective endocarditis in vulnerable individuals.

Maintaining optimal oral health is more important than administering antibiotic prophylaxis before dental procedures in patients with valvular heart disease. Patients with good oral health are less likely to develop bacteremia during daily activities. Therefore, non-pharmacologic prevention should be prioritized over pharmacologic prophylaxis. Non-pharmacologic prophylaxis against infective endocarditis includes reinforcing the importance of excellent oral health and increasing the frequency of dental visits from twice per year, as recommended for the general population, to 4 times per year. Importantly, many dental conditions associated with infective endocarditis, such as gingivitis and periapical endodontic lesions, cause few symptoms.⁴⁵⁰

Body art procedures, including tattoos and piercings, should be contraindicated in these patients. Piercings in particular create a tract that must undergo epithelialization and remain a continuous source of bacteremia until the

tract is closed. Numerous cases of infective endocarditis, including fatal cases, associated with piercing placement have been reported. Patients must be informed of the risks of these procedures, and physicians should routinely address this issue during consultations with patients who have or are considering body art.⁴⁵¹

Each patient should be assessed individually to determine the need for antibiotic prophylaxis, considering both the underlying cardiac condition and the type of procedure. Patients at high risk should be educated about the importance of prophylaxis and the need to inform their health care professionals of their cardiac condition.

17. Pregnancy in Women with Valvular Heart Disease

Pregnancy involves hemodynamic changes that may be poorly tolerated by women with valvular heart disease. Therefore, when planning a pregnancy, which is considered high risk from an obstetric perspective, clinical evaluation by a specialist in valvular heart disease is essential.^{452,453} This evaluation should consider functional capacity, the characteristics of the valve lesion, right and left ventricular function, cardiac rhythm, the presence of pulmonary hypertension, the use of potentially teratogenic medications, and whether criteria are present for valve intervention before pregnancy.⁴⁵²

17.1. Pre-Pregnancy Counseling

When pregnancy is being planned, clinical evaluation, including physical examination with cardiac auscultation, is recommended to screen for valvular heart disease. When suggestive findings are present, further evaluation by a cardiologist is indicated to confirm the diagnosis.

Risk stratification of valvular heart disease during pregnancy should be based on the presence of symptoms, the severity of the valve lesion, and adverse prognostic features, including AF, pulmonary hypertension, ventricular dysfunction, and previous thromboembolic events. This assessment allows valvular heart disease to be classified as high, intermediate, or acceptable risk (Chart 84).⁴⁵⁴

In addition to transthoracic echocardiography, which establishes the diagnosis and severity of valvular heart disease, ECG allows characterization of cardiac rhythm, and exercise stress testing may assist decision-making in asymptomatic

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Chart 82 – Antibiotic prophylaxis regimen for gastrointestinal and genitourinary tract procedures

Route of administration	Antibiotic	Single dose 1 hour before the procedure
Parenteral (intravenous)	Ampicillin and gentamicin	2 g 1.5 mg/kg
Parenteral (intravenous) <i>If allergic to penicillin</i>	Vancomycin and gentamicin	1 g 1.5 mg/kg

Chart 83 – Recommendations for antibiotic prophylaxis against infective endocarditis

Recommendations for antibiotic prophylaxis against infective endocarditis	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Antibiotic prophylaxis is recommended for dental extractions, oral surgery, or other procedures requiring manipulation of the gingival or periapical region of the teeth in patients at high risk of infective endocarditis	Strong / Moderate	Ila C	I B
Systemic antibiotic prophylaxis should be considered in patients at high risk of infective endocarditis undergoing diagnostic or therapeutic procedures involving the gastrointestinal or genitourinary tract	Strong / Low	III B	IIb C

AHA: American Heart Association; ESC: European Society of Cardiology; SBC: Brazilian Society of Cardiology.

patients.⁴ When concomitant aortic disease is present, imaging of the ascending aorta is recommended.⁴⁵²

Valve intervention before pregnancy should be performed in patients who already meet the conventional indications described in these guidelines. More recently, intervention has also been considered for patients classified as high risk (Chart 85) with a desire for pregnancy, even when asymptomatic, because of the high frequency of complications and risk of maternal death. In these cases, detailed clinical assessment, specialized echocardiography, and exercise stress testing are recommended to inform discussion by the Heart Team. Once the indication is confirmed, a transcatheter approach should be prioritized whenever feasible. The decision should be shared with the patient, with clear discussion of the maternal risks associated with a future pregnancy and the possibility that emergency intervention may be required during pregnancy, a situation associated with a high risk of fetal loss and congenital malformations.^{454,455}

In women with valvular heart disease associated with hereditary aortic diseases, pre-pregnancy counseling should be particularly rigorous. Evaluation should include a precise diagnosis based on clinical characterization and, whenever possible, genetic testing because pathogenic variants may substantially alter risk stratification and decision-making regarding intervention before pregnancy.⁴⁵⁴

The presence of variants associated with a higher risk of aortic complications, such as those occurring in Marfan syndrome, Loeys–Dietz syndrome, and other hereditary aortopathies, may justify reassessment of the thresholds for intervention, even in patients with aortic diameters below those traditionally recommended. Genetic testing should

therefore be considered during pre-pregnancy planning, particularly in patients with a suggestive phenotype or family history, because the results may directly impact management.

Although promising, these approaches should be implemented at centers with expertise in aortic disease and cardiovascular genetics. Referral to a specialized center is recommended when this expertise is unavailable locally.

According to current recommendations, surgical repair should be considered in patients with ascending aortic dilation ≥ 45 mm in Marfan syndrome and ≥ 50 mm in bicuspid aortic valve disease. These thresholds should be interpreted in the context of each patient's clinical and genetic profile.⁴⁵⁴

17.2. Risks of Valvular Heart Disease During Pregnancy

Patients classified as being at high or intermediate risk should be followed at tertiary centers by an established cardio-obstetric team that includes experts in interventional cardiology and cardiac surgery, allowing discussion by the Heart Team when necessary.^{452,453}

Regardless of the severity of valvular heart disease, adverse prognostic features should be considered factors that increase maternal and fetal risk. These include HF, AF, pulmonary hypertension, ventricular dysfunction, previous thromboembolic events, the need for anticoagulation, a history of infective endocarditis, and concomitant aortic disease.^{454,456}

The hemodynamic changes of pregnancy and the postpartum period may precipitate HF in patients with significant valvular heart disease. The overlap between the physiological symptoms of pregnancy and HF manifestations may hinder early recognition, delay treatment, and adversely affect maternal and fetal outcomes. In these cases, initial

Chart 84 – Recommendations for pre-pregnancy counseling, pregnancy, delivery, and anticoagulation in pregnant patients

Clinical condition	SBC (Strength of recommendation/ Certainty of evidence)	AHA	ESC
Pre-pregnancy counseling			
• Women with valvular heart disease should be evaluated by a specialist when planning pregnancy	Strong / Moderate	I B	I C
• Clinical assessment during pregnancy planning should consider functional class, the severity of the valve lesion, ventricular function, cardiac rhythm, signs of pulmonary hypertension, medication use, and whether intervention is indicated	Strong / Low	-	I C
• Exercise stress testing assists in the assessment of asymptomatic patients, and imaging assists in the assessment of concomitant aortic disease	Strong / Low	IIa B	-
• Women who meet criteria for valve intervention should undergo the procedure before pregnancy	Strong / Moderate	I B	I B
• Women with high-risk valvular heart disease should be considered for valve intervention before pregnancy, even if asymptomatic	Strong / Low	IIa C	I C
• Women with concomitant aortic disease should be assessed for intervention before pregnancy, preferably with genetic testing	Strong / Low	-	I C
• The selection of valve type in women planning pregnancy should consider the risks of thromboembolism and anticoagulation associated with mechanical prostheses and the limited durability of bioprosthetic valves	Strong / Moderate	IIa B	I C
• Women with mechanical prostheses who are planning pregnancy should be counseled regarding the risks of anticoagulation across the 5 stages of pregnancy	Strong / Low	I B	-
During pregnancy			
• Pregnant patients classified as being at high or intermediate risk should be followed at a tertiary hospital by a cardio-obstetric team throughout pregnancy, delivery, and the postpartum period	Strong / Moderate	I B	I C
• Pregnant patients with rheumatic valvular heart disease should continue prophylaxis with benzathine penicillin	Strong / Moderate	-	-
• Pharmacotherapy is the initial treatment for symptoms of pulmonary congestion in mitral stenosis and heart failure in mitral or aortic regurgitation	Strong / Moderate	-	I C
• Beta-blockers and diuretics are indicated to control heart rate and pulmonary congestion in pregnant patients with mitral stenosis	Strong / Low	IIa C	I B
• Verapamil, a calcium channel blocker, may be considered for heart rate control in atrial fibrillation, with or without digoxin	Strong / Low	-	-
• Percutaneous or surgical valve intervention should be considered in cases refractory to clinical treatment	Strong / Moderate	IIa C	IIa C
• Percutaneous or surgical valve intervention should be considered in patients with aortic stenosis and heart failure, syncope, or angina	Strong / Moderate	IIa B	IIa C
• Transcatheter valve-in-valve implantation or surgical intervention should be considered for stenotic and calcified bioprosthetic valves	Strong / Moderate	-	-
Anticoagulation and mechanical prostheses			
• Anticoagulation should maintain the same therapeutic targets used outside pregnancy	Strong / Moderate	-	I C
• Unfractionated heparin and low-molecular-weight heparin are alternatives to warfarin during the first trimester and after 36 weeks' gestation	Strong / Moderate	IIa B	IIa B
• Warfarin should be continued between 12 and 36 weeks' gestation using the same INR targets applied outside pregnancy	Strong / Low	-	-

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Delivery

• Cesarean delivery should be considered in patients with high-risk valvular heart disease or those receiving anticoagulation	Strong / Moderate	-	-
• Antibiotic prophylaxis against infective endocarditis at the time of delivery should be considered in patients with prosthetic valves or a history of infective endocarditis	Strong / Low	-	-
• Women with valvular heart disease should receive counseling regarding safe and effective contraceptive methods	Strong / Moderate	-	-
• The World Health Organization Medical Eligibility Criteria and the Pearl Index should guide the choice of contraceptive method in women with valvular heart disease	Strong / Moderate	-	-
• Women with valvular heart disease may benefit from progestin-only contraceptives	Strong / Low	-	-

INR: international normalized ratio; SBC: Brazilian Society of Cardiology; AHA: American Heart Association; ESC: European Society of Cardiology.

Chart 85 – Classification of the risks associated with valvular heart disease during pregnancy

High risk	Intermediate risk	Acceptable risk
• Severe mitral stenosis	• Bioprosthetic valve with moderate dysfunction	• Mild valvular heart disease
• Severe aortic stenosis	• Severe pulmonary stenosis	• Normally functioning bioprosthetic valve
• Stenotic/calcified bioprosthetic valve	• Mechanical prosthesis	• Valvular heart disease + normal LVEF
• Dysfunctional mechanical prosthesis	• Mechanical mitral prosthesis > risk than mechanical aortic prosthesis	• Valvular heart disease without adverse prognostic features
• Valvular heart disease + significant PH (PAP ≥ 50 mmHg)		
• Aortic regurgitation + aortic disease	• Marfan syndrome (ascending aortic diameter 40–45 mm)	
• Marfan syndrome (ascending aortic diameter > 45 mm)	• Bicuspid aortic valve (ascending aortic diameter 45–50 mm)	
• Bicuspid aortic valve (ascending aortic diameter > 50 mm)	• Need for anticoagulants	
• Valvular heart disease + LVEF < 35%		

PH: pulmonary hypertension; LVEF: left ventricular ejection fraction; PAP: pulmonary artery pressure.

management should be clinical, with rest and judicious use of medical therapy with an established fetal safety profile.

The fundamental principle for preventing and treating complications during pregnancy is to prioritize general measures, including restriction of physical activity, limitation of sodium intake to 4 g/day, and continuation of rheumatic fever prophylaxis, except with sulfadiazine.

Drug selection should balance the efficacy of maternal treatment with fetal safety. Because most cardiovascular medications cross the placental barrier, agents with an established safety profile, low teratogenic potential, and a lower risk of fetal toxicity are recommended.

For symptom control in pregnant patients with valvular heart disease, medications with an established fetal safety

profile are recommended at the following usual doses: furosemide up to 80 mg/day, propranolol up to 80 mg/day, metoprolol succinate up to 100 mg/day, carvedilol up to 50–75 mg/day, verapamil up to 240 mg/day, hydralazine up to 100 mg/day, and digoxin up to 0.25 mg/day.⁴⁵⁷

ACEIs and ARBs are contraindicated throughout pregnancy because of the risk of fetal malformations.^{457,458}

Treatment of pulmonary congestion caused by mitral stenosis should be initiated with beta-blockers and diuretics. In patients with AF, anticoagulation should be considered, and digoxin may be used for ventricular rate control. When the clinical response is inadequate, percutaneous mitral valvuloplasty may be indicated if valve anatomy is suitable. If a percutaneous procedure is not feasible, conventional surgery may be considered.⁴⁵⁹

In patients with aortic stenosis, the development of HF, syncope, or angina indicates a higher risk of maternal death and warrants hospitalization, detailed assessment, and discussion by the Heart Team regarding the need for intervention. Medical therapy is limited in this setting and may compromise maternal cardiac output and placental perfusion. Although data remain limited, TAVI may be considered during pregnancy in selected cases.^{459,460}

Regurgitant valve lesions, such as isolated mitral or aortic regurgitation, have a low risk of HF, and complications may result from AF and/or ventricular dysfunction. In most cases, symptoms should be controlled with diuretics, digoxin, and/or beta-blockers, with vasodilators reserved as a last-line option.

However, valve intervention during pregnancy should be considered in refractory cases. For mitral regurgitation, TEER may be considered in selected patients, whereas surgery remains the principal therapeutic option for aortic regurgitation.⁴⁵⁹

TAVI may be considered in exceptional circumstances at specialized centers and in carefully selected patients. However, its application in pure aortic regurgitation is limited, particularly in young patients with minimal valve calcification.

17.3. Prosthetic Valves

Pregnancy in patients with prosthetic valves carries high maternal and fetal risk, regardless of valve type. Therefore, the selection of valve type in women with a desire for pregnancy should consider pregnancy-specific factors.⁴⁶¹

Bioprosthetic valves have the advantage of not requiring long-term anticoagulation. However, their limited durability, with the risk of structural valve deterioration and the need for reintervention, including during pregnancy, is an important limitation, particularly in young women. Patients with degenerated bioprosthetic valves should be considered for reintervention during pregnancy planning, even if asymptomatic, because of the risk of clinical decompensation.⁴⁶¹

Conversely, mechanical prostheses require uninterrupted anticoagulation therapy and are associated with a higher risk of maternal and fetal bleeding complications, as well as warfarin embryopathy, particularly in cases of unplanned pregnancy.⁴⁶² In addition, the prothrombotic state of pregnancy increases the risk of prosthetic valve thrombosis. Patients with mechanical prostheses should be followed at tertiary centers by an experienced multidisciplinary team.⁴⁶¹

From a hemodynamic perspective, both normally functioning mechanical and bioprosthetic valves are generally associated with a favorable clinical course during pregnancy. An increase in the transprosthetic gradient may be a physiological consequence of the hemodynamic changes of pregnancy. However, it should be monitored carefully in patients with preexisting bioprosthetic valve dysfunction and in those with mechanical prostheses, in whom it may raise suspicion of prosthetic valve thrombosis.^{463,464}

During pregnancy, management of prosthetic valve dysfunction should prioritize maternal safety. Therapeutic strategies should be discussed by the Heart Team and shared with the obstetric team.

Bioprosthetic valve dysfunction presenting as regurgitation can generally be managed conservatively with medical therapy and has a low fetal risk. Conversely, stenotic dysfunction, particularly when associated with calcific structural valve deterioration, is associated with a high risk of maternal HF, shock, and sudden cardiac death, as well as preterm birth and fetal loss.

In these situations, surgical or percutaneous valve intervention, including a valve-in-valve procedure, should be considered.

In patients with mechanical prostheses, mild to moderate paravalvular regurgitation without significant HF or clinically relevant hemolysis may be managed conservatively with medical therapy directed at HF and anemia.

In the presence of significant prosthetic regurgitation, particularly in the mitral position, or clinically relevant hemolysis, intervention should be considered. Options include percutaneous closure of the paravalvular leak or surgery, recognizing the risks of recurrence and fetal complications.

Prosthetic valve thrombosis requires emergency intervention with thrombolysis or surgery according to established clinical and hemodynamic criteria.

For prosthetic valve stenosis caused by pannus or PPM, surgery should be considered despite the associated high fetal risk.

17.4. Anticoagulation

Anticoagulation protocols for pregnant patients with mechanical prostheses remain challenging and should be individualized according to clinical conditions and institutional experience. Multidisciplinary cardio-obstetric follow-up is recommended and should be structured according to the following phases: pre-pregnancy, each trimester of pregnancy, delivery, and the postpartum period (Chart 84). Anticoagulation should be rigorously monitored according to conventional therapeutic targets, with maternal safety prioritized.^{452,457}

Warfarin is indicated for preventing thrombotic events in pregnant patients with mechanical prostheses but crosses the placental barrier.^{4,462} Warfarin sodium is considered teratogenic and may cause congenital malformations collectively known as fetal warfarin syndrome, regardless of the daily dose used.⁴⁶⁵ Higher doses are associated with a higher likelihood of miscarriage and maternal and fetal bleeding; however, anticoagulation targets should prioritize maternal survival, with the dose adjusted according to the INR.^{462,466,467}

Therefore, during the first trimester, low-molecular-weight heparin or unfractionated heparin may be substituted for warfarin because neither crosses the placental barrier. Low-molecular-weight heparin should be administered subcutaneously at 1.0 mg/kg every 12 hours, with weekly anti-factor Xa monitoring and a target of 0.8 to 1.2 U/mL.⁴⁶⁸ Unfractionated heparin should be administered by continuous intravenous infusion at 18 IU/kg/h and monitored using the activated partial thromboplastin time, with a target of 1.5 to 2.0 times the control value. One disadvantage of unfractionated heparin is the need for prolonged hospitalization.^{4,452}

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Between 12 and 36 weeks' gestation, warfarin may be used with INR monitoring, targeting 2.5–3.0 for an aortic prosthesis and 3.0–3.5 for a mitral prosthesis.

At 34 to 36 weeks' gestation, warfarin should be replaced with low-molecular-weight heparin, which should be continued until 24 hours before delivery and then replaced with unfractionated heparin until 6 hours before delivery.^{4,452,462} Alternatively, continuous intravenous unfractionated heparin may be used exclusively during this period.^{452,462}

After delivery, anticoagulation with low-molecular-weight or unfractionated heparin should be resumed after 6 hours, and warfarin should be introduced after 48 hours. The therapies should overlap until an INR of 2.0 is achieved, at which point hospital discharge may be considered.

When urgent delivery is required, anticoagulation should be reversed to minimize bleeding risk using specific reversal agents, fresh frozen plasma, or prothrombin complex concentrate. If the patient is receiving warfarin, cesarean delivery should be selected because vaginal delivery carries a higher risk of fetal intracranial hemorrhage.

DOACs, including edoxaban, apixaban, and rivaroxaban, are contraindicated during pregnancy. Furthermore, these agents are not recommended in patients with mechanical prosthetic valves.

17.5. Delivery and Postpartum

Delivery should be planned before term through a multidisciplinary approach involving the cardio-obstetric, anesthesiology, and neonatology teams. Vaginal delivery is generally preferred in patients with low- or intermediate-risk valvular heart disease because it is associated with less blood loss and a lower risk of thromboembolic events and

infections.⁴⁵² Neuraxial anesthesia techniques, particularly when administered sequentially, offer hemodynamic advantages by allowing gradual onset of sympathetic blockade.

In addition to obstetric indications, cesarean delivery should be considered in patients with high-risk valvular heart disease, severe obstructive lesions, ascending aortic disease, or labor occurring while the patient is receiving anticoagulation.^{452,460} General anesthesia is usually used in these cases.

Although controversial, antibiotic prophylaxis against infective endocarditis at the time of delivery should be considered in patients with prosthetic valves or a history of infective endocarditis. The suggested regimen is intravenous ampicillin 2 g plus intramuscular gentamicin 1.5 mg/kg administered 1 hour before delivery.

17.6. Contraception

The choice of contraceptive method for women with valvular heart disease should be individualized through a multidisciplinary approach, prioritizing methods that are safe, highly effective, well tolerated, and readily accessible.

Counseling should be based on 2 principal frameworks: (1) the World Health Organization Medical Eligibility Criteria, which classify the risks and benefits of contraceptive methods according to the patient's clinical condition; and (2) the Pearl Index, which expresses method effectiveness as the number of pregnancies per 100 woman-years during use.^{469,470}

According to these recommendations, progestin-only contraceptives, available as oral formulations, quarterly injections, or implants, are preferred for women with valvular heart disease. Combined formulations containing natural estrogen, such as monthly injectable contraceptives, may also be used.^{377,471}

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