

Evaluation of Different Therapeutic Approaches for Acute Coronary Syndromes in Patients Undergoing Chronic Dialysis: A Retrospective Cohort Study

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Abstract

Background: Cardiovascular disease (CVD) is the leading cause of death among individuals with chronic kidney disease (CKD), particularly those undergoing dialysis, accounting for approximately 40% of deaths. The prevalence of ischemic coronary disease among patients undergoing hemodialysis over the age of 45 reaches 41%.

Objective: To analyze outcomes of symptomatic coronary artery disease (CAD) in patients undergoing chronic dialysis, stratified by invasive assessment, and treated with one of three approaches: medical therapy alone (MTA), percutaneous coronary intervention (PCI), or coronary artery bypass grafting.

Methods: This was a retrospective, analytical, observational cohort study based on data from electronic medical records collected between 2013 and 2023, including a total of 68 patients. Quantitative variables were analyzed using one-way Analysis of Variance (ANOVA), and qualitative variables were assessed using Pearson's chi-square test. A p-value <0.05 was considered statistically significant.

Results: The mean age was 60.2 ± 13.1 years, with a male predominance of 42 patients (62.8%). The highest mortality was observed in the MTA group with 25 deaths (69.4%), followed by PCI with 10 deaths (56.6%), and the lowest in the coronary artery bypass grafting group with six deaths (42.9%). Among patients who did not use statins, 19 (82.6%) died ($p < 0.01$). The lowest rate of readmission due to coronary syndrome occurred in the MTA group (two patients; 18.2%), while the highest was in the PCI group (six patients; 54.5%) ($p = 0.02$).

Conclusion: Although no statistically significant difference in mortality was found among the three therapeutic strategies, MTA was associated with lower rates of readmission and repeat cardiac catheterization. In contrast, PCI was linked to a higher risk of readmission due to coronary syndrome.

Keywords: Renal Dialysis; Coronary Artery Disease; Drug Therapy; Percutaneous Coronary Intervention; Coronary Artery Bypass.

Introduction

Cardiovascular disease (CVD) is the leading cause of death among individuals with chronic kidney disease (CKD), which is defined as an estimated glomerular filtration rate (eGFR) below $60 \text{ mL/min/1.73 m}^2$.¹ Cardiovascular mortality is inversely related to the glomerular filtration rate, with the risk increasing as renal function declines.²

Patients undergoing dialysis due to end-stage renal disease (ESRD) face the highest mortality risk within this population.

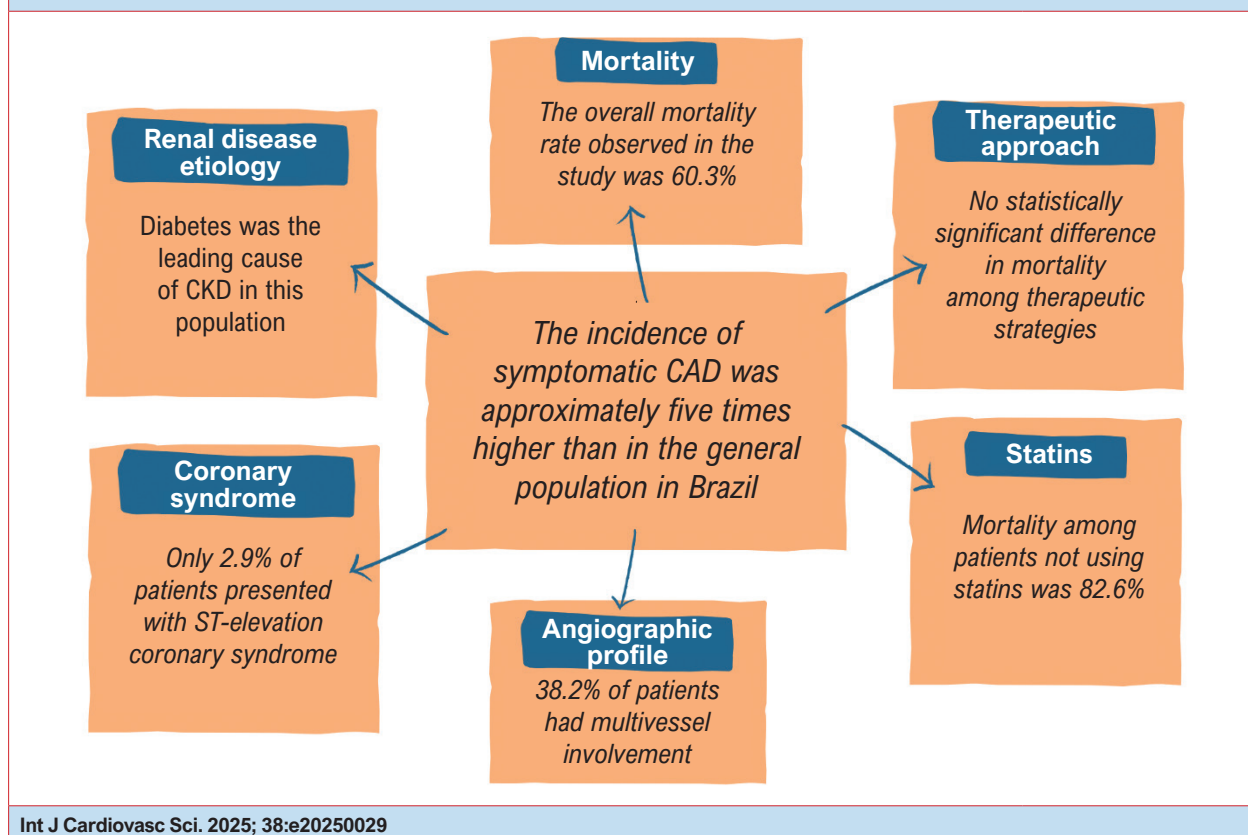
In the United States, the mortality rate among dialysis patients was 173 per 1,000 individuals in 2019, and the prevalence of coronary artery disease (CAD) reached 22% among younger patients and 41% in those over 45 years of age in 2020.³

In patients with CKD, the pathophysiology of CAD involves traditional risk factors such as smoking, hypertension (HTN), and diabetes mellitus (DM).⁴ However, CKD-specific factors also play a significant role. These include marked vascular medial calcification due to the transformation of smooth muscle cells into osteoblast-like cells, driven by hyperphosphatemia and hypercalcemia, as well as the accumulation of uremic toxins such as asymmetric dimethylarginine, which impairs nitric oxide synthase activity.⁵ Elevated levels of interleukin-6 and C-reactive protein in CKD indicate a pro-inflammatory state characterized by endothelial dysfunction and increased production of free radicals. A hypercoagulable state is also present, resulting from elevated platelet-derived procoagulant factors, although platelet activation response is typically reduced.^{5,6}

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Central Illustration: Evaluation of Different Therapeutic Approaches for Acute Coronary Syndromes in Patients Undergoing Chronic Dialysis: A Retrospective Cohort Study



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Summary of results. Evaluation of Different Therapeutic Approaches for Acute Coronary Syndromes in Patients Undergoing Chronic Dialysis: A Retrospective Cohort Study. CKD: chronic kidney disease; CAD: coronary artery disease.

Patients with CKD are often excluded from acute coronary syndrome (ACS) trials because they represent a higher-risk group, making treatment evaluation more challenging.^{7,8} Those with ESRD undergoing dialysis are less likely to receive invasive treatments, with only 12% undergoing percutaneous coronary intervention (PCI) and 3% undergoing coronary artery bypass grafting (CABG).⁹

There are discrepancies in literature regarding the optimal treatment for CAD in the CKD population.¹⁰⁻¹² Since the well-documented prevalence of ischemic events among individuals with CKD, the present study aims to analyze both the epidemiology and the most effective therapeutic approach for reducing mortality and complications related to ACS in patients with ESRD undergoing dialysis in the studied population.

Methods

This article is based on an observational, analytical, and retrospective study with a cohort epidemiological design. Data collection began after approval from the Human Research Ethics Committee at Centro Universitário para o Desenvolvimento do Alto Vale do Itajaí under opinion no. 6.552.015.

Data were collected from electronic medical records at a tertiary hospital in southern Brazil, in partnership with the regional dialysis center, by using a standardized data collection instrument.

The study population consisted of patients undergoing chronic dialysis who were diagnosed with and treated for ACS. Inclusion criteria were (1) undergoing chronic dialysis; (2) presenting symptoms attributable to CAD; and (3) undergoing invasive stratification through coronary angiography. Exclusion criteria were (1) individuals under 18 years of age; (2) lack of follow-up at the same health care facility; (3) having received a kidney transplant prior to the cardiac event; and (4) experiencing the cardiac event before starting dialysis.

A total of 753 patients undergoing chronic dialysis between January 1, 2013, and December 31, 2023, were identified. Next, we identified patients who underwent invasive cardiac stratification through coronary angiography during the same period, totaling 97 individuals. The exclusion criteria were then applied (Figure 1).

After defining the study population, data were collected and stored in a database using Google Sheets. The information was organized into the following sections: (1) population characteristics and lifestyle habits; (2) clinical aspects, including

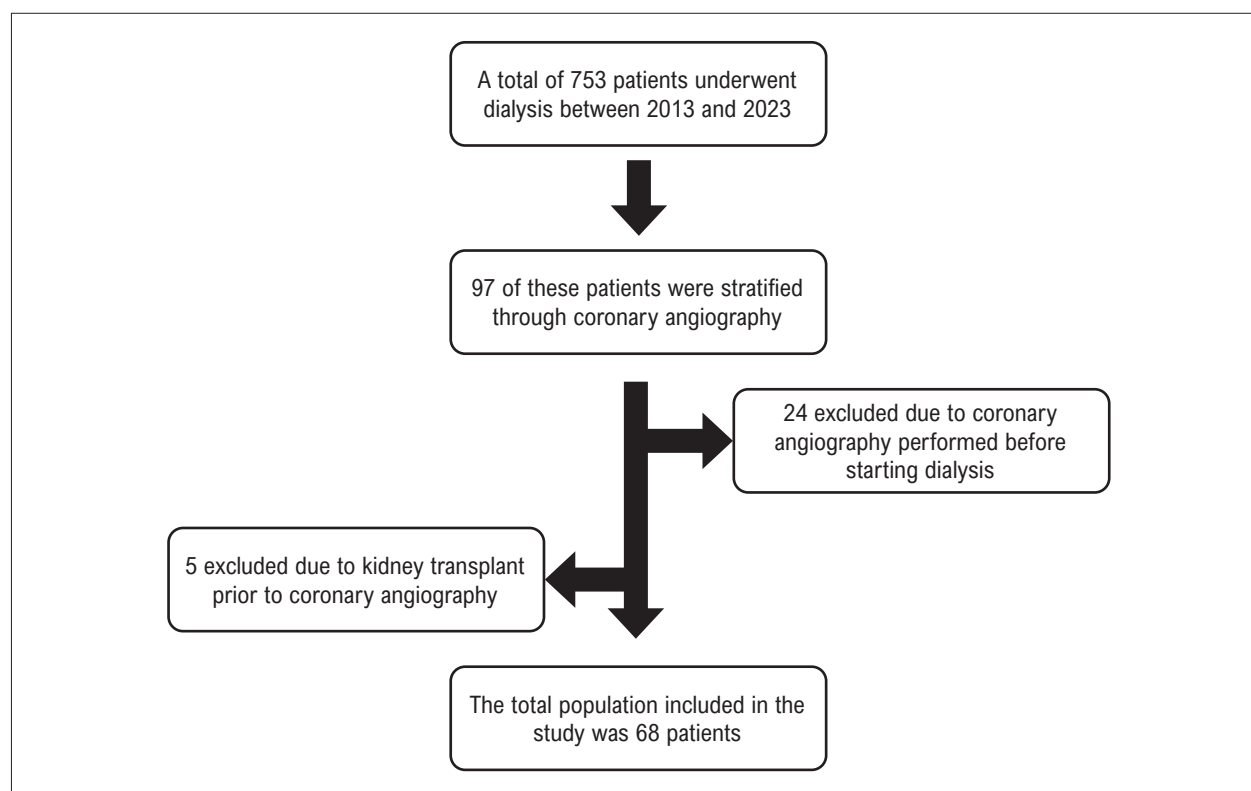


Figure 1 – Patient selection flowchart for the study.

dialysis and ACS characteristics; (3) medications used; (4) therapeutic approaches; and (5) outcomes and mortality.

Statistical analysis

Data were organized and analyzed by using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, N.Y., USA). For group comparisons in tables, therapeutic approaches were categorized into three groups: Group 1 (G1), medical therapy alone (MTA); Group 2 (G2), PCI; and Group 3 (G3), CABG.

To compare quantitative variables between groups, the Shapiro-Wilk test was first applied to assess normality. For variables with normal distribution, the parametric one-way ANOVA test was used, followed by Tukey's post-hoc test. Data were expressed as mean and standard deviation ($\pm$ SD).

For associations between qualitative variables and group comparisons, Pearson's chi-square test was used. When $p < 0.05$, standardized adjusted residual (ar) analysis was conducted, and values were considered statistically significant if $ar > 1.96$. Data were expressed as absolute numbers (n) and percentages (%). A p-value of < 0.05 was considered statistically significant for all analyses.

Results

Epidemiology and risk factors

A total of 753 patients undergoing chronic dialysis between 2013 and 2023 were analyzed. Among them, 97 patients

(12.9%) underwent coronary angiography due to symptomatic CAD. After applying the exclusion criteria, 68 patients (9.0%) remained and were divided into three groups: 36 (52.9%) received MTA (G1), 18 (26.5%) underwent PCI (G2), and 14 (20.6%) underwent CABG (G3).

The mean age at the time of the coronary event was approximately 60.2 years. The youngest group was the CABG group, while the oldest was the G2 (Table 1). There was a predominance of males, accounting for about 60% of the sample, while females comprised 40% (Table 1). However, women experienced the event at a younger age, with a mean of 56.6 ± 12.7 years, compared to 62.4 ± 13.0 years in men. Most patients had low educational attainment, with 40 individuals (58.8%) having completed only elementary school (5th grade).

Approximately 50% of the total sample had DM, with the highest prevalence observed in G1, where around 60% of participants were affected (Table 1). About 91% of patients in the study had HTN. More than 60% of the study population had dyslipidemia, with prevalence reaching nearly 80% among patients who underwent CABG (Table 1). The mean total cholesterol level near the time of the event was 172.8 ± 55.3 mg/dL, low-density lipoprotein cholesterol was 101.6 ± 44.7 mg/dL, and high-density lipoprotein cholesterol was 41.5 ± 10.8 mg/dL.

When combining current and former smokers, the total accounted for approximately 38%. However, smoking status was not recorded in the medical records of more than 23%

of patients (Table 1), limiting the ability to properly assess this risk factor.

Regarding body mass index, 64 patients (94.1%) were classified between normal weight and class I obesity. Among these, MTA was the most commonly used approach, with 12 (50%) patients in the normal weight category, 14 (50%) overweight, and nine (75%) with class I obesity. Only three patients had class II obesity, evenly distributed across the treatment groups. One patient had class III obesity and underwent CABG.

Among the patients included in the study, 18 (26.4%) had a previous coronary ischemic event, and 10 (14.7%) had a history of stroke. There was no difference in mortality compared to the overall sample.

Dialysis-related findings

The main underlying conditions leading to dialysis were diabetic nephropathy in 23 patients (33.8%), hypertensive nephropathy in 14 (20.6%), and polycystic kidney disease (PKD) in 9 (13.2%). Among these etiologies, the diabetic nephropathy group showed the highest final mortality rate, with 19 deaths (82.6%).

Most ACS occurred within the first 4 years after the initiation of dialysis, accounting for 57 patients (83.8%). However, there was no statistically significant association between dialysis duration and mortality (Graph 1).

Clinical profile and therapeutic choice

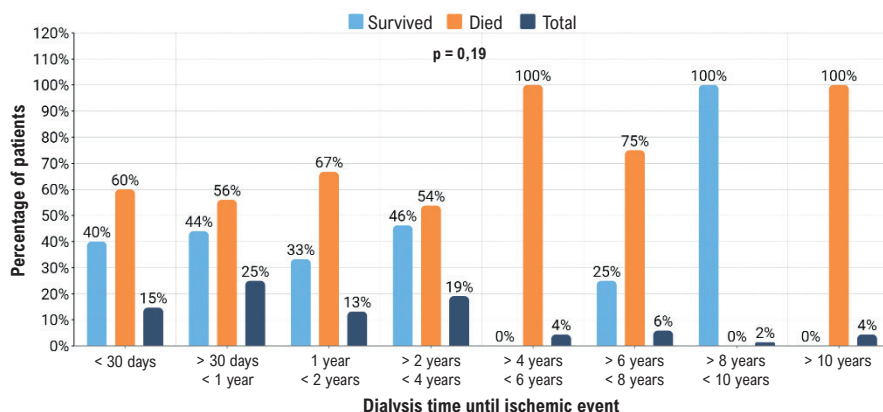
Patients without significant atheromatosis in the coronary angiography study, defined as <50% of the affected vessel diameter, all remained on MTA (G1). Patients with single-vessel involvement represented about 20% of the sample, and the majority stayed on MTA. Bifocal involvement occurred in approximately 15% of patients, most of whom were treated with PCI. Multi-vessel patients accounted for more than 38% of the study population, and the majority were treated with CABG (Table 2).

Non-ST-segment elevation ACS represent the largest portion of the sample, with more than 54% of patients. Chronic symptomatic CAD accounts for approximately 43% of the population, with MTA (G1) as the main therapeutic choice. ST-segment elevation ACS (STEACS) represents less than 3% of the sample.

Table 1 – Epidemiological profile by treatment groups and overall sample

	G1 (n = 36)	G2 (n = 18)	G3 (n = 14)	Total (n = 68)	p
Age (years)	59.6 ± 13.3	64.1 ± 12.1	56.7 ± 13.2	60.2 ± 13.1	0.26 ^a
Sex					0.10b ^b
• Male	19 (45.2%)	11 (26.2%)	12 (28.6%)	42 (62.8%)	
• Female	17 (65.4%)	7 (26.9%)	2 (7.7%)	26 (38.2%)	
DM					0.25 ^b
• No	16 (45.7%)	9 (25.7%)	10 (28.6%)	35 (51.5%)	
• Yes	20 (60.6%)	9 (27.3%)	4 (12.1%)	33 (48.5%)	
HTN					1.00 ^b
• No	3 (50.0%)	2 (33.3%)	1 (16.7%)	6 (8.8%)	
• Yes	33 (52.9%)	16 (25.8%)	13 (21.0%)	62 (91.2%)	
Dyslipidemia					0.31 ^b
• No	16 (64.0%)	6 (24.0%)	3 (12.0%)	25 (36.8%)	
• Yes	20 (46.5%)	12 (27.9%)	11 (25.6%)	43 (63.2%)	
Smoking status					0.38 ^b
• No	12 (46.2%)	8 (30.8%)	6 (23.1%)	26 (38.2%)	
• Yes	9 (81.8%)	1 (9.1%)	1 (9.1%)	11 (16.2%)	
• Former smoker	6 (40.0%)	4 (26.7%)	5 (33.3%)	15 (22.1%)	
• Not reported	9 (56.3%)	5 (31.3%)	2 (12.5%)	16 (23.5%)	

Group: Group 1 (G1): MTA; Group 2 (G2): PCI; Group 3 (G3): coronary artery bypass grafting. Note: Data are expressed as absolute number (n) and percentage (%) or mean ± standard deviation (±SD). Statistical method used: ^aOne-way ANOVA test; ^bPearson's chi-square test; p < 0.05 was considered statistically significant. DM: diabetes mellitus; HTN: hypertension.



Graph 1 – Association between dialysis duration until ischemic event and overall mortality. Data are expressed as percentages (%). Statistical method used: Pearson's chi-square test. $p < 0.05$ was considered statistically significant.

Table 2 – Therapeutic choice according to clinical presentation

	G1 (n = 36)	G2 (n = 18)	G3 (n = 14)	Total (n = 68)
Angiographic profile				
				<0.01*
• No significant atheromatosis	18 (100.0)**	0 (0.0)	0 (0.0)	18 (26.5)
• Single-vessel disease	9 (64.3)	4 (28.6)	1 (7.1)	14 (20.6)
• Two-vessel disease	1 (10.0)	7 (70.0)**	2 (20.0)	10 (14.7)
• Multi-vessel disease	8 (30.8)	7 (26.9)	11 (42.3)**	26 (38.2)
ACS classification				
				0.05*
• Chronic symptomatic CAD	21 (72.4)**	5 (17.2)	3 (10.3)	29 (42.6)
• Non-ST-elevation ACS	14 (37.8)	13 (35.1)	10 (27.0)	37 (54.4)
• ST-elevation ACS	1 (50.0)	0 (0.0)	1 (50.0)	2 (2.9)

Group: Group 1 (G1): MTA; Group 2 (G2): PCI; Group 3 (G3): coronary artery bypass grafting. Note: Data are expressed as absolute number (n) and percentage (%). Statistical method used: Pearson's chi-square test, followed by analysis of standardized adjusted residuals >1.96 . $p < 0.05$ was considered statistically significant (*). CAD: coronary artery disease; ACS: acute coronary syndrome.

Medications used in treatment

Statin use showed statistical significance in the overall analysis of the study ($p < 0.01$). Among patients who did not use statins, only 4 (17.4%) survived, while 19 (82.6%) died.

Of the 36 patients in G1, 35 had a recorded list of medications in their medical records. The use of calcium channel blockers (CCBs) and hydralazine was associated with significantly higher mortality (Graph 2).

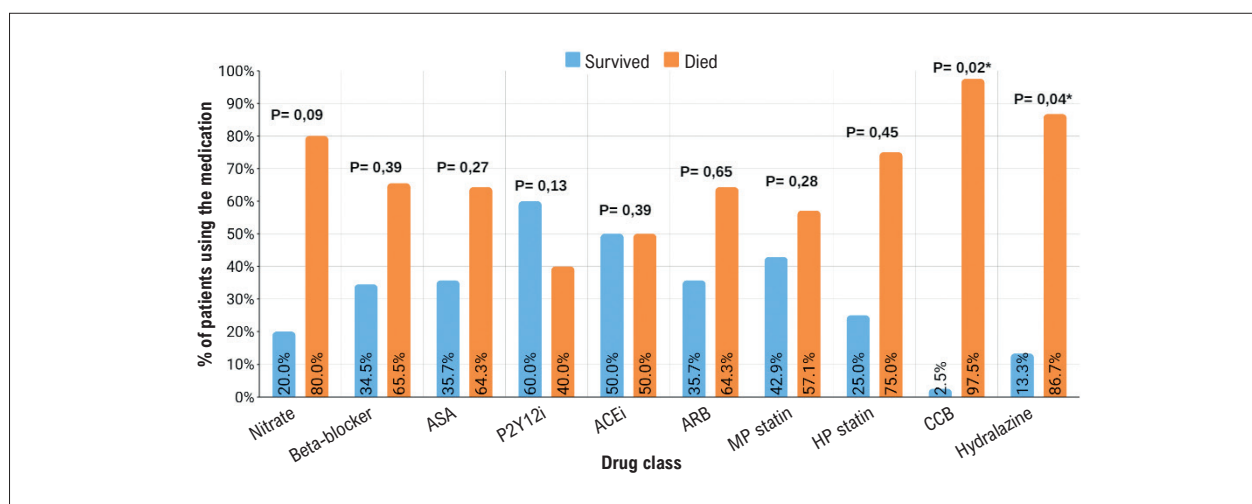
Overall and group-specific mortality

Among the 68 patients in our study, 41 (60.3%) died by the end of the study period. The group with the highest mortality rate was G1, with nearly 70%, followed by G2 with

approximately 57%, and G3 with the lowest mortality rate at around 43% (Table 3). Regarding angiographic profile, the highest mortality was observed in patients with single-vessel disease (71.4%), followed by those with multi-vessel disease (65.4%), no significant atheromatosis (61.1%), and the lowest mortality in those with two-vessel disease (40.0%).

Complications following treatment for ACS

The highest number of rehospitalizations due to ACS and repeat coronary angiography occurred in G2, accounting for approximately 50% of cases (Table 4). In contrast, the lowest rates were observed in G1, with 18.2% and 12.5%, respectively.



Graph 2 – Association between medications used and mortality in the MTA group (G1). Data are expressed as percentages (%). Statistical method used: Pearson's chi-square test. $p < 0.05$ was considered statistically significant (*). ASA: acetylsalicylic acid; P2Y12i: P2Y12 inhibitor; ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; MP statin: moderate-potency statin; HP statin: high-potency statin; CCB: calcium channel blocker.

Table 3 – Relationship between angiographic profile and mortality by treatment group

	No significant atheromatosis (n = 18)	Single-vessel (n = 14)	Two-vessel (n = 10)	Multi-vessel (n = 26)	Total (n = 68)	p
G1						0,78
• No	7 (38.9%)	2 (22.2%)	0 (0.0%)	2 (25.0%)	11 (30.6%)	
• Yes	11 (61.1%)	7 (77.8%)	1 (100.0%)		25 (69.4%)	
G2						0.60
• No	0 (0.0%)	2 (50.0%)	4 (57.1%)	2 (28.6%)	8 (44.4%)	
• Yes	0 (0.0%)	2 (50.0%)	3 (42.9%)		10 (56.6%)	
G3						0.48
• No	0 (0.0%)	0 (0.0%)	2 (100.0%)		8 (57.1%)	
• Yes	0 (0.0%)	1 (100.0%)	0 (0.0%)	5 (45.5%)	6 (42.9%)	

Group: Group 1 (G1): MTA; Group 2 (G2): PCI; Group 3 (G3): coronary artery bypass grafting. Note: Data are expressed as absolute number (n) and percentage (%). Statistical method used: Pearson's chi-square test. $p < 0.05$ was considered statistically significant.

Major bleeding was defined as requiring transfusion of ≥ 2 units of packed red blood cells or a ≥ 2 g/dL drop in hemoglobin. It was most frequent in G1, representing approximately 60% of the cases. The main findings described above are summarized in Central Illustration.

Discussion

In the present study, the incidence of CAD among patients with ESRD on dialysis was 9.0% — almost five times higher than the CAD rate in the general Brazilian population, which

was 1.85% in 2019.¹³ The literature shows that the incidence of CAD in the population with CKD increases with age, particularly in individuals over 65 years old.¹⁴ The mean age found in this study was 60.2 ± 13.1 years, with women experiencing coronary events at a younger age (56.6 ± 12.7 years).

Patients with CKD have an elevated risk of developing CAD, which increases further once dialysis is initiated.¹⁵ Our findings revealed a mortality rate of 60.3% among patients who developed an ACS.

Table 4 – Complications After Treatment by Groups and Overall Sample

Complications	G1 (n = 36)	G2 (n = 18)	G3 (n = 14)	Total (n = 68)	p
Rehospitalization due to ACS					0.02*
• No	34 (59.6)**	12 (21.1)	11 (19.3)	57 (100.0)	
• Yes	2 (18.2)	6 (54.5)**	3 (27.3)	11 (100.0)	
Repeat coronary angiography					0.05
• No	35 (58.3)**	14 (23.3)	11 (18.3)	60 (100.0)	
• Yes	1 (12.5)	4 (50.0)	3 (37.5)	8 (100.0)	
Stroke					0.82
• No	34 (52.3)	17 (26.2)	14 (21.5)	65 (100.0)	
• Yes	2 (66.7)	1 (33.3)	0 (0.0)	3 (100.0)	
Major bleeding					0.30
• No	20 (47.6)	14 (33.3)	8 (19.0)	42 (100.0)	
• Yes	16 (61.5)	4 (15.4)	6 (23.1)	26 (100.0)	

Group: Group 1 (G1): MTA; Group 2 (G2): PCI; Group 3 (G3): coronary artery bypass grafting. Note: Data are expressed as absolute number (n) and percentage (%). Statistical method used: Pearson's chi-square test, followed by analysis of standardized adjusted residuals >1.96. $p < 0.05$ was considered statistically significant (*). Values marked with * indicate statistically significant associations within the row. ACS: acute coronary syndrome.

HTN, DM, and smoking are well-known shared risk factors for both CKD and CAD.^{1,13,16} In our study, the prevalence of DM was 48.5%, dyslipidemia was observed in 63.2%, and HTN was present in 91.2% of patients. However, the prevalence of smoking was low, though this may be underestimated due to incomplete documentation in medical records.

According to the 2022 Brazilian Dialysis Census, the main etiologies of CKD among dialysis patients were HTN, DM, glomerulonephritis, and PKD.¹⁷ In our study, 33.8% of patients had diabetic nephropathy, 20.6% had hypertensive nephropathy, 13.2% had PKD, and 5.9% had glomerular diseases.

STEACS is not commonly seen in patients with ESRD, who often present with atypical or silent symptoms.¹⁸ Consistent with this, only 2 patients (2.9%) in our study presented with STEACS.

Therapeutic decisions vary depending on the angiographic profile, type of ACS, and surgical risk factors of the patient. In line with precious research, we observed a predominance of MTA in patients with no significant atheromatosis and in those with single-vessel disease.^{1,8,9} Among patients with two-vessel disease, PCI was the most common approach, while CABG was predominantly used in those with multi-vessel involvement. However, patients with contraindications to surgery remained on MTA.

The currently recommended treatment for HTN in dialysis patients begins with beta-blockers, which have shown superiority over ACE inhibitors. This is followed by CCBs, whose benefits compared to other antihypertensives remain uncertain.^{19,20} In our study, the use of CCBs was associated with significantly increased mortality ($p = 0.02$). The use of

antiplatelet agents should be individualized, as they reduce the incidence of myocardial infarction but increase bleeding risk and do not impact overall mortality.²¹ The use of statins in dialysis patients is recommended if already initiated before dialysis, particularly in the presence of established CVD.²² In our study, patients not using statins had a markedly higher mortality rate (82.6%).

The main trial that evaluated patients with CKD in the context of stable CAD outcomes was the ISCHEMIA-CKD trial, which concluded that interventional strategies were not superior to MTA in terms of mortality over 2.2 years.²³ However, the invasive strategy was associated with a lower incidence of recurrent cardiac events.¹²

In our study, there was also no statistically significant difference in mortality between the MTA, PCI, and CABG groups. However, among patients with multivessel disease, those who received conservative treatment had a higher mortality rate (75.0%) compared to those who underwent CABG (45.5%).

The main complications of ACS in dialysis patients include recurrent cardiac events, strokes, and bleeding episodes.^{24,25} In our population, MTA was protective against rehospitalization for coronary events and the need for repeat coronary angiography. In contrast, PCI was associated with a higher risk of rehospitalization, affecting 33.3% of patients ($p = 0.05$).

There is significant underrepresentation of patients with ESRD in clinical trials, which limits the evidence available to support recommendations for optimal therapeutic strategies in this group.²⁶ This highlights the need for studies that include a larger number of patients from this population.

This study faced limitations in effective analysis due to the small sample size and heterogeneity across treatment groups. The retrospective design and inconsistency of medical record documentation also hindered the evaluation of certain variables.

Conclusion

In our study, patients with ESRD on dialysis showed an incidence of CAD approximately five times higher than that of the general Brazilian population, along with an elevated mortality rate. DM, HTN, and dyslipidemia were prevalent risk factors in this population. The absence of statin use among patients undergoing chronic dialysis was associated with increased CAD-related mortality.

Our data did not reveal a statistically significant difference in mortality among the groups treated with MTA, PCI, or CABG. However, MTA proved to be a protective factor against rehospitalization for ACS and repeat coronary angiography over the 10-year study period. In contrast, PCI was associated with a higher risk of rehospitalization for ACS. These findings highlight the need for multicenter studies with larger patient populations to allow for broader analysis and more robust conclusions on the subject.

Author Contributions

Conception and design of the research and critical revision of the manuscript for intellectual content: França ME, Ribeiro LC, Toniazzo SRF; acquisition of data: França ME, Fragas AL; analysis and interpretation of the data: França ME, Fragas AL, Rocha FR, Toniazzo SRF; statistical analysis: França ME, Rocha FR; writing of the manuscript: França ME, Rocha FR, Toniazzo SRF.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the UNIDAVI under the protocol number 6.552.015. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

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