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## The Characteristics of Chest Pain in the Emergency Setting among Patients with Chronic Kidney Disease

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### ABSTRACT

**Background:** Chronic kidney disease (CKD) is considered a major public health issue, not only due to the possibility of progressing to end-stage renal disease but also because it is closely related to the development of acute coronary syndrome (ACS). It is still unclear in the literature whether individuals with renal dysfunction present particularities in the clinical manifestations during acute myocardial infarction, similar to individuals with diabetes.

**Aims:** To evaluate the characteristics of clinical manifestations in patients with CKD and ACS.

**Methods:** The Chi-square test and Student's t-test were used to analyze the profile of patients with coronary syndrome and renal disease who were admitted for chest pain at the analyzed hospital.

**Results:** The majority of individuals with renal dysfunction present highly suspicious characteristics, with statistical significance by presenting a p-value equal to 0.01 and a 95% confidence interval (0.04-0.14). **Conclusion:** Individuals with kidney disease predominantly exhibit highly suspicious clinical manifestations for acute coronary syndrome.

**Keywords:** chest pain, clinical manifestations, acute coronary syndrome, chronic kidney disease

## Introduction

Chronic Kidney Disease (CKD) is defined as the progressive and irreversible loss of kidney function<sup>1,2</sup>. Currently, it is regarded as a significant public health concern both in Brazil and worldwide, owing to its impact on the quality of life for the affected population and healthcare expenditures<sup>3,4</sup>. Data from the World Health Organization (WHO) estimates that by 2040, CKD is poised to become the fifth most common chronic disease globally<sup>5</sup>.

The substantial concern surrounding kidney disease extends beyond its progression to a terminal condition that requires renal replacement therapy, such as kidney transplantation and dialysis<sup>6</sup>. It encompasses its correlation with the development of cardiovascular events, particularly Acute Coronary Syndrome (ACS), which stands as a primary cause of global mortality<sup>7,8</sup>. Numerous studies have already elucidated that the decline in renal function constitutes a pivotal risk factor in the development of cardiovascular events, and is also associated with elevated in-hospital mortality rates in cases of coronary disease<sup>9,10</sup>. This association between the two diseases, as evidenced in the literature, begins with a decrease in the glomerular filtration rate (<60 ml/min/1.73m<sup>2</sup>) and appears to be linked with vascular calcification and heightened levels of markers such as Osteoprotegerin (OPG) and Fibroblast Growth Factor 23 (FGF-23), which are associated with an increase in heart-related mortality<sup>11,12</sup>.

Recognizing acute coronary syndrome, however, is not always an easy task. There exists a substantial subset of individuals who exhibit clinical presentations highly suggestive of ACS, characterized by the American Heart Association as retrosternal pain triggered by rest or stress (both physical and emotional), often radiating to other areas (left arm, jaw), accompanied by associated symptoms (dyspnea, nausea)<sup>13,14</sup>.

The classic presentation, however, is not always observed. In several patients, initial complaints can be vague and highly nonspecific, as observed in instances involving women, the elderly, and diabetics<sup>15-17</sup>. In women and the elderly, for instance, the clinical presentation is often associated with symptoms such as nausea, tachypnea, dizziness, abdominal pain, and even falls in the latter group. In individuals with diabetes, numerous studies demonstrate either an absence or atypical nature of chest pain, which can be attributed to the neuropathic involvement characteristic of the disease, altering pain perception<sup>18,19</sup>. In this

context, it is evident from various studies that these specific subpopulations often exhibit a less suspicious clinical profile and this could contribute to underdiagnosis of the disease, as well as delays in treatment and potentially worse outcomes compared to other subpopulations<sup>20,21</sup>.

Although existing literature offers valuable insights into the unique presentations of Acute Coronary Syndrome (ACS) in various subpopulations, there is a lack of research examining whether individuals with renal disease tend to exhibit less or more indicative symptoms of coronary syndrome. Therefore, this study aims to identify specific clinical characteristics in individuals with both chronic kidney disease and acute coronary syndrome, with the ultimate objective of improving the identification and diagnosis of the disease in these subpopulations.

## Methods

This is a prospective cohort study conducted at a hospital situated in the city of Curitiba, Brazil. The study encompassed an analysis of data from patients admitted for chest pain at the aforementioned site, spanning the years 2012 to 2019. The data were extracted from a pre-existing study database, duly approved by the Ethics and Research Committee of the Pontifical Catholic University of Paraná.

The present study was structured into three distinct phases. Initially, was conducted an individual analysis of the profiles of individuals affected by acute coronary syndrome and chronic kidney disease, through the assessment of variables such as age, presence of comorbidities, history of prior myocardial infarction, and lifestyle habits. In a second stage, the focus shifted to investigating the characteristics of chest pain in individuals with and without renal dysfunction, considering aspects such as the type of chest pain, its location, its radiation, factors that worsen or alleviate it, associated symptoms, and the presence of ischemic disease. Finally, based on the analyzed variables, participants were categorized into three groups according to the clinical suspicion of chest pain: high suspicion, moderate suspicion, or low suspicion.

The inclusion criteria for the study were individuals admitted with chest pain to the mentioned hospital, whose data, including records of their comorbidities, lifestyle habits, and clinical status at the time of admission, were included in the databases used. The exclusion criteria applied were individuals with incomplete data. The determination of ischemic disease was defined by the attending physician

based on the analysis of the chest pain characteristics of admitted patients, aided by electrocardiographic exams, laboratory tests, and mortality risk scores. From the results of laboratory tests, the glomerular filtration rate (GFR) was calculated using the CKD-EPI formula based on the creatinine value. Kidney disease was defined as a GFR below 60 mL/minute/1.73 m<sup>2</sup>.

#### STATISTICAL ANALYSIS

Regarding data tabulation, the Microsoft Excel program was initially employed, followed by statistical analysis using the IBM SPSS Statistics software. These data were organized into tables, with quantitative variables presented as mean and standard deviation, while qualitative variables were detailed in the tables according to frequencies and percentages. The Chi-square test was also employed to analyze these variables. Furthermore, the Student's t-test was utilized for the comparison of two distinct populations: those presenting ACS and those not, as well as those exhibiting or not exhibiting CKD.

In this study, a p value < 0,05 was considered for statistical significance. Additionally, the confidence interval was employed to estimate the precision of the obtained measures, allowing for an assessment of result variability and the reliability of the

conclusions drawn. The selection of this statistical method aims to provide a robust and reliable approach for data interpretation.

#### Results

A total of 281 patients admitted with chest pain were analyzed at the Hospital. The analysis of patient profiles concerning the presence or absence of ACS and CKD is presented in Table 01 and Table 02 respectively, while the characteristics and classification of chest pain are shown in Table 03 and Table 04, respectively.

As indicated in Table 1, the mean age of individuals with or without coronary syndrome was 66 (±12,21) years. Among the most prevalent comorbidities in patients with and without ACS were systemic arterial hypertension (77,5% and 64,2%), dyslipidemia (56,8% and 30%), and diabetes mellitus (37,9% and 24,3%). Notably, the presence of prior myocardial infarction (MI) was higher in individuals with ACS (29,3%) compared to those who had not experienced it previously (18,4%). Furthermore, obesity (33,9%), sedentary lifestyle (12,1%), alcohol consumption (12%), and smoking (24,1%) were more frequently reported by individuals with ACS.

Table 01 – Analysis of patient profiles with and without ACS

Variable analyzed	Presence of ACS	Absence of ACS	p value
Age	66 (±12,21)	66 (±16,92)	0,058
Hypertension	45 (77,5%)	133 (64,2%)	0,056
Dyslipidemia	33 (56,8%)	61 (30%)	0,00
Diabetes Mellitus	22 (37,9%)	50 (24,3%)	0,041
Obesity	19 (33,9%)	42 (21,6%)	0,059
Prior myocardial infarction	17 (29,3%)	38 (18,4%)	0,072
Sedentary lifestyle	5 (12,1%)	3 (1,7%)	0,02
Alcohol consumption	7 (12%)	10 (5%)	0,061
Smoking	14 (24,1%)	21 (10,3%)	0,007

Table 02 presents the characteristics of patients with the presence and absence of CKD admitted to the hospital with the complaint of chest pain. The mean age of the evaluated patients was 64 (±15,19) years for those with kidney disease and 62 (±16,22) years for those without it. Concerning comorbidities, more than half of the patients had systemic arterial hypertension (75%), nearly half of

them had dyslipidemia (40%), 27,5% had diabetes mellitus, and 17,5% reported a history of previous Myocardial Infarction (MI). Furthermore, among individuals with CKD, approximately 23,6% were obese, 6,8% reported a sedentary lifestyle, 5,2% had an alcohol habit, and 17,9% reported being smokers.

Table 02 – Analysis of patient profiles with and without CKD

Analyzed variable	Presence of CKD	Absence of CKD	p value
Age	64(± 15,19)	62 (± 16,22)	0,462
Hypertension	30 (75%)	80 (67,5%)	0,392
Dyslipidemia	16 (40%)	42 (37,1%)	0,751
Diabetes Mellitus	11 (27,5%)	35 (29,9%)	0,772

Analyzed variable	Presence of CKD	Absence of CKD	p value
Prior myocardial infarction	7 (17,5%)	25 (21,3%)	0,600
Obesity	9 (23,6%)	26 (22,8%)	0,911
Sedentary lifestyle	2 (6,8%)	5 (5,2%)	0,729
Alcohol consumption	2 (5,2%)	12 (10,5%)	0,331
Smoking	7 (17,9%)	21 (17,9%)	1,000

Regarding chest pain, as demonstrated in Table 03, the majority of individuals reported pain as tightness (16%), burning sensation (11,9%), pressure (9,5%), or stabbing (4,7%). The location of the pain was quite variable: 21,4% of patients mentioned precordial pain, 16,6% retrosternal pain, 9,5% pain in the hemithorax, and 4,7% diffuse pain. Around 16,6% and 11,9% of patients reported radiation to the left arm and left shoulder respectively, and additionally, about 7,1% of patients reported radiation to the right shoulder and 2,3% to the right arm. More than half of the

assessed individuals (61,9%) did not report any improving factors for the pain, but 7,1% noted exacerbation with physical exercise and 2,3% with ventilation. Around 69% of patients related no worsening factors. In terms of associated symptoms, 4,7% of patients experienced sweating, 7,1% mentioned malaise, 35,7% denied associated symptoms and more than a half (57%) mentioned other symptoms. Among the total individuals with CKD analyzed, approximately 27,9% exhibited ischemic disease.

Table 03 – Characteristics of chest pain in patients with and without CKD

Characteristic of pain	Presence of CKD	Absence of CKD	P value
Tightness	7 (16%)	24 (19%)	0,435
Burning sensation	5 (11,9%)	10 (7,9%)	0,435
Pressure	4 (9,5%)	2 (1,5%)	0,016
Stabbing	2 (4,7%)	15 (11,9%)	0,184
<b>Pain location</b>			
Precordial	9 (21,4%)	27 (21,6%)	0,981
Retrosternal	7 (16,6%)	21 (16,8%)	0,984
Hemithorax	4 (9,5%)	15 (12%)	0,662
Diffuse	2 (4,7%)	10 (8%)	0,475
<b>Pain radiation</b>			
Left arm	7 (16,6%)	13 (10,3%)	0,271
Left shoulder	5 (11,9%)	10 (7,9%)	0,435
Right shoulder	3 (7,1%)	2 (1,5%)	0,067
Right arm	1 (2,3%)	1 (0,7%)	0,411
<b>Factors improving/worsening</b>			
No improving factors	26 (61,9%)	88 (69,8%)	0,340
Physical exercise	3 (7,1%)	8 (6,3%)	0,857
Ventilation	1 (2,3%)	5 (3,9%)	0,631
No worsening factors	29 (69%)	99 (78,5%)	0,209
<b>Associated symptoms</b>			
Sweating	2 (4,7%)	0 (0%)	0,014
Malaise	3 (7,1%)	5 (3,9%)	0,403
No associated symptoms	15 (35,7%)	38 (30,1%)	0,502
Other symptoms	24 (57%)	70 (55,5%)	0,858
<b>Presence of ischemic disease</b>	12 (27,9%)	29 (22,8%)	0,502

Lastly, as depicted in Table 04, the majority of patients with CKD were classified, upon admission, with highly suspicious chest pain for ACS, with this

analysis holding noteworthy significance at a p-value of 0.01 and a 95% confidence interval of 0.04-0.14.

Table 04 – Classification of chest pain in patients with CKD and ACS

Suspicious for ACS	Presence of CKD	Absence of CKD	p value	Confidence interval
Highly suspicious	10 (23,8%)	11 (8,6%)	0,01	CI 95% (0,04-0,14)
Moderately suspicious	8 (19%)	40 (31,4%)	0,121	CI 95% (0,07-0,31)
Slightly suspicious	8 (19%)	25 (19,6%)	0,928	CI 95% (0,07-0,31)

## Discussion

The findings reveal that within the study sample, irrespective of the presence or absence of kidney disease, there exists an age group above 60 years in individuals with acute coronary syndrome. Similar observations have been documented in various studies, which also report an average age range of acute myocardial infarction in patients between 55 to 74 years<sup>22</sup>. The higher prevalence of the disease in elderly patients can be explained by the fact that older individuals undergo various age-related changes. The aging process is marked by a reduction in physiological function, attributed to chronic inflammation inherent to aging, which promotes cellular senescence. This, in turn, leads to the progression of atherosclerosis, a pivotal factor contributing significantly to the heightened vulnerability to cardiovascular diseases in the elderly population.<sup>23,24</sup>

Concerning the prevalence of comorbidities, the current study revealed a higher incidence of coronary syndrome in individuals with systemic arterial hypertension, dyslipidemia, and diabetes mellitus, irrespective of the presence or absence of renal dysfunction. Another study yielded comparable results, indicating that approximately 82.6% of patients had arterial hypertension, and 30.1% had diabetes<sup>25</sup>. It is evident that these conditions are intrinsically linked to acute coronary syndrome, playing a crucial role as fundamental risk factors for its development<sup>26,27</sup>. Through their pathophysiologies, these conditions result in endothelial dysfunction, triggering a systemic inflammatory response. Systemic arterial hypertension, for instance, heightens cardiovascular risk by inducing a pro-inflammatory state through changes in the medial layers of blood vessels, such as hypertrophy and hyperplasia. Similarly, Diabetes Mellitus, with insulin resistance and hyperglycemia in its pathophysiology, among other changes, amplifies oxidative stress and endothelial injury. Dyslipidemia, also associated with various factors, contributes to increased systemic inflammation. All these elements, as extensively documented in the medical literature, converge to elevate the risk of developing cardiovascular diseases<sup>28, 29</sup>.

Furthermore, the study identified an association between individuals with chronic kidney disease and heart ischemic disease. Similar to hypertension, diabetes, and dyslipidemia, CKD also represents a significant risk factor for the development of coronary artery disease, and consequently, acute myocardial infarction and the connection between the two diseases has been extensively discussed

and is well-established in the literature<sup>30, 31</sup>. It is acknowledged that the primary risk factors associated with the development of ACS are linked to endothelial dysfunction and systemic inflammatory changes and individuals with kidney disease present risk factors intertwined with the pathophysiology of the disease itself, including increased oxidative stress and an elevated pro-inflammatory state, resulting in atherosclerotic alterations and cardiac remodeling<sup>32,33</sup>. Moreover, it's recognized that individuals with renal dysfunction face a worse prognosis for cardiovascular events when compared to those without the disease, and are more likely to succumb to heart-related conditions and their ramifications rather than the renal disease itself<sup>34</sup>.

Concerning clinical manifestations, it's noteworthy to emphasize the type of chest pain found in patients with both kidney and ischemic disease, as this was a significant focus of the study. Patients with renal dysfunction predominantly exhibited localized chest pain, typical character, characteristic radiation, and absence of relieving factors, which was deemed highly suspicious and statistically significant. Few studies in the literature have focused on assessing whether there are distinct clinical characteristics in the presentation of heart attacks in individuals with chronic kidney disease, similar to the focus on women, the elderly, and diabetics<sup>35-37</sup>.

Some studies suggest that patients with renal disease are more likely to report associated symptoms, such as dyspnea, possibly due to volume overload caused by renal insufficiency<sup>33,38</sup>. However, it is crucial to note that many of these studies focused solely on the clinical presentation of myocardial infarction at different stages of renal disease, suggesting that individuals with advanced renal disease, namely those requiring renal replacement therapies, may exhibit a less suspicious clinical profile, where chest pain may not be the initial symptom<sup>39,40</sup>. In the context of this study, however, the aim was not solely to assess the characteristics of chest pain at different stages of renal disease but rather to investigate the most prevalent clinical manifestations in individuals with chronic kidney disease, irrespective of disease severity. In this regard, it was observed that the majority of individuals with chronic kidney disease present typical chest pain as the primary symptom.

Furthermore, a noteworthy conclusion drawn from this study is that, despite individuals with renal disease being able to display various associated symptoms, typical chest pain still remains the most prevalent symptom, regardless of renal function. In other words, despite CKD patients manifesting more

associated symptoms during acute coronary syndrome, the prevailing complaint continues to be typical chest pain, consistent with the findings of the current study.

Given this, one might question the underlying relationship between the study's findings. In this context, two possible hypotheses for the findings can be considered. One is that the pathophysiology of renal dysfunction might be linked to the development of a typical clinical presentation. The other could stem from evaluator subjectivity in classifying chest pain during the initial assessments of individuals admitted with chest pain and kidney disease.

The present study was conducted at a single center and has a relatively small sample size.

Consequently, the results obtained within the studied population may not be generalized to all other populations. Therefore, similar studies may be necessary to assess the reproducibility of the findings.

## **Conclusion**

The present study demonstrated a higher incidence of acute coronary syndrome in elderly patients with specific associated comorbidities. In individuals with chronic kidney disease, the study showcased a clinical profile that was classified as highly suspicious, characterized by typical localization, radiation, and character.

## **Conflicts of interest statement**

The authors have no conflicts of interest to declare

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