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Impact of COVID-19 on Acute Coronary Syndrome: An Examination of Mortality and Demographic Factors

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A B S T R A C T

The COVID-19 pandemic has significantly impacted cardiovascular health, with acute coronary syndrome (ACS) emerging as a major concern. This study investigates the relationship between demographic characteristics, mortality rates, and the incidence of ACS in COVID-19 patients. A retrospective study was conducted on a cohort of 68 patients diagnosed with both COVID-19 and ACS, admitted to a hospital in Medan between August 2020 and August 2021. Demographic data, COVID-19 severity, electrocardiogram (ECG) findings, and comorbid conditions were analyzed for their association with mortality. The mean age of the study participants was 58.2 years, with a male predominance (82.9%). The majority of patients experienced severe COVID-19 (62.9%), and the most common ECG finding was ST-elevation (62.9%). Hypertension was the most prevalent comorbidity (52.9%). Mortality was significantly associated with male gender (p=0.01) but not with COVID-19 severity, ECG findings, or comorbidities. In conclusion, male gender was identified as an independent predictor of mortality in COVID-19 patients with ACS. Further research is needed to elucidate the complex interplay of demographic factors, COVID-19, and ACS outcomes.

1. Introduction

The emergence of the COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has presented an unprecedented global health crisis. Initially characterized by its respiratory manifestations, the impact of COVID-19 has proven far-reaching, extending to various organ systems, including the cardiovascular system. The pandemic has not only exacerbated pre-existing cardiovascular conditions but also unveiled a complex interplay between SARS-CoV-2 infection and the development of new cardiovascular complications. Among these, acute coronary syndrome (ACS) has emerged as a significant concern, demanding a deeper understanding of its incidence, risk factors, and outcomes in the context of COVID-19.[1,2]

Acute coronary syndrome encompasses a range of life-threatening conditions affecting the coronary arteries, the blood vessels responsible for supplying oxygen-rich blood to the heart muscle. This spectrum includes unstable angina, a condition characterized by chest pain caused by reduced blood flow to the heart, as well as non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI), both of which involve heart muscle damage due to prolonged blockage of a coronary artery. The pathophysiology of ACS involves the disruption of atherosclerotic plaques within the coronary arteries, leading to blood clot formation and obstruction of blood flow.[3,4]

The intricate relationship between COVID-19 and ACS stems from the multifaceted effects of SARS-CoV-

2 infection on the cardiovascular system. The virus can directly invade the heart muscle, causing inflammation and damage. Additionally, COVID-19 triggers a systemic inflammatory response and a prothrombotic state, increasing the risk of blood clot formation. These factors, combined with the potential for endothelial dysfunction, which impairs the ability of blood vessels to dilate and constrict properly, create a milieu that can destabilize existing atherosclerotic plaques and precipitate ACS.[5,6]

Demographic factors, including age, gender, ethnicity, and socioeconomic status, have been recognized as important determinants of health outcomes in various diseases. In the context of COVID-19, these factors have been shown to influence susceptibility to infection, disease severity, and mortality. Understanding the role of demographic factors in COVID-19-related ACS is crucial for risk stratification and the development of targeted interventions.[7,8]

This research is motivated by the need to unravel the complex interplay between COVID-19, ACS, and demographic factors. While previous studies have explored the association between COVID-19 and ACS, there remains a gap in knowledge regarding the specific demographic characteristics that may influence outcomes in this patient population.[9,10] This study aims to address this gap by examining the relationship between demographic factors, COVID-19 severity, and mortality in a cohort of patients diagnosed with both COVID-19 and ACS.

2. Methods

This research employed a retrospective observational study design, utilizing data extracted from the medical records of patients admitted to a tertiary care hospital in Medan, Indonesia, between August 2020 and August 2021. This period was chosen to capture the surge of COVID-19 cases during the pandemic's early phases and to assess the impact of the virus on cardiovascular health in a real-world setting. The hospital serves as a major referral center for a diverse population, ensuring a representative sample of patients with varying demographics and clinical presentations. The retrospective nature of the study allowed for the examination of a substantial number of cases, providing a robust dataset for analysis. However, it also inherent limitations associated with retrospective data collection, such as potential biases in medical record documentation and the inability to control for all confounding factors.

The study population comprised adult patients aged 18 years or older who were admitted to the hospital during the specified study period with a confirmed diagnosis of both COVID-19 and ACS. The inclusion criteria were meticulously defined to ensure a homogenous study sample and to minimize the influence of confounding variables. To be eligible for inclusion, patients had to meet the following criteria; Confirmed COVID-19 Infection: A positive result on a reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2, obtained from a nasopharyngeal or oropharyngeal swab. This criterion ensured that only patients with laboratory-confirmed COVID-19 were included in the analysis; Diagnosis of Acute Coronary Syndrome: A clinical diagnosis of ACS, encompassing unstable angina, non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI), based on the patient's presenting symptoms, electrocardiogram (ECG) findings, and cardiac biomarker levels. The diagnosis of ACS was made by the attending cardiologist, following established clinical guidelines and diagnostic criteria. Patients were excluded from the study if they had incomplete medical records, a history of prior coronary artery disease, or any other coexisting medical condition that could confound the relationship between COVID-19 and ACS. These exclusion criteria were implemented to enhance the internal validity of the study and to ensure that the observed associations were primarily attributable to the interplay between COVID-19 and ACS.

Data were extracted from the electronic medical records of eligible patients using a standardized data collection form. The form was developed by a team of experienced clinicians and researchers, ensuring its comprehensiveness and relevance to the study objectives. The following data elements were collected; Demographic Characteristics: Age, gender, ethnicity, and socioeconomic status. These variables were chosen to assess the potential influence of demographic factors on COVID-19-related ACS outcomes; Clinical Characteristics: COVID-19 severity (mild, moderate, or severe), ACS type (STEMI, NSTEMI, or unstable angina), and the presence of comorbidities such as hypertension, diabetes mellitus, hyperlipidemia, and chronic lung disease. These clinical variables were included to characterize the study population's clinical profile and to explore their potential impact on mortality; Laboratory and Diagnostic Findings: Results of RT-PCR tests for SARS-CoV-2, electrocardiogram (ECG) findings, and cardiac biomarker levels (troponin and creatine kinase-MB). These findings provided objective evidence of COVID-19 infection and ACS, aiding in the accurate classification of patients; Treatment and Interventions: Medications received (antiplatelet agents, anticoagulants, statins, etc.), revascularization procedures performed (percutaneous coronary intervention or coronary artery bypass grafting), and other relevant therapeutic interventions. This information allowed for an assessment of the treatments received by patients and their potential influence on outcomes; Outcomes: Mortality, defined as all-cause mortality during hospitalization. This outcome was chosen as the primary endpoint of the study, reflecting the severity and potential lethality of COVID-19-related ACS. To ensure the accuracy and completeness of data extraction, two trained research assistants independently reviewed each patient's medical record. Any discrepancies between the two reviewers were resolved through consensus or by consulting a third reviewer. This rigorous data collection process aimed to minimize errors and enhance the reliability of the study findings.

Descriptive statistics were used to summarize the demographic and clinical characteristics of the study cohort. Continuous variables were presented as means with standard deviations or medians with interquartile ranges, depending on their distribution. Categorical variables were presented as frequencies and percentages. To assess the association between demographic factors, COVID-19 severity, and mortality, appropriate statistical tests were employed. Chi-square tests or Fisher's exact tests were used to compare categorical variables, while t-tests or Mann-Whitney U tests were used to compare continuous variables, as appropriate. Logistic regression analysis was performed to identify independent predictors of mortality. Variables found to be significant in univariate analyses were entered into a multivariable logistic regression model. The results were presented as odds ratios with 95% confidence intervals. The statistical software SPSS (version 25) was used for all data analyses. A p-value of less than 0.05 was considered statistically significant.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Approval was obtained from the hospital's Institutional Review Board before the commencement of the study. As the study involved the retrospective analysis of de-identified patient data, informed consent was not required. All data were handled confidentially to protect patient privacy.

The sample size for this study was determined based on the availability of eligible patients admitted to the hospital during the study period. While a formal power calculation was not performed, the sample size of 68 patients was deemed adequate to detect meaningful associations between demographic factors, COVID-19 severity, and mortality. However, it is acknowledged that a larger sample size would have provided greater statistical power and allowed for more

detailed subgroup analyses.

3. Results and Discussion

Table 1 provides a descriptive overview of the 68 participants involved in the study examining the impact of COVID-19 on Acute Coronary Syndrome (ACS). The average age was 58.2 years, with a typical range (interquartile range) between 56 and 70. This indicates that the study population primarily consisted of older adults, who are generally at higher risk for both COVID-19 complications and cardiovascular issues. There was a striking male predominance (82.9%), suggesting a potential disparity in how COVID-19 affects men and women in relation to ACS. This aligns with existing knowledge about gender differences in cardiovascular disease risk. Most participants (62.9%) experienced severe COVID-19. This high proportion indicates that the study focused on individuals with significant COVID-19 illness, which could have implications for the observed relationship between COVID-19 and ACS. Hypertension was the most common comorbidity (52.9%), followed by diabetes (17.1%). The presence of these conditions is important as they are known risk factors for both ACS and severe COVID-19. A notable proportion (20%) had both hypertension and diabetes, further increasing their risk profile. The mortality rate was high (61.8%), highlighting the serious implications of developing ACS in the context of COVID-19. This underscores the need for effective management strategies for this patient population.

Table 1. Participants characteristic.

Variable	Category	Frequency	Percentage
Age (years)	Mean (SD)	58.2 (12.1)	
	Median (IQR)	64 (56-70)	
	Range	35-90	
Gender	Male	58	82.9%
	Female	12	17.1%
COVID-19 severity	Mild	13	19.1%
	Moderate	20	29.4%
	Severe	44	62.9%
Comorbidities	Hypertension	37	52.9%
	Diabetes	12	17.1%
	Hypertension and Diabetes	14	20.0%
	No Comorbidities	7	10.0%
Mortality	Deceased	42	61.8%
	Alive	26	38.2%

Table 2 presents the association between various factors (demographic, ECG-related, and comorbidities) and mortality in COVID-19 patients with ACS. No significant association was found between age group and mortality (p=0.453). This suggests that age, while a known risk factor for both COVID-19 and ACS individually, might not be an independent predictor of death in this specific patient group. A statistically significant association was observed between male gender and mortality (p=0.010). Males were more likely to die from COVID-19 with ACS compared to females. This reinforces the observation from Table 1 about the

male predominance in mortality and highlights a potential area for further investigation into gender-specific risk factors or treatment responses. No significant association was found between COVID-19 severity and mortality (p=0.232). This implies that the severity of the COVID-19 infection itself might not be the primary driver of death in these patients. Other factors, such as the presence of ACS and potentially underlying comorbidities, could play a more significant role. No significant association was found between ECG findings (ST depression vs. ST elevation) and mortality (p=0.215). This suggests that the specific type of ACS, as reflected by ECG changes, might not be a strong predictor of death in this context. No significant association was found between the presence of hypertension, diabetes, or both, and mortality (p=0.793). This finding is somewhat unexpected, as these comorbidities are generally associated with worse outcomes in both COVID-19 and ACS. It's possible that the small sample size limited the ability to detect a significant difference.

Table 2. Association between demographic factors, ECG overview, comorbidities, and mortality.

Variable	**Category**	**Deceased**	**Alive**	**p-value**
Age (years)	<50	10	8	0.453
	50-59	15	10	
	≥60	17	8	
Gender	Male	39	19	0.10
	Female	3	9	
COVID-19 Severity	Mild	7	6	0.232
	Moderate	11	9	
	Severe	24	11	
ECG Overview	ST Depression	13	13	0.215
	ST Elevation	29	15	
Comorbidities	Hypertension	23	14	0.793
	Diabetes	7	5	
	Hypertension and Diabetes	7	7	
	No Comorbidities	5	5	

The significant association between male gender and increased mortality in COVID-19 patients with acute coronary syndrome (ACS) points towards potential differences in how men and women respond to this disease. While various factors contribute to this disparity, the influence of sex hormones, particularly estrogen and testosterone, is of particular interest. Estrogen, the predominant female sex hormone, exerts a variety of effects that may protect against cardiovascular disease and its complications, including ACS. Estrogen promotes the dilation of blood vessels, increasing blood flow and reducing the workload on the heart. This effect may be particularly beneficial in ACS, where coronary arteries are narrowed or blocked, reducing oxygen supply to the heart muscle. By enhancing blood flow, estrogen may help maintain adequate oxygenation and prevent further damage to the heart. Estrogen plays a crucial

role in modulating the immune response and reducing inflammation throughout the body. In the context of COVID-19, where systemic inflammation is a key driver of disease severity, estrogen's anti-inflammatory effects may protect against the virus's damaging effects on the cardiovascular system. Estrogen inhibits platelet aggregation, the clumping together of platelets that can lead to blood clot formation. This effect is crucial in preventing coronary artery blockage, a major cause of ACS. By reducing the risk of blood clots, estrogen may help prevent ACS events or limit their severity. Estrogen supports the health of the endothelium, the inner lining of blood vessels. A healthy endothelium is essential for proper blood vessel function, including dilation and constriction, as well as preventing blood clot formation. By maintaining endothelial health, estrogen may contribute to overall cardiovascular protection. Estrogen has a favorable effect on lipid metabolism, promoting lower levels of LDL cholesterol ("bad" cholesterol) and higher levels of HDL cholesterol ("good" cholesterol). This effect may contribute to a reduced risk of atherosclerosis, the buildup of plaque in the arteries that can lead to ACS. In contrast to estrogen's cardioprotective effects, testosterone, the primary male sex hormone, may contribute to a pro-inflammatory and prothrombotic state, increasing the risk of cardiovascular events. Testosterone can enhance the inflammatory response, potentially exacerbating the systemic inflammation triggered by COVID-19. This may increase the risk of cardiovascular complications, including ACS. Testosterone may promote platelet aggregation, increasing the risk of blood clot formation and coronary artery blockage. This effect may contribute to a higher risk of ACS in men. Testosterone may have unfavorable effects on lipid metabolism, potentially promoting higher levels of LDL cholesterol and lower levels of HDL cholesterol. This may contribute to an increased risk of atherosclerosis and ACS. The interplay of these hormonal influences may partially explain why men are more vulnerable to severe COVID-19 and its cardiovascular complications, including ACS. Estrogen's cardioprotective effects may provide women with a degree of resilience against these conditions, while testosterone's potential pro-inflammatory and prothrombotic effects may increase men's susceptibility. It is important to note that hormonal influences are just one piece of the puzzle. Other factors, such as behavioral differences, genetic predisposition, and access to healthcare, also contribute to the observed gender disparity in COVID-19 outcomes. However, understanding the role of sex hormones is crucial for developing gender-specific approaches to prevention and treatment. Healthcare providers should be aware of the potential influence of sex hormones when assessing and managing COVID-19 patients, particularly those with ACS. Recognizing these hormonal differences can help guide clinical decision-making and tailor treatment strategies to the individual patient's needs. While hormonal differences play a significant role in the observed gender disparity in COVID-19-related ACS mortality, they are not the sole determinant. Behavioral and lifestyle factors also contribute significantly to this complex interplay, further increasing men's vulnerability to severe COVID-19 and its cardiovascular complications. Smoking is a well-established risk factor for both cardiovascular disease and severe COVID-19. Men are more likely to smoke than women, and this behavioral difference contributes significantly to their increased risk of adverse outcomes. Smoking damages blood vessels, promoting inflammation and the buildup of plaque (atherosclerosis). This process narrows the arteries, reducing blood flow to the heart and increasing the risk of ACS. Smoking impairs lung function, making individuals more susceptible to respiratory infections, including COVID-19. It also increases the risk of developing severe complications, such as pneumonia and acute respiratory distress syndrome (ARDS). Smoking weakens the immune system, making it less effective at fighting off

infections. This can lead to more severe COVID-19 infections and a higher risk of complications. Excessive alcohol consumption is another behavioral factor that disproportionately affects men and contributes to their increased risk of cardiovascular disease and severe COVID-19. Excessive alcohol intake can lead to high blood pressure, heart failure, and stroke. It can also damage the heart muscle directly, leading to a condition called alcoholic cardiomyopathy. Alcohol can suppress the immune system, making individuals more vulnerable to infections, including COVID-19. It can also interfere with the body's ability to mount an effective immune response, increasing the risk of severe complications. Dietary habits also play a crucial role in cardiovascular health. Men tend to have less healthy dietary habits than women, consuming more red meat, processed foods, and saturated fats. Obesity is a major risk factor for cardiovascular disease and severe COVID-19. It increases the risk of developing high blood pressure, diabetes, and other conditions that strain the cardiovascular system. Diets high in saturated and trans fats can lead to high cholesterol, which contributes to atherosclerosis and increases the risk of ACS. Processed foods and sugary drinks can promote inflammation throughout the body, further exacerbating the cardiovascular risks associated with COVID-19. Stress can have a profound impact on cardiovascular health. Men and women often cope with stress differently, and men may be more likely to engage in unhealthy coping mechanisms, such as excessive alcohol consumption or suppressing emotions. These behaviors can negatively impact cardiovascular health and increase the risk of complications from COVID-19. Chronic stress can lead to elevated levels of cortisol, a stress hormone that can increase blood pressure, heart rate, and inflammation. This can contribute to the development of cardiovascular disease and worsen outcomes in COVID-19. Unhealthy coping mechanisms, such as excessive alcohol consumption, smoking, or overeating, can further exacerbate the cardiovascular risks associated with stress. These behavioral and lifestyle factors, combined with hormonal differences, create a complex interplay that increases men's vulnerability to severe COVID-19 and its cardiovascular complications. Understanding this interplay is crucial for developing effective prevention and treatment strategies. Encouraging smoking cessation through education, counseling, and support programs can significantly reduce the risk of cardiovascular disease and severe COVID-19. Promoting moderate alcohol consumption or abstinence can help protect against cardiovascular damage and immune suppression. Encouraging a healthy diet rich in fruits, vegetables, whole grains, and lean protein can help maintain a healthy weight, lower cholesterol, and reduce inflammation. Promoting healthy stress management techniques, such as exercise, mindfulness, and relaxation techniques, can help reduce the negative impact of stress on cardiovascular health. While hormonal and lifestyle factors contribute significantly to the observed gender disparity in COVID-19-related ACS mortality, emerging evidence suggests that genetic factors may also play a crucial role. These genetic influences can affect various aspects of disease susceptibility and progression, further complicating the interplay between COVID-19 and cardiovascular health. The RAAS is a complex hormonal system that plays a crucial role in regulating blood pressure, fluid balance, and inflammation. It involves a cascade of enzymes and hormones, including angiotensin-converting enzyme (ACE), angiotensin II, and aldosterone. These components interact with receptors found in various tissues throughout the body, including the heart and blood vessels. Genetic variations in the genes encoding these components and receptors can influence their expression and activity, potentially affecting an individual's susceptibility to both COVID-19 and ACS. The ACE2 receptor, which serves as the entry point for SARS-CoV-2 into cells, is expressed differently in men

and women. Some studies suggest that men may have higher levels of ACE2 expression in certain tissues, potentially increasing their susceptibility to infection. Variations in the ACE gene, which encodes the angiotensin-converting enzyme, have been linked to differences in blood pressure regulation and inflammation. Certain polymorphisms may be more prevalent in men and contribute to their increased risk of cardiovascular disease. Variations in the aldosterone synthase gene, which encodes an enzyme involved in aldosterone production, may also influence susceptibility to cardiovascular disease. Aldosterone can promote inflammation and fibrosis in the heart, potentially contributing to ACS development. These genetic variations in the RAAS pathway may partially explain why men are more vulnerable to severe COVID-19 and its cardiovascular complications. Genes involved in immune response and inflammation also contribute to the observed gender differences in COVID-19 outcomes. Variations in these genes can affect the body's ability to fight off the virus and regulate the inflammatory response, potentially leading to more severe outcomes in men. TLRs are a family of receptors that play a crucial role in recognizing pathogens and initiating the immune response. Variations in TLR genes can affect their ability to recognize SARS-CoV-2 and trigger an appropriate immune response. Cytokines are signaling molecules that regulate inflammation. Variations in cytokine genes can affect their production and activity, potentially leading to an exaggerated inflammatory response in some individuals. This "cytokine storm" is a hallmark of severe COVID-19 and can contribute to cardiovascular complications. HLA genes are involved in presenting antigens to immune cells, triggering an immune response. Variations in HLA genes can affect the body's ability to recognize and fight off SARS-CoV-2, potentially influencing disease severity. These genetic variations in immune response and inflammation pathways may contribute to the observed gender differences in COVID-19 outcomes, including the increased risk of ACS and mortality in men. The interplay between genetic factors, hormonal influences, and lifestyle choices creates a complex web that determines an individual's susceptibility to COVID-19 and its cardiovascular complications. Unraveling these complexities is crucial for developing personalized prevention and treatment strategies. The disproportionate impact of COVID-19 on men, particularly those with acute coronary syndrome (ACS), underscores the critical need for gender-specific approaches in clinical practice. Healthcare providers must recognize and address these disparities to optimize care and improve outcomes for this vulnerable population. Male patients with COVID-19 and ACS require heightened vigilance and close monitoring for signs of deterioration. Continuous electrocardiogram (ECG) monitoring to detect changes in heart rhythm or signs of ischemia (reduced blood flow to the heart muscle). Close monitoring of blood pressure, heart rate, and oxygen saturation to assess cardiovascular stability. Careful observation of respiratory rate, effort, and oxygenation to detect any signs of respiratory distress. Regular assessment of cardiac biomarkers (troponin, creatine kinase-MB) to monitor for ongoing heart muscle damage. Utilizing early warning systems to identify subtle changes in a patient's condition that may indicate impending deterioration. Early recognition of these signs can prompt timely intervention and potentially prevent adverse outcomes. Treatment strategies for COVID-19 patients with ACS should be tailored to the individual patient's needs, considering their gender, age, comorbidities, and COVID-19 severity. Prompt consideration of revascularization procedures (percutaneous coronary intervention or coronary artery bypass grafting) to restore blood flow to the affected coronary arteries. Optimization of pharmacological therapies, including antiplatelet agents, anticoagulants, statins, and beta-blockers, to reduce the risk of further cardiovascular events. Judicious use of anti-inflammatory medications, such

as corticosteroids, to modulate the inflammatory response and prevent complications. Providing respiratory support, including oxygen therapy or mechanical ventilation, if necessary, to manage respiratory distress. Healthcare providers should educate male patients about their increased risk of complications from COVID-19 and ACS. Teaching patients to recognize the signs and symptoms of ACS, such as chest pain, shortness of breath, and discomfort in the arms, back, neck, jaw, or stomach. Emphasizing the importance of seeking prompt medical attention if they experience any symptoms suggestive of ACS. Encouraging healthy lifestyle choices, such as smoking cessation, moderate alcohol consumption, a healthy diet, and regular exercise, to reduce their risk of future cardiovascular events. Reinforcing the importance of adhering to prescribed medications and attending follow-up appointments. Public health initiatives play a crucial role in addressing the gender disparity in COVID-19-related ACS mortality. Increase public awareness of the increased risk of cardiovascular complications in men with COVID-19. Encourage healthy lifestyle choices to reduce the risk of cardiovascular disease and severe COVID-19. Develop targeted campaigns to educate men about their risk factors and encourage them to seek medical attention when necessary. Implement community-based programs to provide education and support to men, helping them adopt healthy behaviors and reduce their risk of cardiovascular disease. Continue research to further elucidate the mechanisms underlying the gender disparity in COVID-19-related ACS mortality. Surveillance systems should track gender-specific outcomes to monitor the effectiveness of interventions and identify areas for improvement.[11-13]

This study delved into the complex relationship between age, COVID-19 severity, and mortality in patients diagnosed with both COVID-19 and acute coronary syndrome (ACS). While our findings did not reveal statistically significant associations between age or COVID-19 severity and mortality in this specific patient population, it is crucial to acknowledge the intricate interplay of these factors and their potential clinical implications. Age is an undeniable risk factor for both COVID-19 and ACS, with older individuals generally experiencing more severe manifestations and outcomes from both conditions. The immune system undergoes a gradual decline with age, known as immunosenescence. This involves reduced function of immune cells, decreased antibody production, and impaired inflammatory responses, making older adults more susceptible to infections and less equipped to fight them off effectively. Older adults are more likely to have multiple comorbidities, such as hypertension, diabetes, and chronic kidney disease, which can exacerbate both COVID-19 and ACS. These comorbidities can strain the cardiovascular system, increase inflammation, and impair immune function. Aging is associated with a decrease in physiological reserve, meaning that older adults have less capacity to compensate for the physiological stress imposed by severe illness. This can lead to a more rapid decline and worse outcomes in the face of COVID-19 and ACS. However, despite these well-established age-related vulnerabilities, our study did not find a significant association between age and mortality in this specific patient population. The relatively small sample size of our study may have limited the statistical power to detect subtle age-related differences in mortality. Larger studies with more participants may be able to identify such differences. Our study population consisted primarily of older adults, with a mean age of 58.2 years. This may have limited the variability in age within the sample, potentially masking any age-related differences in mortality. All patients in our study had ACS, a serious condition that carries a high risk of mortality regardless of age. It is possible that the presence of ACS overshadowed any potential impact of age on mortality. Age may interact with other factors, such as comorbidities, COVID-19 severity, and treatment strategies, in influencing mortality. Further

research is needed to disentangle these complex interactions. Similarly, COVID-19 severity was not significantly associated with mortality in our study. This observation, while seemingly counterintuitive, highlights the complex interplay between COVID-19 and ACS. All patients in our study had ACS, a life-threatening condition with a high inherent risk of mortality. It is plausible that the presence of ACS overshadowed any potential impact of COVID-19 severity on mortality. The limited sample size may have hindered the ability to detect a significant association between COVID-19 severity and mortality. Larger studies with greater statistical power are needed to explore this relationship further. The severity of ACS can vary widely among patients, potentially influencing the impact of COVID-19 severity on mortality. Further research should investigate whether the relationship between COVID-19 severity and mortality differs across different levels of ACS severity. Despite the lack of significant associations in our study, age and COVID-19 severity remain crucial considerations in the management of patients with COVID-19 and ACS. Age and COVID-19 severity should be integrated into the overall risk assessment of patients with COVID-19 and ACS. This can guide clinical decision-making and prioritize resources for those at highest risk. While our study did not find significant associations, age and COVID-19 severity may influence treatment decisions in certain cases. For example, older patients or those with severe COVID-19 may be more likely to benefit from intensive care, mechanical ventilation, or specific pharmacological therapies. Healthcare providers should counsel patients about the potential impact of age and COVID-19 severity on their overall prognosis. This includes discussing the potential benefits and risks of different treatment options and setting realistic expectations for recovery.[14,15]

This study aimed to unravel the complex interplay between COVID-19, ACS, and patient characteristics, specifically focusing on the impact of ECG findings and comorbidities on mortality. While our findings did not reveal statistically significant associations between ECG findings or comorbidities and mortality, it is crucial to acknowledge their intricate roles in the overall clinical picture and their potential implications for patient management. Electrocardiogram (ECG) findings are cornerstone in the diagnosis and risk stratification of ACS patients. Traditionally, ST-segment elevation on the ECG, indicative of complete coronary artery occlusion, is associated with a higher risk of adverse outcomes, including mortality. However, in the context of COVID-19, our study did not find a significant association between ECG findings and mortality. COVID-19 exerts a wide range of effects on the cardiovascular system, extending beyond the direct involvement of coronary arteries. COVID-19 triggers a robust inflammatory response that can affect the entire body, including the heart and blood vessels. This systemic inflammation can contribute to myocardial injury, arrhythmias, and thrombosis, increasing the risk of adverse outcomes regardless of the specific coronary artery involvement. COVID-19 can impair the function of the endothelium, the inner lining of blood vessels, disrupting its ability to regulate blood flow and prevent blood clot formation. This endothelial dysfunction can contribute to both ACS and other cardiovascular complications, potentially obscuring the prognostic significance of ECG findings. COVID-19 can directly injure the heart muscle through various mechanisms, including direct viral invasion, inflammation, and microvascular thrombosis. This myocardial injury can lead to heart failure, arrhythmias, and even sudden cardiac death, irrespective of the presence or absence of ST-segment elevation on the ECG. COVID-19 is associated with a hypercoagulable state, meaning an increased tendency for blood clot formation. These blood clots can travel to various organs, including the heart, lungs, and brain, causing life-threatening complications such as pulmonary embolism and stroke. The relatively small sample size of our study

may have limited the statistical power to detect subtle differences in mortality based on ECG findings. Larger studies with greater statistical power are needed to explore this relationship further. The specific characteristics of our study population, including the high prevalence of comorbidities and severe COVID-19, may have influenced the observed lack of association between ECG findings and mortality. The severity of ACS can vary widely among patients, even within those with similar ECG findings. It is possible that the impact of ECG findings on mortality may be different for patients with different levels of ACS severity. Further research should investigate whether the relationship between ECG findings and mortality differs across different levels of ACS severity. Comorbidities, such as hypertension, diabetes, and chronic kidney disease, are well-established risk factors for both COVID-19 and ACS. These conditions can exacerbate the underlying pathophysiological processes involved in both diseases, increasing the risk of severe complications and mortality. However, our study did not find a significant association between comorbidities and mortality in COVID-19 patients with ACS. Our study population had a high prevalence of comorbidities, with over 50% having hypertension and over 20% having both hypertension and diabetes. This high prevalence may have limited the ability to detect differences in mortality based on comorbidity status, as the majority of patients already had significant cardiovascular risk factors. The small sample size of our study may have limited the statistical power to detect subtle differences in mortality based on comorbidities. Comorbidities may interact with other factors, such as age, COVID-19 severity, and treatment strategies, in influencing mortality. Further research is needed to disentangle these complex interactions and identify specific comorbidity profiles that may be associated with higher mortality risk in COVID-19 patients with ACS. As discussed earlier, COVID-19 can exert a multitude of systemic effects that contribute to mortality independently of the presence or absence of comorbidities. This may overshadow the prognostic value of comorbidities in this specific patient population. Despite the lack of significant associations in our study, ECG findings and comorbidities remain important considerations in the management of patients with COVID-19 and ACS. ECG findings and comorbidities should be integrated into the overall risk assessment of patients with COVID-19 and ACS. This can guide clinical decision-making and prioritize resources for those at highest risk, even if these factors were not independently associated with mortality in our study. While our study did not find significant associations, ECG findings and comorbidities may influence treatment decisions in certain cases. For example, patients with ST-segment elevation or multiple comorbidities may be more likely to benefit from early revascularization procedures, intensive care admission, or specific pharmacological therapies. Healthcare providers should counsel patients about the potential impact of ECG findings and comorbidities on their overall prognosis, even in the context of COVID-19. This includes discussing the potential benefits and risks of different treatment options and setting realistic expectations for recovery.[16-18]

The findings of this study have several implications for clinical practice, particularly in the management of COVID-19 patients with acute coronary syndrome (ACS). Healthcare providers should be aware of the increased risk of mortality in male COVID-19 patients with ACS. Early risk stratification based on gender and other clinical factors, such as age, comorbidities, and COVID-19 severity, can help identify patients who may benefit from more intensive monitoring and treatment. This may involve closer monitoring of vital signs, more frequent laboratory testing, and early referral to specialized care for high-risk individuals. The management of COVID-19 patients with ACS should be tailored to the individual patient's needs, taking into account their gender, age, comorbidities, and COVID-19 severity. This may involve more aggressive

interventions, such as early revascularization procedures or the use of specific medications, for high-risk individuals. For example, male patients with COVID-19 and ACS may benefit from early angiography and percutaneous coronary intervention (PCI) to restore blood flow to the affected coronary arteries. Additionally, the use of antiplatelet agents, anticoagulants, and statins should be optimized based on individual patient characteristics. The management of COVID-19 patients with ACS requires a multidisciplinary approach, involving cardiologists, intensivists, infectious disease specialists, and other healthcare professionals. Effective communication and collaboration among these specialists are essential to ensure that patients receive comprehensive and coordinated care. Healthcare providers should educate patients about the potential cardiovascular complications associated with COVID-19, particularly among men. This includes emphasizing the importance of seeking prompt medical attention if they experience any symptoms suggestive of ACS, such as chest pain, shortness of breath, or discomfort in the arms, back, neck, jaw, or stomach. Patients should also be advised on lifestyle modifications to reduce their risk of cardiovascular disease and severe COVID-19, such as smoking cessation, moderate alcohol consumption, a healthy diet, and regular exercise. The findings of this study also have implications for public health interventions aimed at reducing the burden of cardiovascular complications in the COVID-19 population. Public health initiatives should focus on raising awareness of the cardiovascular complications associated with COVID-19, particularly among men. This can be achieved through public awareness campaigns that disseminate information about the signs and symptoms of ACS, the importance of seeking prompt medical attention, and lifestyle modifications to reduce cardiovascular risk. Public health interventions should target high-risk populations, such as men with pre-existing cardiovascular risk factors or those who have experienced severe COVID-19. This may involve community-based screening programs to identify individuals at high risk of developing cardiovascular complications and targeted interventions to promote healthy lifestyle choices. Continued surveillance and research are needed to monitor the trends in cardiovascular complications associated with COVID-19 and to evaluate the effectiveness of public health interventions. This includes collecting data on the incidence, prevalence, and outcomes of cardiovascular complications in COVID-19 patients, as well as evaluating the impact of public health interventions on these outcomes.[19,20]

4. Conclusion

This study underscores the complex interplay between COVID-19, acute coronary syndrome (ACS), and patient characteristics. Male gender emerged as a significant predictor of mortality in COVID-19 patients with ACS, highlighting potential sex-specific differences in disease susceptibility and outcomes. The intricate relationship between age, COVID-19 severity, ECG findings, comorbidities, and mortality warrants further investigation to optimize risk stratification and patient management strategies. Our findings emphasize the need for heightened vigilance in male COVID-19 patients with ACS, especially those with older age, severe COVID-19 infection, ST-segment elevation on ECG, and multiple comorbidities. While these factors may not be independently associated with mortality, their presence should prompt careful consideration of treatment options, including early revascularization procedures, intensive care admission, and tailored pharmacological therapies. Moreover, this study highlights the importance of educating patients about the potential cardiovascular complications of COVID-19 and encouraging them to seek prompt medical attention if they experience any symptoms suggestive of ACS. Promoting healthy lifestyle choices, such as smoking cessation, moderate alcohol consumption, a healthy diet, and regular

exercise, is crucial to reduce the risk of cardiovascular disease and severe COVID-19. Public health initiatives should prioritize raising awareness of the cardiovascular complications associated with COVID-19, particularly among men. Community-based screening programs and targeted interventions can help identify high-risk individuals and promote healthy behaviors. Continued surveillance and research are essential to monitor trends, evaluate public health interventions, and further elucidate the complex interplay between COVID-19, ACS, and patient outcomes.

5. References

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