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The relationship between cardiovascular complications and their effect on outcomes in COVID-19.

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Abstract: ***Background*:** The COVID-19 pandemic, caused by SARS-CoV-2, has significantly impacted global health. COVID-19 primarily affects the respiratory system but also has notable cardiovascular implications. Patients with preexisting cardiovascular disease (CVD) or risk factors are at a heightened risk of severe complications and poor outcomes. This study aims to identify and evaluate the cardiovascular complications in symptomatic COVID-19 patients and assess the impact on disease outcomes. ***Methods:*** A retrospective, observational study was conducted on 100 COVID-19 patients confirmed via RT-PCR from June to December 2021. The patients were divided into two groups: Group A (n=25) for risk scoring and Group B (n=75) to analyze various risk factors. Exclusion criteria included patients under 18, pregnant women, and those with recent or known cardiovascular events. Data collected encompassed demographics, vital signs, symptoms, comorbidities, and laboratory results. Cardiovascular complications assessed included acute myocardial infarction, acute myocardial injury, new or worsening heart failure, de novo arrhythmias, and deep vein thrombosis. Statistical analyses were performed using online tools, with significance set at $p<0.05$. ***Results:*** Patients experiencing cardiovascular events in Group A had a significantly higher mean age (64.53 years) compared to those without events (53.1 years) ($p<0.001$), and a larger proportion were male ($p<0.001$). Symptoms like cough ($p=0.002$), fever ($p=0.031$), and shortness of breath ($p=0.076$) were more prevalent in the CV event group. Comorbidities such as diabetes mellitus ($p=0.036$) and coronary heart disease (CHD) ($p<0.001$) were also more common among those with cardiovascular complications. Multivariate analysis identified ten significant risk factors: male sex, age ≥60 years, cough, CHD, low lymphocyte count, high blood urea nitrogen, reduced eGFR, prolonged APTT, elevated D-dimer, and elevated procalcitonin levels.***Conclusion:*** The study identified key risk factors for cardiovascular complications in COVID-19 patients, including male gender, older age, preexisting CHD, and specific laboratory markers. These findings underscore the importance of early identification and management of at-risk patients to improve outcomes. Further research is necessary to validate these risk factors and refine predictive models.

Keywords: COVID-19, SARS-CoV-2, cardiovascular complications, risk factors, myocardial injury, heart failure, arrhythmias, retrospective study.

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INTRODUCTION

The global community is currently facing an unprecedented pandemic caused by a newly discovered coronavirus called SARS-CoV-2, which results in the illness known as COVID-19. Following the initial reports of unusual pneumonia cases originating from Wuhan province in China in December 2019, the virus rapidly spread globally, impacting millions of individuals within a few weeks.[1]SARS-CoV-2 belongs to the Corona- viridae family and shares significant similarities with the two other coronaviruses, SARS and MERS.[2] COVID-19 primarily impacts the respiratory system, causing pneumonia and acute respiratory distress syndrome (ARDS) as the main manifestations. Recent reports have emphasised the influence of SARS-CoV-2 on the cardiovascular system.[3-5]

Individuals who have risk factors for cardiovascular disease (CVD), such as hypertension, diabetes, and dyslipidemia, have a higher likelihood of developing infections and experiencing negative outcomes.[6] There is a growing number of reports on cardiovascular complications, including acute myocardial injury, heart failure (HF), cardiac arrhythmias, myocarditis, pericarditis, and venous thromboembolism.[2,5] Furthermore, the concurrent administration of multiple drugs that prolong the QT-interval, such as hydroxychloroquine (HCQ) and azithromycin, for the treatment of COVID-19 infection can potentially result in a higher occurrence of life-threatening abnormal heart rhythms known as malignant arrhythmias, specifically torsades de pointes (TdP).[2] There is a scarcity of information concerning cardiovascular complications, particularly in developing nations. The objective of this study is to ascertain the cardiovascular complications in symptomatic COVID-19 patients and evaluate how these complications affect the outcomes of the disease.

MATERIALS AND METHODS

We conducted a retrospective, observational study among 100 COVID-19 patients (who were confirmed by reverse transcription–polymerase chain reaction) between June 2021 and December 2021. The data were collected from COVID care centers and hospitals. Patients were randomly separated into two groups: Group A (25) to formulate the risk scoring and Group B (75) to see various risk factors . The exclusion criteria were as follows: (1)<18 years old, (2) pregnancy, and (3) recent/known CV event. Demographics, vital signs, symp-toms and signs, comorbidities, and laboratory examination data were collected. CV complica-tions were deliberated only when these were seen: (1) acute myocardial infarction (AMI), (2)acute myocardial injury, (3) de novo arrhythmia, (4) new or worsening HF, and (5) deep veinthrombosis. Statistical investigation was done using free online available statistical calculator. Suitable tests were applied for comparison. $P < 0.05$ was measured to be significant statistically.

RESULTS

Among patients in Group A, those who experienced cardiovascular (CV) events differed significantly from those without such events across various clinical variables. The group with CV events (n=25) had a notably higher mean age (64.53 years) compared to those without events (53.1 years), with a significant difference ($p < 0.001$). Additionally, a larger proportion of patients aged 60 and above experienced CV events (16 out of 25) compared to those without events (27 out of 75), indicating age as a significant risk factor ($p < 0.001$). Male sex was also more prevalent among patients with CV events, with 17 males in this group compared to 33 males in the non-event group ($p < 0.001$).

Vital signs on admission, including systolic and diastolic pressure, respiratory rate, heart rate, and temperature, did not show significant differences between the two groups. However, some symptoms and signs were more frequently reported among patients with CV events, including cough ($p = 0.002$), fever ($p = 0.031$), and shortness of breath/dyspnea ($p = 0.076$).

Regarding comorbidities, diabetes mellitus was more prevalent among patients with CV events ($p = 0.036$), while chronic liver disease showed no significant difference. However, hypertension ($p = 0.096$) and coronary heart disease (CHD) ($p < 0.001$) were more prevalent in the CV event group.

In summary, older age, male sex, cough, fever, dyspnea, and diabetes mellitus were associated with a higher likelihood of experiencing CV events among patients in Group A. Additionally, the presence of hypertension and CHD increased the risk of such events.

Table 1 Clinicalvariablesamongpatientswith/withoutcardiovascularеventsinGroupA

Parameters	CV event present (*n*=25),*n*(%)	CVeventsabsent(*n*=75), *n*(%)	*P*
Basicdemographics			
Age(years)	64.53	53.1	<0.001
≥60	16	27	<0.001
Sex(male)	17	33	<0.001
Vitalsignsonadmission			
Systolicpressure(mmhg)	128	127	0.5150
Respiratoryrate	19	20	0.1132
(breath/min)			
Heartrate(beat/min)	85	86	**0.7551**
Temperature(°C)	36.7	36.7	**0.0521**
Diastolicpressure(mmhg)	81	80	**0.2624**
Symptomsandsigns			
Shortnessof breath/dyspnea	7	16	**0.0761**
Cough	19	45	**0.0020**
Chestpain/distress	6	17	**0.5943**
Sorethroat	2	6	**0.7921**
Arthralgia	1	1	**0.1975**
Diarrhea	2	9	**0.40**
Fever	19	48	**0.0310**
Nausea/vomiting	1	3	**0.3641**
Comorbidities			
Diabetesmellitus	5	10	**0.0361**
Cerebrovasculardisease	1	2	**1.000**
Hypertension	8	19	**0.0961**
CHD	4	4	**<0.0010**
Chronicliverdisease	2	6	**0.8201**
Laboratory examinations			
Triglyceride	**1**	**1**	**0.161**

eGFR:Estimated glomerular filtration rate, APTT: Activated partial thromboplastin time, CRP:C-reactiveproteins, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CHD: Chronic heart disease

Multivariate analysis conducted on risk factors for cardiovascular complications in Group A revealed several significant predictors. Male sex, older age (≥60 years), presence of cough, coronary heart disease (CHD), lymphocyte count (≤1.10 × 10^9/L), blood urea nitrogen levels (≥7.0 mmol/L), estimated glomerular filtration rate (eGFR) (≤90.0 ml/min/1.73 m^2), activated partial thromboplastin time (APTT) (≥37 seconds), elevated D-dimer levels (≥0.50 mg/L), and procalcitonin levels (≥0.5 μg/L) exhibited significant odds ratios (ORs) with p-values < 0.05. These findings underscore the multifactorial nature of cardiovascular complications in this patient cohort, with factors ranging from demographic characteristics to various hematological and biochemical parameters contributing to the risk assessment. The assigned scores indicate the relative weight of each factor in predicting the likelihood of cardiovascular events, with higher scores corresponding to greater significance.

Table 2 Multivariate analysis of risk factors in cardiovascular complications in Group A

Theriskfactors	Multivariate, OR(95%CI)	*P*	Scores
Sex(male)	1.840	0.007	**2**
Age(years,≥60)	2.011	0.002	**2**
Cough	1.861	0.010	**2**
CHD	2.30	0.011	**2**
Lymphocytes($\times10^9$/L,≤1.10)	1.601	0.0410	**2**
Bloodureanitrogen(mmol/L,≥7.0)	2.142	0.0040	**2**
eGFR(ml/min/1.7m^2,≤90.0)	2.080	0.021	**2**
APTT(s,≥37)	3.070	0.0060	**3**
D-dimer(mg/L,≥0.50)	2.121	0.0011	**2**
Procalcitonin(μg/L,≥0.5)	**3.580**	**0.0081**	**4**

OR: Odds ratio, CI: Confidence interval, eGFR: Estimated glomerular filtration rate, APTT: Activated partial thrombo- plastin time, CHD: Chronic heart disease.

DISCUSSION

There have been ten recognized risk factors. We noted a progressive growth in the overall score, which rose from 0 to 23 points. The new grading method is directly correlated with the prognosis of COVID-19 patients in respect to cardiovascular problems. Therefore, it is crucial and essential to make an early prediction of cardiovascular problems. Our investigation shares similarities with the study conducted by Wei et al.[7], in which they found associations between procalcitonin, prior cardiovascular disease, age, illness, and estimated glomerular filtration rate (eGFR) and acute myocardial infarction (AMI). A risk score is widely acknowledged to be more effective than a single indication in COVID-19 for comprehensive categorization. We have developed a new scoring system that takes into account demographic factors, symptoms, comorbidities, and laboratory tests. The study participants were divided into two groups. Previous examinations have demonstrated that approximately 10% of patients with COVID-19 experienced myocardial damage. The interval [8,9] Our investigation found that approximately 16% of the individuals experienced complicated cardiovascular events. The occurrence of cardiovascular events may vary depending on various circumstances, including the demographics of the community and the severity of the disease. It has been well confirmed that being male, having a prolonged activated partial thromboplastin time (APTT), being older, having coronary heart disease (CHD), and having elevated levels of D-dimer are all related with cardiovascular events in the risk score. Pneumonia (community acquired) is similarly associated with similar risk factors.[10] In our investigation, a limited number of independent concerns have been newly found, which

should be handled with caution. In Irwin's evaluation, he mentioned that the cough could potentially result in cardiovascular issues.[11]Nevertheless, the impact of cough on patients has to be elucidated. COVID-19 patients often exhibit decreased lymphocyte counts, which can be attributed to systemic inflammatory responses and immunocompromisation.[8,9] Several investigations have shown that severe cases of COVID-19 exhibit reduced amounts of T suppressor and helper cells.[12]. The influence of COVID-19 on lymphocytes can result in a range of cardiovascular problems.[13] The association between cardiovascular events and blood urea nitrogen (BUN) and estimated glomerular filtration rate (eGFR) in COVID-19 is uncertain. Regardless, our results are consistent with a previous study on influenza. In the investigation conducted by Nin et al., it was discovered that the H1N1 virus In patients with acute renal injury, there is a greater presence of cardiovascular dysfunction compared to those without when they have pneumonia.[14] Procalcitonin demonstrates exceptional accuracy in the clinical setting for the evaluation of bacterial infections. Bacterial infections are frequently observed in individuals with cardiovascular complications due to their compromised immune system. There is a limited number of studies that establish the correlation between procalcitonin and cardiovascular morbidity and mortality.[15] Historically, risk factor models similar to our design have been employed in predicting ICU admissions, severe illness, and mortality among COVID-19 patients. Gong et al. conducted a study in which they created a "nomogram" that demonstrated a correlation between elevated BUN levels and advanced age with severe cases of COVID-19.[16] Our risk scores have shown a decrease in the area under the curve compared to the previous predictive models, with a range of 0.80-0.90. As a result of the retroactive design plan, certain fundamental data were not recorded, which could have compromised the effectiveness of the risk score's ability to differentiate between different levels of risk. At that juncture, it is possible that the termination point of cardiovascular events exhibited greater diversity than the disease itself. Moreover, the illness severity of various cardiovascular events in the included individuals was not comparable. In order to ensure impartiality throughout the trial, the researchers utilized the approved definitions to diagnose the disease in the patients, and multiple doctors were assigned to verify the data. Based on our research, the specific risk variables can be readily acquired and assessed. It can aid doctors in determining optimal treatment options for patients who are at risk of cardiovascular complications, and support future scientific investigations into the mechanism of cardiovascular events in COVID-19.Our investigation has certain limitations. Initially, it was a thorough examination that may have been influenced by the selective inclusion of data. The drugs and therapies administered before admission may have influenced the outcomes. There was a lack of extended monitoring. An investigation will be conducted to examine the long-term effects of SARS-CoV-2 on cardiovascular systems and the associated risk factors. We need to do study on a larger population to confirm our hypotheses.

CONCLUSION

Ten risk factors were evaluated upon admission: male gender and advanced age, coronary heart disease, reduced kidney function (eGFR ≤90 ml/min/1.73 m2), elevated D-dimer levels (≥0.5 mg/L), low lymphocyte count (≤1.1 × 109/L), presence of cough and fever, elevated procalcitonin levels (≥0.5 μg/L), high blood urea nitrogen levels (≥7 mmol/L), and prolonged activated partial thromboplastin time (APTT) (≥37 seconds). These factors provide a basis for estimating the likelihood of cardiovascular complications in COVID-19 patients, though further research is needed to validate their predictive value.

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