




Cardiovascular Risk Factors Among Patients Infected with COVID-19 in Saudi Arabia

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Background: Coronavirus disease (COVID-19) is a global pandemic with more than 60 million cases worldwide and over 1.5 million deaths by March 2021. Its outbreak has caused a huge burden on healthcare systems all over the world. Several studies in the medical literature have suggested that patients with underlying cardiovascular disease (CVD) are at higher risk for developing severe symptoms, poor prognosis, and high mortality rates. The aim of this study was to assess the prevalence of CVD risk factors among COVID-19 patients based on the Framingham risk score (FRS), and to evaluate the association of CVD risk factors with clinical outcomes.

Patients and Methods: In this retrospective cross-sectional study, we identified 264 confirmed cases with COVID-19 at King Saud University Medical City in Riyadh, Saudi Arabia. Patients aged 18–80 years were included, and their electronic records were reviewed. They were classified into low, intermediate, and high risk of CVD according to FRS classification.

Results: Two-hundred-six patients (67% male) were included in this study. The mean age was 55.3 ± 15.1 years. Most patients had comorbidities: the most common were hypertension (48.1%), diabetes (45.1%), and ischemic heart disease (11.2%). More than half required intensive care admission, and 58 (28.2%) patients died. Pneumonia was the most frequently observed complication (85%), followed by mechanical ventilation (28.3%) and acute kidney injury (27.7%). Age, male gender, hypertension, and diabetes mellitus showed significant differences between FRS categories, and were associated with intermediate and high-risk groups of FRS ($p < 0.05$). Pneumonia and length of stay were associated with the Intermediate risk group of FRS.

Conclusion: Cardiovascular disease risk factors are prevalent in Saudi patients infected with COVID-19. FRS could be a useful tool to identify CVD risk factors among COVID-19 patients and predict a complicated course.

Keywords: Framingham risk score FRS, COVID-19, cardiovascular risk factors, Saudi Arabia

Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by the newly discovered SARS-COV 2 virus. By March 2021, COVID-19 has affected more than 60 million persons globally, with over 1.5 million deaths.¹ This has caused a huge burden on healthcare systems all over the world. Nationally, in the Kingdom of Saudi Arabia (KSA), there have been 357,623 confirmed cases of COVID-19, with more than 5000 deaths, according to the Saudi Ministry of Health and the Saudi Centre of Disease Prevention and Control (report on December 1st 2020).²

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A large analysis was conducted on COVID-19 patients by the Chinese Centre for Disease Control and Prevention, suggesting that patients with a previous history or underlying cardiovascular disease (CVD) are at higher risk for developing severe symptoms and poor prognosis.³ High mortality rates were associated with CVD (10.5%) and hypertension (HTN) (6.0%). The overall mortality rate was (2.3%).³ Another study by the US Department of Health and Human Services (Centers for Disease Control and Prevention) concluded that the hospitalization rate of COVID-19 patients was highest in those 65 years old and above (13.8%), and among adult patients, 89.3% had one or more underlying conditions; HTN (49.7%) and CVD (27.8%).⁴

A meta-analysis of seven studies with a total of 6922 patients had shown that dyslipidemia is associated with severe COVID-19 infections, and suggested that patients with dyslipidemia should be monitored closely to minimize the risk of COVID-19.⁵ Diabetes mellitus (DM) has also been highlighted as an important predictor of poor outcome among patients with COVID-19, which is probably related to its proinflammatory state.⁶

Nationally, in KSA, Alsafayan et al had analyzed data of 1519 cases of COVID-19 and found 20.1% of the patients had underlying comorbidities; Hypertension in 8.8%, and diabetes in 7.6% of all the cases, 71.6% of studied patients were admitted to hospitals and 4.7% required ICU treatment.⁷

This high prevalence of CVD among COVID-19 patients is particularly relevant to Saudi Arabia. The last survey by the Saudi General Authority of Statistics in 2018 reported that 1.21% of the Saudi population were diagnosed with CVD, 7.6% reported a diagnosis of HTN, and 48.2% of Saudis aged 65 years or older have HTN.⁸ A population-based study conducted in Riyadh City to assess the risk of CVD using Framingham risk scores (FRS) found that a significant percentage of the general Saudi population have intermediate-to-high scores (FRS ≥ 10).^{9–11} This high prevalence of CVD in KSA may predispose Saudis to an even higher risk of COVID-19 complications as patients with CVD are more vulnerable to COVID-19 infection, and the infection itself might exacerbate their underlying CVD condition and lead to death.¹² This is also true for another species of the Coronavirus family, Middle East respiratory syndrome (MERS), that hit the country in 2012.¹³

Cardiac diseases were present in 30% and obesity in 16% of MERS cases based on a systematic review and

meta-analysis of 637 MERS-CoV cases, with a mortality rate of approximately 35%. The authors had suggested that these conditions down-regulate the synthesis of proinflammatory cytokines and impair the host's innate and humoral immune systems.¹⁴ A descriptive study by Assiri et al in 2013 had shown that 96% of 47 laboratory-confirmed MERS-CoV had underlying comorbidities; hypertension 34%, chronic cardiac disease 28%, and chronic renal disease 49%. They had noticed that the case-fatality rate rose with increasing age.¹⁵ Another Saudi study found an association between severe MERS-CoV illness and patients with pre-existing health morbidity.¹⁶ This past experience with the MERS outbreak has paved the road for the Saudi authorities in controlling the spread of the current pandemic.¹³ Here we assess the prevalence of CVD risk factors based on FRS among a sample of COVID-19 patients admitted to hospitals in Saudi Arabia.

Patients and Methods

This study is an observational, retrospective, cross-sectional study conducted between May and August 2020 at King Saud University Medical City (KSUMC) in Riyadh, Saudi Arabia. All COVID-19 cases that confirmed by real-time reverse transcription-polymerase chain reaction (RT-PCR) nasopharyngeal swab were enrolled in this study. We Included the records of alive and dead patients aged 18–80 years old. We excluded oncology patients, and pregnant or lactating women.

Data Collection

The following data were collected from patients' electronic charts:

1. Demographic data (age, sex, comorbidities).
2. Clinical presentation of COVID-19.
3. Framingham risk score "FRS" based on age, gender, systolic blood pressure, diabetes, smoking, and blood cholesterol have been calculated, Medscape website calculator: <https://reference.medscape.com/calculator/252/framingham-risk-score-2008>¹⁰
Patients were categorized based on the 10-year FRS into three groups: low risk (<10%), intermediate risk (10–20%) and high risk (>20%).
4. History of smoking.
5. The baseline of all the metrics (Blood pressure, Body mass index (BMI), Glycosylated haemoglobin (HbA1C), total lipid profile values obtained during previous outpatient visits, D-dimer, Complete Blood

Count (CBC) with differential, serum ferritin, Lactate dehydrogenase (LDH), and coagulation parameters).

6. Administered medications.

In case of missing elements in the patient history, direct contact was made with the surviving impacted patients or the families of those who died.

Outcomes to be evaluated:

1. Length of stay in hospital (including ICU admission).
2. Pneumonia
3. ARDS (Acute Respiratory Distress Syndrome) According to Berlin definition.^{17,18}
4. Mechanical ventilation.
5. Shock
6. Acute kidney injury, defined as an abrupt (within 48 hours) reduction in kidney function based on an elevation in serum creatinine level, a reduction in urine output, the need for renal replacement therapy (dialysis), or a combination of these factors.¹⁹
7. Acute heart failure. Acute heart failure is defined as a rapid onset of new or worsening signs and symptoms of HF.²⁰
8. In-hospital mortality.

Ethical Approval

The study was approved by the KSUMC Institutional Review Board, reference number (Ref. No. 20/0497/IRB). This study was conducted in accordance with the Declaration of Helsinki. Patient consent to review their medical records was not required by the KSUMC Institutional Review Board due to the anonymized data collection and maintained with confidentiality.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences software, version 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as the means \pm standard deviations (SDs) and compared using one-way ANOVA to test the difference between variables and three groups of FRS. The categorical data were presented as numbers and percentages (%) and compared using the Chi-square test to determine whether there are significant differences between variables and three levels of FRS. Multiple logistic regression analysis was used to examine the association

between the independent risk factors and 10-year risk for cardiovascular disorders according to FRS scoring as dependent variables. All the statistical tests were considered statistically significant if having a p-value < 0.05 .

Results

Baseline Patient Characteristics

A total of 264 patients with COVID-19 were identified at King Saud University Medical City, who enrolled in this study. Fifty-eight patients were excluded due to missing data. Ultimately, 206 patients (70%) were included in the final analysis. The baseline characteristics of COVID-19 patients are summarized in Table 1. As shown in this table, patients were classified into low, intermediate, and high risk of CVD according to FRS classification.

Eighty-six patients (41.7%) were in the high-risk score group. Overall, the mean age for the participants was 55.3 ± 15.1 years, and most patients were male (67%). Their mean BMI was 30.1 ± 6.8 kg/m² (obese). Comorbidities were reported in most of the patients, and the most common comorbidities were hypertension (48.1%), diabetes (45.1%), and ischemic heart disease (11.2%). The most common clinical symptoms during admission were shortness of breath and fever, followed by cough and diarrhoea (Table 2). In terms of treatment given, most patients received antibiotics (90.3%) and azithromycin (58.7%). Pneumonia (85%) was the most frequently observed outcome complication, followed by mechanical ventilation, acute kidney injury, ARDS, and heart failure. The detailed clinical symptoms, medications, treatments, and outcomes of COVID-19 patients are shown in Table 2. Generally, the frequency and the mean of high-risk category in most of the variables were more than low-risk and intermediate-risk categories. COVID-19 patients in the highest categories of FRS had significantly higher age, male gender, more likely to have hypertension, diabetes mellitus, ischemic heart disease, cerebrovascular disease, pneumonia, and heart failure outcomes compared to those in the low or intermediate FRS categories ($p < 0.05$). More than half of the patients were admitted to the ICU units, and the length of stay in the hospital was 18.9 ± 15.5 days. Fifty-eight (28.2%) of COVID-19 patients died, and most were male (81%); 27 (46.5%) of them were in the high-risk group with a mean age of 65 years. Similarly, acute kidney injury developed in 57 patients, 28 (49%) of them were in the high-risk group.

Table 1 Baseline Characteristics of COVID-19 Patients Classified by Framingham Risk Score

Variables	Total (n = 206)	Low Risk (n =71)	Intermediate Risk (n = 49)	High Risk (n = 86)	P value
Demographic data					
Age (yr)	55.3± 15.1	41.9 ± 10.6	57.3 ± 7.4	63.8 ± 6.7	< 0.001*
Sex, male	138 (67)	41 (57.7)	30 (61.2)	67 (77.9)	0.017*
SBP (mmHg)	126.1 ± 20.8	117.5 ± 14.9	125.2 ± 17.1	136.3 ± 20.1	0.536
DBP (mmHg)	70.3 ± 12.6	69.3 ± 11.4	72.3 ± 12.0	72.7 ± 16.6	0.191
Body mass index (kg/m ²)	30.1 ± 6.8	30.1 ± 6.9	30.8 ± 6.3	30.3 ± 6.5	0.674
Smoking status					0.329
Never	188 (91.3)	64 (90.1)	44 (89.8)	80 (93.0)	
Former	9 (4.4)	2 (2.8)	3 (6.1)	4 (4.6)	
Current	9 (4.4)	5 (7.0)	2 (4.1)	2 (2.3)	
Comorbidities					
Hypertension	99 (48.1)	14 (19.7)	21 (42.8)	64 (74.4)	< 0.001*
Diabetes mellitus	93 (45.1)	13 (18.3)	17 (34.7)	63 (73.2)	< 0.001*
Ischemic Heart Disease	23 (11.2)	4 (5.6)	3 (6.1)	16 (18.6)	0.016*
Chronic Kidney Disease	18 (8.7)	3 (4.2)	5 (10.2)	10 (11.6)	0.241
Chronic lung Disease	17 (8.3)	7 (9.9)	3 (6.1)	7 (8.1)	0.764
Heart Failure	19 (9.2)	3 (4.2)	4 (8.2)	12 (13.9)	0.106
Cerebrovascular accident	15 (7.3)	1 (1.4)	2 (4.1)	12 (13.9)	0.007*

Notes: Data are presented as mean ± standard deviation or number (%); *Statistically significant.

Abbreviations: LOS, length of stay; DBP, diastolic blood pressure; SBP, systolic blood pressure.

As presented in Table 3, a multiple logistic regression model was used to evaluate the association between risk factors characteristics of COVID-19 patients and FRS levels. The low-risk group was considered as the reference group, and 19 independent risk factor variables and outcomes associated with FRS had been identified as a consequence of their p-value at univariate analysis as well as the most risk factors for COVID-19. We found that age (OR 1.36; 95% CI, 1.19, 1.54; $p < 0.000$), male gender (OR 0.06; 95% CI, 0.01, 0.43; $p = 0.005$), diabetes mellitus (OR 23.02; 95% CI, 2.43, 218.28; $p = 0.006$), pneumonia (OR 21.19; 95% CI, 1.41, 318.65; $p = 0.027$), and length of stay (OR 1.06; 95% CI, 1.01, 1.12; $p = 0.028$) were independently associated with the Intermediate risk group of FRS. However, the high-risk category of FRS was significantly associated with age (OR 1.62; 95% CI, 1.39, 1.90; $p < 0.000$), male gender (OR 0.004; 95% CI, 0.00, 0.05; $p < 0.001$), hypertension (OR 10.98; 95% CI, 1.75, 68.95; $p = 0.011$), and diabetes mellitus (OR 210.57; 95% CI, 18.26, 2428.16; $p < 0.001$).

Discussion

The present study confirms that CVD risk factors, such as age, male gender, diabetes mellitus, and hypertension, are

prevalent in COVID-19 patients admitted to hospitals in KSA. To our knowledge, this is the first study in the Middle East that stratified patients with COVID-19 according to cardiovascular disease factors based on FRS and assessed the association of CVD risk factors with clinical outcomes.

During pandemics such as COVID-19, the clinical consequences and pathogenic effects can be variable and more profound in a specific population. Several studies have reported that old age is a significant risk factor for COVID-19 mortality and morbidity.^{21,22} In addition to older age, a large body of evidence has highlighted an increased susceptibility of patients with diabetes to infectious diseases,²³ which might be attributed to malfunctioning of the immune system in diabetics.^{24,25} A recent systematic review and meta-analysis of 30 articles revealed an association between diabetes with poor outcomes in patients with COVID-19.²⁶

Obesity has become a worldwide epidemic. Recent studies show that obesity might aggravate the course of COVID-19.^{21,27} The current study found that obesity was common among the patients with COVID-19; the mean BMI was 30.1 ± 6.8 regardless of their FRS risk classification.

Table 2 Clinical Symptoms, Medications, Treatments and Outcomes of COVID-19 Patients Classified by Framingham Risk Score

Variables	Total (n = 206)	Low Risk (n = 71)	Intermediate Risk (n = 49)	High Risk (n = 86)	P value
Clinical symptoms					
Cough	128 (62.4)	41 (57.7)	34 (69.4)	53 (62.4)	0.433
Fever	151 (73.7)	48 (67.6)	36 (73.5)	67 (78.8)	0.285
SOB	154 (75.9)	49 (70)	43 (87.8)	62 (73.8)	0.071
Sputum	33 (16)	4 (5.6)	13 (26.5)	16 (18.6)	0.006*
Hemoptysis	3 (1.5)	1 (1.4)	0 (0)	2 (2.3)	0.555
Sore Throat	22 (10.7)	5 (7)	6 (12.2)	11 (12.8)	0.469
Neurological symptoms	22 (10.7)	8 (11.3)	6 (12.2)	8 (9.3)	0.851
Diarrhea	53 (25.9)	18 (25.4)	13 (27.1)	22 (25.6)	0.975
Nausea and vomiting	50 (24.3)	16 (22.5)	9 (18.4)	25 (29.1)	0.346
Abdominal Pain	19 (9.2)	8 (11.3)	2 (4.1)	9 (10.5)	0.357
Treatments					
Steroids	116 (56.6)	33 (46.5)	33 (67.3)	50 (58.8)	0.066
Antibiotics	186 (90.3)	60 (84.5)	46 (93.9)	80 (93)	0.125
Hydroxychloroquine	5 (2.4)	3 (4.2)	2 (4.1)	0 (0)	0.159
Azithromycin	121 (58.7)	33 (46.5)	33 (67.3)	55 (64)	0.032*
Anti-viral	8 (3.9)	4 (5.6)	2 (4.1)	2 (2.3)	0.564
Laboratory Results					
HgA1C	8.1 ± 5.9	7.1 ± 2.7	7.9 ± 2.6	9.3 ± 9.4	0.182
D-dimer	3.3 ± 4.9	2.7 ± 4.6	2.0 ± 2.0	4 ± 5.9	0.407
HDL	0.9 ± 0.44	1 ± 0.5	0.8 ± 0.5	0.9 ± 0.3	0.200
LDL	2.0 ± 0.9	2.3 ± 1.1	1.9 ± 0.8	1.9 ± 1.0	0.495
PT	15.1 ± 3.4	15.4 ± 3.1	15.1 ± 5	15.5 ± 3.5	0.579
APTT	41.2 ± 15.6	42.2 ± 19.8	39.9 ± 9.6	42.1 ± 17.9	0.221
Ferritin	1100.8 ± 1298.3	1184.2 ± 1627.6	1334.4 ± 1343.9	1034.6 ± 1166.2	0.322
LDH	540.1 ± 818.1	655 ± 1560	524 ± 244	473 ± 204	0.270
Outcomes					
Pneumonia	175 (85)	52 (73.2)	47 (95.9)	76 (88.4)	0.001*
ARDS	21 (10.2)	6 (8.5)	7 (14.3)	8 (9.3)	0.547
Mechanical Ventilation	58 (28.3)	18 (25.4)	20 (41.7)	20 (23.3)	0.061
Shock	15 (7.3)	4 (5.6)	5 (10.2)	6 (7)	0.632
Acute Kidney Injury	57 (27.7)	16 (22.5)	13 (26.5)	28 (32.6)	0.369
Heart Failure	17 (8.3)	1 (1.4)	6 (12.2)	10 (11.6)	0.035*
ICU admission	119 (57.8)	38 (53.5)	35 (71.4)	46 (53.5)	0.085
LOS (day)	18.9 ± 15.5	17.5 ± 16.6	23.6 ± 16.7	17.9 ± 14.9	0.193
Death	58 (28.2)	15 (21.1)	16 (32.7)	27 (31.4)	0.263

Notes: Data are presented as mean ± standard deviation or number (%); *Statistically significant.

Abbreviations: SOB, shortness of breath; HgA1C, hemoglobin a1c; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; PT, prothrombin time; APTT, activated partial thromboplastin time; LDH, lactic dehydrogenase; ARDS, acute respiratory distress syndrome; LOS, length of stay.

This study also found that males were more affected by COVID-19 than females, and the majority were intermediate and high FRS risk (61.2% and 77.9%, respectively, $p = 0.017$). This coincides with published epidemiological studies which highlighted that males are more likely to be infected with COVID-19 and more susceptible to its complications, including death.^{21,22,28,29}

There was no significant difference in the presenting symptoms and the laboratory parameters between different FRS risk categories, including markers of disease severity (LDH, D-Dimer, Ferritin).³⁰ The most common clinical symptoms were shortness of breath and fever, followed by cough and diarrhoea, which matches with most of the symptoms reported in the literature.³¹

Table 3 Multiple Logistic Regression Analyses of Risk Factors Associated with Framingham Risk Score for COVID-19 Patients

Risk Factor Variables	Framingham Risk Scoring								
	Low Risk (< 10%) (ref)			Intermediate Risk (10–20%)			High Risk (> 20%)		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Age (yr)	–	–	–	1.35	1.19, 1.54	< 0.001*	1.62	1.38, 1.90	< 0.001*
Male sex (vs female)	–	–	–	0.06	0.01, 0.43	0.005*	0.01	0.00, 0.04	< 0.001*
Smoker (vs non-smoker)	–	–	–	5.52	0.29, 104.99	0.256	7.09	0.13, 396.99	0.340
Comorbidity present (vs not present)									
Hypertension	–	–	–	5.65	1.08, 29.33	0.039*	10.98	1.75, 68.95	0.011*
Diabetes mellitus	–	–	–	23.02	2.43, 218.28	0.006*	210.57	18.26, 2428.16	< 0.001*
Ischemic Heart Disease	–	–	–	0.07	0.00, 6.17	0.246	0.16	0.00, 15.64	0.430
Chronic Kidney Disease	–	–	–	2.66	0.07, 99.90	0.596	0.42	0.00, 21.34	0.668
Chronic lung Disease	–	–	–	6.99	0.59, 83.57	0.124	14.69	0.70, 308.08	0.083
Heart Failure	–	–	–	2.76	0.07, 98.62	0.578	3.75	0.08, 159.57	0.489
Cerebrovascular accident	–	–	–	0.31	0.01, 7.19	0.471	1.55	0.07, 31.73	0.777
Outcomes									
Pneumonia	–	–	–	21.19	1.41, 318.65	0.027*	13.63	0.81, 229.50	0.070
ARDS	–	–	–	2.17	0.21, 21.99	0.512	5.59	0.40, 78.60	0.202
Mechanical Ventilation	–	–	–	0.91	0.12, 7.01	0.663	0.45	0.04, 5.18	0.523
Shock	–	–	–	0.12	0.00, 3.14	0.205	0.07	0.00, 2.09	0.124
Acute Kidney Injury	–	–	–	1.94	0.29, 12.75	0.491	3.16	0.35, 28.83	0.308
Heart Failure	–	–	–	12.09	0.20, 733.84	0.234	13.29	0.20, 886.21	0.227
ICU patients	–	–	–	0.65	0.09, 3.38	0.529	0.93	0.11, 7.89	0.951
LOS (day)	–	–	–	1.06	1.01, 1.12	0.028*	1.05	0.98, 1.11	0.169
Death	–	–	–	0.45	0.05, 3.97	0.476	0.47	0.04, 6.29	0.570

Note: *Statistically significant.

Abbreviations: ARDS, acute respiratory distress syndrome; ICU, intensive care unit; LOS, length of stay.

With regards to the outcome of the study group, pneumonia was higher in intermediate and high-risk CVD; similarly, more patients with intermediate and high FRS risk patients developed heart failure ($p = 0.035$). This points to a higher rate of complications in patients with CVD, as reported previously in the literature.^{12,32}

FRS has long been used to estimate the 10-year risks of CVD based on disease risk factors.³³ It has been validated in many studies, with a higher score indicating more CVD risk factors. In addition, it is widely applied and available as online networking applications.³⁴

In the present study, 86 (41.4%) COVID-19 patients had a high FRS score, suggesting that those with high FRS are more prone to COVID-19. We have also detected a trend toward more cardiorespiratory complications among patients with higher FRS score. This is in agreement with Barry et al, who highlighted the challenges of rapidly detecting and properly isolating patients with

MERS-CoV with underlying congestive heart failure (CHF) and chronic kidney disease (CKD) who present with the unexplained deterioration of their chronic conditions.³⁵ Hence, it is increasingly evident that the disease tends to be more prevalent and more severe in patients with CHF or CKD.^{35,36} In addition, there is growing evidence that a significant number of COVID-19 patients develop cardiovascular complications, and these were associated with higher mortality.³⁷

One of the limitations of this study is that it is a single-centre experience with a small sample size, which limited the generalization of the data; thus, future studies with larger sample sizes are now needed to investigate the difference in the outcome, including death among the different FRS categories. Another limitation is that it is retrospective data analysis. Some information, such as socioeconomic characteristics, occupation, and level of education, was difficult to collect. Further study is needed

to determine the relation of CVD risk factors of COVID-19 patients and their socioemotional status. Similarly, the exact medication that every patient was receiving was not collected and compared among FRS groups. This could be important as some previous studies have suggested a relation between metformin and statin, for example, with the outcome.^{6,38}

Conclusion

Patients with CVD are more vulnerable to COVID-19 infection, which might worsen their underlying condition and lead to a poor outcome. FRS can identify COVID-19 patients with high-risk CVD and should be confirmed in a larger sample size and different population. It is highly recommended to consider FRS when triaging COVID-19 patients, with timely recognition of high-risk patients while treating cases with a communicable disease.³² Public health authorities need to motivate hospitals and primary care clinics to consider CVD risk factors in risk stratification and treatment decisions for patients with COVID-19. They also need to be more vigilant in controlling CVD risk factors since it not only increases the morbidity of non-communicable diseases, but also predisposes to and worsens the outcome of communicable diseases.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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