Original Article

Cardiac Comorbidities Impact on the Outcomes in Severe COVID-19 Infection

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Abstract

Background: COVID-19 is now a global pandemic, with the officially recorded number of affected individuals approaching 4 billion patients. **Aim of the Work:** Our purpose is to study the effect of cardiac comorbidities on the outcomes of severely infected COVID-19 patients. **Patients and Methods:** This study included 147 patients with severe COVID-19. All data were analyzed regarding demographic risk factors, associated diseases, mode of oxygen therapy administration, and echocardiography. **Results:** The death rate (DR) in patients with severe COVID-19 and no comorbidities was 7.7%. In patients who had only one risk factor as smoking, hypertension (HTN), or diabetes mellitus (DM), the DR was 16.7%, 33.3%, and 8.3%, respectively. The addition of one risk factor to HTN increased DR in the case of DM (36.8%) and in the case of smoking (40%). Regarding the outcomes, the percentage of the patients affected was as follows: impaired left ventricular ejection fraction (LVEF) <50% (19.7%), dilated right ventricular (RV) basal dimension (12.2%), decreased tricuspid annular plane systolic excursion <17 mm (8.2%), increased SPAP >30 mmHg (53.7%), and pericardial effusion (23.1%). Patients were subclassified according to the presence of HTN. The hypertensive group had increased LV wall thickness and LV end-systolic dimension and impaired LVEF and fraction of shortening than normotensive patients. DR for females and males treated by high-flow nasal cannula was (3.3% vs. 6.9%), continuous positive airway pressure (0% vs. 3.2%), and mechanical ventilation (100% vs. 90.5%). The suggested score was significantly higher in the death group (P < 00001). The DR increased markedly with the incremental rising score. **Conclusions:** Comorbidities, age, and delayed presentation with decreased oxygen saturation had a cumulative risk that can predict the outcome of COVID-19 patients. The presence of HTN alone or associated with other risk factors had a higher DR than other risk factors.

Keywords: Comorbidity score, COVID-19, echocardiography, hypertension, oxygen saturation, ventricular function

Introduction

The coronavirus disease (COVID-19) has been declared a global pandemic by the WHO. With 80% of the patients having mild illness, 14% severe illness, and 6% critical illness.[1] Outbreaks caused by coronaviruses are considered a more recent phenomenon; the first reported outbreak was caused by severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1) in 2003[2] and the most recent is the still ongoing pandemic caused by SARS-CoV-2.[3] Outbreaks related to coronavirus infections are a global concern, but the dynamics of these outbreaks and their effects on mortality are still being studied.[4]

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Patients and Methodology

This study is a retrospective cross-sectional study that included 147 patients who were admitted to our University Hospital from December 2020 to June 2021. The current study was approved by the Research Ethics Committee; (FMG-IRB); ID: 1167 and was performed following the Helsinki declaration. Patients were diagnosed to have documented severe COVID-19. All their data in the files were analyzed regarding

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demographic risk factors (smoking, hypertension [HTN], diabetes mellitus [DM], ischemic heart disease [IHD], and associated diseases [bronchial asthma, cerebral, and chronic kidney disease (CKD)]). Their treatment in the intensive care unit was documented regarding methods of oxygen therapy or mechanical ventilation. Medical therapies were performed according to the Egyptian Ministry of Health protocol.

Severe COVID-19 cases were defined according to the clinical and radiographic criteria, including respiratory rate >30 and computed tomography (CT) chest revealing CORADs 4–5 and/or low O2 saturation (<92%). Only intrahospital mortality due to confirmed COVID-19 was considered COVID-19-related mortality.

During admission, all patients were examined clinically; CT chest and laboratory results were collected for analysis. All patients underwent full echocardiographic examination, including left ventricular (LV) dimensions, fraction of shortening (FS), LV ejection fraction (EF), right ventricular basal dimension (RVBd), tricuspid annular plane systolic excursion (TAPSE) and estimated systolic pulmonary artery pressure (SPAP), and the presence of mitral or aortic regurgitation and pericardial effusion. The diagnosis of impaired LVEF if <50%, RVBd dilatation if >41 mm, increased SPAP >30 mmHg, and abnormal TAPSE if <17 mm.

The medical status at admission was analyzed in all patients and according to several classifications: first, according to gender. The second was according to the presence of HTN or not in each gender.

Statistical analysis

Numerical variables were expressed as mean and standard deviation. The Social Science Statistical (SSS) calculators were used:

- t-test calculator for two independent means when data are normally distributed
- Mann–Whitney *U*-test calculator was used to compare two independent groups or conditions or treatments to be compared without making the assumption that values are normally distributed. The data are continuous or the scale of measurement should be ordinal, interval, or ratio
- Statistical significance was set at a level of $P < 0.05$, and ≤0.001 is highly significant
- Qualitative measures (categorical) data, either nominal or ordinal, were expressed as percent for comparison. Odds ratios (ORs), 95% confidence interval (CI), and *P* values are calculated using MedCalc statistical software
- Multivariate logistic regression analysis using stats.Blue calculator.

Ethical statement

The current study was approved by the Research Ethics Committee Al-Azhar University; (FMG-IRB); ID:1167.

Results

The study included 147 patients. The study population included 65 males representing 44.2% and 82 females representing 55.8%. Age ranged from 19 years to 86 years old. The mean age was 61.6 ± 12.5 and 58.9 ± 15.7 years for male and female patients, respectively, with no significant difference. The total deaths were 44 (29.9%) patients; 23 (15.6%) females and 21 (14.3%) males, with no significant difference.

Individual risk factors were recorded among the studied patients, whether as a sole comorbidity or combined risk factors, and the death rate (DR) for each risk factor represented in Table 1.

Regarding age (<40 years, 41–60 years, and ≥61 years), the DR was 6.7%, 19.2%, and 41.3%, respectively. Logistic regression analysis of outcomes and age was statistically significant ($P \leq 0.01$).

Regardless of age, the COVID patients with no comorbidities had a DR of 7.7%. Smokers had a DR of 16.7%. Hypertensive patients had a higher DR than diabetic patients (33.3% vs. 8.3%, respectively). DRs in hypertensive patients with the addition of one other risk factor such as DM or smoking were 36.8% and 40%, respectively.

Echocardiographic parameters showed a decrease of LVEF <50% in 29 (19.7%) patients, dilated RV basal dimension >41 mm in 18 (12.2%) patients, decreased TAPSE <17 mm in 12 (8.2%) patients, pericardial effusion in 34 (23.1%) patients, and increased SPAP >30 mmHg in 79 (53.7%) patients.

Classification of the male and female groups according to the presence and absence of hypertension

The female group included 82 patients, of which 36 were hypertensives and 46 normotensives. The male group included 65 patients, of which 31 were hypertensives and 34 normotensives. Hypertensive and normotensive female patients showed no significant difference regarding age, length of stay (LOS), and oxygen saturation (O_2%) at admission.

Hypertensive and normotensive males showed no significant difference regarding LOS and oxygen saturation (O_2%) on admission, but the mean age of normotensive male patients was significantly younger ($P < 0.005$).

Table 1: Age, risk factors (single or combined), and death percentage among each group

Risk factors in (*n*=147) patients	Total number	Death number	Death (%)
Age≤40 years	15	1	6.7
Age 41-60 years	52	10	19.2
≥61 years	80	33	41.3
No risk factors/other diseases	26	2	7.7
HTN	6	2	33.3
DM	12	1	8.3
CKD	4	2	50
Smoking	12	2	16.7
HTN + DM	19	7	36.8
HTN + smoking	5	2	40

HTN: Hypertension, DM: Diabetes mellitus, CKD: Chronic kidney disease

Echocardiographic parameters showed that both hypertensive males and females had increased interventricular septum (IVS) thickness ($P < 0.00001$), posterior wall thickness ($P < 0.00001$), increase of left ventricular end-systolic dimension (LVESd) ($P < 0.002$ for females and $P < 0.008$ for males), and LV systolic functions were significantly lower in hypertensive groups.

Pericardial effusion was detected in hypertensive patients more than in normotensive. The OR was 2.77 and 95% CI: 1.24–6.15 ($P \leq 0.0123$) [Table 2].

CT chest findings regarding CORADs scores were reported in female and male patients, and the number of deaths and their percent in each CORADs level are summarized in Table 3. CT chest and CORADs scores revealed no significant difference in DR between female and male groups in CORADs 4 and CORADs 5 ($P = 0.97$ and $P = 0.358$, respectively).

The lower O_2% at admission was related to a higher DR in all patients (males and females). Multivariate logistic regression analysis of outcomes and O_2% was highly significant ($P \leq 0.0001$), and the multivariate logistic regression and CKD were also significant ($P \leq 0.037$). The number of patients who required mechanical ventilation was 42 (representing 28.6% of the study population); all of them were admitted with O_2% <71%. The DR among them was 95.2%. DR for patients treated by high-flow nasal cannula was 3.3% in females and 6.9% in males, whereas treatment by Continuous positive airway pressure was associated with 0% mortality versus 3.2% mortality in males and females, respectively [Table 3].

Our suggested COVID scores [Table 4] depended on the analysis of all data and variables at the time of admission. The associated comorbidities had a cumulative risk for prediction of outcome with COVID infection. These risks include age,

Table 2: Comparison between hypertension and non-hypertension groups in female and male gender

	Females (*n*=82)			Males (*n*=65)		
	HTN (*n*=36)	Non-HTN female (*n*=46)	*t*-test *P*	HTN (*n*=31)	Non-HTN male (*n*=34)	*t*-test *P*
Age (years)	62±12	56.3±17	0.297	65.9±9.3	57.5±13.7	0.005
LOS (days)	7.3±5.5	6±5.1	0.382	7.65±7.2	6.68±5.5	0.544
O_2%	84.8±9.2	84±11.5	0.523	83.4±9.9	83.7±11.4	0.913
IVS (mm)	13.2±1.2	10.7±1.7	0.00001**	13.3±1.7	10.5±1	0.00001*
LVEDd (mm)	50.6±5.7	48.3±4.9	0.054	53.1±5.3	50.5±5.3	0.045*
PWT (mm)	11.8±0.9	9.5±1.9	0.00001**	12.3±0.9	9.6±1.1	0.0001**
LVESd (mm)	34.5±7.9	29.3±7	0.002*	37.4±6.6	32.9±7.3	0.008*
FS (%)	32.5±7.8	40±6.8	0.00005**	30.3±7.3	36.3±10	0.002*
EF (%)	60.1±11	68.8±8.1	0.0001**	56.5±11.4	63.1±10.1	0.01*
RVBd (mm)	37.8±4.4	35.7±3.4	0.0138	37.9±3.5	36.8±3.4	0.21
TAPSE (mm)	19.6±3.1	21±2.5	0.033*	18.7±2.1	19.5±2.9	0.22
SPAP (mmHg)	36.0±8.4	31.7±8.3	0.021*	35.1±7.1	32.7±6.3	0.18

*Statistically significant, **Statistically high significant. LOS: Length of stay, O_2%: Oxygen saturation, IVS: Interventricular septum thickness, LVEDd: Left ventricular end-diastolic dimension, PW: Posterior wall thickness, LVESd: Left ventricular end-systolic dimension, FS: Fraction of shortening, EF: Ejection fraction, RVBd: Right ventricular basal dimension, TAPSE: Tricuspid annular plane systolic excursion, SPAP: Systolic pulmonary artery pressure, HTN: Hypertension

Table 3: Death rate in relation to computed tomography chest COVID-19 reporting and data system, oxygen saturation, and methods of oxygen supply

	Female (*n*=82)			Male (*n*=65)		
	Patients number	Deaths number Total (*n*=23)	Percentage of death	Patients number	Death number Total (*n*=21)	Percentage of death
CT chest findings at admission						
CORADs 4	52	14	27.5	54	16	29.6
CORADs 5	30	9	30	11	5	45.5
O_2% at admission						
≤80	21	13	61.9	18	13	72.2
81-90	35	9	25.7	36	8	22.2
≥91	26	1	3.8	11	0	0
Methods of oxygen supply						
High-flow nasal cannula	30	1	3.3	29	2	6.9
CPAP	31	1	3.2	15	0	0
Mechanical ventilation	21	21	100	21	19	90.5

CORADs: COVID-19 reporting and data system, CPAP: Continuous positive airway pressure, O_2%: Oxygen saturation

O_2% at admission, smoking, HTN, DM, IHD, PE, CKD, and rescue from cardiac arrest or shock.

The calculated COVID score for patients is summarized in Table 5 and its correlation with the DR. The mean ± standard deviation of the total score was 5.86 ± 2.04 in the patients who died, whereas it was 3.7 ± 2.02 in the patients who survived (P < 00001). The logistic regression analysis of outcomes and COVID score was highly significant ($P < 0.0001$).

Discussion

Although acute respiratory complications are common in COVID-19, cardiovascular complications are increasingly being recognized. These include acute myocardial injury, arrhythmias, and heart failure (HF). Therefore, there is a need for a high index of suspicion of cardiovascular complications since there is an overlap in the symptoms and signs.[5] In the previous epidemics, it was noted that coexisting cardiovascular disease (CVD) with or without myocardial injury was associated with higher mortality.[6] Data from Europe and the US have confirmed the disturbing relationship between diabetes, HTN, CVD, and COVID-19 outcomes.[7,8] A study including 5700 patients reported a similar message that HTN (56.6%), obesity (41.7%), diabetes (33.8%), coronary artery disease (11.1%), and congestive HF (6.9%) were the most common comorbidities.[9]

Table 4: COVID score for prediction of death outcome

Risk	Score
Age (years)	
<40	0
41-60	1
>61	2
O_2% at admission (%)	
≥91	0
90-81	1
80-71	2
≤70	3
Presence of risk factors	
Smoking	1
HTN	1
DM	1
IHD	1
Other diseases	
Pericardial effusion	1
CKD	1
Rescue of cardiac arrest/shock	2

HTN: Hypertension, DM: Diabetes mellitus, IHD: Ischemic heart disease, CKD: Chronic kidney disease, O_2%: Oxygen saturation

Table 5: Estimated COVID score for COVID admitted patients and the death rate

The score	Total patients		
	Patient number	Death number	Death (%)
0	14	0	0
1			
2	43	4	9.3
3			
4	50	16	32
5			
6	27	15	55.5
7			
8	13	9	69.2
9			
10			
Total	147	44	29.9

Case fatality rates vary by country from <0.1% to >20% and are influenced by testing strategies that define the infected population, economics, health-care resources, comorbidity rates, demographics, and politics.[10] Our admitted patients were severe cases only and their CORADs were 4 and 5. DR in different age categories (<40 years, 41–60 y, and ≥61 years) was 6.7%, 19.2, and 41.3%, respectively. However, the estimated case fatality ratio was 0.32 in patients aged <60 years in comparison with 6.4% in patients aged >60 years.[11] In Italy, case fatalities ranged from 0% below age 30 years to 3.5% for ages 60–69 years and 20% above age 80 years.[12] The relative risk of fatal outcomes in young patients with HTN, diabetes, and CVD was higher than in elderly patients.[13]

Gender has no significant difference regarding the mean of age, LOS, and oxygen saturation at admission. Despite the higher rate of HTN, DM, smoking, IHD, CKD, and DR in the male gender, the OR revealed no significant difference between the male and female gender except for smoking due to the higher prevalence of smoking among males ($P < 0.0001$).

The DR among COVID-19 patients with no comorbidities or other diseases was 7.7%. The presence of one risk factor as HTN, DM, or smoking was associated with an increase of DR to 33.3%, 8.3%, and 16.7%, respectively. DRs in hypertensive patients with the addition of one other risk factor as diabetes or smoking were 36.8% and 40%, respectively.

Echocardiography was performed for all patients included in our study population although it has been recommended that performing echocardiograms would be only limited to cases where the derived information is likely to produce clinical benefit.[14,15] In our study, echocardiography was done for all admitted patients with complete personal protective equipment worn by the medical staff. The echo-derived data helped to understand COVID-19 impact on the heart and was also of additive value for follow-up.

In our study, decreased LV systolic function (LVEF <50%) was detected in 19.7% of patients. Hypertensive patients had significantly increased both LVEDd and LVESd with a decrease both EF and FS. Echocardiography variables were compared in both genders according to the presence of HTN or not, because of the impact of HTN on myocardial structure and function. In the hypertensive group, there was a highly significant increase of IVS, PW thickening, and LVESd in both genders. LVEDd was higher in hypertensive males. The systolic functions (EF and FS) were reduced significantly in both male and female hypertensive groups.

Although it was mentioned that SARS-CoV infection was found to be associated with cardiomyopathy.[16] Other studies recorded reversible cardiomegaly without HF in 10.7% of the cases.[17] Transient atrial fibrillation is an uncommon feature.[17]

The incidence of acute HF was 23% (44 out of 191 patients with COVID-19) and that multiple precipitating etiologies, including acute coronary syndrome, cardiac arrhythmias, stress-induced cardiomyopathy, and fulminant myocarditis, might result in acute HF or cardiogenic shock in patients with COVID-19.[18] Although COVID-19 is predominantly a respiratory illness,[19] this may be secondary to lung disease since acute lung injury itself leads to increased cardiac workload and can be problematic, especially in patients with preexisting HF.[20]

The unique pathophysiology of COVID-19 places the RV at higher risk of failure.[21] In our study, dilated RV basal dimension >41 mm was present in 18 (12.2%) patients, decreased TAPSE <17 mm in 12 (8.2%) patients, pericardial effusion in 34 (23.1%) patients, and increased SPAP >30 mmHg in 79 (53.7%) patients.

Pericardial effusion was detected in hypertensive patients more than in normotensives. The OR of pericardial effusion was significantly higher.

In our study, analysis of CT chest and CORADs grading revealed no significant difference regarding DR between female and male groups at CORADs 4 and 5 ($P = 0.97$ and $P = 0.358$, respectively). Moreover, there was no significant difference between hypertensive and non-hypertensive patients regarding CORADs grading. The P values for CORADs 4 and 5 were $P = 0.148$ and $P = 0.93$, respectively.

Factors associated with outcomes in 187 patients with COVID-19 were previously noted and recorded, up to 35% had underlying CVD (HTN, coronary heart disease, or cardiomyopathy), and 28% showed evidence of acute myocardial injury (defined as elevated troponin T).[22] However, a number of chronic diseases are associated with an increased frequency of elevated troponin, including systemic HTN, left ventricular hypertrophy, HF, pulmonary HTN, and CKD.[23]

In our hypertensive females, the mean of RVBd was dilated, TAPSE was decreased, and SPAP was increased significantly, reflecting the COVID effect on the lungs and their impact on the right ventricle. The male gender had the same changes but did not reach statistical significance.

The identification of factors that may influence the heterogeneity of COVID-19 onset and outcome can optimize care services. In this regard, advanced age and preexisting chronic diseases, two strictly related aspects, have shown to substantially affect the COVID-19 prognosis, leading to dramatic increases in case fatality rates.[12,24] However, they assigned no weight to individual conditions, although the differing impact of multimorbidity depending on the severity of the disorders has been previously acknowledged. Weighting is particularly useful if the purpose of the measurement is to predict future outcomes such as mortality.[24]

Our suggested COVID score included several points, patient's age, oxygen saturation at admission, and comorbidities including smoking, HTN, DM, IHD, pericardial effusion, CKD, and rescue from cardiac arrest or shock. The mean score was significantly lower in recovered patients than in dead patients. Moreover, logistic regression of the outcome and score was highly significant ($P < 0.0001$). The DR increased markedly with the incremental rising score.

Study limitations

The study comprised a small number of patients suffering from severe COVID-19 only. In addition, the number of patients who had isolated comorbidities such as IHD and CKD alone was small for analysis.

Conclusions

Comorbidities had a cumulative risk that can predict the outcome of COVID-19 patients. Applying the suggested score at the time of admission can predict the danger of death and the need for mechanical ventilation. Patients who have high scores should attract attention for special medical care and treatment from the start.

The presence of HTN risk factors alone or associated with other risk factors has a higher DR than others. The suggested score needs to be evaluated in a prospective study with a large number of patients

Complications in hypertensive patients are significantly higher as dilated LV, decreased systolic function, and development of pericardial effusion. Long-term follow-up of those patients who may proceed to HF in future is essential.

Consents

The written informed consent was obtained from all patients at admission and all required consents according to the hospital by law.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Authors' Contributions

This research is a collaboration between 4 departments in 2 universities.

The researchers from 1 to 4 contributed by data collection.

The fifth researcher contributed by scientific data analysis, paper writing, revision and publication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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