Original Article

Correlation between Cardiac Output and Disease Severity in Intubated COVID-19 Patients: Insights from Ultrasonic Cardiac Output Monitoring in Intensive Care Unit Settings

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Abstract

Background: The COVID-19 pandemic has affected millions globally, and still continues to do so. Regarding the cardiovascular influences of COVID-19, this study aimed to investigate the relationship between cardiac indices, particularly cardiac output (CO), and severity of disease. **Methods:** This retrospective cohort study was conducted on intubated COVID-19 patients admitted to the intensive care unit (ICU). The study involved analyzing data from mechanically ventilated patients, excluding those with preexisting cardiovascular or pulmonary comorbidities. Hemodynamic parameters were evaluated by ultrasonic cardiac output monitoring (USCOM), and the severity of disease was evaluated by acute physiology and chronic health evaluation (APACHE II) and sequential organ failure assessment (SOFA) scoring systems. **Results:** The study included 41 patients, predominantly male with an average age of 63.1 years. Hemodynamic parameters and scores were reported for 6 days. This showed significant changes in CO, SOFA, and APACHE II over time (with $P = 0.02, 0.04, 0.03$, respectively). A negative correlation was found between CO and both SOFA and APACHE II scores ($P < 0.05$), indicating that as CO increased, the severity scores decreased. **Conclusion:** This study emphasizes the importance of continuous hemodynamic monitoring in ICU settings for COVID-19 patients. The correlation between CO and severity scores suggests that USCOM, along with APACHE II and SOFA, can be crucial in assessing the dynamic clinical state of patients, contributing to better management and potentially improving outcomes.

Keywords: Acute physiology and chronic health evaluation, COVID-19, sequential organ failure assessment and cardiac output, ultrasonic cardiac output monitoring

Introduction

The COVID-19 epidemic, which commenced 3 years ago, continues to impact all facets of life. By March 2023, the number of confirmed cases of infection surpassed 670 million and resulted in mortality rates exceeding 6.8 million people, necessitating the multipillar management of this pandemic.[1-3] Although most patients present with mild or no symptoms, some may have a septic shock from acute respiratory distress syndrome (ARDS), multiorgan failure, or even die.[4-7] Initially, it was thought that COVID-19 only affects the respiratory system. However, subsequent research revealed that it involves

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other organs, which is associated with increased mortality rates.[8-11] In comparison to SARS and MERS, COVID-19 has a greater impact on the cardiovascular system (CVS), particularly causing severe damage to the pulmonary vessels and cardiac dysfunction, both with and without direct harm to the heart muscle.[10,12] Nonetheless, the exact hemodynamic effects of COVID-19 on CVS are not well known.

Initially, individuals may have hypovolemia due to fever and the prescribed limitation of fluid intake, which is advised upon hospital admission to prevent pulmonary edema.[13,14] Similar to other systemic inflammations, patients with COVID-19 exhibit varying levels of vasodilation, which can be aggravated by sedative medications during mechanical ventilation. Circulating cytokines have the potential to trigger ventricular dysfunction.[15] In addition, postmortem investigations indicated that coronavirus may infrequently cause myocarditis, which can impair both systolic and diastolic function.[16-18] Mechanical ventilation using positive end-expiratory pressure can hinder right ventricular ejection and subsequently cause right ventricular dilation and decreased left ventricular filling.[19] In addition, among intensive care unit (ICU) admitted patients, those with COVID-19 appear to have a higher incidence of pulmonary embolism.[20,21]

Acute physiology and chronic health evaluation (APACHE II) and sequential organ failure assessment (SOFA) scores are two major scoring systems that can evaluate the severity of COVID-19 involvement and predict mortality.[22,23] Given that myocardial injury and cardiovascular comorbidities play a substantial role in the mortality of COVID-19, where new COVID-19 variants appear with their specific characteristic,[2] it is crucial to conduct early cardiological evaluations and identify high-risk patients.[24] Hence, particularly in intubated and severe cases, dynamic evaluation of cardiac indices may have the potential to evaluate not only the CVS function but also systemic inflammation. It can thus guide the decision-makers to examine the response to treatment and modify the therapeutic strategy. Therefore, we aimed to evaluate the cardiac function using ultrasonic cardiac output monitoring (USCOM) along APACHE II and SOFA scoring systems.

Methods

Ethical consideration

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The research and ethic committee of Shahid Beheshti University of Medical Sciences approved the study protocol (IR.SBMU.NRITLD.REC.1403.015).

Type of sampling and reason for selection

In this retrospective cohort study, the documented data of the patients with severe COVID-19, who were admitted to the ICUs of a university hospital due to COVID-19 involvement, were analyzed. We employed a convenience sampling method to select intubated, mechanically ventilated patients due to COVID-19 involvement and assessed all eligible cases throughout the study duration between January and June 2022.

Patients consent statement

All the patients signed the consent agreement forms provided to them and they were fully informed about study."

Inclusion criteria

The patients diagnosed with COVID-19 and severe lung involvement who were admitted to the ICU between January and June 2022 were included in this study. The diagnosis of COVID-19 was confirmed by the real-time reverse transcription polymerase chain reaction test and lung involvement was shown through computed tomography imaging. In addition, we only included those being mechanically ventilated due to severe lung involvement.

Exclusion criteria

Exclusion criteria included individuals with preexisting cardiac or pulmonary conditions such as ischemic heart disease, congestive heart failure, valvular heart disease, history of coronary artery bypass graft surgery as well as those with chronic kidney disease, individuals requiring vasopressors or inotropes on day 1 of admission, and patients in the prone position. In addition, cases with incomplete or insufficient medical records, including missing diagnostic test results or imaging studies essential for confirmation of COVID-19 diagnosis or assessment of lung involvement, were excluded from the analysis.

Patient assessment and data collection

All patients received the best possible therapies, and if necessary, goal-directed therapy. The ICU trainees assessed and monitored all the cases for 10 days. A conventional monitoring device used to measure vital signs and USCOM was employed by a single expert operator to evaluate the hemodynamic parameters. In addition, the severity of disease was examined by APACHE II and SOFA scoring systems every day.

Ultrasonic cardiac output monitor

The USCOM-1A® device employs continuous-wave Doppler technology, using a nonimaging probe placed in the suprasternal notch, to measure the velocity–time integrals of blood flow across the aortic valve at the left ventricular outflow tract. The participants maintained a partially reclined posture, whereas a small quantity of conducting gel was placed on their skin near the suprasternal notch. USCOM-1A® utilizes an internal anthropometric algorithm that establishes a correlation between the outflow tract diameter and the patient's height. By multiplying the velocity–time integral by the aortic root diameter, USCOM-1A® calculates the stroke volume (SV, cm^3). Cardiac output (CO) and systemic vascular resistance (SVR) can be determined using the following formulas: CO = SV × heart rate; SVR = mean arterial pressure divided by CO. Flow time corrected (FTc), an indication of left ventricular preload, and Smith–Madigan inotropic index (SMII), a discrete measure of heart inotropy, were also measured by USCOM. The hemodynamic examinations were conducted by skilled physicians, using standardized protocols.

Acute physiology and chronic health evaluation and sequential organ failure assessment

The acute physiology score, the chronic health evaluation, and the age-based score are the three components that makeup APACHE II.[25] It encompasses a total of 12 physiological factors. The APACHE II score ranges from zero "0" to 71 points, with a maximum of 60 points for physiological variables, up to 6 points for age, and up to 5 points for the past health conditions. The SOFA score assesses the dysfunction of six organs: respiratory, renal, circulatory, hepatic, hematological, and central nervous systems. Each system is evaluated on a scale of 0 (normal function) to 4 (severe dysfunction).[26]

Statistical analysis

The data were analyzed using IBM SPSS version 27 (IBM Corp., Armonk, NY, USA). The categorical variables are expressed as proportions and frequencies. Kolmogorov–Smirnov test was applied to test the normality distribution. The quantitative variables with normal distribution are summarized as mean ± standard deviation and also median. To explore the impacts of categorical independent variables, the Chi-square test was used. Mean values were compared between two groups using the independent *t*-test, as well as using nonparametric tests, such as the Mann–Whitney *U*-test. Pearson or Spearman correlation coefficient was applied to show the association between two variables. $P < 0.05$ were considered to indicate statistical significance.

Results

Baseline characteristics of patients

A total number of 41 patients were examined. Thirty-one patients (75.6%) were male and 10 (24.4%) were female. The average age of the patients was 63.1 ± 15.1 years and for women and men, it was 64.5 ± 13.5 and 58.7 ± 19.5 years, respectively. There is a significant difference between men and women in height and BMI as shown in Table 1 ($P < 0.05$). As it could be seen, the two groups have no difference in terms of other baseline characteristics, such as baseline SOFA, APACHE II, and length of ICU stay.

Temporal trends in hemodynamic parameters

Table 2 shows the evaluation of hemodynamic parameters trend within 6 days follow-up. Patients were evaluated by USCOM, APACHE II, and SOFA for 10 consecutive days, but because of the incomplete data in the past 4 days, Table 2 is structured only for the first 6 days. CO, SOFA, and APACHE II have changed significantly. SOFA and APACHE II experienced a decreasing trend and CO has increased, inversely.

Association between cardiac output, sequential organ failure assessment and acute physiology and chronic health evaluation scores

To show the association between CO, SOFA, and APACHE II changes, the means of these variables have been considered

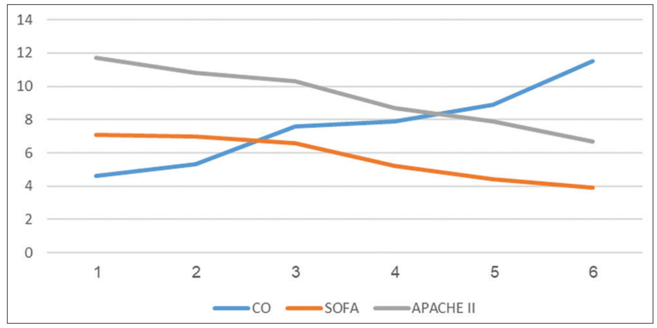

Figure 1: Trend of changes in CO, SOFA, and APACHE II score means through time. CO: Cardiac output, SOFA: Sequential organ failure assessment, APACHE II: Acute physiology and chronic health evaluation

each day. Figure 1 contains the trend of CO, SOFA, and APACHE II means in a line chart. As it is shown, SOFA and APACHE II decrease simultaneously and CO moves in an inverse direction in comparison to both of them. Correlation coefficients of three items emphasized that CO was significantly correlated with SOFA and APACHE II with Spearman coefficients of −0.689 and −0.702 ($P < 0.05$). SOFA and APACHE II correlation coefficients also are significant, 0.88 ($P = 0.001$).

Discussion

The present study demonstrated a significant enhancement in CO levels along with the alterations in APACHE II and SOFA scores during the first 6 days of administration in the ICU.

The mortality prediction ability of APACHE II and SOFA has been evaluated in COVID-19 patients. The death prediction accuracy using these scoring systems was not favorable, of which SOFA provided better accuracy. However, their scores were significantly higher in nonsurvival patients, indicating their potential in evaluating the severity of COVID-19 involvement.[27] In our study, due to the limited number of mortalities during the study, we could not determine the accuracy and potential of these scoring systems in predicting mortality. Nonetheless, APACHE II and SOFA scores significantly steadily decreased during the first 6 days of admission to the ICU, with a higher reduction in APACHE II scores.

Given the fact that COVID-19 has a considerable influence on CVS function, particularly in severe intubated patients, constant hemodynamic monitoring seems to be crucial.[10,12] For instance, Caravita *et al*. examined the hemodynamic profile of COVID-19 patients with mechanical ventilation. They demonstrated that CO and pulmonary vascular resistance were lower, but pulmonary artery wedge pressure was higher in COVID-19 patients than in the control group of mechanically ventilated patients with typical ARDS.[28] In addition, it has been shown that hemodynamic parameters evaluated by USCOM altered more significantly and the mortality rate was significantly more in intubated patients with COVID-19 rather than nonCOVID-19 patients.[29] In this regard, we have reported hemodynamic indexes examined by USCOM, which include

Table 1: Patient's characteristics

Variables	Mean±SD			*P*
	Male (*n*=31)	Female (*n*=10)	Total (*n*=41)	
Age (year)	64.5±13.5	58.7±19.5	63.1±15.1	0.299
Height (cm)	170.3±7.4	160.4±4.9	167.9±8.1	<0.001*
Weight (kg)	64.5±13.5	58.7±19.5	61.5±15.2	0.180
BMI	33.5±6.4	26.9±6.3	28.5±6.9	0.007*
APACHE II	11.74±4.9	11.57±5.4	11.64±5.3	0.387
SOFA	7.0±3.1	8.0±3.0	7.6±3.2	0.100
Length of stay in ICU (day)	8.6±4.2	9.0±4.0	8.8±4.2	0.578
Systolic pressure	126.5±23.2	128.4±16.2	126.9±21.5	0.810
Diastolic pressure	81.8±19.1	84.7±9.5	82.5±17.1	0.652
Hemoglobin	13.9±1.6	13.6±2.2	13.8±1.8	0.520
Mortality, *n* (%)	1 (3.2)	1 (10.0)	2 (4.9)	0.689

Patients were followed up for 10 days from admission to ICU and deaths during this period were counted as mortality. ICU: Intensive care unit, BMI: Body mass index, APACHE II: Acute physiology and chronic health evaluation, SOFA: Sequential organ failure assessment, SD: Standard deviation, *: Significant

Table 2: Haemodynamic parameters and severity of disease

Variables	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	*P*
CO	4.6±1.6	5.3±1.7	7.6±2.0	7.9±2.5	8.9±2.8	11.5±2.8	0.023*
SV	30.4±14.6	32.4±13.5	33.8±14.9	36.3±12.5	32.4±12.2	35.3±15.9	0.672
SVR	3375.6±1542.0	3177.6±1199.3	3015.4±1536.9	2568.9±915.1	2757.2±1637.9	2277.6±1327.7	0.100
FTc	288.9±83.2	287.9±74.8	293.6±65.2	298.4±70.7	299.9±59.3	304.2±72.7	0.973
SMII	2.3±2.9	0.8±0.2	0.8±0.3	0.7±0.2	0.6±0.2	0.7±0.2	0.664
SOFA	7.1±2.6	7.0±2.8	6.6±3.2	5.2±2.7	4.4±3.1	3.9±2.3	0.046*
APACHE II	11.7±3.1	10.8±3.5	10.3±2.9	8.7±3.2	7.9±3.4	6.7±3.0	0.033*

*Significant at 0.05 level. CO: Cardiac output, SV: Stroke volume, SVR: Systemic vascular resistance, FTc: Flow time corrected, SMII: Smith–Madgian inotropic index, APACHE II: Acute physiology and chronic health evaluation, SOFA: Sequential organ failure assessment

CO, SV, SVR, FTc, and SMII. Among these variables, only CO has been significantly increased. Using USCOM, Emami *et al*. evaluated hemodynamic indexes for 5 days.

in COVID-19 and non-COVID-19 patients and demonstrated similarly that CO increased significantly in COVID-19 group (from 3.03 ± 1.1 to 3.80 ± 1.4).[29] In addition, they showed an insignificant decrease in SVR levels (from 2904 ± 1176 on Day 1 to 2524 ± 113 on Day 5), which is consistent with our findings (from 3375 ± 1542 on Day 1 to 2277 ± 1327 on Day 6).

Conclusion

This study highlights the importance of evaluating hemodynamic parameters along SOFA and APACHE II scoring systems and indicates significant changes in CO and scoring system values during the initial ICU period. As far as CO evaluated by USCOM was correlated with the severity of disease shown by APACHE II and SOFA, it emphasizes the role of continuous monitoring in ICU settings to examine the dynamic clinical state of COVID-19 patients, thereby improving their overall management.

Outcomes of the study

Due to the correlation of severity scores with CO, USCOM monitoring appeared significant dynamic clinical state evaluator of critically ill patients.

Rationale of the study

This study contributes to the growing body of evidence on the cardiovascular manifestations of COVID-19 and underscores the importance of integrated hemodynamic monitoring in guiding clinical management which may improve patient outcomes in the ICU setting.

Limitation of the study

Owing to the retrospective cohort nature of this study, we could not reveal the actual influence of daily cardiac function evaluation on the management and clinical outcome. In addition, since we used the convenience sampling method, selection bias may be introduced which limits the generalizability of the results. The selection criteria of including intubation and mechanically ventilation with severe COVID-19 may not fully represent the broader population of COVID-19 patients, including those with less severe illness. Since the cardiac index changes have been shown in this study, we suggest researchers focus on the practical part and demonstrate its effects on decision-makers to modify the treatment strategy.

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Conflicts of interest

There are no conflicts of interest.

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