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Ultrasonic cardiac output monitoring in intubated patients with and without COVID-19 in the ICU: a prospective cohort study

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Abstract: **Objective:** The present study was conducted to compare mechanically ventilated patients with and without COVID-19 in terms of hemodynamic instability using cardiovascular indicators.

Methods: This prospective cohort study assigned intubated and mechanically ventilated patients to two groups, i.e. with COVID-19 and without COVID-19. The hemodynamic parameters measured and compared between the two groups on the first day of intensive care unit (ICU) admission and the following four consecutive days using an ultrasonic cardiac output monitor (USCOM) included cardiac output (CO), systemic vascular resistance (SVR), stroke volume (SV), flow time corrected (FTc), minute distance (MD) and potential kinetic energy (PKE).

Results: Forty-three patients (males: 62.7%) were assigned to the COVID-19 group and 40 (males: 64.1%) to the one without COVID-19. Insignificant differences were observed between the two groups at baseline in terms of the mean homodynamic variables measured using the USCOM (P>0.05). The mean CO increased (P=0.020), the mean SVR insignificantly changed (P=0.267), the mean MD increased (P=0.005) and PKE decreased (P=0.066) in the COVID-19 group during the five days of evaluation. In the same period, the mean CO insignificantly changed (P=0.937), the mean SVR increased (P=0.028) and changes in MD (P=0.808) and PKE (P=0.539) were insignificant in the group without COVID-19. The two groups were not significantly different in terms of the other homodynamic parameters during the follow-up (P>0.05).

Conclusion: The five-day changes in the USCOM-measured homodynamic parameters were lower in the group without COVID-19 compared to in that with COVID-19. In the group without COVID-19, no statistically-significant differences were observed between the mean follow-up values of the variables, excluding SVR, and their baseline values.

Keywords: Artificial Respiration; Cardiac Output; COVID-19; Intensive Care Units; Point of Care; Ultrasonography

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1. Introduction

Today, the world is experiencing a devastating pandemic caused by the novel coronavirus disease 2019 (COVID-19) (1). Although COVID-19 was first believed to mainly involve the respiratory system, later it was found that rapid involvement of other organs was related to poorer outcomes and higher mortality rates (2-4). Although most cases remain asymptomatic or present with only mild symptoms, a number of cases may suffer from acute respiratory distress syndrome (ARDS), septic shock, multi organ failure or even death (5-7). Accurately monitoring intravascular volume (IVV), cardiac output (CO) and hemodynamic parameters is essential for these severe cases that are normally mechanically ventilated (8-11). To the best of the authors' knowledge, hemodynamic instability has not been compared yet between patients with and without COVID-19 in terms of cardiovascular parameters. The present research was therefore conducted to compare these parameters between mechanically ventilated patients with COVID-19 and those without COVID-19.

2. Methods

2.1. Study design and setting

This prospective cohort study was conducted in the intensive care unit (ICU) of Sina Hospital, Tehran, Iran, from December 2019 to November 2020 and approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.SINAHOSPITAL.REC.1399.102), Tehran, Iran. Conducting this study did not interfere with the patient management process. Informed written consent was obtained from all the participants or their guardians.

2.2. Study population

The present study selected intubated mechanically ventilated patients using convenience sampling and evaluated all the eligible cases during the study period. Comparison was performed between one group with COVID-19 and another without it. COVID-19 was diagnosed using real time reverse transcription polymerase chain reaction (RT-PCR) test and potential lung involvement was observed in a CT scan. Subjects in the second group with no cardiovascular and pulmonary history had been intubated due to medical conditions other than COVID-19 such as postoperative care. The two groups were matched in terms of gender rather than age. The exclusion criteria comprised underlying cardiac or pulmonary diseases such as ischemic heart disease, congestive heart failure, valvular heart disease and Cor pulmonale, chronic kidney disease, and sepsis as well as shocks and, vasopressor or inotrope requirements on the first day of admission.

2.3. Ultrasonic cardiac output monitor (USCOM)

The invasive or non-invasive hemodynamic monitoring techniques and devices used in intensive care units (ICUs) include echocardiography, esophageal Doppler monitoring, the FloTrac system and pulmonary artery catheters (12-14). As a Doppler probe, USCOM is used on the suprasternal notch in non-invasive monitoring to measure the aortic blood flow velocity (15,16). This accurate and reliable technique can also be used for the real-time assessment of cardiac output (CO), intravascular volume (IVV) and fluid responsiveness (12).

2.4. Patient assessment and data collection

The patients in each group received appropriate treatments and goal-directed therapy if needed. All the cases were evaluated and followed up by an ICU fellow during the five consecutive days. Vital signs were recorded using a standard monitoring device and hemodynamic parameters were estimated using the USCOM (USCOM 1A, Uscom Ltd., Sydney, NSW, Australia) placed on the suprasternal notch. The aortic blood flow velocity, CO, systemic vascular resistance (SVR), stroke volume (SV), flow time corrected (FTc), minute distance (MD) and potential kinetic energy (PKE) were also measured and recorded upon admission and on the four following days. Furthermore, demographic data, underlying diseases, doses of vasopressor and inotrope and mortality were compared between the two groups.

2.5. Statistical analysis

Quantitative variables were described using mean±standard deviation (SD) and qualitative variables using frequency and percentage. Relationships among the categorical variables were evaluated using the Chi-square test. Between-group relationships among the quantitative variables were assessed using the independent t-test. Repeated-measures ANOVA was performed to obtain between- and within-group mean differences in the homodynamic variables. The level of statistical significance was adjusted as $P<0.05$, and $0.05<P<0.10$ was considered marginally significant. All the data were analyzed in IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA).

3. Results

This study assigned 43 patients (males: 62.7%) to the COVID-19 group and 40 (males: 64.1%) to the non-COVID-19 group. Gender distribution was not significantly different between the two groups (P=0.986), whereas patients in the COVID-19 group were significantly older than those in the other group (P<0.001). At least one underlying disease was found in 79.1% of the cases in the COVID-19 group and 67.5% in the non-COVID-19 group and the difference was statistically insignificant (P=0.233). Only the history of hypertension was significantly more frequent in the COVID-19 group (58.1% vs 35.0%, P=0.035). Figure 1 shows the distribution of underlying diseases in the two groups.

The administered rate of vasopressor (39.5% vs 12.5%, P=0.005) and inotrope (27.9% vs 12.5%, P=0.087) were significantly higher in the COVID-19 group than in the non-COVID-19 group during 5-day patient evaluation; meanwhile, 15 (34.9%) cases died in the COVID-19 group and 4 (10.0%) in the other group (P=0.007). Table 1 compares basic data between the two groups.

At baseline, the mean diastolic blood pressure (DBP) (73.3±12.7 mmHg vs 66.0±16.7 mmHg, P=0.028) and the mean oxygen saturation (SpO2) (90.8±6.3% vs 98.6±2.1%, P<0.001) were significantly lower in the COVID-19 group than in the non-COVID-19 group. The mean systolic blood pressure (SBP) (P=0.076) and heart rate (P=0.088) were also insignificantly lower in the COVID-19 group than in the other group. According to table 2, the mean values of the homodynamic variables, including CO, SVR, SV, FTc, MD and PKE, estimated using the USCOM were not significantly different between the two groups at baseline (Table 2).

This study ended with 24 patients remaining in the COVID-19 group and 19 in the other group. The mean SBP increased from 120.1 mmHg on day 1 to 125.7 mmHg on day 5 in the COVID-19 group (P=0.044); this change was, however, insignificant in the non-COVID-19 group (P=0.275) (Figure 2a). Similarly, the mean heart rate increased from 81.1 bpm

Table 1 Comparison of basic data between the two groups

Variable		Group		P
		COVID-19 N (%)	Non-COVID-19 N (%)	
Gender	Male	27(62.7)	25(62.5)	0.986
	Female	16(37.3)	15(37.5)	
Age; year±SD		62.8±9.9	51.1±16.5	<0.001
Underlying diseases		34(79.1)	27(67.5)	0.233
Vasopressor rate administration		3.4(39.5)	3.5(12.5)	0.005
Inotrope rate administration		12(27.9)	5(12.5)	0.087
Mortality		15(34.9)	4(10.0)	0.007

Table 2 Comparison of vital signs and homodynamic parameters between the two groups

Variable	Group		P^a	P^b
	COVID-19	Non-COVID-19		
	(Mean±SD)			
Systolic blood pressure (mmHg)	119.5±23.2	128.4±21.7	0.076	0.532
Diastolic blood pressure (mmHg)	66.0±16.7	73.3±12.7	0.028	0.570
Heart rate (bpm)	87.7±20.9	95.6±20.4	0.088	0.515
Oxygen saturation (%)	90.8±6.3	98.6±2.1	<0.001	<0.001
Cardiac output (L/min)	3.4±1.2	3.5±1.5	0.594	0.365
Systemic vascular resistance (mmHg.min/L)	2635.1±1113.1	2594.9±1037.3	0.866	0.756
Stroke volume (mL)	39.2±12.1	36.9±14.7	0.446	0.584
Flow time corrected (ms)	331.8±68.9	328.2±53.5	0.794	0.775
Minute distance (cm)	11.2±4.3	12.0±5.0	0.461	0.154
Potential kinetic energy (J)	123.0±85.9	137.7±105.0	0.488	0.296

a: Mean difference at baseline (day 1); b: Mean difference during the follow-up; bpm: Beats per minute; ms: Millisecond, J: Joule

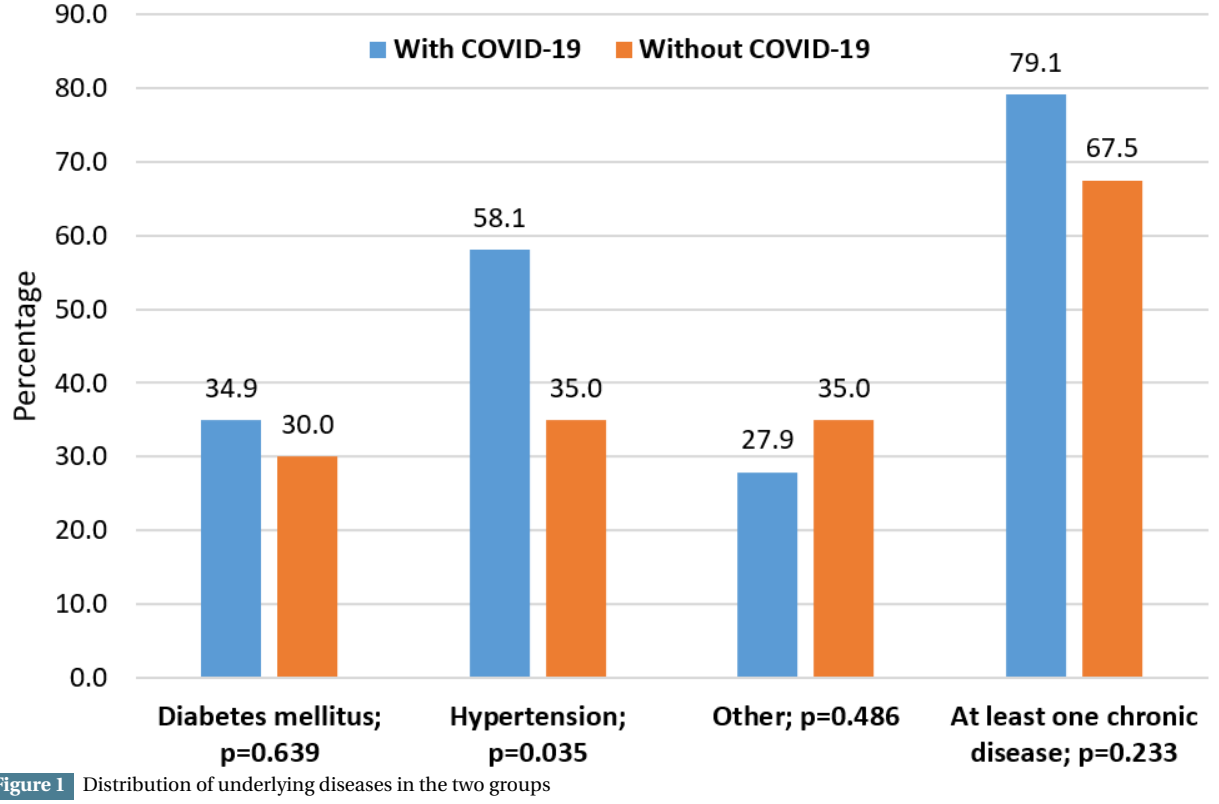

Figure 1 Distribution of underlying diseases in the two groups

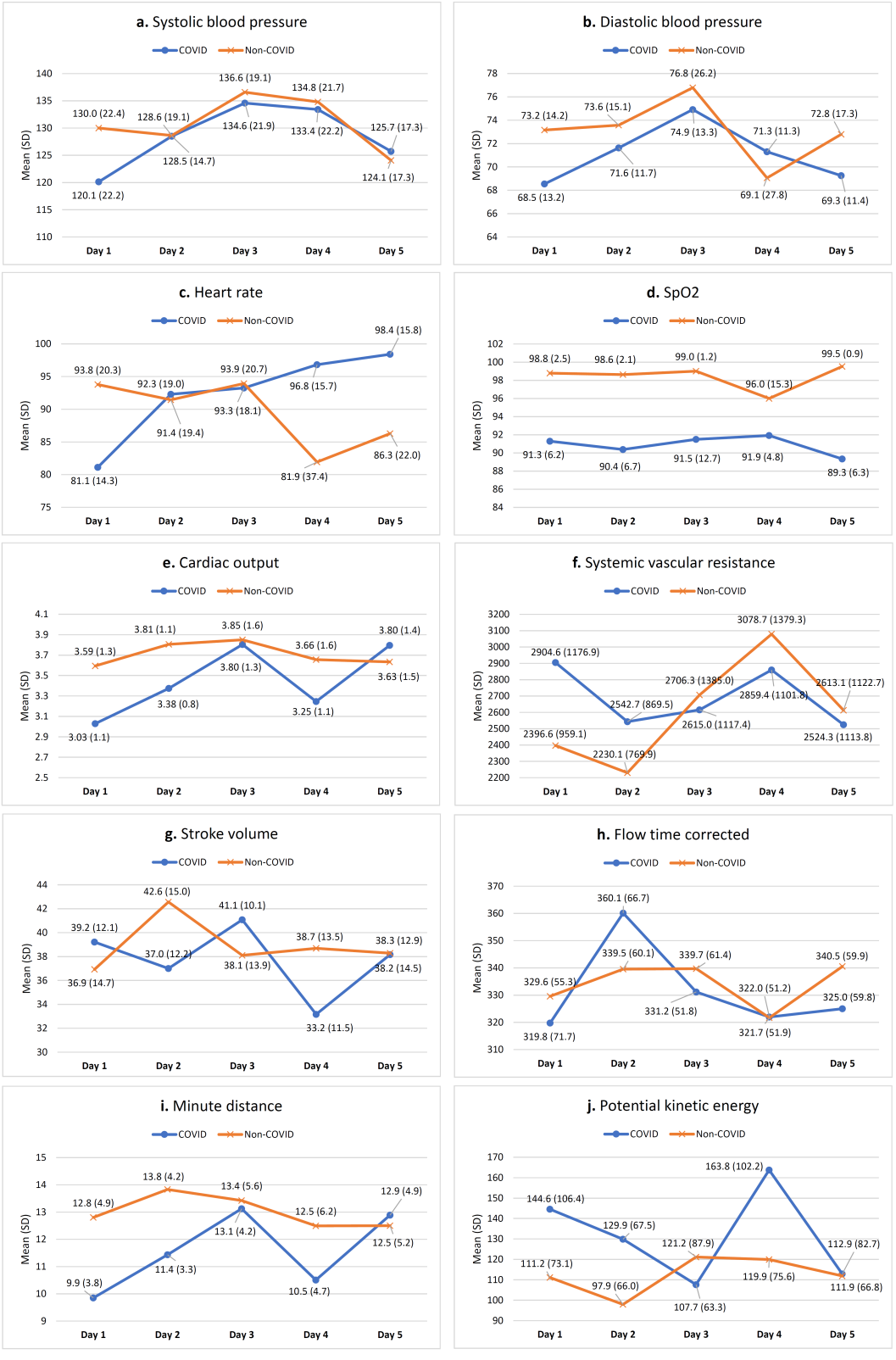

Figure 2 Mean levels of the homodynamic parameters in the COVID-19 and non-COVID-19 groups at follow-up, based-on the completed data after 5 days

(beats per minute) on day 1 to 98.4 bpm on day 5 in the COVID-19 group (P=0.001), and this change was insignificant in the other group (P=0.323) (Figure 2c). Repeated-measures ANOVA showed no significant differences between the two groups in terms of the mean levels of vital signs and homodynamic parameters at follow-up (P>0.05), except for the lower SpO2 in the COVID-19 group (P<0.001) (Figure 2d).

The mean CO increased from 3.03 L/min on day 1 to 3.80 L/min on day 5 in the COVID-19 group (P=0.020), though this change was insignificant in the non-COVID-19 group (P=0.937) (Figure 2e). The mean SVR increased from 2396.6 mmHg.min/L on day 1 to 2613.1 mmHg.min/L on day 5 in the non-COVID-19 group (P=0.028), despite the corresponding insignificant change in the COVID-19 group (P=0.267) (Figure 2f). The mean MD also rose from 9.9 cm to 12.9 cm (P=0.005) in the COVID-19 group, whereas PKE decreased from 144.6 J to 112.9 J (P=0.066). The changes in MD (P=0.808) and PKE (P=0.539) were insignificant in the non-COVID-19 group. The changes in the other homodynamic parameters were also insignificantly different between the two groups at follow-up (P>0.05).

4. Discussion

The present study reported no significant difference between the two groups in terms of CO, SVR, SV, FTc, MD and PKE (P>0.05).

Given the lack of a definitive treatment for COVID-19 at the time of writing this article, continuous hemodynamic monitoring and supportive management are crucial for restoring tissue vascularization and organ function in intubated patients with COVID-19 and more severe cases (17).

In 2020, Michard et al. reported vasopressor requirements and changes in the cardiac function in the majority of patients with COVID-19 admitted to the ICU (18). Hemodynamic evaluation therefore appeared essential before the disease progresses to a critical state. They also reported no significant hemodynamic alterations in approximately 50% of the patients and found their majority in the hyperdynamic state owing to the virus-induced systemic inflammation. In addition, systolic dysfunction was as rare as 20% in patients with COVID-19 (18,19).

The majority of the hemodynamic variables estimated with the USCOM changed more significantly and mortality was significantly higher in the COVID-19 group compared to the non-COVID-19 group. The rate of vasopressor and inotrope administered in the COVID-19 group were also higher than in the other group.

In 2020, Caravita et al. reported combined cardiopulmonary alterations in the hemodynamic profile of mechanically ventilated patients with COVID-19 (20). They performed pulmonary artery catheterization as an invasive procedure in mechanically ventilated patients with acute respiratory distress syndrome (ARDS), compared their hemodynamic variables with those receiving no mechanical ventilation and found a higher cardiac index and pulmonary artery wedge pressure and the same pulmonary vascular resistance in the patients with ARDS compared to the control group. They also reported hypertension and diabetes mellitus as the most prevalent underlying diseases in the COVID-19 group, which is consistent with the present findings. To the best of the authors' knowledge, this study pioneered the investigation and comparison of hemodynamic parameters in patients with and without COVID-19 in the ICU using the USCOM. Moreover, using USCOM was found to yield the same outcomes as those obtained using other invasive methods (21-24).

Asar et al. analyzed retrospectively 17 patients with COVID-19 and 16 patients diagnosed with other types of diseases with moderate and severe ARDS, mechanically ventilated and admitted in ICU (25). They performed advanced hemodynamic monitoring via the transpulmonary thermodilution method and they concluded that pulmonary vascular permeability indexes of COVID-19 ARDS patients were significantly higher than non-COVID-19 patients. The ICU mortality rate was 59% in COVID-19 ARDS group and 50% in ARDS patients due to other causes. This difference was not significant in their study.

5. Limitations

The present study limitations included its unicenter type and small sample and operator dependency of USCOM as a non-invasive and accessible hemodynamic monitor. Swan-Ganz catheterization was also not performed in the patients owing to their critical and unstable condition and the invasive nature of the method.

6. Conclusion

Lower changes in the homodynamic parameters were observed during the study period in the non-COVID-19 group than in the COVID-19 group. Compared to baseline, no statistically-significant changes were observed in the mean follow-up values of these variables, excluding SVR, in the non-COVID-19 group. In contrast, the mean levels of SBP, HR, CO and MD significantly changed in the COVID-19 group at follow-up.

7. Declarations

7.1. Acknowledgment

None.

7.2. Authors' contribution

AN and KHE contributed to the design of the article. MM and HS conceived the study idea. RSM and AA helped prepare the manuscript draft. SHE and TZ revised the article. EV collected the data. All the authors reviewed and approved the final manuscript.

7.3. Conflict of interest

Authors declared no conflicts of interest.

7.4. Funding

None.

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