The Ability of Cardiac Output to Predict Mortality in Patients with Septic Shock of Surgical Origin: A Pilot Study

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Abstract

Background: The aim of this study is to evaluate the ability of cardiac output (CO) to predict 28-day mortality in patients with septic shock.

Methods: This prospective observational study included adult patients with septic shock after surgical control of the source of infection. The CO using transthoracic echocardiography, heart rate, mean arterial pressure, acute physiology and chronic health evaluation (APACHE) score, and sequential organ failure assessment (SOFA) score, and laboratory data were collected within 3 hours of the admission to the ICU. Patients were followed up for outcome until hospital discharge and/or 28 days after first ICU admission. The primary outcome was the ability of the CO to predict to predict 28-day mortality using the area under receiver operating characteristic curve (AUC) analysis. Secondary outcomes were the ability of severity scores and laboratory data to predict 28-days mortality.

Results: Twenty-four patients were analyzed, and 7/24 (29%) patients died. The AUC (95% confidence interval) for the CO to predict 28-day mortality was 0.78 (0.57-0.92). AT a cut-off value of ≤5.5 L/min, the CO can predict 28-mortality with negative predictive value of 93%. The AUC for the APACHE II score, SOFA score, and laboratory data to predict 28-days mortality was not statistically significant.

Conclusion: Echocardiography-derived CO can be a useful predictor of 28-day mortality in surgical critically ill patients with septic shock. A CO >5.5 L/min can suggest patient survival with a predictive value of 93%.

Keywords: Sepsis; Septic shock; Postoperative; Mortality; Cardiac Output

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Introduction

Culex species are the most wides pread Septic shock is a leading cause of intensive care unit (ICU) admission and is characterized by seriously high mortality rates worldwide. Septic shock represents the most common cause of circulatory failure [1]. Septic shock is usually due to vasoplegia which results in re-distribution of the effective blood volume causing profound hypotension with a preserved cardiac function and normal-to-high cardiac output (CO); however, sepsis sometimes produces septic cardiomyopathy resulting in impaired left ventricular systolic and diastolic functions; and right ventricular function [2]. It is hypothesized that left ventricular systolic dysfunction would be associated with poor patient outcomes in patients with septic shock. However, previous studies which evaluated the association of sepsis-induced cardiac dysfunction and patient outcomes showed conflicting results [3–5].

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All previous studies evaluated cardiac function at terms of ejection fraction, tissue doppler indices, and diastolic dysfunction. No studies to the best of our knowledge evaluated the association of low cardiac output and patient outcomes in patients with septic shock. The aim of this study is to evaluate the relation of CO and 28-day mortality in patients with septic shock. we aimed also to find the predictive ability of CO for patient mortality.

Patients and Methods

This prospective observational study was conducted at Cairo University Hospital in the surgical ICU for trauma and emergency operations. The study was approved by the institutional research ethics committee and written informed consent was obtained from patient next-of-kin. The study included patients with septic shock according to Sepsis-3 agreement [6]. All included patients were postoperative admitted from the emergency operating theatre after surgical intervention for eliminating the source of sepsis. Patients were included according to the following criteria: age between 18-65 years, ejection fraction > 40%, no significant valvular cardiac lesions, on norepinephrine infusion. Patients with the following criteria were excluded from the study: poor echocardiographic window, metastatic cancer, pre-admission cardiac arrest, patients with potentially undrained source, and patients with refractory hypotension who are expected to die within 24 h.

Patient management

Patients were managed according to the local protocols and the surviving sepsis campaign guidelines [7]. As all patients were admitted from the operating theatre, the early resuscitation, fluid, and vasopressor management was performed in the emergency room and/or the operating room. On admission to the ICU, patients were evaluated using point-of-care echocardiography for the evaluation of the type of shock and for determination of the cardiac output.

Measurement of the cardiac output.

An experienced intensivist with more than 100 supervised cases of transthoracic examinations performed the echocardiographic assessment. The stroke volume was calculated as the product of the subaortic velocity time integral (VTI) and the left ventricular outflow tract (LVOT) diameter. The VTI was obtained by placing the pulsed wave Doppler sampling cursor in the middle of the LVOT proximal to the aortic valve in the apical five-chamber view. The LVOT diameter measured as the distance between the inflection points at the base of the aortic valve cusps from the left parasternal long-axis view during systole. The LVOT area was calculated, according to the following equation: $\pi \text{ X } \left(\text{LVOT}\frac{\text{diameter}}{2}\right)^2 = \left(\text{LVOT}\frac{\text{diameter}}{2}\right)^2 \text{ X } 0.785.$ Finally, the stroke volume was calculated as the product of the VTI and the LVOT diameter [8]. The CO was calculated as the product of the stroke volume and the heart rate. Ultrasound measurements were obtained using a GE Vivid E9 machine. The measurements were obtained within 3 h from ICU admission. Patients were followed up for outcome until hospital discharge and/or 28 days after first ICU admission. Patients were divided into survivors and dead according to their status after 28 days and the two groups were compared for baseline properties, severity scores, and clinical data.

Primary outcome

The accuracy of the CO to predict 28-day mortality using the area under receiver operating characteristic curve (AUC) analysis.

Secondary outcomes

The secondary outcomes included: the ability of central oxygen saturation, severity scores and laboratory data to predict 28-days mortality. Other outcomes included baseline heart rate and mean arterial pressure, age, sex, source of infection, days of mechanical ventilation and ICU stay.

Sample size calculation and statistical analysis

The sample size was calculated using MedCalc version 12.1.4.0 (MedCalc Software bvba, Belgium) to detect AUC of 0.85 for the CO to predict 28-day mortality. The null hypothesis was set at 0.5. The study power was set at 80% and the alpha error was set at 0.05. The minimum number of patients was calculated to be 21, with at least 7 positive cases (mortality) and 14 negative cases (survival).

Data were presented as the means (standard deviations), medians (quartiles), and frequencies (%) as appropriate. Data were checked for normality using the Shapiro-Wilk test. The two study groups were compared using the Unpaired Student's *t* test or Mann-Whitney *U* test for continuous variables; and either the Chi-squared test or Fisher's exact test for the categorical variables. MedCalc version 12.1.4.0 (MedCalc Software bvba, Mariakerke, Belgium) generated receiver operating characteristic curves and the AUC were calculated. Values with the highest sensitivity and specificity (Youden index) were obtained. The level of significance was set at $p \leq 0.05$.

Results:

Thirty patients were evaluated for the eligibility to the study and 24 patients were included and were available for the final analysis. The mean age of the included cohort was 53 ±12 years and 12/24 (50%) were males. The number of survivors was 17/24 (71%) patients, while the number of patients who died was 7/24 (29%). The median (quartiles) duration of mechanical ventilation was 2.0 (1.0, 3.5) days and the length of hospital stay was 8.0 (6.5, 9.5) days. The baseline data of the participants are displayed in Table 1. The patients who died had higher mean arterial pressure and likely to have lower cardiac output in comparison to the survivors. (Table 2) Other hemodynamic and laboratory data were comparable between the two groups. (Table 2).

The AUC (95%CI) for the CO to predict 28-day mortality was 0.78 (0.57-0.92). AT a cut-off value of ≤5.5 L/min, the CO can predict 28-mortality with sensitivity of 86% and negative predictive value of 93%. (Table 3) The AUC for the ability to predict 28-days mortality was not statistically significant in the APACHE II score, SOFA score, and laboratory data. (Table 3).

Table 1: Demographic data and baseline clinical severity scores. Data presented as mean ±standard deviation, median (quartiles), and frequency (%)

	Dead (n=7)	Survivors (n=17)	P-values
Age (years)	53 ±13	53 ±12	0.927
Male gender	1 (14%)	11 (65%)	0.069
Body mass index (kg/m^2)	32 ±4	32 ±4.5	0.825
Source of infection Abdomen Soft tissue	 6 (86%) 1 (14%)	 15 (88%) 2 (12%)	 1.000 1.000
APACHE II score	10 ±5	12 ±4	0.530
SOFA	6 ±2	6 ±2	0.841
Duration of mechanical ventilation (days)	7 (2, 10)	2 (1, 3)	0.047

APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment

Table 2: Hemodynamic and laboratory data. Data presented as mean ±standard deviation, median (quartiles), and frequency (%)

	Dead (n=7)	Survivor (n=17)	P value
Heart rate (bpm)	106 ±28	111 ±19	0.679
Mean arterial pressure (mmHg)	95 ±11	79 ±11	0.003 *
Central venous oxygen saturation (%)	61 ±14	64 ±10	0.578
Central venous pressure (cmH_2O)	11 ±7	8 ±5	0.210
Cardiac output (L/min)	5.0 ±2.4	8.4 ±4.3	0.064
Serum lactate (mg/dL)	4.3 ±1.8	3.6 ±1.3	0.332
C-reactive protein (mg/dL)	262 ±101	240 ±101	0.627
Urea (mg/dL)	103 ±92	57 ±14	0.701
Creatinine (mg/dL)	1.8 ±1.8	1.9 ±1.3	0.873
Interleukin-6 (IU/mL)	389 (113, 1442)	314 (198, 1193)	0.901
Interleukin-10 (IU/mL)	4.8 (4.8, 59.0)	4.8 (4.8, 10.5)	0.757

APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment. * denotes statistical significance

Table 3: AUC analysis for the ability to predict 28-day mortality

	AUC (95%CI)	Sensitivity	Specificity	PPV	NPV	Cut-off value
Cardiac output	0.78 (0.57-0.92) *	86%	82%	67%	93%	≤5.5 L/min
Central venous saturation	0.64 (0.42-0.83)	57%	82%	58%	82%	≤55%
APACHE	0.59 (0.38-0.79)	71%	59%	42%	83%	≤10
SOFA	0.60 (0.38-0.79)	57%	71%	44%	80%	≤5
Lactate	0.58 (0.36-0.78)	43%	88%	38%	75%	>4.5 mg/dL
C-reactive protein	0.57 (0.36-0.77)	100%	35%	39%	100%	>156 mg/dL
Interleukin-6	0.52 (0.31-0.73)	57%	59%	36%	77%	>337.7 IU/mL
Interleukin-10	0.54 (0.33-0.75)	29%	88%	50%	75%	>53.2 IU/mL

APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation II, AUC: area under receiver operating characteristic curve, CI: confidence interval, SOFA: Sequential Organ Failure Assessment. * Denotes statistical significance

Discussion

We report that low CO can predict poor patient outcomes in septic shock. The AUC for 28-day mortality was highest for the CO in our cohort of surgical critically ill patients. Other variables, namely lactate, central venous saturation, and inflammatory makers showed low predictive properties in this cohort.

Septic shock is usually associated with profound vasodilatation and preserved cardiac systolic function; this combination of low afterload and preserved contractility is responsible for the high CO which is a characteristic feature for distributive shock [1]. However, being a dysregulated host response to infection with possible failure of any organ, sepsis sometimes produces myocardial depression which impair the systolic function, diastolic function, or both [9]. Having a low CO in some septic patients might denote that the pathology is severe and advanced which resulted in a low stroke volume despite the low afterload. This might explain our findings which shows that low CO is a predictor of poor outcomes in this population.

Previous data showed conflicting results with regard the relation of initial cardiac function and final outcomes in patients with septic shock. Sanfilippo et al reported that there is no association with left ventricular systolic function (evaluated by tissue doppler) and patient outcomes in septic shock [3]. Sevilla Berrios et al found a similar finding to Sanfilippo et al study; however, they evaluated the left ventricular function according to the ejection fraction [4]. Jentzer et al found that left ventricular dysfunction does not predict poor outcomes in post-arrest patients [5]. The difference between the mentioned studies and our results is probably because they evaluated the systolic function in a different way from ours. Our study focused on the CO as a final product of the cardiac function. Supporting out results Yuriditsky et al found that the low VTI is associated with poor outcomes in pulmonary embolism [10].

Our findings suggest that early evaluation of the CO could be an important tool for risk stratification of patients with septic shock. Detecting of patients with more severe disease could be useful in benchmarking. Furthermore, measurement of the CO could help in the follow-up of patient during their ICU stay and detect their progress and response to therapeutic interventions. The study is considered a pilot study which should be confirmed in larger cohorts. Some limitations are present such as being a single-centre study which included strictly surgical patients. other limitations such as the lack of sophisticated echocardiographic measurements because the examination was a point-of-care one.

Conclusion:

In conclusion echocardiography-derived CO can be a useful predictor of 28-day mortality in surgical critically ill patients with septic shock. A CO >5.5 L/min can suggest patient survival with a predictive value of 93%.

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