ORIGINAL ARTICLE

The Predictive Value of Echocardiography for Evaluation of Sepsis-Induced Cardiac Dysfunction and Mortality Outcomes in Critically-ill Septic Patients in Comparison with APACHE II and qSOFA Clinical Scores

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Abstract

Background: ***Sepsis remains a major global health issue, characterized by a systemic inflammatory response to infection that leads to widespread organ dysfunction.***

Aim of the work: ***This work aimed to evaluate the prognostic value of echocardiography in predicting sepsis-induced cardiac dysfunction (SICD) and compare its effectiveness with clinical scoring systems like APACHE II and qSOFA.***

Methods: ***In the intensive care unit (ICU) of Al-Azhar University Hospitals, 90 patients with sepsis were included in this prospective observational cohort study. This study'sstudy's primary focus was the evaluation of echocardiographic parameters. In addition, evaluation of Clinical scores such as APACHE II and qSOFA.***

Results: ***The presence of diabetes mellitus (DM) and hypertension (HTN) significantly increased the risk of mortality (P>0.05). Higher serum lactate level is a well-established marker of sepsis severity and mortality. Cardiomyopathy was significantly associated with higher mortality (P>0.05). LVEF at day 3 (LVEF_3) and LVEF at day 7 (LVEF_7) were significant predictors of mortality. APACHE II Score was a significant indicator of mortality (P>0.05). The combined analysis of the APACHE II score and LVEF at day 3 (LVEF_3) was a strong independent predictor (94.8%) of the variability in mortality among critically ill septic patients.***

Conclusions: ***Lower LVEF values at different time points (initial, day 3, and day 7) are linked to higher mortality rates. Echocardiography provides additional prognostic value compared to traditional clinical scores like APACHE II and qSOFA. Older patients with comorbidities like diabetes and hypertension have worse outcomes.***

Keywords: Cardiomyopathy; Left Ventricular Ejection Fraction; Echocardiography; Sepsis

1. Introduction

Sepsis is a condition of pathologic, physiologic, and metabolic abnormalities brought on by infection that can lead to tissue hypoxia, mitochondrial dysfunction, and release of inflammatory cytokines, which can cause numerous organ dysfunctions.[1] In the intensive care unit (ICU), septic cardiomyopathy occurs, and it ranges between 10 and 70 % in septic patients.[2] This variation across studies is probably caused by underrecognition and a lack of official diagnostic criteria. The suggested diagnostic standards for cardiomyopathy brought on by sepsis included an acute and reversible onset of global biventricular dysfunction with decreased contractility, dilatation of the left ventricle, diminished responsiveness to fluid and pressors, and lack of acute coronary syndrome as a contributing factor.[3]

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The three main characteristics of sepsis-induced cardiomyopathy are dilatation of the left ventricle (LV), decreased EF, and recovery in seven to ten days.[4] Importantly, by identifying the predictors of the condition, it is possible to distinguish sepsis-induced cardiomyopathy from other heart conditions and avoid invasive procedures like coronary angiography. Early detection of sepsis-induced cardiomyopathy contributes to mitigating the burden of sepsis.[5] Transthoracic echocardiography (TTE) is a popular noninvasive, reliable bedside examination that has made it simple to assess hemodynamic variability, including right ventricular (RV) dysfunction, systolic or diastolic LV failure.[6] The Acute Physiology and Chronic Health Evaluation II (APACHE II) score system is a popular model for prognostic scoring in ICUs. For patients in critical condition, it has demonstrated itself to be an excellent predictor of patient severity and has a strong association with the outcome.[7] Quick Sequential Organ Failure Assessment (qSOFA) was designed to quickly detect infected individuals who are at a high risk of death.[1] This study aimed to evaluate the prognostic value of echocardiography in predicting sepsis-induced cardiac dysfunction (SICD) and compare its effectiveness with clinical scoring systems like APACHE II and qSOFA.

2. Patients and methods

This prospective observational cohort study involved 90 patients with sepsis who were admitted to the critical care unit at Al-Azhar University Hospitals between April 2023 and October 2024. All patients or their authorized representatives provided informed written consent, and the Institutional Review Board granted ethical approval. Adults aged 18 years and older with a diagnosis of sepsis, as per the Sepsis-3 criteria, were included in the study. The study's primary focus was the evaluation of echocardiographic indices, including LVEF, Mitral Annular Plane Systolic Excursion (MAPSE), Tissue Doppler Imaging (TDI) parameters for left ventricular diastolic function, and Tricuspid Annular Plane Systolic Excursion (TAPSE) for right ventricular function. These measurements were conducted at ICU admission, three days, and one week after admission. In addition, laboratory tests, such as C-reactive protein (CRP), serum lactate, and blood cultures, were collected. Clinical scores such as APACHE II and qSOFA were also evaluated on the first day of ICU admission. Criteria for exclusion included chronic renal failure, ischemic heart disease, pre-existing cardiomyopathy, or LVEF <50% at baseline.

Study design:

All patients included in the study were assessed by:

Baseline characteristics, including age, sex, estimated body weight, height, and comorbidities that already existed.

Vital signs: At ICU admission, noninvasive (Systolic, Diastolic, Mean Arterial Blood Pressure) measured in both upper limbs and the highest reading obtained, Heart Rate (HR), SpO2, Electrocardiogram (ECG), Respiratory Rate, Central Venous Pressure (CVP), Urinary Output (UOP).

Echocardiographic parameters within 48 hours of diagnosis of sepsis.

Laboratory tests, including blood culture, liver function, renal function, serum lactate, total leukocyte count (TLC), and C-reactive protein (CRP)

Clinical scores: APACHE II and qSOFA scores.

Technique and measurement:

After standard continuous electrocardiogram (ECG) monitoring, arterial blood pressure and respiratory rate monitoring, and central venous catheter placement. fluid resuscitation, empirical antibiotics, and tests such as blood culture, liver function, renal function, TLC, serum lactate, and CRP have been ordered. Hemodynamic measurements MAP, HR and CVP also recorded.

Echocardiographic parameters:

LV ejection fraction (LVEF):

LVEF has been measured from the perspectives of the parasternal long axis (PLAX) or parasternal short axis (PSAX) using the standard M-Mode technique. Then, we calculated LVEF using the Modified Simpson Method. In order to quantify LVEF using this method, the endocardial border must be traced in both the apical four-chamber view and two-chamber view during end-diastole and end-systole. Normal EF ranges between 55% and 75%.

Mitral annular plane systolic excursion (MAPSE):

MAPSE have been measured using M-mode across the annulus of the mitral valve, which corresponds to the left ventricular lateral wall segments, in the four-chamber apical view. The mitral annulus's systolic excursion is shown by measuring the distance between the peak during mitral valve closure and the lowest point at end diastole. The Average normal values have been reported in the range of 12-15mm.

LV diastolic function:

Tissue Doppler imaging (TDI) parameters of the peak early (e′) of the septal and lateral mitral annulus have been evaluated to evaluate the diastolic filling patterns of the left ventricle. From the Doppler recordings, the early (MV E) and late (MV A) phases of the mitral inflow were measured for peak velocities, and the E/A ratio was

estimated. Using apical two-chamber (A2C) and apical four-chamber (A4C) images, the LA volume index was calculated. The lateral mitral annulus and septal peak early diastolic velocity (e′) were measured. The TR peak velocity was calculated, and according to the findings, patients have been classified into normal diastolic function or diastolic dysfunction.

Right ventricle (RV) function:

Tricuspid annular plane systolic excursion (TAPSE), which is quantified using M-mode in the apical four-chamber view, has been used to evaluate RV function. The precursor should be as parallel to the lateral tricuspid annulus and as aligned along the RV's free wall as possible.

Normal TAPSE was ≥ 1.6 cm.

Fraction area change (FAC)

It's a two-dimensional measure of the right ventricle's global systolic function. It was acquired using the apical four-chamber view and calculated as the difference between the end-diastolic area and the end-systolic area divided by the end-diastolic area. Normal FAC is 35% or higher.

Sample Size Analysis

Power analysis was carried out using G*Power software (latest ver. 3.1.9.7; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) to determine the representative sample and ensure the validity of the results. Considering a confidence level of 95%, a power of 80%, an α error of 5% and according to the data obtained from a previous study, which revealed that the proportion of mortality related to sepsis-induced cardiomyopathy (P)= 0.3, the representative sample should be at least 81 patients with sepsis-induced cardiomyopathy in this study. Estimating a 10% dropout during follow-up (f), then the total number of cases would be 90.

Statistical analysis

The data was statistically analyzed by SPSS v26 (IBM©, Chicago, IL, USA). The Kolmogorov–Smirnov test will check the normality of data. The paired t-test is used to compare quantitative data that are expressed as mean and standard deviation (SD). The chi-square (x2) test is used to examine qualitative variables that are displayed as frequency and percentage (%). The 'Mann-Whitney U' test is utilized for continuous non-parametric variables. Kaplan–Meier survival time-to-event analysis is used to compare survival between groups. Statistical significance is determined using a p-value of 0.05 and the standard 95% confidence limit.

3. Results

The study population consists of 41.8% females and 57.1% males. Diabetes Mellitus (DM) is present in 49.5% of the patients, indicating a balanced presence between diabetic and non-diabetic individuals. Hypertension (HTN) affects 42.9% of the patients, while 36.3% are smokers Table 1

Table 1. Demographic data

VARIABLE		FREQUENCY	PERCENT
SEX	Female	38	41.8
	Male	52	57.1
DM	No	45	49.5
	Yes	45	49.5
HTN	No	51	56.0
	Yes	39	42.9
SMOKING	No	57	62.6
	Yes	33	36.3

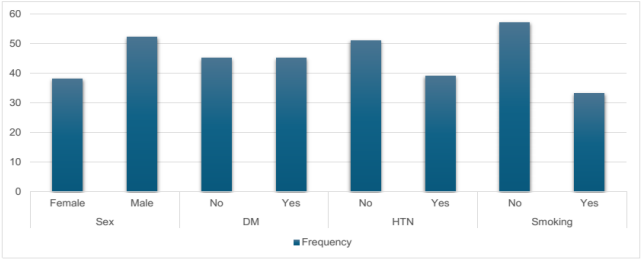

Figure 1. Descriptive parameters

Table 2. Demographic Characteristics and Their Association with ICU Mortality

		ICU MORTALITY		P VALUE
		No MEAN ± SD/ N(%)	Yes MEAN ± SD/ N(%)	
AGE (YEARS)		60.62 ± 7.344	71.86 ± 7.827	.000*
WEIGHT (KG)		77.69 ± 9.335	72.73 ± 8.293	.029*
HIGHT (METER)		1.7104 ± .03735	1.7155 ± .03949	.591
BMI		26.5706 ± 3.23531	24.7745 ± 3.23280	0.26
SEX	Female	32 (47.1%)	6 (27.3%)	0.102
	Male	36 (52.9%)	16 (72.7%)	
DM	No	43 (63.2%)	2 (9.1%)	0.000
	Yes	43 (63.2%)	20 (90.9%)	
HTN	No	44 (64.7%)	7 (31.8%)	0.007
	Yes	24 (35.3%)	15 (68.2%)	
SMOKING	No	49 (72.1%)	8 (36.4%)	0.003
	Yes	19 (27.9%)	14 (63.6%)	

Older age and lower weight are significantly associated with higher ICU mortality, with mean ages of 71.86 years (SD = 7.827) for deceased patients compared to 60.62 years (SD = 7.344) for survivors (p = .000), and mean weights of 72.73 kg (SD = 8.293) for deceased patients compared to 77.69 kg (SD = 9.335) for survivors (p = .029). While height and BMI did not show significant differences, gender distribution

indicated a trend with more males (72.7%) among deceased patients compared to survivors (52.9%), though not statistically significant (p = .102). Diabetes mellitus (DM) and hypertension (HTN) significantly increased the risk of mortality, with 90.9% of deceased patients having DM (p = .000) and 68.2% having HTN (p = .007). Smoking also showed a significant association, with 63.6% of deceased patients being smokers compared to 27.9% of survivors (p = .003).

Table 3. Clinical Outcomes and Their Association with ICU Mortality

		ICU MORTALITY		P VALUE
		No MEAN ± SD/ N(%)	Yes MEAN ± SD/ N(%)	
APACHE II SCORE		16.76 ± 3.746	27.77 ± 2.181	.000*
VENTILATION TIME (HOURS)		0.88 ± 4.307	88.36 ± 33.442	0.000
ICU LENGTH OF STAY (DAYS)		5.53 ± 1.732	8.91 ± 1.571	0.000
HOSPITAL LENGTH OF STAY (DAYS)		10.79 ± 2.422	8.91 ± 1.571	0.000
Q SOFA	2	67 (98.5%)	15 (68.2%)	0.000
	3	1 (1.5%)	7 (31.8%)	
CARDIOMYOPATHY	No	68 (100.0%)	4 (18.2%)	0.000
	Yes	0 (0.0%)	18 (81.8%)	

Higher APACHE II scores are significantly associated with ICU mortality, with deceased patients having a mean score of 27.77 (SD = 2.181) compared to 16.76 (SD = 3.746) for survivors (p = .000). Deceased patients also had significantly longer ventilation times (mean = 88.36 hours, SD = 33.442) and ICU lengths of stay (mean = 8.91 days, SD = 1.571) compared to survivors (mean = 0.88 hours, SD = 4.307 and mean = 5.53 days, SD = 1.732, respectively) (p = .000 for both). However, deceased patients had shorter hospital stays (mean = 8.91 days, SD = 1.571) compared to survivors (mean = 10.79 days, SD = 2.422) (p = .000). Higher qSOFA scores and the presence of cardiomyopathy were also significantly associated with higher mortality (p = .000).

Table 4. Roc curve of LVEF to predict mortality:

	CUTOFF	SENSITIVITY	SPECIFICITY	PPV	NPV	AUC	P
LVEF_1	≤54	72.73	57.35	35.6	86.7	0.678	0.007
LVEF_3	≤53	90.91	94.12	83.3	97.0	0.925	<0.0001
LVEF_7	≤55	90.91	95.59	87.0	97.0	0.923	< 0.001

PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve.

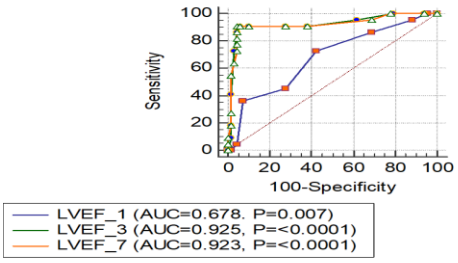

Figure 2. Roc curve of LVEF to predict mortality:

The ROC curve analysis of Ejection Fraction of left ventricle at different time points provides valuable insights into mortality prediction in critically-ill septic patients. The results show that LVEF_1 with a cutoff of ≤54 has a sensitivity of 72.73% and specificity of 57.35%, indicating a fair level of accuracy with an Area Under the Curve (AUC) of 0.678 and a significant p-value of 0.007. This suggests that lower LVEF1 is associated with high mortality, although its predictive power is moderate.

Table 5. Clinical Outcomes and Their Association with ICU Cardiomyopathy

VARIABLE		ICU CARDIOMYOPATHY		P VALUE
		No MEAN ± SD/ N(%)	Yes MEAN ± SD/ N(%)	
APACHE II SCORE		17.25 ± 4.205	28.28 ± 1.674	.000
VENTILATION TIME (HOURS)		4.5 ± 16.783	93.33 ± 32.813	.000
ICU LENGTH OF STAY (DAYS)		5.71 ± 1.872	8.94 ± 1.589	.000
HOSPITAL LENGTH OF STAY (DAYS)		10.68 ± 2.425	8.94 ± 1.589	.005
Q SOFA	2	70 (97.2%)	12 (66.7%)	0.001
	3	2 (2.8%)	6 (33.3%)	
MORTALITY	No	68 (94.4%)	0 (0.0%)	0.000
	Yes	4 (5.6%)	18 (100.0%)	

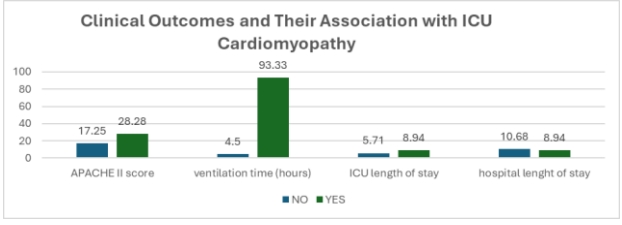

Figure 3. Clinical outcomes and their association with ICU cardiomyopathy

Clinical outcomes revealed significantly worse prognoses for patients with ICU cardiomyopathy. They had higher APACHE II scores (28.28, SD = 1.674 vs. 17.25, SD = 4.205, p = .000), longer ventilation times (93.33 hours, SD = 32.813 vs. 4.5 hours, SD = 16.783, p = .000), and longer ICU stays (8.94 days, SD = 1.589 vs. 5.71 days, SD = 1.872, p = .000). However, they had shorter overall hospital stays (8.94 days, SD = 1.589 vs. 10.68 days, SD = 2.425, p = .005). The qSOFA

score was higher in patients with ICU cardiomyopathy, with 33.3% scoring 3 compared to 2.8% of those without (p = .001). Mortality was significantly higher in patients with ICU cardiomyopathy (100% vs. 5.6%, p = .000).

4. Discussion

Sepsis remains a major global health issue, characterized by a systemic inflammatory response to infection that leads to widespread organ dysfunction.[8] Among the organs most affected by sepsis is the heart, where sepsis-induced cardiomyopathy (SICM) is commonly observed.[3]

The current study showed that the presence of diabetes and hypertension significantly increased the risk of mortality, with 90.9% of deceased patients having DM (p = .000) and 68.2% having HTN (p = .007). Smoking also showed a significant association, with 63.6% of deceased patients being smokers compared to 27.9% of survivors (p = .003). In agreement with Ke et al.[9], who revealed that individuals with both DM and HTN face significantly heightened risks for ischemic heart disease (IHD) and stroke.

The present study showed higher serum lactate levels in deceased patients (2.595 mmol/L) in comparison with survivors (2.412 mmol/L) (p = .002), suggesting greater metabolic stress, which is a well-established marker of sepsis severity and mortality. In agreement with Salottolo et al.[10] who revealed that lactate level > 2.5 was independently linked to a 2.6-fold higher risk of death in elderly trauma patients.

The current study revealed that the presence of cardiomyopathy was significantly associated with higher mortality. In agreement with Havaldar, A. A.[11 m]who revealed that After day 7, a follow-up echocardiogram revealed that the survivors'survivors' ejection fraction had improved.

Also, present study revealed that LVEF at day 3 (LVEF_3) and LVEF at day 7 (LVEF_7) were significant predictors of mortality. In agreement with Angaran et al.[12] who demonstrated that the risk of a number of outcomes, including overall mortality, cardiovascular death, hospitalizations for cardiovascular disease, and hospitalizations for heart failure, could be stratified using LVEF as a significant predictor.

The current study showed that TAPSE_3 and TAPSE_7 values were significantly reduced in deceased patients, and TAPSE was identified as a robust predictor of death in agreement with Gajanana et al.[13] who revealed that death was observed to be highly associated with TAPSE <2.4 cm, regardless of age or BNP, troponin, or APACHE disease severity scores.

The current study showed little significant change in FAC over time, with no notable associations with mortality. Like our findings, Vallabhajosyula et al.[14] found that FAC did not exhibit a consistent relationship with mortality outcomes.

According to the results of our study, the APACHE II Score is a significant predictor of death. In the same line with a retrospective analysis of 200 patients in an Iranian intensive care unit, an APACHE II score of 15 is the most accurate way to predict the mortality of critically ill patients, and a score of 17 is the best cut-off to determine whether a patient is at high or low risk of dying.[15]

The present study showed that the combined analysis of the APACHE II score and LVEF at day 3 (LVEF_3) was a powerful independent predictor (94.8%) of the variability in mortality among critically ill septic patients. The APACHE II score assesses the overall severity of illness and organ dysfunction, which has been a strong mortality predictor. [16]

Study limitations included a relatively small sample size. The study was in a single center. The study did not assess how interventions (e.g., fluid resuscitation, vasopressor use, or specific antibiotic therapies) influenced echocardiographic parameters and outcomes.

4. Conclusion

Lower LVEF values at different time points (initial, day 3, and day 7) are linked to higher mortality rates, indicating that echocardiography is a useful tool for outcomes prediction in critically ill septic patients. Echocardiography provides additional prognostic value compared to traditional clinical scores like APACHE II and qSOFA. Older patients with comorbidities like diabetes and hypertension have worse outcomes.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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