Original Research Article

Study of sepsis-induced myocardial dysfunction and its correlation with SOFA score and Creatine kinase-MB

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Abstract

Background: Incidence of Sepsis-Induced Myocardial Dysfunction (SIMD) is reported at 18% to 65%, and the mortality rate is 40% to 70%. Few studies have explored the role of Creatine kinase-MB (CK-MB) as a biomarker for SIMD. Previous studies have proved that levels of cardiac biomarkers were higher in non-survivors.**Aims and objectives:**To study the frequency and spectrum of myocardial dysfunction in patients with sepsis by transthoracic echocardiography and evaluate the association between CK-MB and Sequential Organ Failure Assessment (SOFA) score.**Materials and Methods:**One hundred patients aged>18 years satisfying the sepsis definition with SOFA score ≥2 were studied at the Department of General Medicine and Cardiology on an in-patient basis. The cohort was grouped into SOFA score <5, between 5 and 7, and > 7.Clinical evaluation, assessment of complete blood counts, liver and renal function tests, serum electrolytes, arterial blood gas analysis, and 12-lead electrocardiography was performed. All patients were also subjected to two-dimensional transthoracic echocardiography.**Results:**The majority of the patients had a SOFA score <5 (53%), 30 had a SOFA score between 5-7, and 17 had a SOFA score >7. Out of 17 patients who had SOFA score >7, all had elevated CK-MB, similarly out of 30 patients who had SOFA score between 5-7; the majority had elevated CK-MB (86.7%) (P<0.001). Out of 17 patients who had SOFA score >7, all of them had an abnormal myocardial function; out of 30 patients who had SOFA score between 5-7, the majority had abnormal myocardial function (80%) (P<0.001).**Conclusion:**SOFA score and CK-MB are vital tools for assessing myocardial dysfunction in patients suffering from sepsis. Early detection can reduce the risk of mortality.

Keywords: Sequential Organ Failure Assessment, myocardial dysfunction, electrocardiography, sepsis

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Introduction

Sepsis, as per the Sepsis-3 revised criteria, has been defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. The severity of organ dysfunction has been assessed with various scoring systems that quantify abnormalities according to clinical findings, laboratory data, or therapeutic interventions[1].The predominant score in current use is the Sequential Organ Failure Assessment (SOFA). A higher SOFA score is associated with an increased probability of mortality. For clinical considerations, organ dysfunction in sepsis is represented by an increase in the SOFA score of 2 points or more[2,3].Myocardial dysfunction is one of the manifestations of greater clinical relevance in sepsis and one of the organic dysfunctions that most early occurs in septic shock. Cardiac dysfunction is referred to as sepsis-induced myocardial dysfunction (SMD). SMD is a reversible myocardial depression caused by sepsis and characterized by left ventricular dilation, depressed ejection fraction (EF), and a recovery period of seven to 10 days[4].The incidence of SMD has been reported at 18% to 65%, and the mortality rate is 40% to 70%.[5].Numerous studies have described different types of myocardial dysfunction in sepsis. These efforts have evolved from focusing only on left ventricular (LV) systolic dysfunction to recognizing other types of myocardial dysfunction as a part of the spectrum of this organ failure, which may have different treatment options and prognostic implications. Even though different types of myocardial dysfunction have been evaluated to some extent, there is a lack of consensus on this entity's definition and clinical spectrum. Therefore, its true frequency, especially in the Indian sub-population, remains elusive. Few studies have explored the role of Creatine kinase-MB (CK-MB) as a biomarker for SMD. However, previous studies have proved that levels of cardiac biomarkers were higher among the non-survivors [5]. Interestingly, CK-MB showed the best correlation with severity of sepsis and left ventricular dysfunction on echocardiography, suggesting that CK-MB could be a valuable biomarker of septic cardiomyopathy,especially in centers where bedside echocardio-graphy is not available.

In this study, we attempt to determine the frequency of myocardial dysfunction, describe the different types, and determine the association between SOFA score and CPKMB.

Materials and Methods

A present prospective cross-sectional study was performed on 100 patients at the Department of General Medicine and Cardiology, G.R. Medical College, Gwalior (M.P.), on an in-patient basis. Individuals above the age of 18 years consenting to the study admitted to the Medicine ICU satisfying the Sepsis definitions with SOFA score equal to, or more than 2 were included.Patients with age below 18 years,history of definitive coronary artery disease, pre-existing abnormal echocardiography, pre-existing abnormal cardiac electro-physiology/cardiac arrhythmias, implanted pacemaker/ cardio verter-defibrillator,with history of cardiac intervention including such as catheterization, pericardial tap, cardiopulmonary resuscitation,

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CABG, valvular replacement, having pre-existing valvular heart disease, history of anti-arrhythmic drugs, anti-ischemic or beta-blockers and those who do not provide consent for the study were excluded. The subjects were stratified into three groups:SOFA score less than 5, between 5 and 7, and more than 7.All patients underwent detailed clinical evaluation, including history and systemic examination, anthropometric evaluation, assessment of routine biochemical parameters, including complete blood counts, liver and renal function tests, serum electrolytes, arterial blood gas analysis, and 12-lead electrocardiography. All patients were subjected to two-dimensional transthoracic echocardiography in the Department of Cardiology. All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross-tabulation were used to prepare the tables. Categorical data were expressed as a percentage. PRISM and Microsoft office were used to prepare the graphs. The Chi-Square test was used to compare the categorical data. P-value of < 0.05 is considered as significant.

Results

The majority of the patients had age ≥60 (48%), followed by 40-59 years (34%) and 20-39 years (13%). The majority of the patients were males (58%), followed by females (42%). The most common source of infection was respiratory (46%) followed by abdominal (27%) and urinary (15%). The most common co-morbidity associated with patients was hypertension (34%), followed by diabetes mellitus (28%) and COPD (19%).Majority of the patients had serum bilirubin <1.2 (50%), platelet count <150 (86%), GCS score of 15 (81%) and serum creatinine level between 2.0-3.4 (62%).

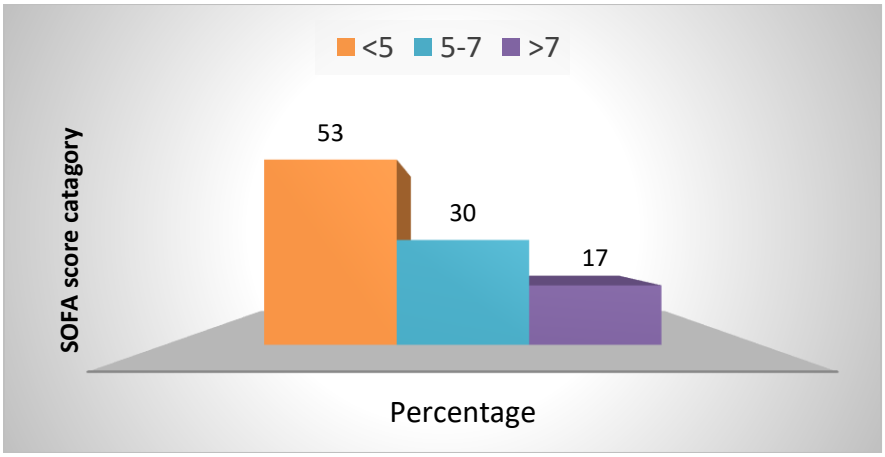

Fig 1: Distribution of patients according to SOFA score

Table 1: Comparing SOFA score with CPKMB

SOFA score	CPKMB (IU/L)		Total	P-value
	<25	>25		
<5	43 (81.1)	10 (18.9)	53 (100)	<0.001
5-7	4 (13.3)	26 (86.7)	30 (100)	
>7	0 (0)	17 (100)	17 (100	
Total	47 (47)	53 (53)	100 (100)	

SOFA; Sequential Organ Failure Assessment, CPKMB; Creatine kinase-MB, Data are expressed as a number of patients (percentage), Chi-Square test was applied. A P-value of <0.05 is considered significant.

Table 2: Comparing SOFA score with myocardial function

SOFA score	Myocardial function		Total	P-value
	Abnormal	Normal		
<5	21 (39.6)	32 (60.4)	53 (100)	<0.001
5-7	24 (80)	6 (20)	30 (100)	
>7	17 (100)	0 (0)	17 (100)	
Total	62 (62)	38 (38)	100 (100)	

SOFA: Sequential Organ Failure Assessment, Data is expressed as a number of patients (percentage), Chi-Square test was applied. A P-value of <0.05 is considered significant.

The majority of the patients with SOFA score >7 had severe LV systolic dysfunction (35.3%) followed by moderate LV systolic dysfunction (47.0%); of the patients with SOFA score between 5-7, the majority of them had mild LV systolic dysfunction (50%) followed by moderate LV systolic dysfunction (26.7%). The distribution between SOFA and the LV systolic dysfunction was highly significant, as revealed by the highly significant value of <0.001.

Discussion

Sepsis is characterized by life-threatening organ dysfunction with dysregulated immune responses. Cardiac dysfunction seen in sepsis is unique as it is reversible within 7–10 days. An initial study by Parker et al. in 1984 showed a paradoxically lower ejection fraction in survivors of septic shock[6].The majority were ≥60 years of age with male preponderance. In line with that, Narváez et al. reported that the mean patient age was 62.1±16.3 years, and 57.9% were males[7].Several previous studies are in agreement with the present study findings where the majority of the patients with sepsis had old age[8,9].The most common source of infection was respiratory (46%), abdominal (27%), and urinary (15%). In agreement with this, Lina De Geer et al. reported that the mostcommon source of sepsis was pulmonary (34%), gastrointestinal (22%), and genitourinary in

(22%), and seven patients (14%) were neutropenic,with hematology-ical malignancies[10].Narváez et al. found that the primary infection site corresponded to the urological tract, which is in line with the present study findings[7].Acute, profound circulatory collapse resulting in multi-organ failure is the hallmark of septic shock. During septic shock, vasodilatory effects of bacterial endotoxin and endogenous vasopressin deficiency alter the systemic vascular resistance resulting in misdistribution of blood flow and inadequate oxygen delivery[11].As per Sepsis 3 criteria, the diagnosis of sepsis is made by an acute increase in organ dysfunction as assessed by the SOFAscore by 2 or more points consequent to the infection[1].A variety of cardiac biomarkers are available, including isoenzymes of lactate dehydrogenase (LDH) and cardiac muscle-specific creatine kinase (CK - MB) isozyme, cardiac troponins, natriuretic peptides (atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and C-type natriuretic peptide), endothelins, and cardiotrophins[12].In the present study, we used CPKMB as the biomarker and compared it with the SOFA score. Troponin is a Cardiac biomarker that has been extensively studied. It may be elevated in 36 to 86% of patients with sepsis and is associated with increased mortality[13].In the present study, on comparing SOFA score with the CPKMB, it was found that out of 17 patients who had SOFA score >7, all had elevated CPKMB, similarly out of 30 patients who had SOFA score between 5-7, the majority had elevated CPKMB (86.7%). This shows that elevated CPKMB levels are one of the risk factors for increasing SOFA score, as revealed by the highly significant p-value of <0.001. A similar series by Eldeen et al. studying the predictive value of Cardiac troponins(cTn) on mortality and adverse complications in patients with sepsis and septic shock and to explore the relation of cTn with CU scoring systems reported that patients with elevated cTn were more critically ill as reflected by higher APACHE scores at study entry and SOFA score on admission and 2nd day:APACHE was (34.6±10.9vs.17.8±5.4,p-value=0.001),SOFA on admission (14.9 ±4.2vs.6.9±4.5, p-value=0.0001) and SOFA at 2nd day (15.8±5.4vs. 5.5±4.4, p-value=0.0001)[14].Myocardial dysfunction is a common morbid consequence of severe sepsis and septic shock that has become increasingly recognized over the past 3 decades. Sepsis-induced cardiac dysfunction is characterized by impairment in contractility,diastolic dysfunction(DD),or both. Diastolic dysfunction is equally prevalent in the presence of sepsis, occurring in approximately 40% of the patients[15].However, this number may vary according to the criteria used to evaluate the diastolic function. This has been observed in a study conducted by Clancy et al., in which 60% of the patients assessed on the first day of an episode of severe sepsis or septic shock presented diastolic dysfunction, and 23% presented indeterminate diastolic function according to the guidelines published in 2016 by the American Society of Echocardiography along with the European Association of Cardiovascular imaging, while 21% and 74% had diastolic dysfunction or indeterminate diastolic function, respectively, according to the 2009 guidelines of the American Society of Echocardiography[16].Whereas Landesberg et al. found 6-fold higher mortality in septic patients with DD, Pulido and colleagues found no association between DD and mortality in sepsis[17].In a recent meta-analysis of 7 observational studies involving 636 patients with sepsis and septic shock, it was found that DD was standard (20%-57%) and was associated with increased mortality [18].In a group of patients with sepsis and preserved LVEF, Dalla et al. demonstrate that the prevalence of depressed longitudinal LV function is as common as 50%, compared to 8.7% in critically ill patients without septic shock[19].Our relatively large study finds that LV systolic dysfunction is prognostically relevant in the short term, mainly when LV systolic function is assessed by GLS, even when the SOFA score is accounted for. In a previous study from our institution in relatively unselected patients from the same population source, we find that LVEF predicts prognosis in the short term[20].In the present study, the majority of the patients with SOFA score >7, majority of them had severe LV diastolic dysfunction(47.1%) followed by moderate LV diastolic dysfunction (29.4%). Out of 30 patients with SOFA scores between 5-7, 26.7% had moderate LV diastolic dysfunction, followed by 16.7 patients with mild LV diastolic dysfunction. The distribution between LV diastolic dysfunction and the SOFA score was highly significant, as revealed by the highly significant p-value of <0.001. The most probable reason for cardiac dysfunction is myocardial edema due to inflammation-induced vascular leakage might also influence cardiac compliance and function. In addition, ventricular function is affected by changes in afterload. Pulmonary hypertension will worsen right-heart function, whereas right-heart dilation will impair left-heart function. Endothelial cells producing vasoactive molecules that regulate peripheral vascular resistance are impaired during septic shock, and thus, endothelial dysfunction plays a crucial role in its pathophysiology. This is because impaired endothelium-derived NO release could alter the physiological regulation of blood flow distribution via coronary vasospasm combined with increased peripheral vascular resistance and the associated elevation of cardiac workload and myocardial oxygen demand[21].

Conclusion

We found a higher prevalence of sepsis among the male population of the older age group. The most common source of infection was respiratory, abdominal, and urinary. LV dysfunction followed by LV systolic dysfunction and LV diastolic dysfunction was the most common among patients with abnormal SOFA scores. The SOFA score and CPKMB are important tools for assessing myocardial dysfunction in patients suffering from sepsis. Early detection can reduce the risk of mortality. The LV function to be assessed early in sepsis if the patient is not improving for which serial echo and serial biomarkers should be done as a prognostic and diagnostic tool.Further study is needed on a large number of patients in a developing country, so that early detection of severe sepsis can be done.

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