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Original Article

Internal Medicine Section

Prognosis of Left Ventricular Systolic Dysfunction in Septic Shock Patients

M.MUKHYAPRANA PRABHU[1], SURESH KUMAR YALAKALA[2], RANJAN SHETTY[3], ASHOK THAKKAR[4], TULSEE SITAPARA[5]

ABSTRACT

Introduction: The prognosis of myocardial dysfunction in critically ill patients with sepsis and its association with mortality is controversial. We aim to determine the significance of left ventricular systolic dysfunction in septic shock patients and their associated outcome.

Materials and Methods: A prospective, single center, observational study was carried out at an intensive care unit of a tertiary care hospital. A total of 66 patients diagnosed with septic shock were enrolled in the study from September 2010 to June 2012. The 2D echocardiography was performed for all the patients. Ejection fraction < 50% was the diagnosing parameter for the patients with systolic dysfunction in septic shock. Acute Physiology and Chronic Health Evaluation III (APACHE III) score was calculated.

Results: The mean age of patients were found to be 53.71 ± 16.76 years. The mortality rate was found to be 48.48% and among them 43.75% patients had ejection fraction < 50%. Non-survivors exhibited significantly lower mean blood pressure (74.19 ± 10.28 versus 80.59 ± 11.31; p = 0.008), lower ejection fraction (52.59 ± 16.37 versus 62.56 ± 8.31; p = 0.029) and higher APACHE III score (89.34 ± 15.41 versus 70.65 ± 13.27; p < 0.001). The receiver operating characteristic curves APACHE III score (area under curve = 0.830) and ejection fraction (area under curve = 0.656) were used to predict the mortality in septic patients.

Conclusion: Low ejection fraction, a marker to measure left ventricular systolic dysfunction is a predictor of mortality in septic shock patients. However, more research is needed to confirm the findings.

Keywords: Echocardiography, Ejection fraction, Mortality

INTRODUCTION

Sepsis is a serious medical condition affecting millions of patients each year. The average documented incidence of sepsis worldwide is 56-91 cases per 1,00,000 people, with a reported mortality rate of 30% [1]. Myocardial dysfunction is a common feature of sepsis. Cardiac dysfunction in septic shock is a crucial component of multiple organ dysfunction [2] and is an important cause of fatality [3,4]. Dysfunction of left ventricle (LV) associated with sepsis has been reported decades ago [2], but was not absolutely recognised until the widespread use of echocardiography in intensive care unit (ICU) [5,6]. The mechanism is still unclear and is probably multifactorial [7].

The pathophysiology and various types of myocardial dysfunction are well documented in literature. Numerous echocardiographic parameters have been developed to assess the LV function in sepsis [8]. Among these parameters, ejection fraction (EF) is most commonly used to evaluate LV systolic function [4,9].

In spite of larger data, the presence of LV systolic dysfunction and its relation with the outcome is still conflicting especially in septic shock patients [5,10]. The correlation between low ejection fraction and mortality is not clear [2,10,11]. The aim was to evaluate the significance of LV systolic dysfunction in the patients with septic shock and its association with the mortality in these patients.

MATERIALS AND METHODS

Study Design and Patient Population

A prospective, single centre, observational study was carried out at Kasturba Medical College & Hospital, Manipal, India, from September 2010 to June 2012. A total of 66 patients with septic shock were enrolled in the study after complying with inclusion and exclusion criteria. The enrollment procedure of patients is shown in [Table/Fig-1]. Informed consent was obtained and the study was approved by the Institutional Ethics Committee. (177/2010 meeting held on 14th December 2010).

The patients have been diagnosed with septic shock as per the guidelines of ACCP/SCCM Consensus Conference Committee [12]. The inclusion criteria included organ dysfunction and acute circulatory failure characterized by (a) persistent arterial hypotension (defined as a systolic arterial blood pressure <90 mm Hg or reduction from baseline by >40 mm Hg), despite adequate volume resuscitation (septic shock) (b) presence of infection, documented or strongly suspected, with a systemic inflammatory response, together with two or more of the following:

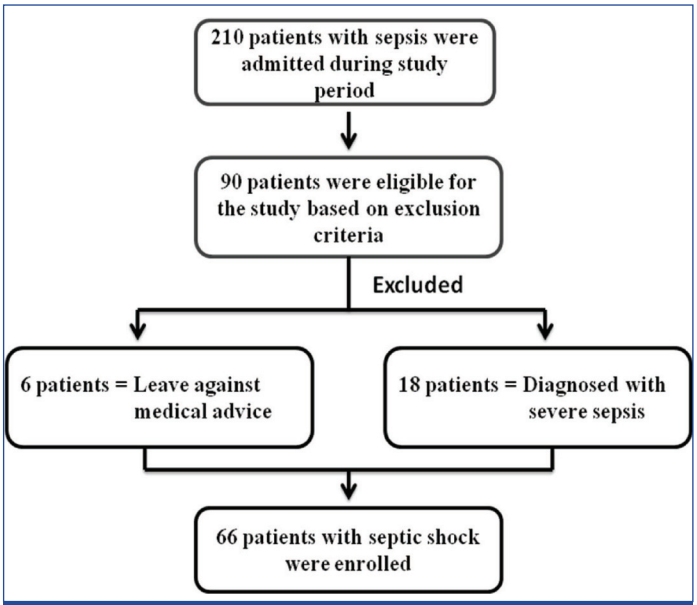
- Temperature > 38°C or < 36°C
- Heart Rate > 90 bpm
- Respiratory Rate 30/min with $PaCO_2$ < 32
- Total leukocyte count > 12 x 109 /L or < 4x 109 /L or > 10% staff cells

Exclusion criteria included patients with age lesser than 18 years, pregnancy, patients who documented with valvular heart disease, known ischemic heart disease, dilated cardiomyopathy, hypertension, myocarditis, connective tissue diseases, abuse of drugs such as alcohol and cocaine, arrhythmias, diabetes mellitus, hypothyroidism or hyperthyroidism.

Baseline clinical variables were collected including age, gender, co-morbidities, hemodynamic parameters, requirement and dose of inotropes and Acute Physiology and Chronic Health Evaluation (APACHE) III score.

Echocardiography

All patients underwent 12 lead electrocardiogram and 2D echocardiography using Vivid e portable echo machine from GE healthcare using 2.5 MHz transducer and Doppler echocardiography including Tissue Doppler Imaging. Left lateral position was used to analyse the patients. Assessments were made using parasternal long axis, short axis, apical four chamber and two chamber images according to the American Echocardiography Association Criteria. The modified Simpson's method was used to measure the LV



[Table/Fig-1]: Enrollment procedure of study patients

Variables	Septic Shock
Demographic Parameters	
Age (years)	53.71 ± 16.76
Male, n (%)	34 (51.5%)
Length of hospital stay	9.76 ± 4.21
Length of ICU stay	6.09 ± 3.45
APACHE III Score	79.71 ± 17.07
Laboratory Parameters	
Serum creatinine (mg/dL)	1.66 ± 1.18
pH	7.13 ± 0.75
Hemodynamic parameters	
Mean blood pressure (mm Hg)	77.48 ± 11.21
Noradrenaline, n (%)	27 (30.3%)
Dopamine, n (%)	13 (19.7%)
Noradrenaline + Dopamine, n (%)	20 (30.3%)
No medication, n (%)	6 (9.1%)
Echocardiographic Parameters	
Ejection Fraction	57.73 ± 13.72
Cardiac Index	4.17 ± 0.90

[Table/Fig-2]: Baseline characteristics of patients with septic shock

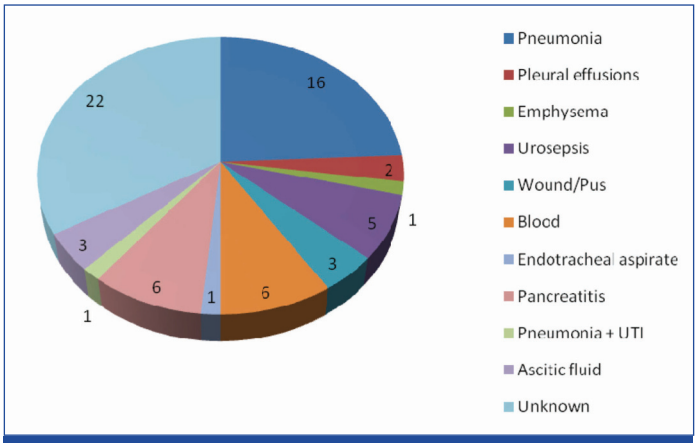
ejection fraction (EF). Left ventricular (LV) systolic dysfunction was defined as LVEF with <50% [13-15]. Cardiac index for assessing systolic dysfunction was calculated by dividing the cardiac output to the body surface area of patients.

STATISTICAL ANALYSIS

All data were analysed using SPSS version 16.0. Categorical data are presented as number of patients (percentage). Descriptive statistical analysis is performed for continuous variables. For comparison between groups, either student's unpaired t-test or Mann-Whitney U test are used for the continuous variables according to the Gaussian distribution. The chi-square test was used to assess differences in categorical variables. All statistical tests were carried out at 5% level of significance. Receiver operating characteristic curve (ROC) analysis was performed to predict the association of APACHE score and ejection fraction with mortality.

RESULTS

The mean age of patients was found to be 53.71 ± 16.76 years and 34 (51.5%) patients were male. Mean blood pressure (MBP) was observed as 77.48 ± 11.21 mmHg. Baseline characteristics of the patients with septic shock are shown in [Table/Fig-2].



[Table/Fig-3]: Sources of infection in septic shock patients

Types of micro-organism	Number of patients (Percentage)
E.coli	7 (10.6)
Klebsiella	5 (7.5)
Leptospirosis	4 (6.06)
Pseudomonas	9 (13.6)
Pseudomonas + Klebsiella	1 (1.5)
Staphylococcus aureus	3 (1)
Streptococcus	1 (1.5)
Acinetobacter	6 (9.09)
Polymicrobial	0 (0.00)
Candida	2 (3.03)
Enterococcus	2 (3.03)
Klebsiella + E coli	1 (1.5)
Rikettsial	1 (1.5)
Not Known	24 (36.36)

[Table/Fig-4]: Types of microbes involved in septic shock patients

The source of infection was not known in most of the patients (42.8%). Among the known source, the most common source of infection was pneumonia (24.2%). The other sources of infection in various patients are depicted in [Table/Fig-3]. The micro-organism associated with septic shock patients was not known in majority of patients (36.36%). Different types of microbial culture observed in septic shock patients are presented in [Table/Fig-4].

A total of 18 (27.27%) patients reported LV systolic dysfunction on the first day of admission. The mortality rate of septic shock patients was found to be 48.48%. The comparisons among the survivor and non survivor patients with sepsis are depicted in [Table/Fig-5]. Among the inotropes used for maintaining the blood pressure in patients, 44.1% of the survivors were resuscitate with noradrenaline and combination of noradrenaline and dopamine (59.4%) being the most often used in non surviving septic shock patients.

Among the indices of systolic dysfunction, MBP, APACHE III score and ejection fraction showed significant difference among the survivors and non survivors. It is clear from the table that mortality was linked to lower MBP. Fourteen patients among the non-survivors had ejection fraction < 50%.

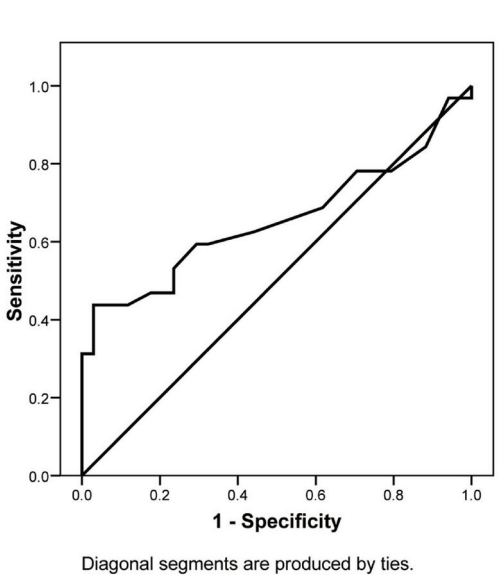
The ability of ejection fraction and APACHE III score to predict the mortality according to ROC curve is shown in [Table/Fig-6,7] respectively. The area under curve for ejection fraction was observed to be 0.656 and that of APACHE III score was found to be 0.830.

DISCUSSION

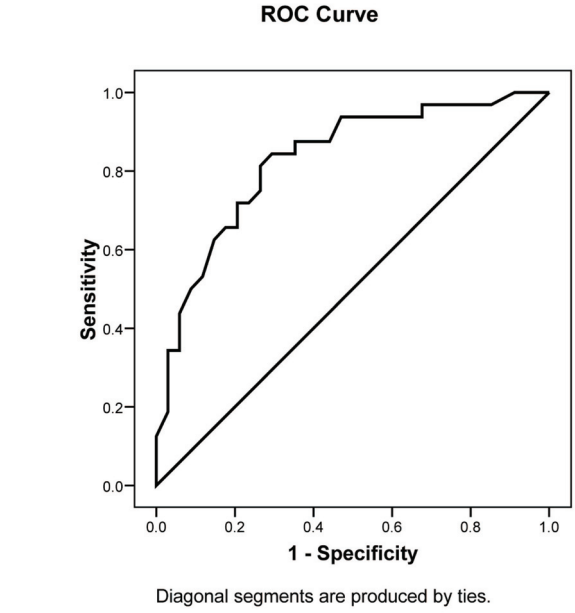
Sepsis is the major cause of death among critically ill patients and accounts for more than 215,000 deaths per year in the United States alone [16,17]. The incidence and frequency of sepsis is continuously growing due to the factors like aging population, more number of

Variables	Survivors (n =34)	Non Survivors (n=32)	p-value
Demographic Parameters			
Age (years)	50.35 ± 17.11	57.28 ± 15.87	0.093
Male, n (%)	21 (61.8%)	13 (38.2%)	0.139
APACHE III Score	70.65 ± 13.27	89.34 ± 15.41	<0.001
Laboratory Parameters			
Serum creatinine (mg/dL)	1.70 ± 1.25	1.62 ± 1.11	1.00
pH	7.07 ± 1.04	7.20 ± 0.08	0.121
Hemodynamic parameters			
Mean blood pressure (mm Hg)	80.59 ± 11.31	74.19 ± 10.28	0.008
Noradrenaline, n (%)	15 (44.1%)	5 (15.6%)	0.006
Dopamine, n (%)	6 (17.6%)	7 (21.9%)	
Noradrenaline + Dopamine, n (%)	8 (23.5%)	19 (59.4%)	
No medication, n (%)	5 (14.7%)	1 (3.1%)	
Echocardiographic Parameters			
Ejection fraction	62.56 ± 8.31	52.59 ± 16.37	0.029
Ejection fraction <50%, n (%)	4 (11.76%)	14 (43.75%)	0.005
Cardiac index	4.03 ± 0.77	4.32 ± 1.01	0.311

[Table/Fig-5]: Comparative analysis between survivors and non survivors in septic shock patients



[Table/Fig-6]: Receiver-operating characteristic curve for predicting mortality by using ejection fraction. Area under curve is 0.656



[Table/Fig-7]: Receiver-operating characteristic curve for predicting mortality by using APACHE III score. Area under curve is 0.830

patients with compromised immune systems, and the increased number of patients who had undergone prolonged, high risk surgery [18]. The progression of sepsis often occurs when the host cannot contain the primary infection, a problem frequently related to the characteristics of the micro-organism, the large burden of infection, persistent presence of super-antigens and other virulence factors, resistance of phagocytosis and opsonization often associated with antibiotic resistance [19]. Abnormalities in cardiac function is common in sepsis.

In this study, the mean age of patients with septic shock was found to be 53.71 ± 16.76 years which was comparatively less than the studies reported by David et al., [9]. However, the APACHE III score in septic shock patients (79.71 ± 17.07) was observed to be similar with the other reported study [9].

A prospective study conducted over 106 patients by Pulido et al., demonstrated that lower mean atrial pressure (MAP) in non-survivors is associated with mortality, although they do not show significant difference among survivors and non-survivors. The significant difference in MBP was reported in our study [7]. The risk of subsequent renal replacement therapy increases as there is increase in the time spent below the MAP of 75 mm Hg which was reported by Dunser et al., [20]. Such findings suggest the importance of addressing ischemic acute renal failure in the absence of frank hypotension [21]. This correlates that vasoactive substance plays an important role in septic patients.

In our study, LVEF was depressed in 18 (27.27%) septic shock patients. A cohort study on the ICU patients by Landsberg et al., reported 9.1% isolated systolic dysfunction [4]. Studies using echocardiography reported a 20-60% incidence of reduced EF in septic shock which was reversible in patients who survive [22-24].

In a landmark study by Parker and colleagues, 50% of the septic shock patients exhibited ventricular dilatation and hypokinesia during the first 48 h after admission [2]. Furthermore, compromised LVEF (43.9% ± 18% versus 55% ± 15%) was observed in survivors during the first 24 h [11]. In other similar studies [25], evidence of septic myocardial dysfunction in survivors was shown by depressed LVEF, although the difference in LVEF between survivors and non-survivors is not significant [4,13]. These results are contrary to our results. In the present study, survivors had better LVEF than non survivors signifying that the low EF is a measure of mortality in these patients. However, a study on 57 septic patients demonstrated by Breukmann et al., found that LVEF is a tool for determining systolic dysfunction [14].

In our study, APACHE III score showed significantly higher values in non-survivors. Amongst the ROC curves of APACHE III score and ejection fraction for predicting the mortality, APACHE III score is considered as a better predictor (AUC= 0.830) of mortality in critically ill patients than ejection fraction (AUC=0.656). Subsequently, other studies had reported the good association of APACHE III score and mortality in intensive care unit patients [26,27].

CONCLUSION

In a nutshell, left ventricular systolic dysfunction was observed in our study with an association of mortality in septic shock patients. Decreased ejection fraction may be considered as sole criteria for diagnosing systolic dysfunction and predicting mortality. However, further studies are still needed to provide clear and confirmatory diagnosis.

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PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Medicine, Kasturba Medical College and Hospital, Manipal, Karnataka, India.
2. Junior Resident, Department of Medicine, Kasturba Medical College & Hospital, Manipal, Karnataka India.
3. Professor, Department of Cardiology, Kasturba Medical College & Hospital, Manipal, Karnataka India.
4. Senior Manager - Clinical Research & Medical Writing, Department of Clinical Trials, Sahajanand Medical Technologies Pvt. Ltd., Surat, Gujarat, India.
5. Trainee Medical Writer, Department of Clinical Trials, Sahajanand Medical Technologies Pvt. Ltd., Surat, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ranjan Shetty,
Professor, Department of Cardiology, Kasturba Medical College & Hospital, Manipal-576104, Karnataka, India.
E-mail : ranjanshettyk@yahoo.com

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