N-terminal pro-brain natriuretic peptide is an independent predictor of mortality in patients with sepsis

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ABSTRACT

This study aims to evaluate the role of cardiac enzymes N-terminal pro-brain natriuretic peptide (NT-proBNP) and cardiac troponin-I (CTnI) as predictors of outcomes in patients with sepsis.

78 cases with a diagnosis of sepsis were enrolled over a 2-year period. Baseline demographic, Acute Physiology and Chronic Health Evaluation-II (APACHE-II), Simplified Acute Physiology Score-II (SAPS-II), hematologic and biochemical parameters were noted. Serum NT-proBNP and CTnI were evaluated at 24 and 72 hours of admission along with echocardiography. Patients were prospectively followed up until death or discharge.

Mean APACHE-II score was 19.8±9.6 and SAPS-II was 44.8±17.2. Survival rate in the study was 47.5% (36 of 78 patients). NT-proBNP was significantly higher in non-survivors with values over 4300 pg/mL at 24 hours and 5229 pg/mL at 72 hours associated with poor outcomes ($p<0.05$). CTnI was higher among non-survivors than in survivors, but the difference was not significant. APACHE-II score combined with NT-proBNP predicted a poor outcome in 51.2% cases compared with 14.6% cases with APACHE-II alone ($p<0.05$), while SAPS-II combined with NT-proBNP predicted a poor outcome in 53.6% cases as compared with 9.6% cases with SAPS-II alone ($p<0.05$). SAPS-II greater than 45 and NT-proBNP values at 72 hours were independent predictors of mortality in patients with sepsis.

NT-proBNP is an independent predictor of mortality in patients with sepsis and its combination with APACHE-II and SAPS-II improves the predictive values of the scoring systems.

Significance of this study

What is already known about this subject?

- Sepsis is a state of host immune dysfunction in response to infection.
- Cardiac dysfunction is a prominent organ failure in sepsis.
- Multiple scoring systems exist for identifying prognosis but fare poorly in predicting outcomes in such patients.

What are the new findings?

- N-terminal pro-brain natriuretic peptide (NT-proBNP) is an independent predictor of mortality in patients with sepsis.
- Serial measurements at 24 and 72 hours post-admission are useful in predicting outcome in such patients.
- Cardiac troponin-I is useful as a marker of in-hospital mortality but serial measurements have no prognostic value.
- Both cardiac biomarkers are more sensitive in identifying cardiac dysfunction in sepsis as compared with echocardiogram.
- Both biomarkers enhance predictive ability of Acute Physiology and Chronic Health Evaluation and Simplified Acute Physiology Score-II scoring systems in predicting outcome.

How might these results change the focus of research or clinical practice?

- Use of NT-proBNP as a prognostic tool in sepsis.
- Development of scoring systems based on NT-proBNP or incorporation of NT-proBNP into currently used severity of illness scores and prospective validation of the same.

INTRODUCTION

Sepsis is a condition of life-threatening organ dysfunction caused by dysregulated host response to infection.[1] It affects 20 million individuals globally every year and current management guidelines focus on adequate resuscitation and organ support combined with eradication of the underlying infection through appropriate antibiotics and source control.[2]

Cardiac involvement is the second most common organ involvement in sepsis after pulmonary (46%).[3] An intensive care unit (ICU)-based study in Europe revealed that 75%–80% patients with sepsis have at least two organ failures, most commonly respiratory failure (50%–75%) and cardiac failure or shock (50%–63%) requiring life support.[4] Cardiac dysfunction in sepsis includes distributive shock, myocardial dysfunction and dysrhythmias. Currently used

severity of illness (SOI) scores such as Acute Physiology and Chronic Health Evaluation-II (APACHE-II), Simplified Acute Physiology Score-II (SAPS-II) and Sequential Organ Failure Assessment (SOFA) score rely on distributive shock as an assessment of cardiac dysfunction.

N-terminal pro-brain natriuretic peptide (NT-proBNP) is a 76 amino acid prohormone, which in its active form, promotes natriuresis to relieve stress on the ventricular wall.[5] Cardiac troponin-I (CTnI) is an essential component of the myocardial apparatus and assists in cardiac contraction.[6] Both biomarkers have been studied in sepsis as early markers of cardiac dysfunction and studies have reported higher levels of NT-proBNP in non-survivors as compared with survivors with CTnI being a predictive biomarker for mortality in sepsis which is not an independent risk factor for poor outcomes.[7 8]

There are limited data available on the role of serial NT-proBNP and CTnI measurements and the impact of combining the biomarkers with conventional SOI scores in predicting outcomes in patients with sepsis.

METHODOLOGY

We conducted a single-center, prospective observational study over 2 years (October 2017–October 2019) at the All India Institute of Medical Sciences, New Delhi, a tertiary care referral center in North India. All patients admitted in the Department of Medicine with a diagnosis of new onset (within 24 hours) sepsis with or without septic shock were reviewed for inclusion. For the purpose of this study, sepsis was defined clinically as an identified source of infection with a rise in SOFA score by ≥2 points above baseline. Septic shock was defined as a state with vasopressor requirement to maintain a mean arterial pressure ≥65 mm Hg and a serum lactate ≥2 mmol/L, as outlined by the Sepsis-3 criteria.[1] Inclusion criteria included patients greater than 18 years of age who consented to participate in the study. Patients who had undergone trauma and any surgical intervention, and had received care at other hospitals for ≥24 hours prior to admission were excluded. Any patient with coexistent illnesses known to cause elevated levels of our studied biomarkers—acute coronary syndrome, cor pulmonale, chronic renal insufficiency, pre-existing heart failure, post-cardiopulmonary resuscitation, known arrhythmia—was excluded at baseline (figure 1).

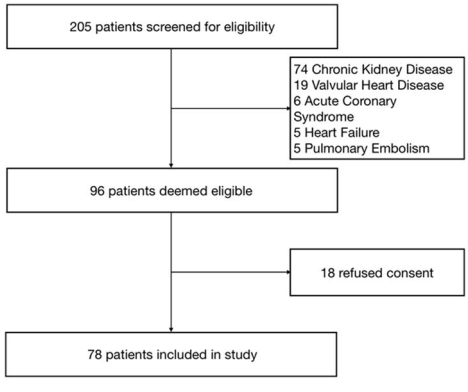

Figure 1 Flow diagram depicting the screening, exclusion and recruitment.

The patients' demographic records, coexisting comorbid conditions and vital parameters were recorded at baseline, along with requirement for life support in the form of mechanical ventilation, inotropic use and need for hemodialysis. Hemogram, liver and renal function tests were sent at baseline and subsequently based on the patient's clinical status. Samples for blood and urine culture were taken from all patients on the day of admission preferably prior to the initiation of antibiotics and processed per standard protocol. Other samples for culture (eg, sputum, cerebrospinal fluid, wound swab, endotracheal aspirate) were obtained using a case-based approach, as per the decision of the treating physician. Values of NT-proBNP (assay: VIDAS NT-proBNP2 analyzer based on ELISA; manufactured by: ThermoFisher Scientific; license partner: bioMérieux; New Delhi, India) and CTnI (assay: VIDAS high sensitivity troponin-I analyzer based on ELISA; manufactured by: ThermoFisher Scientific; license partner: bioMérieux; New Delhi, India) were assessed at 24 hours and 72 hours of admission.

A detailed echocardiographic examination (ultrasound system: Phillips EPIQ CVx Cardiac Ultrasound System) was performed within 24 hours of admission and repeated at 72 hours. Simultaneously, each patient underwent serial clinical status assessment, disease severity assessment (employing three severity scoring systems: with the APACHE-II and the SAPS-II assessed within 24 hours of admission and the SOFA score assessed serially at baseline and 72 hours).

The data thus obtained were analyzed using Stata V.14 software (StataCorp 2011, College Station, Texas, USA). The key outcome measures assessed included mortality and duration of hospital or ICU stay. To compare the baseline demographic, clinical characteristics and biochemical parameters between the two groups of patients, X^2 tests were used for categorical variables and Student's t-tests were used for continuous variables with normal distribution. For all statistical tests, a p value of <0.05 was considered to be statistically significant. For the purpose of multivariate analysis, a generalized linear model (glmnet) was constructed using all at-admission parameters found significant on univariate analysis, using fivefold cross-validation for each outcome (severity and mortality). Using area under receiver operating characteristic (ROC) curve as a marker of predictive accuracy, the model with best performance characteristics (alpha and lambda) was chosen. The variables with the highest beta parameter were then sequentially added in a multivariate logistic regression model to identify the best combination of predictive variables for each outcome. Similar methodology was followed for both severity and mortality.

RESULTS

Over the study period, 205 patients with an admitting diagnosis of sepsis with or without septic shock were screened. Seventy-eight patients satisfied criteria for inclusion and were subsequently enrolled in our study (figure 1). Of the recruited patients, 41 (52.56%) succumbed to their illness and the remaining 37 (47.44%) were discharged following recovery. The recruited patients had a mean age of 45.4±17.4 years with the maximum number of patients (20 (26%)) belonging to the age group of 55–65 years. Of

78 subjects enrolled, 41 subjects were male (53%) and 37 subjects were female (47%). There was no significant age or gender-based predilection toward severe disease or poor outcome in the subjects.

Diabetes mellitus and hypertension were the most commonly encountered comorbid illnesses accounting for 21 (27%) cases each. Others included autoimmune diseases (5 patients), malignant neoplastic disorders (2 patients), thyroid illness (2 patients), chronic liver disease (5 patients) and obesity (3 patients). While the number of subjects was too small to draw definitive conclusions about differences in patient outcome, it was noted that patients with malignant disorders and those with chronic liver disease had higher severity of illness scores at baseline, all seven of these patients eventually succumbing to their illness.

Laboratory parameters including complete blood counts, renal and liver function testing and arterial blood gas analysis were assessed for all patients at baseline. Comparing the values obtained in survivors and non-survivors, it was observed that patients who succumbed to their disease had significantly higher total leukocyte counts and lactate levels, with poorer arterial oxygen tension/fractional inspired oxygen ratio, lower platelet counts, lower Glasgow Coma Score and lower urine output in the first 24 hours after admission. Importantly, renal and hepatic function assessment at baseline did not differ significantly among survivors and non-survivors. Lower respiratory tract infections (33 patients (42%)) and intra-abdominal infections (23 patients (29%)) accounted for the majority of studied cases. The remaining cases were related to skin and soft tissue infections (12 patients (15.4%)) while no source of sepsis could be identified in 10 cases. The baseline demographic, clinical and laboratory data have been summarized in table 1.

APACHE-II, SAPS and SOFA scores were calculated for all patients at the time of baseline assessment. Each of the three scores was significantly higher in non-survivors as compared with survivors (table 2). Obtained scores were employed in a predictive ROC analysis for the measure of adverse patient outcome (mortality) in our cohort. All three scores had high and comparable predictive accuracy (table 2, figure 2).

As described previously, levels of cardiac enzymes were assessed at baseline (within 24 hours of admission) and at 72 hours after admission. At baseline, values of NT-proBNP were significantly higher in non-survivors (5811 pg/mL) as compared with survivors (3230 pg/mL) (p=0.002). The trend continued to be observed at 72 hours following admission with higher values of NT-proBNP in non-survivors (8448.5 pg/mL) than survivors (2377 pg/mL) (p<0.001). There was no statistically significant difference in the admission values of CTnI among survivors and non-survivors. At 72 hours of hospitalization, values of CTnI were higher in non-survivors (69.37±6.26 ng/mL) than survivors (50.08±9.77 pg/mL) (p=0.045). This level of significance was considered weak in view of multiple outlier values and hence was not used further to construct ROC curves for establishment of cut-off values. Predictive ROC analysis was performed to define patient outcomes with levels of baseline and day 3 NT-proBNP levels. It was found that values of NT-proBNP greater than 4300 pg/mL at baseline were associated with a poor outcome (area under the curve (AUC): 0.6928, sensitivity: 65.85%, specificity: 64.86%, PPV (Positive Predictive Value): 69.2%, NPV (Negative Predictive Value): 64.1%). At 72 hours, it was seen that values greater than 5229 pg/mL were associated with poor outcome (sensitivity: 85.29% specificity: 83.78%, AUC: 0.8486, PPV: 82.9%, NPV:

Table 1 Baseline demographic, clinical and laboratory parameters of enrolled patients

Variable	All patients (N=78)	Survivors (N=41)	Non-survivors (N=37)	P value
Comorbid illnesses (no (%))				
Hypertension	21 (26.9)	12 (29.2)	9 (24.3)	0.62
Diabetes mellitus	21 (26.9)	13 (31.7)	8 (21.6)	0.32
Chronic liver disease	5 (6.4)	0	5 (13.5)	**0.05**
Obesity	3 (3.8)	2 (4.8)	1 (2.7)	1
Autoimmune disease	5 (6.4)	1 (2.4)	4 (10.8)	0.18
Hypothyrodism	2 (2.6)	2 (4.9)	0	0.49
Malignancy	2 (2.6)	0	2 (5.4)	0.22
Laboratory parameters				
Hemoglobin (g/L) (mean±SD)		112±25	100±24	0.20
Total leukocyte count (10^9/L) (median (IQR))		15.49 (8.90)	17.0 (14.30)	**0.06**
Platelet count (10^9/L) (median (IQR))		200,000 (231,000)	1 46,000 (177,000)	**0.01**
Blood urea (mg/dL) (median (IQR))		41 (64)	79 (89)	0.07
Serum creatinine (mg/dL) (median (IQR))		1.1 (1.1)	1.4 (2.7)	0.06
Serum bilirubin (mg/dL) (median (IQR))		0.9 (1.5)	1.2 (1.4)	0.77
pH (mean±SD)		7.30±0.07	7.27±0.10	0.07
PaO_2/FiO_2 (mean±SD)		290±86.9	231.9±98.5	**0.007**
Lactate (mmol/L) (median (IQR))		1.8 (0.7)	2.18 (2.64)	**0.01**
Urine output (L/24 hours) (median (IQR))		1200 (1000)	800 (750)	**0.001**
GCS (mean±SD)		11.75±3.3	9.3±3.9	**0.002**

Values in bold are considered statistically significant (p<0.05).
GCS, Glasgow Coma Score; PaO_2/FiO_2, arterial oxygen tension/fractional inspired oxygen.

Table 2 Severity of Illness indices: impact on patient outcome

Scoring system		Score (mean±SD)			P value	Predictive accuracy (ROC analysis)			
		All patients (N=78)	Survivors (N=41)	Non- survivors (N=37)		Area under the curve	Optimum cut-off value	Sensitivity	Specificity
APACHE-II	Score	19.8±9.6	17.24±6.08	22.29±7.19	**0.001**	0.714	20	70.73	67.57
	Predicted mortality		30%±17%	45%±22%					
SOFA	Score	7.2±3.8	5.62±2.96	8.7±3.9	**<0.001**	0.73	7	68.29%	70.27%
	Predicted mortality		<20%	Up to 50%					
SAPS-II	Score	44.8±7.2	35.72±12.05	53.17±17.20	**<0.001**	0.809	45	78.05%	81.08%
	Predicted mortality		30%±20%	50%±25%					

Values in bold are considered statistically significant (p<0.05).
APACHE-II, Acute Physiology and Chronic Health Evaluation-II; ROC, receiver operating characteristic; SAPS-II, Simplified Acute Physiology Score-II; SOFA, Sequential Organ Failure Assessment.

86.1%). Furthermore, it was found that a composite of cut-offs combining severity of illness indices with NT-proBNP levels improved odds of predicting adverse patient outcome compared with either index alone (table 3). Finally, higher values of NT-proBNP (per the cut-offs above) on day 1 and day 3 were associated with an adverse patient outcome as demonstrated by Kaplan-Meier survival analysis (figure 3).

Detailed transthoracic echocardiography was performed at baseline and at 72 hours, assessed parameters included left ventricular ejection fraction (LVEF) (assessed by Simpson's biplane method of disks), inferior vena cava (IVC) diameter, peak velocity of the tricuspid regurgitant (TR) jet (where applicable) and the ratio of E and A velocities (E/A ratio) (assessed by mitral inflow pulsed wave Doppler). Observed E/A ratio on both day 1 and day 3 was significantly higher in survivors as compared with non-survivors. Predictive ROC analysis for patient outcome used variables of day 1 and day 3 E/A ratio. An E/A ratio >0.90 on day 1 was predictive of a better outcome (AUC: 0.8487, sensitivity: 70.3%, specificity: 85.4%, PPV: 81.3%, NPV: 76.1%), similarly an E/A ratio >0.90 on day 3 also predicted better outcome (AUC: 0.8410, sensitivity: 73%, specificity: 73.5%, PPV: 75%, NPV: 71.4%). No significant differences were noted among

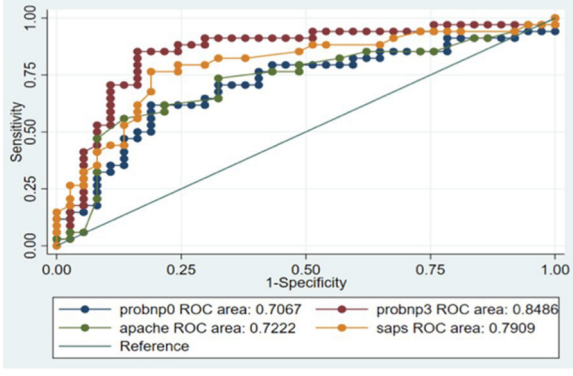

Figure 2 Predictive ROC analysis for severity of illness indices and serial NT-proBNP levels as predictors of adverse outcomes. APACHE, Acute Physiology and Chronic Health Evaluation; NT-proBNP, N-terminal pro-brain natriuretic peptide; ROC, receiver operating characteristic.

survivors and non-survivors in the observed values of ejection fraction or IVC diameter on day 1 or 3 or peak TR velocity on day 1. However, a statistically significant negative correlation of modest strength was observed between NT-proBNP values on day 3 and the calculated ejection fraction on day 3 with an r-value of −0.35. Echocardiographic data thus obtained are summarized in table 4.

Finally, length of ICU or ward stay was compared among survivors and non-survivors. It was noted that survivors (median (IQR): 14 days (14 days)) had a significantly (p<0.001) longer ward stay as compared with non-survivors (median (IQR): 6 days (7 days)). Likewise, it was found that survivors (median (IQR): 11 days (11.5 days)) had a significantly (p 0.023) longer ward stay as compared with non-survivors (median (IQR): 7 days (6 days)).

DISCUSSION

Multiple biomarkers have been identified over the years for potential roles in the diagnosis and management of sepsis such as adrenomedullin, CD64, sTREM-1, etc, but none of them hold a well-defined role in the treatment and prognosis of sepsis at present.[9] The FINNSEPSIS Study, conducted in 2007 across 24 ICU settings in Finland with 254 patients with sepsis, reported significantly higher value of NT-proBNP in non-survivors (median 7908 ng/mL) as compared with survivors (median 3498 ng/mL) (p=0.002). NT-proBNP values at 72 hours and SAPS within 24 hours were independent predictors of hospital mortality.[10] Papanikolaou *et al* in their 3-year single-centre study prospectively followed up 42 cases of sepsis with serial BNP values for the first 5 consecutive days of admission and reported that patients in septic shock have higher BNP values which correlate with the SOI scores (APACHE-II and SOFA) as well as peak norepinephrine dose on day 1. Plasma BNP levels declined faster in survivors than in non-survivors, both in sepsis and septic shock (p<0.02) and the inability to decrease BNP levels <500 pg/mL was associated with increased mortality (p<0.03).[11]

In our study, non-survivors had a higher baseline value at 24 hours (median 5811 pg/mL) as compared with survivors (3230 pg/mL). This difference persisted until 72 hours with non-survivors having a higher value at 72 hours (median

Table 3 Odds of adverse patient outcome by severity of illness indices: effect of combining NT-proBNP levels

Predictive variable	OR for adverse outcome (OR (95% CI))	P value
APACHE-II score >20 **OR** NT-proBNP >4300 pg/mL	2.47 (0.77 to 8.03)	0.13
APACHE-II score >20 **AND** NT-proBNP >4300 pg/mL	14.88 (3.60 to 61.39)	**<0.001**
SAPS-II score >45 **OR** NT-proBNP >4300 pg/mL	5 (1.38 to 18.18)	**0.014**
SAPS-II score >45 **AND** NT-proBNP >4300 pg/mL	55 (9.07 to 333.45)	**<0.001**
SOFA score >7 **OR** NT-proBNP >4300 pg/mL	1.56 (0.50 to 4.86)	0.44
SOFA score >7 **AND** NT-proBNP >4300 pg/mL	24 (4.38 to 131.47)	**<0.001**

Values in bold are considered statistically significant (p<0.05).
APACHE-II, Acute Physiology and Chronic Health Evaluation-II; NT-proBNP, N-terminal pro-brain natriuretic peptide; SAPS-II, Simplified Acute Physiology Score-II; SOFA, Sequential Organ Failure Assessment.

8448.5 pg/mL) as compared with survivors (median 2377 pg/mL). Cut-off values established on the basis of ROC curves generated predicted that NT-proBNP values greater than 4300 pg/mL (sensitivity 65.85% and specificity 64.86%) at 24 hours and values greater than 5229 pg/mL (sensitivity 85.29% and specificity 83.78%) at 72 hours predicted poorer outcomes in these patients. Thus, a higher value at baseline with a rising trend at 72 hours generally indicated a poorer outcome, although the values at 72 hours had greater sensitivity and specificity in predicting outcome than values at 24 hours.

Favory and Neviere reported up to 50% cases of sepsis to have some form of myocardial dysfunction which is difficult to assess by bedside methods and suggested that troponin-I be used as a marker for poor outcome.[12] Subsequent studies by Yang *et al* in 2015 among 586 cases with non-coronary artery disease having elevated CTnI identified sepsis to be the strongest independent cause of CTnI elevation (p<0.01).[13] Zochios and Valchanov also reported the association of higher values of troponins would not only be indicative of increased hospital mortality but could also be incorporated in sepsis bundles as a prognostic tool.[14] However, Vallabhajosyula *et al* in their retrospective study of 944 patients admitted with sepsis over a 7-year period (2007–2014) reported elevated troponin-T values on admission in 90% cases. The elevated values were associated with unadjusted in-hospital (OR 1.6; p=0.003) and 1-year mortality (OR: 1.3; p=0.04) but did not correlate with longer hospital stay. They concluded that troponin-T values were associated with higher short-term and long-term mortality but routine testing did not aid prognosis in these patients.[15]

In our study, there was no significant difference in CTnI values among non-survivors (mean 54.1±4.8 ng/mL) as compared with survivors (56.9±6.8 ng/mL) at 24 hours. Non-survivors had a higher value at 72 hours (mean 69.4.1±6.2 ng/mL) as compared with survivors (mean 50.1±9.8 ng/mL) (p<0.05). Thus, CTnI appears to be helpful in identifying patients with short-term mortality but does not have much utility (when measured serially) as a prognostic marker. Yang *et al* reported similar findings in their retrospective study of 375 patients with cancer with sepsis.[16]

The duration of hospital stay was higher in survivors than in non-survivors. Median ICU stay in survivors was 14 days as compared with 6 days in those who did not survive (p<0.001). Similarly, median stay in the ward was higher in survivors (median 11 days) than in non-survivors (median 7 days) (p=0.023). The difference is likely due to the requirement of supportive care for management of organ failures—hemodialysis for persistent renal failure and need of gradual weaning for those on mechanical ventilation. A study by Chatterjee *et al* however reported shorter duration of stay for survivors in the medical wards as compared with non-survivors.[17]

In terms of SOI scores, survivors have significantly lower mean APACHE-II, SAPS-II and SOFA scores than non-survivors (table 2). A previous study by Mohan *et al* had

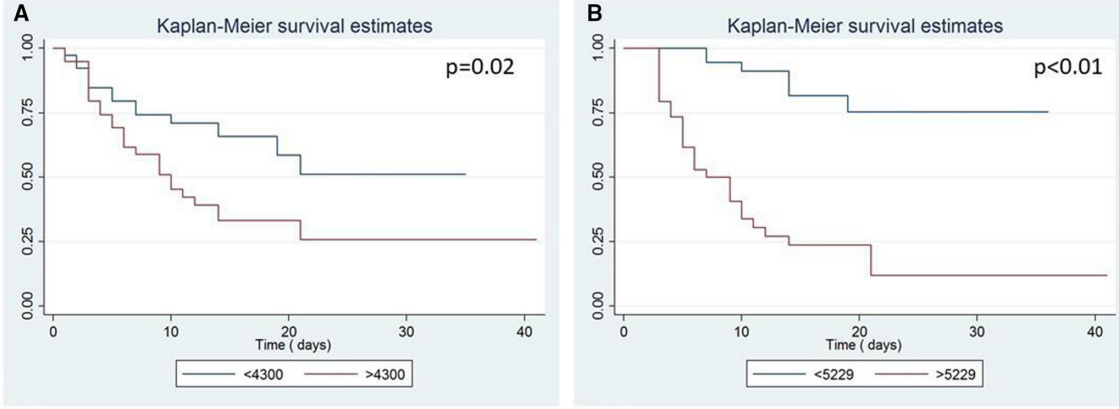

Figure 3 Kaplan-Meier survival analysis demonstrating an adverse outcome for patients with NT-proBNP >4300 pg/mL on day 1 (A) and NT-proBNP >5229 pg/mL on day 3 (B). NT-proBNP, N-terminal pro-brain natriuretic peptide.

Table 4 Serial echocardiographic assessment: comparison with patient outcome

Parameter		Value (mean±SD) Survivors (N=41)	Non-survivors (N=37)	P value
E/A ratio	Day 1	1.03±0.22	0.81±0.15	**<0.001**
	Day 3	1.03±0.21	0.82±0.17	**<0.001**
Peak TR velocity (cm/s)	Day 1	251±19.8	257.2±18.6	0.16
	Day 3	249.7±12.04	261.5±19.8	**0.003**
IVC diameter (cm)	Day 1	1.65±0.31	0.81±0.15	0.48
	Day 3	1.61±0.29	1.68±0.31	0.13
LV ejection fraction (%)	Day 1	56.2±6.7	54.9±9.2	0.48
	Day 3	54.1±10.0	59.0±5.7	0.13

Values in bold are considered statistically significant (p<0.05).
E/A ratio, ratio of E and A velocities; IVC, inferior vena cava; LV, left ventricular; TR, tricuspid regurgitant.

identified APACHE-II greater than 14, SAPS-II greater than 35 and a SOFA score greater than 7 on day 1 to be predictive of a poor outcome in patients with sepsis. In our study, APACHE-II greater than 20 and SAPS-II greater than 45 indicated poor outcome in patients. The difference could have arisen due to our cohort of patients being more ill than the cohort in the previous study. In terms of SOFA score, however, both studies are in agreement that a score greater than 7 at baseline indicates poor outcome.[18] Combining the scores in APACHE-II and SAPS-II with NT-proBNP led to significantly improved ability to predict poorer outcomes in these patients than with the SOI scores alone. APACHE-II score alone could predict mortality in 34.2% cases as compared with 51.22% cases when used in combination with NT-proBNP (OR 14.87, p<0.05). Similarly, SAPS-II could predict the outcome correctly in 36.59% cases as compared with 53.66% cases when used in combination with NT-proBNP (OR 55, p<0.05).

Echocardiographic assessment of patients with sepsis and myocardial dysfunction poses several challenges. Most notably, changes in echocardiographic parameters are frequently subtle and may not be sensitive enough to accurately or completely represent the extent of myocardial injury in the relatively short course of illness.[19] These observations were asserted in a recent systematic review by Sanfilippo *et al* that demonstrated LVEF to not have any prognostic value in patients with sepsis. They found instead that the less widely available but more sensitive technique of global longitudinal strain assessment could be a better prognostic indicator in these patients.[20] Other studies have reported diastolic dysfunction to be an earlier and more common manifestation of cardiac dysfunction in sepsis.[21] Our study corroborates these findings demonstrating no significant differences in ejection fraction among patients with favorable and adverse outcomes but a significantly lower E velocity and E/A ratio both at baseline and on repeat assessment at 72 hours in non-survivors. Additionally, while TR velocity did not significantly differ among the two groups at baseline, by the time the patients were reassessed at 72 hours, it was found that patients who went on to have adverse outcomes had higher peak TR velocities as compared with their better faring counterparts. These findings signify that myocardial damage, while difficult to establish, portends a poor prognosis in patients with sepsis and demonstrably progresses rapidly in these patients. Hence, assessment of diastolic function or estimation of pulmonary pressures may thus be the easiest echocardiographic parameters for the evaluation of myocardial dysfunction in sepsis.

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