

Correlation between Sequential Organ Failure Assessment (SOFA) Score with Right Ventricular Systolic Function and Left Ventricular Filling Pressure in Sepsis Patients

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ABSTRACT

This research aimed to evaluate the relationship of sepsis severity assessed using SOFA scores with RV systolic function and LVFP. Methods: This cross-sectional observational study involved 25 dr. Kariadi General Hospitals septic patients without cardiac disease. The SOFA score as a study subject was calculated up to a maximum of 3 times per patient parallel to the RV function examination. Echocardiographic RV function parameter we used Tricuspid Annular Plane Systolic Excursion (TAPSE), Right Ventricle Fractional Area Change (RV-FAC), Right Ventricle Free Wall Strain (RV-FWS), Right Ventricle-Pulmonary Artery (RV-PA) coupling, and LVFP using the Nagueh formula and ASE/EACVI 2016 criteria. Correlation tests were conducted between SOFA scores with TAPSE, RV-FAC, RV-FWS, RV-PA coupling, and LVFP. Results: There were 56 samples of SOFA scores and echocardiography. There was a significant correlation between SOFA scores and TAPSE ($r = -0.44$, $p = 0.001$), RV-FAC ($r = -0.54$, $p = <0.001$), RV-FWS ($r = -0.52$, $p = <0.001$), RV-PA coupling ($r = -0.32$, $p = 0.014$). No significant correlation was found between SOFA and LVFP scores with Nagueh ($r = 0.11$, $p = 0.42$) and the 2016 ASE/EACVI criteria ($r = -0.022$, $p = 0.09$). RV-FWS can detect RV dysfunction earlier than other parameters. Conclusion: SOFA score is associated with RV function but not with LVFP. Echocardiography in septic patients can be considered to detect early RV dysfunction.

KEYWORDS SOFA score, TAPSE (Tricuspid Annular Plane Systolic Excursion), RV-FAC (Right Ventricle Fractional Area Change), RV-FWS (Right Ventricle Free Wall Strain), LVFP (Left Ventricle Filling Pressure).



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INTRODUCTION

Sepsis is a clinical syndrome resulting from the body's maladaptive response to infection, which triggers a destructive inflammatory reaction and causes disturbances at the cellular level in various organs (Vignon & Huang, 2015; Zhang et al., 2020; Vallabhajosyula et al., 2017; Anavekar et al., 2017). The Third International Consensus Definition for Sepsis emphasizes identifying septic patients based on the organ dysfunction that occurs, using the Sequential Organ Failure Assessment (SOFA) score as the primary criterion for diagnosing sepsis (Greer, 2015; Lanspa et al., 2020; Narváez et al., 2018; Leenhardt, 2018). Myocardial dysfunction frequently occurs in sepsis, with an incidence of approximately 50–64%, and can increase short-term mortality in intensive care unit

patients by 3 to 4 times. This dysfunction generally occurs acutely and is reversible. Left ventricular global dysfunction characterized by dilatation and decreased ejection fraction without an increase in left ventricular filling pressure is a distinctive feature of septic cardiomyopathy (Prihadi et al., 2019; Spencer & Flachskampf, 2019; Anavekar et al., 2017; Vignon & Huang, 2015). Right ventricular dysfunction also occurs in 30–50% of cases.

Loss of systemic vascular tone, decreased cardiac output, and inadequate fluid resuscitation cause a decline in right ventricular preload, while increased pulmonary vascular resistance (*Pulmonary Vascular Resistance / PVR*), hypoxic vasoconstriction, metabolic acidosis, and pulmonary vascular thrombosis contribute to increased right ventricular afterload (Lanspa et al., 2020; Martin et al., 2019; Narváez et al., 2018; Leenhardt, 2018). Echocardiography is a non-invasive test that can directly assess cardiac function (Martin et al., 2019; Order et al., 2014; Vallabhajosyula et al., 2017; Zhang et al., 2020).

Conventional echocardiography is commonly used to evaluate right ventricular (*RV*) function; however, it may underestimate the extent of myocardial injury. Strain imaging can accurately quantify global and segmental myocardial function by assessing the displacement of myocardial tissue. Right ventricular free wall strain (*RV-FWS*), as measured by echocardiography, has been proposed as a reliable indicator of RV function, being relatively easy to perform and offering high temporal resolution.

Cardiac dysfunction in sepsis, particularly right ventricular systolic impairment, is a well-documented but understudied phenomenon, occurring in 30–50% of septic patients and significantly worsening prognosis (Vallabhajosyula et al., 2017, *Annals of Intensive Care*). Despite advances in critical care, the relationship between sepsis severity, assessed by *SOFA* scores, and RV function remains ambiguous, with conflicting evidence on whether *SOFA* scores reliably predict RV dysfunction. For instance, while some studies report a correlation between higher *SOFA* scores and RV impairment (Narváez et al., 2018, *Medicina Intensiva*), others find no significant association (Vieillard-Baron et al., 2014, *Intensive Care Medicine*), highlighting a critical gap in the literature.

A significant research gap lies in the inconsistent timing and methods of echocardiographic assessment in sepsis. Most studies evaluate cardiac function within the first 24 hours of ICU admission, potentially missing dynamic changes in RV performance as sepsis progresses (Dugar et al., 2020, *BMJ*). Furthermore, conventional echocardiography may underestimate RV dysfunction, as newer techniques like speckle-tracking echocardiography (*STE*) reveal subclinical myocardial injury earlier (Orde et al., 2014, *Critical Care*). This gap calls for longitudinal studies incorporating advanced imaging to capture the full spectrum of sepsis-induced RV dysfunction.

The urgency of this research is underscored by the high mortality associated with sepsis-induced RV dysfunction, which increases short-term death risk by 3 to 4 times (Pulido et al., 2012, *Mayo Clinic Proceedings*). Early detection of RV impairment could guide tailored therapies, such as optimized fluid management or vasoactive drug selection, to improve outcomes. However, without robust evidence

linking *SOFA* scores to RV function, clinicians lack reliable tools to identify high-risk patients, perpetuating a one-size-fits-all approach to sepsis management.

This study's novelty lies in its comprehensive evaluation of multiple RV function parameters (*TAPSE*, *RV-FAC*, *RV-FWS*, and *RV-PA* coupling) alongside *SOFA* scores, addressing limitations of prior single-parameter analyses. By employing *STE*—a more sensitive tool for detecting subclinical dysfunction—the research aims to clarify whether *SOFA* scores can serve as a surrogate for RV impairment, filling a critical knowledge void. Additionally, the inclusion of left ventricular filling pressure (*LVFP*) assessment provides a holistic view of sepsis-induced cardiac dysfunction, a dimension rarely explored in existing literature.

The primary purpose of this study is to determine the correlation between *SOFA* scores and RV systolic function in septic patients using advanced echocardiographic techniques. By establishing whether *SOFA* scores reflect RV dysfunction, the research seeks to validate a readily available clinical tool (*SOFA*) for risk stratification, potentially eliminating the need for specialized imaging in resource-limited settings. Secondary objectives include evaluating the prognostic value of *RV-FWS* in detecting early RV dysfunction and assessing the relationship between *SOFA* scores and *LVFP*.

This research contributes to the field by providing evidence-based insights into the cardiac manifestations of sepsis, particularly RV dysfunction, which has historically been overshadowed by left ventricular-focused studies. The findings could refine current diagnostic criteria, enabling earlier intervention and personalized management strategies. Moreover, the study highlights the clinical utility of *STE* in sepsis, advocating for its integration into routine critical care practice to enhance diagnostic accuracy and patient outcomes.

The implications of this research are far-reaching, offering potential improvements in sepsis management protocols. If *SOFA* scores are strongly correlated with RV dysfunction, they could be used to identify patients who would benefit from closer hemodynamic monitoring or targeted therapies. For healthcare systems, this could translate into reduced ICU stays and lower mortality rates. Furthermore, the study's emphasis on RV function may spur further research into RV-specific treatments, such as pulmonary vasodilators or inotropes, tailored to septic patients' unique pathophysiology.

Ultimately, this study bridges a critical gap in sepsis research by elucidating the relationship between *SOFA* scores and RV function, with implications for both clinical practice and future research. By leveraging advanced echocardiography and rigorous statistical methods, the findings aim to enhance the precision of sepsis care, ultimately improving survival and quality of life for affected patients. The results may also inform guidelines on the timing and methods of cardiac assessment in sepsis, ensuring earlier detection and intervention for high-risk individuals.

RESEARCH METHOD

. This study aimed to determine the relationship between the severity of sepsis, assessed using the *SOFA* score, and right ventricular systolic function as well as left ventricular filling pressure in septic patients. We employed an observational, cross-sectional design with consecutive sampling of patients admitted to the Intensive

Care Unit (*ICU* and *HCU*) of Dr. Kariadi Semarang. The study was conducted from May 2020 to September 2020. This research was supported by Dr. Kariadi Hospital Semarang and the Department of Cardiology and Vascular Medicine, FK UNDIP, and was approved by the Ethics Committee for Health and Medical Research, FK UNDIP / RSUP Dr. Kariadi Semarang.

The definition of right ventricular (*RV*) dysfunction varied depending on the echocardiographic parameter used. We defined *RV* dysfunction according to the following criteria: *TAPSE* < 17 mm,¹³ *RV-FAC* < 35%,¹³ *RV-FWS* < -20%,¹³ *RV-PA* coupling < 1, and for left ventricular filling pressure (*LVFP*), quantitative criteria > 15 mmHg, as well as qualitative criteria based on the ASE/ECVI 2016 guidelines, where the presence of two positive criteria out of three was considered indicative of *RV* dysfunction.

Research subjects

Informed consent was obtained from the patients' families. Inclusion criteria were patients diagnosed with sepsis, while exclusion criteria included a history of congenital heart disease or valvular heart disease (corrected or not), history of coronary heart disease or myocardial infarction with ECG evidence and regional wall motion abnormalities, history of arrhythmia or presence of a pacemaker, chronic renal failure, chronic obstructive pulmonary disease, history of stroke or head injury, hematologic malignancy, chronic liver disease, and patients with poor echocardiographic image quality. Our study involved 23 septic patients in the intensive care unit. Patients were re-examined if there were changes in the *SOFA* score as determined by the intensivist, with a maximum of two examinations per patient. Ultimately, we collected 56 echocardiographic data samples.

Research procedure

Patients diagnosed with sepsis who met the inclusion criteria and did not meet the exclusion criteria were registered as study subjects. Informed consent was obtained from the patients' families. Patient data such as demographic information, *SOFA* score, blood pressure, heart rate, use of mechanical ventilation, vasoactive drugs, and volume status were collected during examination. Echocardiographic data were acquired using the Philips Epiq CVx system, including 2D parameters, M-mode, Doppler, and myocardial strain imaging. Myocardial strain calculations were performed using Tomtec echocardiography software.

Research variables

In this study, the *SOFA* score was defined as the independent variable, while *RV* systolic function parameters were the dependent variables. We analyzed the correlation between *SOFA* scores and *RV* systolic function as well as left ventricular filling pressure.

Statistical analysis

Statistical analysis was performed using SPSS version 23.0 (IBM Corporation, USA). Descriptive data were presented as mean ± standard deviation or median with interquartile range, frequency, and percentage. The minimum total sample size was estimated to be 40 *SOFA* scores at 80% power. To control for type I error, the alpha level was adjusted by dividing it according to the ratio of

each *SOFA* score, assuming a correlation coefficient of 0.5 between each statistical test. An interim analysis with independent data yielded a figure of 1.96, which was considered statistically significant in the final analysis. A 95% confidence level was used, and results were reported with two-sided p-values.

RESULT AND DISCUSSION

A total of 56 samples of echocardiography data were examined during the period May-September 2020. We presented the demographic characteristics and clinical data in Table 1. Mean age is 47.96 years + 13.76, and 56% are female. The main sources of infection were the abdominal organs (88%), respiratory (4%), and others (8%).

Based on the RV function parameter, there was a decrease of RV-FWS in all research subjects, RV-PA coupling decreased in 73.2% of research subjects, and RV-FAC decreased in 51.8% of research subjects, while the TAPSE parameter decreased in 28.6% of subjects. The Venn diagram in Figure 1 showed an RV dysfunction based on parameters TAPSE, RV-FAC, RV-FWS, and RV-PA coupling.

Relationship between SOFA score with Right Ventricular Function

Pearson correlation test was used to correlate SOFA scores and TAPSE, RVFAC, RVFWS, and RV-PA Coupling. There was a significant negative correlation between SOFA scores with TAPSE, RVFAC, RVFWS, and RV-PA Coupling with a p-value < 0.05. Tables 2 and 3 showed the correlation test of SOFA scores with TAPSE, RVFAC, RVFWS, RV-PA Coupling, and LVFP.

Relationship between SOFA score with Left Ventricular Filling Pressure

Spearman correlation test was used to correlate SOFA scores and LVFP. It showed that there was a negative correlation between SOFA scores and LVFP calculated quantitative and qualitative, but it was not significant statistically, with a p-value > 0.05. Table 3 shows a correlation analysis between the SOFA score and the LVFP.

Comparative analysis of SOFA scores with Right Ventricular Function and left ventricular filling pressure

We divide the SOFA score into two groups based on the curve analysis Receiver Operating Characteristic (ROC) and Area Under The Curve (AUC) to find the cut-off point of the SOFA score for the occurrence of right ventricular dysfunction (Figure 2). Determination of the cut-off value is carried out based on the RV function of the FAC parameter data and obtained the cutting point results of the SOFA score are > 6.5 with sensitivity 72.4% and specificity 77.8%, AUC 81.7% (95% CI 70% - 93%) and p-value = 0.000. Table 4 shows comparative analyzes of clinical and echocardiographic characteristics based on SOFA scores.

Comparative analysis between SOFA scores and RV function

Comparative analysis using an independent T-test showed that there was a correlation between SOFA scores and TAPSE, RVFAC, RVFWS, and RV-PA coupling statistically significant with a p-value < 0.05. Table 5 showed a comparative analysis between the SOFA score and the RV function.

Comparative analysis between SOFA score and left ventricular filling pressure

Comparative analysis using the Mann-Whitney test showed that there was no correlation between SOFA scores and LVFP quantitative and qualitative with a p-

value>0.05. Table 6 showed a comparative analysis between the SOFA score and the LVFP. The reliability and validity of the measurements using Bland-Altman indicate a good match between the results of the measurements tested. The intra-observer suitability test showed no significant difference in the subjectivity of measurements ($p > 0.05$), and the data were 100% in the 95% area limit of agreement. The inter-observer suitability test showed no significant difference in the subjectivity of measurements ($p > 0.05$), and the data were 100% in the 95% area limit of agreement.

Discussion

This study showed a significant correlation statistically between the SOFA score and the RV function, but there was no significant correlation between the SOFA score and the LVFP. Cardiac dysfunction often occurs with the increasing severity of sepsis. RV dilatation does not always occur in septic patients. In this study, there was no RV anatomical abnormality. Besides, if using RV dilation criteria based on ESC 2015¹⁵ where RV dilatation occurs when the basal diameter RV / LV ratio is >1 , there is no increase in the RV / LV ratio either from univariate analysis with a mean of 0.82 ± 0.16 and bivariate analysis was 0.81 ± 0.13 in SOFA scores <6 and 0.84 ± 0.18 in SOFA scores >6 ($p=0.584$). Orde et al. showed no RV dilatation in septic patients generally (basal RV mean 39 ± 7) and Singh et al.¹⁵ showed only 9% RV dilatation in septic patients (Lee et al., 2018; Mahjoub et al., 2012; Chan & Klinger, 2018).

In addition to myocardial dysfunction, sepsis also disrupts both systemic and pulmonary vascular function. In general, this study showed that the median SVR was normal but had a high median PVR, but there was no significant difference between the SOFA score groups from the bivariate analysis as shown in table 4. During sepsis, abnormal regulation of Nitric Oxide (NO) in the systemic circulation will cause vasodilation, but in hypoxic conditions that occur with increasing sepsis severity, NO production is reduced in the pulmonary circulation and will cause pulmonary vasoconstriction circulation.¹⁷ The SVR value that did not differ between groups could be due to vasoactive drugs, wherein the SOFA >6 group was 80.4% using vasoactive drugs and having a mean MAP that was not significantly different from the SOFA score group ≤ 6 . Increasing PVR not only due to vasoactive use but also use of mechanical ventilators and the incidence of acidosis, hypothermia can also play a role in increasing PVR in septic patients (Vieillard-Baron & Cecconi, 2014; Lang et al., 2016; Nagueh et al., 2016).

Relationship between SOFA score and right ventricular function

This study obtained moderate strength of correlation between SOFA scores and TAPSE ($r = -0.44$), RVFAC ($r = -0.54$), and RVFWS ($r = -0.52$), while the relationship between SOFA and RV-PA scores coupling has a weak correlation strength ($r = -0.32$). This study also showed that the higher the SOFA score, the higher the decrease in RV function. Comparative analysis showed significant differences in the mean of each parameter of the RV function. Research Narvaez et al.¹⁹ showed that patients with sepsis who had RV dysfunction (mean TAPSE 16.3 ± 3.14) had a higher mean SOFA score than patients without RV dysfunction (mean TAPSE 21.8 ± 3.82 , $p < 0.001$) with a SOFA score of 9.91 ± 3.82 compared to 7.47 ± 3.41 ($p = 0.037$).

In our study, RVFWS is a parameter that can detect RV dysfunction earlier than other parameters of RV function in septic patients among the four parameters of RV function used. If we assessed RV dysfunction using the TAPSE parameter, only 28.6% of the study subjects experienced RV dysfunction. However, when using RVFWS, RVFAC, or RV-PA parameters coupling in assessing RV function, more than 50% of samples can be identified as having RV dysfunction. RVFWS decreased in 100% of samples, and 6

samples had decreased RVFWS function without any other decrease in RV function. The sensitivity of RVFWS to detect RV dysfunction is similar to the research of Orde et al.²⁰, which shows speckle tracking echocardiography (STE) can increase the detection rate of RV dysfunction compared with conventional echocardiography examinations. Orde et al.²⁰ showed that isolated RV dysfunction was 32% on conventional echocardiography, whereas STE examination showed its presence in isolated RV dysfunction in 72% of the sample. Orde et al.²⁰ showed RV free wall strain in the group patient with a SOFA score of 10 ± 4 are -18.1 ± 5.4 while in the group with an average SOFA score of 13 ± 3 is -16.9 ± 5.6 .

Prihadi et al.²¹ also said RV FWS could detect RV dysfunction higher than other RV function parameters. Many factors that may not directly affect RV function in septic patients during intensive care, such as hypoxia, acidosis, decreased preload, or a ventilator, do not consider a protective ventilation strategy. RVFWS can detect subendocardial disorders, so this examination is essential to detect subclinical myocardial dysfunction.

In this study, FAC is more able to detect RV dysfunction earlier than TAPSE. The meta-analysis by Lee et al.²² comparing TAPSE and FAC in estimating RV systolic function showed FAC had a higher correlation with RVEF assessed using CMR than TAPSE (0.56 versus 0.40, $P = 0.018$). Research by Anavekar et al.²³ showed that RV FAC had the strongest correlation to RVEF of CMR than other parameters ($r = 0.80$, $p < 0.001$).

RV-PA coupling takes into account the adaptability of the RV contraction to a given afterload. Average RV-PA value coupling, which < 1 indicates RV dysfunction. There is a significant relationship between SOFA scores and RV-PA coupling in this study; it looks at the mean RV-PA value coupling SOFA score > 6 , which is smaller than the SOFA score group < 6 ($p = 0.012$), also supported by a high PVR value in the SOFA score group > 6 . This relationship also indicates that an increase in afterload increases the likelihood of right ventricular dysfunction in sepsis. Using a ventilator that does not apply a protective ventilation strategy can also further improve afterload RV. As a result of the increased afterload, the RV will adapt acutely by increasing contractility to maintain the RV-arterial coupling and RV output in response to peripheral needs (homeometric adaptation). Zhang et al.²⁴ using TAPSE/PASP as Coupled RV-PA indicator in septic patients on a ventilator showed that TAPSE/PASP ≤ 0.5 mm/mmHg had higher 1-year mortality compared to the TAPSE/PASP group > 0.5 mm/mmHg ($p < 0.01$). In that study, patients in the survivor group had a mean TAPSE/PASP was 0.61 and a mean SOFA score of 12 compared with nonsurvivors who had a mean of 0.36 and mean SOFA score was 14. TAPSE/PASP ratio was also independently associated with the ICU's mortality rates (HR 0.027, $p = 0.017$).

Several studies show different results compared to our study. Vieillard-Baron et al.⁷ showed no significant difference in the SOFA score between patients with RV dysfunction (as assessed by RV dilation and increased CVP) and without RV dysfunction ($p = 0.527$), and the TAPSE score did not show a significant difference between patients with RV dysfunction compared to the group without RV dysfunction ($p = 0.108$). The study of Vallabhajosyula et al.²⁵ showed that in patients with RV dysfunction assessed using TAPSE and RVFAC, there was no significant difference in the mean SOFA score than patients without RV dysfunction. Our study's different results could be due to the difference in echocardiography timing between this study and the two studies. Vallabhajosyula et al. and Villard-Barron et al. collected data from the initial 24 hours of patients diagnosed with sepsis and admitted to the intensive care room. In contrast, our study took a maximum sample range of 12 hours after the patient was diagnosed with sepsis, but some patients have had longer treatments in the intensive care unit. Dugar et al.²⁶ stated that the incidence of RV dysfunction would increase in echocardiographic studies carried out in the 48-72 hour timeframe compared to the initial 24 hours. Meanwhile, Vignon et al.²⁷ said cardiovascular changes depend on the timing of the hemodynamic assessment performed,

the onset of infection leading to sepsis, and fluid status so that any treatment given in the intensive care unit will impact RV function.

Relationship between SOFA Scores and LVFP

Our study found no statistically significant correlation between SOFA scores and LVFP, either quantitatively or qualitatively. It can occur because, during sepsis and critical illness, other issues influenced the dynamic left ventricular filling pressure, such as the underlying disease, fluids management and administration of vasoactive drugs, and echocardiography timing.⁸ Three main components (the relaxation function LV, effective compliance of LV, and LV filling volume) influenced LVFP.²⁸ Volume status, a determining component of filling pressure, can change according to RV dysfunction. Our study's RV dysfunction occurred in both the low and high SOFA score groups, affecting LV preload. Besides, a mechanical ventilator (the amount of tidal volume and the value of PEEP) and vasoactive drugs (the type and dose of vasoactive drugs) that did not include in our study can also affect the LVFP. Mahjoub et al.²⁹ suggest that adequate fluid administration can improve the relaxation disturbances during sepsis. Increasing mitral annulus early wave velocity (e') before and after giving fluids indicated relaxation disturbance during sepsis ($p < 0.05$). Another study by Farias et al.²⁸ using experimental animal studies showed that mice with sepsis experienced a dynamic change in compliance during sepsis where the compliance on the first day was decreased and returned to near normal on the third day but decreased again on day 7 of sepsis with the same fluid administration compared to the control group without sepsis.

CONCLUSION

This study concludes that the *SOFA* score exhibits a significant negative correlation with right ventricular (*RV*) systolic function, as measured by parameters such as *TAPSE*, *RV-FAC*, *RV-FWS*, and *RV-PA* coupling, but shows no significant association with left ventricular filling pressure (*LVFP*) in septic patients. The findings underscore the utility of the *SOFA* score as a clinical tool for identifying *RV* dysfunction in sepsis, with *RV-FWS* emerging as the most sensitive parameter for early detection. These results highlight the importance of incorporating advanced echocardiographic techniques, particularly speckle-tracking echocardiography, into routine sepsis management to improve risk stratification and patient outcomes.

For future research, longitudinal studies with larger, multicenter cohorts are recommended to validate these findings and explore the dynamic changes in *RV* function over the course of sepsis. Additionally, investigations into targeted therapeutic interventions—such as personalized fluid resuscitation, vasoactive drug selection, or pulmonary vasodilators—based on the severity of *RV* dysfunction could further refine sepsis care. Further studies should also examine the prognostic implications of *RV* dysfunction in sepsis, including its impact on long-term mortality and morbidity, to establish evidence-based guidelines for monitoring and treatment.

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