

Association of fluid balance and diastolic dysfunction in patients with septic shock in the intensive care unit

Summary

Diastolic dysfunction is a common manifestation of sepsis-associated cardiomyopathy and has been associated with poorer outcomes in critically ill patients; however, the factors that contribute to its development during septic shock are not fully defined. This study aimed to determine the association between cumulative fluid balance and diastolic dysfunction in patients with septic shock admitted to the ICU. An observational, prospective, longitudinal, and analytical study was conducted that included 55 adult patients with a diagnosis of septic shock. Cumulative fluid balance and diastolic function were assessed by critical echocardiography using the E/A ratio at admission, 24, and 72 hours. The statistical analysis included descriptive and analytical methods; ROC curves and relative risk calculation were used. It was identified that 40% of the patients had diastolic dysfunction. The most frequent infectious process was abdominal (60%), followed by pulmonary (32.7%). A positive and significant correlation was observed between the accumulated water balance and the mitral E/A ratio at all times evaluated (admission: $r=0.531$; 24 h: $r=0.560$; 72 h: $r=0.466$; $p<0.001$). The relative risk of diastolic dysfunction increased with water balance: 5.4 times the risk at admission, 8.8 at 24 h, and 13.9 at 72 h. In conclusion, the risk of developing diastolic dysfunction consistently increases with the increase in accumulated water balance.

Keywords: Septic shock, diastolic dysfunction, fluid balance, and critical echocardiography

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Abbreviations: ICU; Intensive Care Unit, HGR 196; Regional General Hospital 196.

Introduction

Sepsis and septic shock represent a global public health problem due to their high incidence, high mortality, and considerable consumption of health resources.^{1,2} These entities are characterized by a dysregulated response of the host to an infection, leading to progressive organ dysfunction and, in its most severe form, circulatory collapse with hemodynamic alterations.³

Septic shock is distinguished by a complex interaction between systemic inflammation, microcirculatory alterations, and organ dysfunction.⁴ Within this context, the involvement of the cardiovascular system plays a central role in the clinical evolution of critically ill patients. The inability of the heart to adapt to increased hemodynamic

demands contributes to the deterioration of tissue perfusion and the progression of organ dysfunction, which directly impacts prognosis.⁵⁻⁷

Traditionally, attention to cardiac compromise in septic shock has focused on systolic function; however, in recent years, diastolic dysfunction has gained relevance as an important component of cardiovascular involvement. By convention, left ventricular diastole extends from the moment of aortic valve closure to mitral valve closure and usually lasts two-thirds of the cardiac cycle at rest.⁸ Diastolic dysfunction is characterized by an alteration in ventricular relaxation and diastolic filling, which conditions an increase in intracavitary pressures and limits the ventricle's ability to accommodate changes in preload.^{9,10} One of the fundamental pillars in the treatment of septic shock is the management of intravenous fluids.¹¹ Early water resuscitation aims to restore tissue perfusion and optimize cardiac output; However, excessive fluid administration can lead to a positive fluid balance, with relevant pathophysiological consequences such as

tissue edema, increased interstitial pressure, impaired oxygenation, renal failure, and other organ dysfunctions.¹²

A positive water balance can directly influence ventricular diastolic function by modifying preload conditions and increasing filling pressures; This phenomenon is particularly relevant, since the heart's ability to adapt can be limited to.^{13,14}

Hemodynamic assessment in the intensive care unit (ICU) requires tools that allow accurate, dynamic, and reproducible functional assessment. In this sense, critical echocardiography has established itself as an essential tool for the evaluation of critical patients; its non-invasive nature and its applicability to the patient's bedside make it a particularly useful instrument.¹⁵ The assessment of diastolic function by critical echocardiography, using simple Doppler parameters such as the mitral E/A ratio, allows the identification of ventricular filling alterations. The integration of critical echocardiography in the evaluation of patients with septic shock offers the possibility of individualizing hemodynamic management and optimizing therapeutic strategies.¹⁶⁻¹⁸ Despite the clinical importance of water balance in the evolution of patients with septic shock, its specific relationship with diastolic dysfunction has not been clearly defined in daily clinical practice, which generates uncertainty in decision-making related to fluid administration. Understanding this relationship is critical to inform more accurate clinical decisions and to avoid potentially harmful interventions resulting from unidentified volume overload over time.

In this context, our study sought to systematically analyze the association between accumulated fluid balance and diastolic dysfunction in patients with septic shock, using functional assessment tools accessible in the ICU.

Methodology

An observational, prospective, longitudinal, and analytical study was conducted in the ICU of the Regional General Hospital 196 (HGR 196). A total of 55 patients diagnosed with septic shock aged >18 years were included. Patients with chronic heart failure, chronic kidney disease, ischemic heart disease, and those who did not sign informed consent were excluded from the research. The water balance was recorded at the entrance, at 24 and 72 hours. Diastolic function was assessed by critical echocardiography through pulsed Doppler, using mitral A-wave velocity, mitral E-wave velocity, and E/A ratio

with an Esaote Mylabx 8 device. For statistical analysis, we include descriptive and analytical methods. We used to mean and standard deviations or medians and interquartile ranges, depending on the distribution of the variables. Qualitative variables were expressed in frequencies and percentages. For the analytical analysis, groups were defined according to water balance cut-off points identified with ROC curves, and their association with clinical and echocardiographic variables was evaluated, with which relative risks were calculated. Non-parametric tests such as Spearman's evaluation coefficient were applied to analyze associations.

Results

The present study included a total of 55 adult patients with a diagnosis of septic shock admitted to the ICU. All patients met the criteria for inclusion and had serial echocardiographic evaluations during the first 72 hours of stay, as well as the recording of fluid balance from admission to 72 hours. Initially, a descriptive analysis of the demographic, clinical, and echocardiographic characteristics of the studied population was performed, as well as the variables related to the accumulated water balance (Table 1). The population was made up of a similar distribution between men and women, and the mean age was 58.9 + 8.9 years, 63.3% correspond to men, and 36.4% were women. For the study population, patients who met the diagnosis of septic shock were included; abdominal origin occupied 60%, followed by 32.7% pulmonary origin. During the initial analysis, it was identified that 40% (n=22) of patients developed diastolic dysfunction during the follow-up period (Table 2). Diastolic dysfunction was observed both in early and subsequent evaluations, which allowed its dynamic behavior to be analyzed over time. At the same time, the accumulated water balance at the same time points was documented. When evaluating the association between accumulated water balance and diastolic function, a positive and statistically significant correlation was observed between both variables in the three evaluation moments. On admission, the correlation analysis showed a coefficient $r = 0.531$ ($p < 0.001$), indicating a moderate association between a higher accumulated water balance and alterations in the mitral E/A ratio. At 24 hours, this association was maintained and showed a slightly higher correlation coefficient ($r = 0.560$; $p < 0.001$). At 72 hours, although the coefficient decreased, the correlation remained statistically significant ($r = 0.466$; $p < 0.001$), demonstrating a persistent association over time.

Table 1 General characteristics of patients with septic shock

Variable	N = 55 Media + DS Median (RIQ)	Variable	N = 55 Media + DS Median (RIQ)
Age	58.9 ± 8.9	TAPSE 72 hrs mm	17 (14; 19)
Male	35 (63.3)	Cr mg/dL income	1.9 (0.8; 3.2)
Female	20 (36.4)	Cr 24 hrs mg/dL	1.6 (0.9; 3.1)
MAP mmHg income	63 (55; 75)	Cr 72 hrs mg/dL	1.2 (0.7; 3.7)
MAP 24 hrs mmHg	68 (60; 77)	Urea ingress mg/dL	85 (55; 112)
MAP 72 hrs mmHg	72 (61; 82)	Urea 24 hrs mg/dL	75 (55; 156)
HR Income lpm	107 (80; 120)	Urea 72 hrs mg/dL	66 (40; 165)
HR 24 hrs lpm	90 (75; 105)	Hb income gr/dL	13.2 (11; 14.2)
HR 72 hrs lpm	77 (65; 95)	Hb 24 hrs gr/dL	13.1 (10.4; 14.0)
RR Income rpm	21 (18; 23)	Hb 72 hrs gr/dL	12.2 (10.2; 12.8)
RR 24 hrs rpm	16 (16; 18)	Platelets Intake ×10 ³ /μL	220 (156; 345)
RR 72 hrs rpm	16 (16; 18)	24 hrs platelets ×10 ³ /μL	190 (100; 320)
Entrance Temp °C	37.4 (36.9; 38.6)	Platelets 72 hrs ×10 ³ /μL	175 (112; 310)

Table 1 Continued....

Temp 24 hrs °C	37.0 (36.5; 37.8)	Leukocytes admission ×10 ³ /μL	20.9 (16.5; 24.7)
Temp 72 hrs °C	36.9 (36.5; 37.2)	Leukocytes 24 hrs ×10 ³ /μL	15.8 (13.1; 24.3)
Sat O ₂ Revenue %	90 (88; 90)	Leukocytes 72 hrs ×10 ³ /μL	13.2 (11.9; 26.3)
Sat O ₂ 24 hrs %	92 (90; 92)	Albumin intake gr/dL	3.1 (2.5; 4.0)
Sat O ₂ 72 hrs %	93 (88; 94)	Albumin 24 hrs gr/dL	3.5 (2.5; 4.0)
Wave E Ingress cm/s	90 (80; 110)	Albumin 72 hrs gr/dL	3.5 (2.8; 3.8)
Wave E 24 hours cm/s	80 (70; 100)	Water Balance Income ml	2800 (1451; 3790)
Wave E 72 hours cm/s	78 (62; 100)	Water Balance 24 hrs ml	4060 (1988; 6850)
Wave A inlet cm/s	60 (39; 65)	Water Balance 72 hrs ml	2744 (1608; 9640)
Wave A 24 hours cm/s	50 (40; 55)	SOFA Entrance	13 (10; 20)
Wave A 72 hrs cm/s	50 (40; 60)	24 hrs SOFA	9 (7; 22)
Rel E/A Input	1.5 (1.3; 3.1)	SOFA 72 hrs	7 (6; 22)
Rel E/A 24 hrs	1.6 (1.4; 2.4)	APACHE entered	21 (18; 42)
Rel E/A 72 hrs	1.5 (0.9; 2.3)	Cardiac output income l/min	4.7 (3.6; 5.9)
Diastolic dysfunction	22 (40)	Cardiac output 24 hrs l/min	5.3 (3.9; 5.9)
MAPSE income mm	14 (11; 19)	Cardiac output 72 hrs l/min	5.0 (3.9; 5.4)
MAPSE 24 hrs mm	16 (10; 19)	Days of ICU stay	7 (4; 9)
MAPSE 72 hrs mm	16 (10; 19)	Ventilation days	4 (2; 5)
TAPSE inlet mm	17 (12; 19)	Mortality	18 (32.7)
TAPSE 24 hrs mm	17 (14; 19)		

MAP; Mean arterial pressure, HR; heart rate, RR; respiratory rate, Temp; Temperature, Sat O₂; Oxygen saturation, Cr; Creatinine, Hb; Hemoglobin, SOFA; Sequential Organ Failure Assessment, APACHE; Acute Physiology and Chronic Health disease Classification System, MAPSE; Mitral Annular Plane Systolic Excursion, TAPSE; Tricuspid annular plane systolic excursion

Table 2 Degree of diastolic dysfunction at admission, 24 h and 72 h

Degree of Dysfunction	Upon admission	24 hrs	72 hrs
Grade I Relaxation Disorder	3 (5.5%)	3 (5.5%)	6 (10.9%)
Grade II Pseudonormalized	37 (67.3)	37 (67.3)	33 (60%)
Grade III Restrictive Standard	15 (27.3%)	15 (27.3%)	16 (29.1%)

The ROC analysis was also carried out, which identified optimal cut-off points to predict diastolic dysfunction: admission >3265 mL (AUC=0.876), 24 h >4685 mL (AUC=0.979), and 72 h >5755 mL (AUC=0.927), all with statistical significance p<0.001. Table 3

summarizes the ROC results with their cut-off points and the area under the curve. Subsequently, a relative risk analysis was performed to evaluate the probability of developing diastolic dysfunction in relation to the accumulated fluid balance. The relative risk (RR) of diastolic dysfunction was increasing: 5.4 times at admission, 8.8 times at 24 h, and 13.9 times at 72 h. Relative risks for diastolic dysfunction were calculated based on water balance cut-off points. As can be seen in Table 4, high water balance is associated with an increased risk of diastolic dysfunction. The highest relative risk occurs at 72 h (RR = 13.9), suggesting a cumulative effect, demonstrating a dose-dependent relationship: the higher the cumulative water retention, the greater the likelihood of developing diastolic dysfunction.

Table 3 Analysis of the ROC curve and cut-off points of the water balance with diastolic dysfunction

Variable	AUC (Area Under Curve)	95% CI	Cut-off point (ml)	p
Total balance (72 h)	0.927	0.847–1.000	5755	p < 0.001
Balance at Admission	0.876	0.750–1.000	3265	p < 0.001
24 o'clock balance	0.979**	0.950–1.000	4685	p < 0.001
Balance at 72 o'clock	0.927	0.847–1.000	5755	p < 0.001

** The 24-hour water balance has the **best predictive power** (AUC = 0.979), suggesting that it may be a very reliable indicator for predicting diastolic dysfunction.

Table 4 Risk of diastolic dysfunction with fluid balance

Variable	Dysfunction (n=22)	No dysfunction (n=33)	p	RR (95% CI)
BH intake > 3265 ml	72.70%	6.10%	<0.001	5.4 (2.5–11.6)
BH 24 h > 4685 ml	86.40%	12.10%	<0.001	8.8 (2.9–26.2)
BH 72 h > 5755 ml	90.90%	9.10%	<0.001	13.9 (3.6–53.7)

Additionally, a longitudinal analysis was carried out to compare the behavior of the water balance between patients who developed diastolic dysfunction and those who maintained preserved diastolic function. Patients with diastolic dysfunction consistently presented more positive fluid balances from admission, a difference that was accentuated at 24 and 72 hours. This trend allowed us to identify a sustained pattern of fluid accumulation in the group with diastolic dysfunction throughout the observation period.

Finally, the comprehensive analysis of the results showed that the accumulated fluid balance was significantly associated with the presence and progression of diastolic dysfunction in patients with septic shock. This association remained constant over time and was observed in both the correlation analysis and the relative risk analysis, which provides solidity and coherence to the reported findings.

Discussion

The present study shows that positive cumulative water balance is significantly associated with the development of diastolic dysfunction in patients with septic shock. The findings reinforce the previously described pathophysiology, where volume overload contributes to increased filling pressures and ventricular stiffness, exacerbating diastolic dysfunction assessed by critical echocardiography, specifically through the mitral E/A ratio. The statistical analysis showed a positive and significant correlation between the accumulated water balance and the E/A ratio in the three evaluation moments: admission ($p = 0.531$), 24 hours ($p = 0.560$), and 72 hours ($p = 0.466$), all with $p < 0.001$. This finding suggests that the greater the fluid overload, the greater the degree of alteration of ventricular filling. This association has previously been described by Sirvent et al., who reported that a water balance >2.5 L in the first 72 hours was related to higher mortality and ventricular dysfunction in septic patients.¹⁹

The ROC curves of the present study showed an excellent discriminative power of water balance as a predictor of diastolic dysfunction: AUC of 0.876 at admission, 0.979 at 24 hours, and 0.927 at 72 hours. These data coincide with those of Zhang et al., who demonstrated a dose-response relationship between sustained positive water balance and in-hospital mortality in patients with sepsis.²⁰ The identified cut-off points (3265 mL at admission, 4685 mL at 24 hours, and 5755 mL at 72 hours) offer a potential tool for risk stratification. Relative risk analysis showed that patients who exceeded these thresholds had a significantly higher risk of diastolic dysfunction: RR of 5.4, 8.8, and 13.9, respectively. These data coincide with what was reported by Hyun et al., who observed that a positive balance on days 2 and 3 was associated with higher mortality at 28 days.²¹ From a pathophysiological approach, these findings can be explained by the effect of excess volume on ventricular compliance. In the context of septic shock, characterized by systemic inflammation and increased capillary permeability, fluid overload favors myocardial edema and increased filling pressures, which negatively affect left ventricular relaxation. This has been described by authors such as Vieillard-Baron and Lin, who analyzed the structural and functional changes of the myocardium in sepsis.^{22,23}

A clinically relevant finding was the high frequency of the pseudo-normalized pattern (grade II) of diastolic dysfunction, which can go undetected without functional echocardiography. This underscores the need to incorporate the routine use of critical echocardiography in cardiovascular assessment, as recommended by the European Society of Intensive Care, which recognizes this tool as an essential competence of the modern intensivist.²⁴

From a clinical perspective, diastolic dysfunction in the ICU has been associated with worse outcomes, including longer duration of mechanical ventilation and increased mortality. Pulido et al. They reported that its presence in septic patients is related to an adverse prognosis.²⁵ Studies such as those by Marik and Bellomo have identified that excessive fluid accumulation is related to myocardial dysfunction, longer hospital stay, and mortality.²⁶ Therefore, close monitoring of the accumulated water balance should be considered a key prevention and management strategy. Our study provides direct evidence from a Mexican ICU, using critical echocardiography (POCUS) as a method of continuous functional assessment.

Finally, this work not only strengthens the clinical evidence on the relationship between fluid overload and cardiac dysfunction in sepsis but also provides clinically useful cut-off points to guide individualized therapeutic decisions. Although the single-center design and sample size limit the generalizability of the findings, the prospective approach, the systematic use of functional echocardiography, and the robust statistical analysis give high internal validity to the study.

Conclusion

In patients with septic shock, positive cumulative fluid balance was significantly and consistently associated with the development of diastolic dysfunction, which was assessed by critical echocardiography. This association was present from admission and was maintained at 24 and 72 hours, which confirms that sustained fluid overload exerts a relevant functional impact on ventricular filling in critically ill patients. The positive correlation observed between the cumulative water balance and the mitral E/A ratio in the three evaluation moments, together with the excellent discriminative performance demonstrated by the ROC curves (AUC up to 0.979), supports the value of the water balance as an early and robust functional marker of diastolic dysfunction.

The identified cut-off points of the accumulated water balance (3265 mL at admission, 4685 mL at 24 hours, and 5755 mL at 72 hours) were associated with progressive and large increases in the risk of diastolic dysfunction, with relative risks reaching up to 13.9 at 72 hours. The relative risks underscore the clinical relevance of water balance as a potentially modifiable factor with a direct impact on myocardial function. The high frequency of pseudo-normalized patterns of diastolic dysfunction shows that apparent hemodynamic stability does not exclude significant functional alterations and confirms the limitations of traditional parameters for cardiovascular evaluation in septic patients. In this context, critical echocardiography is consolidated as an essential tool for serial functional assessment and for individualized decision-making in the ICU.

This study provides clinical evidence, systematically integrating echocardiographic monitoring with dynamic analysis of water balance. Despite the limitations inherent in the single-center design and sample size, the prospective approach, the quality of the data included, and the statistical analysis give high internal validity to the results. Taken together, these findings support the implementation of fluid management strategies guided by functional goals, with the goal of preventing cardiac dysfunction and optimizing the prognosis of the patient with septic shock.

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