



## ***Point of care ultrasonography in the evaluation of myocardial dysfunction due to sepsis.***

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### **ORIGINAL ARTICLE**

#### **Summary**

**Background:** Septic shock is commonly diagnosed in critically ill patients and is an important cause of mortality. Techniques used to assess fluid responsiveness and hemodynamic profile with physical examination and central venous pressure have been shown to be insufficient. Thus, the importance of other methods, such as bedside ultrasound (POCUS), is evident. The aim of this study was to analyze patients with septic shock who developed left ventricular dysfunction by POCUS.

**Methods:** Prospective study involving 14 patients diagnosed with septic shock, over 18 years old, without previous cardiac pathologies. Clinical, laboratory and imaging data were collected. POCUS was applied by a cardiology resident; the results were compared with those found by an echocardiographer.

**Results:** Variables were compared between patients with normal and depressed ventricular function (VF). Mean arterial pressure was significantly lower in patients with depressed VF ( $p = 0.01$ ). Vasopressor drug dose and Pro-BNP value were significantly higher in patients with depressed VF ( $p = 0.01$ ). Regarding the POCUS inter-rater comparison, the variables of left ventricular global systolic function, vena cava index and presence of B line were significantly concordant ( $p = 0.02; 0.003; 0.002$ ).

**Conclusions:** Patients with depressed VF had a greater severity of shock, suggesting refractoriness, with cardiac dysfunction as a possible aggravating factor, which was visualized only by POCUS and corroborated by higher Pro-BNP values. A short POCUS training is enough for the non-specialist physician to be able to use this resource in the management of these patients.

**Keywords:** Shock, Septic shock, Left Ventricular Dysfunction, Ultrasound.

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**Dados da publicação:** Artigo recebido em 21 de Agosto e publicado em 01 de Outubro de 2023.

**DOI:** <https://doi.org/10.36557/2674-8169.2023v5n5p22-39>

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## **Background**

Shock is generally defined as a state of cellular and tissue hypoxia due to reduced supply, increased consumption, or inadequate use of oxygen, and may develop because of circulatory failure [1]. Although the definition varies between studies, it is a relatively common situation in the hospital admission of critically ill patients [2].

In the emergency care setting, septic shock is frequently observed (62%) and is considered an independent risk factor for increased mortality [3]. Traditional physical examination techniques, when isolated, may not be as sensitive and specific as the assessment of the shock profile, given its high pathophysiological complexity [4,5]. Studies have shown that a complementary assessment, central venous pressure (CVP), used in certain cases to assess fluid responsiveness, would be a flawed approach in this context [6]. Marik, Baram and Vahid [7] performed a systematic review of the literature showing a very poor relationship between CVP and blood volume, as well as the inability of CVP/DeltaCVP to predict the hemodynamic response to a fluid challenge. Thus, it is advised that CVP should not be used for making clinical decisions regarding fluid management [6].

Currently, the most accurate method to guide fluid administration decisions is through dynamic measurements that estimate the change in cardiac output that occurs in response to a fluid bolus, for which POCUS is very well employed, evaluating the inferior vena cava to estimate preload, and lung ultrasound to identify the early presence of extravascular lung fluid and prevent fluid overload [8]. According to Corl et al [9], in a prospective observational study of critically ill patients, POCUS performs well in distinguishing between fluid responders and non-responders and can be used to guide fluid resuscitation.

Septic shock, when refractory, requires additional evaluations of the patient's clinical condition, one of the evaluation points being the cardiogenic component (left ventricular function), since, in the study by Lanspa et al. [10], which evaluated 393 patients, 63% of individuals evolved with cardiac dysfunction, increasing mortality by up to 3 times in these cases.



Shock patients have high mortality rates, and these rates are related to the magnitude and duration of hypotension [11]. Therefore, the clinical evaluation and the correct etiological diagnosis of shock, as well as its progression regarding other associated components, such as ventricular dysfunction, must be accurate and quickly listed for the best evolution of the patient [4,11].

A randomized clinical trial involving 184 patients with undifferentiated hypotension, published in 2004, showed that immediate and targeted ultrasound increased the rate of correct diagnosis of shock etiology from 50% to 80% [5]. A recent case series proposed point-of-care ultrasound (POCUS) for diagnosing the type of shock and monitoring its evolution [12,13]. It is recommended as a first-choice modality in consensus guidelines [14]. No other investigational bedside tool can offer a similar diagnostic capability, allowing for the exact targeting of underlying cardiac and hemodynamic problems [15,16].

Physicians can become proficient in POCUS with minimal training, and its use has been shown to improve diagnostic accuracy, reduce procedural complications, shorten hospital stays, and improve patient satisfaction [14,17,18,19]. There are several protocols for diagnosing the etiology of shock. In 2010, the RUSH protocol (Rapid ultrasound in shock and hypotension) [20] and the FATE protocol were published, which can be used as a screening, monitoring tool and to evaluate the effects of therapeutic interventions [21,22]. The qualitative assessment of the global systolic function of the left ventricle is known by the term eyeballing, which is very useful and practical to indirectly estimate whether there is any degree of impairment of the systolic function [23].

The present study prospectively analyzed the accuracy of bedside ultrasound in a cohort of critically ill patients with septic shock. Clinical and laboratory signs of poor perfusion were evaluated, as well as left ventricular impairment through ultrasound in conjunction with Pro-BNP and troponin, pulmonary congestion and blood volume. Thus, this study raises the hypothesis that the association of point-of-care ultrasound could influence the management of shock, such as the identification of cardiac dysfunction due to sepsis, which could lead to targeted procedures for this diagnosis. That said, ultrasonography is a useful tool in the differential diagnosis and treatment of shock, not



only in its initial period, but also for continued evaluation, especially when the etiology is undifferentiated or multifactorial.

## **Methods**

### **Recruitment**

The patients were selected by the diagnosis of septic shock, being people admitted to the Emergency Room of the Hospital University Maria Aparecida Pedrossian - HUMAP in Campo Grande - MS, from July 2022 to February 2023, who used the Public Health System. Included were patients of both sexes; aged between 18 and 90 years; diagnosed with septic shock; no previous diagnosis or suspicion of heart failure; in attendance in the sector of emergency medical care. The following were not included: patients under 18 years of age and over 90 years of age; no diagnosis of septic shock; with a previous diagnosis of heart failure; from other sectors of the hospital in question; with suspicion of previous heart failure based on the anamnesis collected from the patient and family members.

### **Research Outline**

The patients invited to participate in the study met the inclusion and non-inclusion criteria and signed the informed consent form. In cases of unconscious patients, the Informed Consent Form was applied to their legal guardian. The protocol consisted of care provided at the Emergency Room with ultrasound at the bedside, for a total n of 14 patients.

### **Data collect**

The individuals underwent anamnesis focusing on the previous history of comorbidities and symptoms that could increase the suspicion of previous heart failure (systemic arterial hypertension, type 2 diabetes mellitus, dyslipidemia, smoking, previous acute myocardial infarction, orthopnea, paroxysmal nocturnal dyspnea, dyspnoea on exertion or knowledge of previous heart failure). Age verification was performed, auscultation with S3 or S4, vital signs with non-invasive mean arterial pressure and heart rate, as well as the focus of septic shock. Secondary variables were

collected, such as date of onset of shock and use of vasoactive drugs, diuresis in the last 6 hours and fraction of inspiratory oxygen.

To exclude suspected heart failure, symptoms related to exertion and rest were explored. According to Mann et al. [21] the most common signs and symptoms include dyspnea, fatigue, limited exertion, orthopnea, and edema. In a review of 22 studies of adult patients who presented to a hospital emergency room with dyspnoea, the possibility of heart failure was best suggested through a previous history of heart failure, paroxysmal nocturnal dyspnoea of a third heart sound, or of atrial fibrillation [24].

### **Central venous blood gases, arterial blood gases and troponin**

Venous blood was collected for central venous blood gas analysis to check central venous oxygen saturation (SVC<sub>O</sub>2) and another sample for troponin and pro-BNP assessment via laboratory tests. Arterial blood was collected for arterial blood gas analysis to check the partial pressure of oxygen (PO<sub>2</sub>), partial pressure of carbon dioxide (PCO<sub>2</sub>), pH, lactate, and bicarbonate (HCO<sub>3</sub>). An evaluation of the CO<sub>2</sub> GAP was carried out using two gasometries, arterial and central venous.

### **Point-of-Care Ultrasound - POCUS**

Bedside ultrasound (EVUS 8 – Saevo, 2020) was performed, recording left ventricular function, measurement of the inferior vena cava (with evaluation of the vena cava index), and the presence of B lines. FATE during the evaluation. The protocol was performed by a first-year cardiology resident, trained in POCUS, with a training time of 12 hours. During the exam, the images were saved and sent to an experienced echocardiographer, who performed his evaluation. The evaluations of the images were carried out in a blind study model in which none of the researchers knew the evaluation of the other. Subsequently, the results were compared.

Oxygen saturation was estimated by pulse oximetry with a Dixtal XR 2010 model device (Biomédica, Manaus, AM, Brazil). Blood pressure was measured manually using a sphygmomanometer (ANEROIDES PREMIUM, China, 2019).

### **Data analysis**

Measures of numeric variables were expressed as median and interquartile range. For comparisons between groups, the Mann-Whitney test was used. To verify the agreement between the examiners, the Kappa Reproducibility Index was used. Data normality was analyzed using the Liliefors test. Values of  $p < 0.05$  were considered significant. Data analysis was performed using the Bioestat 5.0 program.

## **Results**

### **Evaluation of patients and results of laboratory tests**

In the present analysis, 14 patients between 40 and 76 years old were included; all had a confirmed diagnosis of sepsis. The overall mean age was  $59.07 \pm 12.83$  years and 10 (71.4%) were male. The observed age in the depressed VF group was  $46.0 \pm 6.5$  years and in the normal VF group  $67.0 \pm 23.0$  years ( $p = 0.1027$ ).

The baseline comorbidities observed were systemic arterial hypertension (28.5%), type 2 diabetes mellitus (28.5%), HIV (28.5%), smoking (14.2%), stroke (14.2%), chronic obstructive pulmonary disease (7.14%).

The focus of septic shock was predominantly pulmonary (78.5%), followed by abdominal (7.14%), cutaneous (7.14%) and urinary and cutaneous simultaneously (7.14%). Non-invasive mean blood pressure (measured with a cuff suitable for the patient) was  $73.57 \pm 11.20$  and heart rate  $101 \pm 24.55$ . When quantifying the diuresis of the last 6 hours, the presented mean was  $308.92 \pm 292.79$  ml. Regarding arterial blood gases, the pH found was  $7.33 \pm 0.10$ , venous carbon dioxide saturation (SVCO<sub>2</sub>) of  $81.42 \pm 6.81$ , PO<sub>2</sub>/FIO<sub>2</sub> ratio of  $278.78 \pm 129.90$ ,  $19.32 \pm 8.53$ , lactate  $3.53 \pm 3.96$ , CO<sub>2</sub> GAP  $6.27 \pm 3.71$ . Troponin quantification showed results of  $473.78 \pm 1102.47$  and Pro-BNP of  $8157 \pm 11624$ . All patients were under mechanical ventilation at an inspired fraction of oxygen of  $39.71 \pm 16.13$ . All patients used noradrenaline at a mean dose of  $0.33 \pm 0.32$  mcg/kg/min. And only 14.28% of patients needed a second vasoactive drug, using vasopressin.

Mean arterial pressure (MAP) was statistically significant when comparing patients with depressed and normal ventricular function ( $p = 0.0109$ ), and patients with depressed VF had lower MAP values. Another statistically relevant variable was Pro-BNP, which was higher in patients with depressed VF ( $p = 0.0131$ ).

The noradrenaline dose ratio in patients with depressed and normal ventricular function was statistically significant ( $p = 0.0131$ ), with a higher usual dose being observed in patients with depressed VF. The duration of vasoactive drug use in days was  $4.86 + 5.24$ , with patients with depressed ventricular function having a longer duration of use compared to individuals with normal VF ( $p = 0.1332$ ). See table 1.

### **POCUS assessment and comparison between resident and specialist physician**

During the performance of the POCUS by the first-year cardiology resident, data on the global systolic function of the left ventricle found, with the eyeballing technique, were that 28.57% of the patients had depressed VF. The measurement of the vena cava evaluated during inspiration under mechanical ventilation was  $1.80 \pm 0.39$  cm and during expiration under mechanical ventilation,  $1.52 \pm 0.39$ . The vena cava index under mechanical ventilation was classified as turgid ( $< 18\%$ ) in 57.14% of the patients. The presence of B lines was found in 42.85% of the patients.

The data found by the experienced echocardiographer agreed in the assessment of all patients in relation to the global systolic function of the left ventricle using the eyeballing technique. Regarding the vena cava index, agreement was observed at 0.8571, with Kappa index (coefficient of agreement) 0.7143, being statistically significant ( $p = 0.0038$ ). As for the evaluation of the presence of B lines, only 14.28% of the patients presented different results between the evaluators, with a Kappa index (coefficient of agreement) of 0.72, which was statistically significant ( $p = 0.0025$ ). See table 2.

### **Debate**

In the present study, we prospectively evaluated 14 patients diagnosed with septic shock, aged between 40 and 76 years, observing a high prevalence of males, previously published studies also show a higher number of patients of this gender [25]. Patients were divided into 2 subgroups: with depressed VF and with normal VF, evaluated using POCUS. Similar comorbidities (systemic arterial hypertension, diabetes, HIV) were observed among patients. The prevalence of pulmonary focus in septic shock presented by patients is consistent with previously published data [26].

As they were patients in shock, all individuals were hypotensive and using vasoactive drugs, however, when comparing patients with depressed and normal VF,



patients with depressed VF had lower MAP values, while used higher doses of vasopressor drugs.

Therefore, the hypothesis of underdiagnosis of ventricular dysfunction in septic shock should be raised here. The suspicion that these patients could be candidates for inotropic drugs, after the assessment of left ventricular function by POCUS, must be considered. Since patients with depressed VF, despite a higher dose of vasopressor drug, had a lower MAP, it is believed that there is a refractoriness of the shock at this moment, with the possible cause of this being left ventricular dysfunction, which until the time of the bedside ultrasound evaluation, it had not been detected.

Regarding laboratory tests such as arterial lactate, CO<sub>2</sub> GAP and SVCO<sub>2</sub>, no statistically significant difference was found between the groups with depressed VF and normal VF. Another piece of information collected was urine output in the last 6 hours, which also showed no difference between the two studied groups. See Table 1. Such data suggest that in patients with septic shock, with possible progression to refractory shock, such parameters are less significant for assessing cardiac dysfunction due to sepsis.

The Pro-BNP values found were significantly higher in patients with depressed VF. Published studies show higher mean values of Pro-BNP among patients with left ventricular dysfunction [25]. It is known that the plasma BNP level is closely related to the severity of left ventricular dysfunction [27, 28, 29]. This result is important for the present study and corroborates the assessment of ventricular dysfunction assessed by point of care ultrasound.

Troponin tended to higher values in depressed VF, but without statistical significance. In published studies, depressed VF has been reported to significantly correlate with elevated troponins in severe sepsis, [26] this fact may reflect impaired myocardial relaxation and imbalance in oxygen supply demand, possibly resulting from excess catecholamines, tachycardia or microvascular dysfunction [25].

A recent case series proposed POCUS for diagnosing the type of shock and monitoring its progression [12, 13]. It is recommended as a first-choice modality in consensus guidelines [14]. No other investigational bedside tool can offer a similar diagnostic capability, allowing for the exact targeting of underlying cardiac and hemodynamic problems [15, 16]. As a result, there has been a significant increase in the



adoption of POCUS in recent decades [30]. The advent of smaller and more portable machines, combined with improved image quality, has brought ultrasound out of the radiology department [31]. In 2010, the practice of focused assessment of trauma ultrasound (FAST) became widespread and the Royal College of Emergency Medicine introduced POCUS as a mandatory component of the emergency medicine curriculum.

Studies have shown that clinicians can be trained in a short period of time to determine left ventricular function, determine intravascular fluid status, and detect pericardial effusion [14]. When ultrasound was applied to more than 1 anatomical area, the training time ranged from 4 to 320 hours, depending on the level of detail of the exams. For focused POCUS exams, practitioners received 2 to 31 hours of training [32]. The cardiology resident in this study underwent a 12-hour POCUS training. Studies have shown that clinicians can be trained in a short period of time to determine left ventricular function, determine intravascular fluid status, and detect pericardial effusion [14]. The use of ultrasound in emergency care is associated with better results, greater satisfaction, and a decrease in complications in patients [33]. Smalley et al. [34] implemented a successful training curriculum for 106 physicians, showing improvement in urgent and emergency care.

When comparing the findings of the resident physician in cardiology and the specialist in echocardiography, the results of the present study were satisfactory, with a convincing and statistically relevant concordance index in all the evaluated ultrasound variables. That said, what was previously published is confirmed, that a short-term training can be beneficial for the management of patients in shock [14,17,18,19].

Our study has some limitations. We have a relatively small n of patients, and the patients did not have serial ultrasound evaluations. There was a limitation of excluding patients with possible previous heart failure only with a previous clinical history, with symptoms and risk factors that could suggest such a diagnosis. The main strength of our study is the selection of exclusively septic shock cases, with a robust clinical, laboratory and ultrasound evaluation of each case, as well as the double analysis of all ultrasound exams, both by the 1st year cardiology resident and by an experienced echocardiographer, and inter-rater comparison can be performed. In addition, we performed the evaluation of a Brazilian sample, which has a heterogeneous ethnic origin [35].



## **Conclusion**

Patients with depressed VF tend to have lower MAP despite the use of a higher dose of vasopressor drugs, suggesting an evolution with refractory shock, where the cardiac dysfunction factor due to sepsis could only be considered after the use of Point of Care Ultrasound. Other clinical and laboratory data generally used together to evaluate cardiac dysfunction were analyzed, such as diuresis, SVCO<sub>2</sub>, CO<sub>2</sub> GAP and lactate, and in none of them was there any difference between the depressed VF and normal VF groups. This consideration reinforces that the point of care ultrasound was fundamental for the identification of ventricular dysfunction in these cases.

Patients with depressed VF had significantly higher Pro-BNP values, which is important to corroborate the assessment of ventricular dysfunction visualized by point of care ultrasound.

A short period of POCUS training is enough for a non-specialist physician to use point-of-care ultrasound to assist in the diagnosis and management of patients, which may lead to better prognoses.

New studies on the applicability of POCUS in patients with septic shock are encouraged given the importance of early diagnosis for decision-making in critically ill patients. Based on the evaluation of cardiac dysfunction by POCUS, the possibility of introducing an inotropic drug, as well as other conducts aimed at cardiovascular diagnosis, in patients with septic shock, is mentioned. It is believed that more assertive and earlier measures in the management of refractory shock would be implemented with the application of point of care ultrasound in clinical practice, since its use was substantial for the premature diagnosis of ventricular dysfunction in these patients.

## **Disclosure**

**Thanks:** None

**Financing:** None

**Other Disclosures/Conflicts of Interest:** None



**Ethical approval:** This was a prospective randomized study carried out at the University Hospital of Mato Grosso do Sul (HUMAP/UFMS), in Campo Grande, using the physical space of the Emergency Room. This study was conducted in accordance with recognized ethical standards in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the University Hospital (protocol number 5.500.714/CAAE 58756122.0.0000.0021). Written informed consent was obtained from patients or legal representatives.

**Disclaimers:** None

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Tables

Table 01: Comparison of measurements of the variables days of VAD, noradrenaline dose, mean arterial pressure, heart rate, diuresis (last 6 hours), SvCO<sub>2</sub>, lactate, GAP CO<sub>2</sub>, vena cava measurement (inspiration), vena cava measurement (expiration), troponin and Pro-BNP between the studied groups. Campo Grande-MS, 2023 (n = 14).

	<b>Depressed VF</b>	<b>VF Normal</b>	<b>p-value</b>
DVA days	7,0±4,5	3,0±2,0	0,1332
Noradrenaline dose	0,5±0,5	0,3±0,2	0,0131
Mean arterial pressure	65,0±6,0	75,0±13,5	0,0109
Heart rate	111,0±34,0	94,0±20,5	0,7940
Diuresis (last 6 hours)	300,0±300,0	200,0±587,5	0,4334
SvCO <sub>2</sub>	74,0±8,0	80,0±8,5	0,3961
Lactate	3,9±3,5	1,7±1,7	0,2149
GAP CO <sub>2</sub>	10,0±5,0	5,0±4,1	0,1917
Vena cava measurement (inspiration)	1,6±0,2	1,8±0,6	0,6953
Vena cava measurement (expiration)	1,4±0,3	1,4±0,7	0,3608
Troponin	123,0±2106,5	88,0±270,5	0,2400
Pro-BNP	35000,0±15444,5	2098,0±3918,5	0,0131

DVA Days: Vasoactive Drug Days. SvO<sub>2</sub>: Venous Carbon dioxide Saturation. GAP CO<sub>2</sub>: Anion Gap of Carbon dioxide. Pro-BNP: Brain Protein Natriuretic Peptide.

Table 02: analysis of inter-rater reproducibility for measurements of LV global systolic function (LVSGF), vena cava index (CVI) and presence of B line (PLB), Campo Grande-MS, 2023 (n = 14).

	<b>Observed agrément</b>	<b>Kappa index (k)</b>	<b>p-value</b>
LVSF	0,7857	0,5116	0,0262
CVI	0,8571	0,7143	0,0038
PLB	0,8571	0,7200	0,0025
	<b>Replicability</b>	<b>Kappa Concordance</b>	-
LVSF	Good	Regular	-
CVI	Good	Good	-
PLB	Good	Good	-

LVSF: Left Ventricular Global Systolic Function. CVI: Vena Cava Index. PLB: Line B Presence.