

Association of inferior vena cava diameter in the emergency room and early mortality in septic patients

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Abstract

Introduction: Sepsis is a worldwide condition that affects nearly 30 million people and causes about 6 million deaths per year. QuickSOFA (qSOFA) has limitations in identifying at-risk patients in the emergency room. There is no known association of inferior vena cava diameter measured through Point-of-Care Ultrasound (POCUS) and mortality in septic patients. **Methods:** We included 39 septic patients admitted to the emergency room that received a POCUS evaluation with IVC diameter measures. One attending performed all ultrasound evaluations. Patients were analyzed according to non-dilated IVC (less than 20 mm) and dilated (more than or equal to 20 mm). **Results:** Overall in-hospital mortality was 33%, more frequent in the dilated IVC group (66,7% vs 27,3%) without statistical significance. The dilated IVC group had non-significant more frequencies of mechanical ventilation, ICU admission and use of vasopressors. Early-mortality (defined as less than 72 hours) was more frequent in the non-dilated group (70%) vs the dilated group (0%) with a significant p-value 0.01. **Conclusion:** Septic patients in the emergency room with a POCUS IVC diameter less than 20 mm are more likely of early mortality within 72 hours of admission. This finding must be confirmed with prospective research and controlling confounders.

Keywords: POCUS. Inferior vena cava. Sepsis. Mortality.

Asociación del diámetro de la vena cava inferior en el servicio de urgencias y la mortalidad temprana en pacientes con sepsis

Resumen

Introducción: La sepsis es una condición que mundialmente afecta a cerca de 30 millones de personas y ocasiona alrededor de 6 millones de muertes por año. La escala quickSOFA se ha utilizado para identificar pacientes en riesgo de deterioro en el servicio de urgencias, aunque con limitaciones en su capacidad diagnóstica. No se conoce asociación entre el diámetro de la vena cava inferior (VCI) por ecografía clínica (POCUS, Point-of-Care Ultrasound) y la mortalidad temprana en pacientes con sepsis. **Métodos:** Incluimos 39 pacientes que ingresaron al servicio de urgencias a quienes se les realizó una evaluación POCUS al ingreso con medición de la VCI. El médico internista tratante realizó la evaluación. Los pacientes fueron analizados de acuerdo con la condición de la VCI dilatada (≥ 20 mm) o no dilatada (< 20 mm). **Resultados:** La mortalidad intrahospitalaria global en el grupo estudiado fue del 33%, mayor en el grupo de pacientes con VCI dilatada (66,7% vs. 27,3%). El grupo de pacientes con VCI dilatada tuvo mayor frecuencia de ventilación mecánica, ingreso a la unidad de cuidados intensivos y uso de vasopresores. La mortalidad temprana (< 72 horas de ingreso) fue más frecuente en el grupo de pacientes con VCI no dilatada (70%) que en el grupo de pacientes con VCI dilatada (0%) ($p = 0.01$).

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Conclusiones: *Los pacientes sépticos en el servicio de urgencias con una medición de la VCI por POCUS al ingreso < 20 mm tienen más probabilidad de fallecer antes de las 72 horas. Este hallazgo debe ser confirmado por estudios prospectivos con control de confusores y una mayor muestra.*

Palabras clave: *POCUS. Vena cava inferior. Sepsis. Mortalidad.*

Introduction

Sepsis is a worldwide condition that affects nearly 30 million people and causes about 6 million deaths per year. A large part of the mortality and morbidity rates are linked to hosts' dysregulated response to infection leading to shock and death¹. So far, the most important way to mitigate its burden is to approach each patient in a timely manner and provide targeted treatment².

The clinical spectrum of sepsis forces clinicians to prioritize interventions in patients with increased risk of deterioration. One of the most used prediction tools is the quick Sequential Organ Failure Assessment (qSOFA), implemented as a fast bedside clinical score to aid in the identification of specific patients with a higher risk of death. The qSOFA has a good performance predicting in-hospital mortality (AUROC 0.81), nonetheless a sensitivity of 48% and known pitfalls make qSOFA a limited tool regarding the stratification of at-risk patients in the emergency department³. Other studies with the objective of predicting sepsis-related mortality with SOFA (Sequential Organ Failure Assessment Score), qSOFA and lactate clearance have had conflicting findings⁴⁻⁶.

Point-of-care-ultrasound (POCUS) helps clinicians identify critical diagnoses enabling decisive interventions in a timely fashion⁷. Inferior Vena Cava (IVC) visualized through POCUS at the bedside is a rapid way to approximate the volemic state in septic patients and guide fluid management, although with limitations^{8,9}. The use of ultrasound in emergency medicine has grown in the past years, demonstrating an added value to the bedside clinical exam¹⁰. An important goal in sepsis evaluation and management at the emergency room is to have a fast, easy, and reproducible approach to identify patients with elevated risk of death at emergency room admission.

There is no known association of inferior vena cava diameter measured through POCUS and mortality in septic patients. Hence, our study evaluated the relation between IVC diameter and early mortality in septic patients at the emergency room.

Methods

This is a single center cross-sectional study that analyzed patients admitted to the emergency room at a university-based hospital from January 2019 to December 2020. Our Hospital Universidad del Norte is a one hundred and twenty bed institution with 90.000 emergency room visits per year. Patients with sepsis suspected at emergency admission were initially included. The Universidad del Norte Ethics Committee and The Institutional Review Board of Hospital Universidad del Norte approved this protocol (Act 216/2020).

Sepsis diagnosis had to be made at entrance and confirmed at discharge as final diagnosis and was defined as suspected or confirmed infection plus organ dysfunction represented by SOFA score greater than or equal to 2 points. These patients received the standard treatment including intravenous crystalloids, antibiotics and cultures plus supportive measures.

All patients had a POCUS evaluation within the first 6 hours of admission, including IVC diameter measurement, collapsibility index and qualitative systolic function. All ultrasound evaluations were performed by one attending internist in the emergency room, who has POCUS formal training and experience of more than one hundred studies performed in two years. Equipment used was Sonoscape Model S2 2016-03 (Sonoscape Medical Corp. China) using B-mode, M-mode and Doppler as required. The IVC measurements were obtained from the subxiphoid view using the M-mode longitudinal diameter in expiration at 2cm from the atrio-caval union. Calculation of Collapsibility Index (CI) used expiration diameter (ExpD) and inspiration diameter (InsD) of inferior vena cava ($\text{ExpD} - \text{InsD} / \text{ExpD}$)¹¹. We defined collapsibility as a CI $\geq 50\%$. Exclusion criteria were a final diagnosis different to sepsis, patient on mechanical ventilation upon ultrasound exploration, abdominal masses, pulmonary hypertension, or a condition that led to equivocal IVC measurements as non-proper subxiphoid view (Fig. 1).

Patients received standard care according to sepsis guidelines to that moment and attending physician criteria. Intravenous fluids were given before and after IVC measures. Antibiotics and vasopressors were initiated

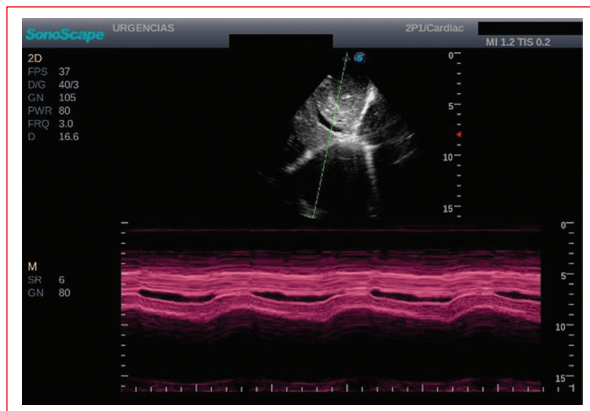


Figure 1. Subxiphoid view of the inferior vena cava (IVC) with M-mode calculating.

if needed and when needed. IVC diameter was not part of decision-making process.

Individuals with a confirmed diagnosis of sepsis and a valid measure of IVC were included in the final analysis. Population was divided in patients with non-dilated IVC (less than 20 mm diameter) and patients with a dilated IVC (more than or equal to 20 mm diameter). Basal characteristics were analyzed in each group. We extracted from medical records all demographic, clinical, laboratory variables and ultrasound evaluations. In-hospital early mortality was the outcome variable, defined as death occurring during the first 72 hours of admission. We chose this definition as previous reports had used it and considering the best moment of the clinical management of the patient that reflected the initial severity and the initial interventions carried out with its impact on mortality¹².

Statistical analysis

The continuous variables are reported as median and interquartile ranges (IQR), and categorical variables are reported as absolute and relative frequencies. Univariate and bivariate analysis were performed. The Mann-Whitney U test was used for comparing continuous variables and chi-square or Fisher's test for qualitative variables. For all comparisons, a two-tailed p-value less than 0.05 was considered statistically significant. Analyses were performed using IBM SPSS Statistics version 25.

Results

A total of 39 patients were included in the analysis. We found a predominantly older than 65 years

population (53.8%), most of them females (59%) with signs of inflammatory response at admission. Median heart rate was 100 beats per minute, median systolic and mean blood pressure were 100 and 73 mmHg, respectively. Median quick SOFA at Emergency Department evaluation was 3 points. Inflammation markers and lactate were elevated. Median Sequential Organ Failure Assessment (SOFA) was 8 points. The predominant source of infection was respiratory (48%), followed by urinary tract infection (23%). Regarding clinical evolution, 19 (48.7%) patients required Intensive Care Unit (ICU) admission, 28 (71.8%) received vasopressor and 24 (61.5%) needed mechanical ventilation. Overall in-hospital mortality occurred in 13 patients (33.3%).

Bivariate analysis considering patients with dilated and non-dilated IVC showed the same median age around 68 years old, greater number of females in the normal IVC group without statistical significance. Clinical presentation regarding heart rate, systolic and mean blood pressure was the same among groups. Lactate was more elevated in the dilated group without statistical significance. There were no differences in laboratory values, source of infection, qSOFA and SOFA scores between both groups. Regarding clinical variables, the dilated IVC group had greater in-hospital mortality (66,7 vs 27,3% p 0.06), vasopressor use (83,3 vs 69,7%), need for mechanical ventilation (83,3 vs 57,6%), all of which had no statistical significance (Table 1).

Regarding early mortality, zero patients died in the dilated group compared to 7 (70%) patients in the non-dilated group with a significant p value 0.018 (Figure 2).

Discussion

In this study we found an association between early mortality in septic patients and the IVC diameter measured through POCUS. A non-dilated IVC was related with more in-hospital mortality during the first 72 hours of admission. Conversely, the overall mortality was more frequent in the dilated-IVC group.

There are several studies that associate IVC with fluid responsiveness and volemia in septic patients^{8,9}. Protocols assessing the use of POCUS to diagnose volemia in septic shock patients have showed encouraging results¹³. Regarding mortality association with IVC diameter or its measurement through POCUS, there is a lack of knowledge with scarce or null evidence, which motivated our study in the first instance.

Table 1. Basal Characteristics of population

	All (n = 39)	Normal (< 20 mm) (n = 33)	Dilated IVC (≥ 20 mm) (n = 6)	p value
Demographic and Clinical Variables				
Age years	69 (55-78)	69 (54-78)	68 (50-77)	0,84
> 65 yo	21 (53,8)	18 (54,5)	3 (50)	0,83
Female	23 (59)	21 (63,6)	2 (33,3)	0,20
Heart rate bpm	100 (88-125)	97 (83-130)	111 (104-120)	0,45
Systolic blood pressure mmHg	100 (76-122)	90 (73-121)	117 (93-132)	0,22
Mean blood pressure mmHg	73 (53-88)	66 (52-87)	82 (68-101)	0,19
C-reactive protein mg/dl	142 (99-160)	148 (99-167)	134 (94-143)	0,21
Creatinine mg/dl	1,5 (1,28-2,50)	1,5 (1,2-2,7)	1,3 (0,8-2,2)	0,22
Serum lactate mmol/L	4,38 (1,7-7,18)	3,9 (1,6-7)	5,3 (3,6-10)	0,45
Community Acquired Pneumonia	19 (48,7)	14 (42,4)	5 (83,3)	0,59
Urinary tract infection	11 (28,2)	10 (30,3)	1 (16,7)	0,59
Other source of infection	9 (23,1)	9 (27,3)	0	0,73
Quick SOFA	3 (2-3)	3 (2-3)	3 (2-3)	0,48
SOFA	8 (4-10)	8 (3-10)	9 (5-11)	0,21
Systolic Dysfunction (POCUS)	7 (17,9)	7 (21,2)	0 (0)	
Clinical Variables				
ICU admission	19 (48,7)	15 (45,5)	4 (66,7)	0,40
Vasopressor	28 (71,8)	23 (69,7)	5 (83,3)	0,65
Mechanical ventilation	24 (61,5)	19 (57,6)	5 (83,3)	0,37
In-Hospital Mortality	13 (33,3)	9 (27,3)	4 (66,7)	0,06

All categorical variables are expressed in absolute frequencies (#) and percentages (%). Quantitative variables are expressed in median and interquartile ranges. Significant p value was considered < 0.005.

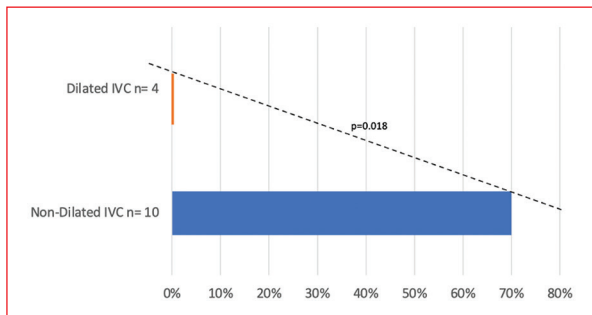


Figure 2. Early Mortality (<72 hrs) according to IVC Diameter. Relative frequencies of early in-hospital mortality according to IVC diameter. Patients with non-dilated IVC (< 20 mm) presented 7 in-hospital deaths (70%) before 72 hours of admission, compared to patients with dilated IVC (≥ 20 mm) whom had no in-hospital death before 72 hours of admission.

One study analyzed the IVC diameter ratio by computed tomography with in-hospital mortality in septic shock patients finding an elevated mortality in the group of dilated IVC (OR 1.48 IC95% 1.09 – 1.99), which is consistent with the in-hospital mortality in our study¹⁴. In this study, patients were given fluids before IVC measurement, same situation happened in our Emergency Room. We found only 6 patients having dilated IVC in our study. Almost all these patients were admitted to the ICU, received vasopressors, went on

mechanical ventilation and eventually died after 72 hours of in-hospital treatment. This set of patients may represent the aggressive fluid challenge during resuscitation phase and all its consequences, such as hypervolemia, cardiac dysfunction related to sepsis, failed mechanical ventilation weaning, common in septic patients and related to in-hospital mortality¹⁵.

On the other hand, we found that only non-dilated IVC patients died in the first 72 hours of admission. This finding is remarkable, denoting an early mortality possibly linked to hypovolemia or a severe vasodilation state leading to relative hypovolemia and death in a short period of time, not correctable with intravenous fluids in resuscitation phase. The first 72 hours of management in septic patients include the resuscitation, optimization and stabilization phases of fluid use thus all the interventions done at this stages of management could explain and affect the outcome evaluated¹⁶. We found an association that does not pretend to establish causality, but to show a possible relation of a simple, easy and fast evaluation at the bedside like POCUS with an important outcome in a specific set of patients with a high mortality.

Our patients were treated as guidelines pointed to be standard of care. Were given a 30cc/kg bolus of crystalloids at sepsis recognition, vasopressors when needed and antibiotics within the first hour of sepsis diagnosis. We did not analyze these interventions given that were

standard of care (all patients received them) and our study was not powered to combine or adjust for this time-dependent variables. It is a fact that a timely-response to septic patients (early antibiotics, vasopressors, IV fluids) improves clinical outcomes and death rates¹⁵.

Our study is a small-sample analysis with inference limitations due to lack of power, not controlled clinical interventions, and confounding factors such as fluids balance, time of antibiotics and vasopressors initiation, but with valuable information about community septic patients that encourages a more detailed analysis of IVC diameter and its relationship with in-hospital sepsis-related mortality. To our knowledge, this is the first study to analyze the association between IVC diameter and mortality, thus promoting more research aiming to include the measurement of IVC diameter through POCUS as a predictor of early death in septic patients, along with evaluation of treatment strategies that lead to early mortality reduction.

Conclusion

In conclusion septic patients in the emergency room with a POCUS IVC diameter less than 20 mm are more likely of early mortality within 72 hours of admission. This finding must be confirmed with prospective research and controlling confounders.

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Conflicts of interest

None of the authors have a conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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