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ORIGINAL PAPER

Prognostic value of Doppler waveform analysis of common femoral vein in septic patients: a prospective cohort study

Nathalia Helbig Dias[1,2] · Douglas Rodrigues Gomes[1] · Ana Claudia Tonelli de Oliveira[1] · José Augusto Santos Pellegrini[1] · Márcio Manozzo Boniatti[1,2]

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Abstract

Objectives To assess whether there is an association between abnormal common femoral vein (CFV) Doppler waveform and intensive care unit (ICU) mortality in patients with sepsis.

Methods Patients admitted to the ICU with sepsis were included. Pulsed-wave Doppler was performed by examining the CFV in the short axis without angle correction and in the long axis with angle correction. An abnormal CFV Doppler waveform was determined by a retrograde velocity peak (RVP) > 10 cm/s in the long axis or RVP > 50% of the antegrade velocity peak in the short axis. TAPSE < 17 mm was defined as right ventricular (RV) dysfunction. The primary outcome was ICU mortality.

Results One hundred and ten patients were included. There was no association between abnormal CFV Doppler waveforms in the long ($p = 0.709$) and short axes ($p = 0.171$) and ICU mortality. TAPSE measurements were performed in 16 patients. RV dysfunction was identified in 8 (50.0%) patients. There was no association between the diagnosis of RV dysfunction based on TAPSE measurement and the identification of abnormal CFV Doppler waveforms in the long axis ($p = 1.000$) and in the short axis ($p = 1.000$).

Conclusion Abnormal CFV Doppler waveforms were not associated with ICU mortality in patients with sepsis. Furthermore, in the exploratory analysis, these alterations were not useful in identifying RV dysfunction in these patients.

✉ Nathalia Helbig Dias
nhdias@hcpa.edu.br

Douglas Rodrigues Gomes
drgomes@hcpa.edu.br

Ana Claudia Tonelli de Oliveira
actoliveira@hcpa.edu.br

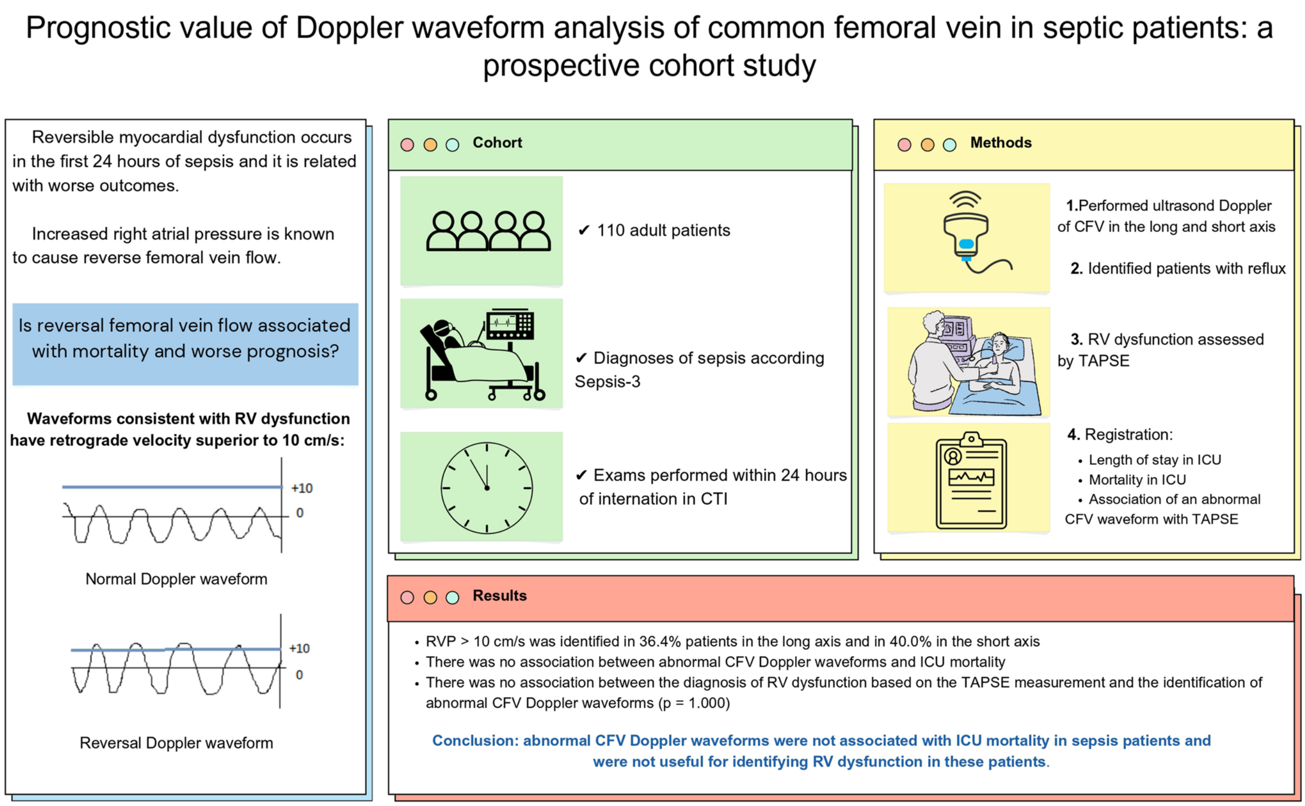
José Augusto Santos Pellegrini
jpellegrini@hcpa.edu.br

Márcio Manozzo Boniatti
mboniatti@hcpa.edu.br

1 Hospital de Clínicas de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil

2 Postgraduate Program in Health Sciences: Cardiology and Cardiovascular Sciences, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil

Graphical abstract



Keywords Common femoral vein · Right ventricular dysfunction · Sepsis · Pulsatility · Doppler ultrasound · Right atrial pressure

Abbreviations

CFV	Common femoral vein
ICU	Intensive care unit
RV	Right ventricular
RAP	In right atrial pressure
PWD	Pulsed-wave Doppler
TAPSE	Tricuspid annular plane systolic excursion
MV	Mechanical ventilation
RRT	Renal replacement therapy
DUS	Duplex ultrasound
RVP	Retrograde velocity peak

Introduction

Sepsis is one of the main causes of admission to the intensive care unit (ICU) [1] and is characterized by multiorgan dysfunction due to dysregulated inflammation in response to infection [2]. Early and timely fluid resuscitation is a basic measure in the treatment of sepsis. Nonetheless, aggressive fluid resuscitation beyond reversal of hypovolemia may have side effects [3, 4]. Previous studies have demonstrated that a positive fluid balance over time is associated with higher mortality in patients with sepsis [5, 6]. Furthermore, right ventricular (RV) dysfunction, associated or not with positive fluid balance, has been frequently reported in patients with sepsis, being associated with worse outcomes [7, 8].

The femoral vein is an extension of IVC and reflects a window to estimate right atrial dynamics [9]. With an increase in right atrial pressure (RAP), due to RV dysfunction, venous congestion and venous distension occurs in the splanchnic circulation and the pressure waveforms is transmitted to more distal venous circulation, including the common femoral vein (CFV). Pulsed-wave Doppler (PWD) of the portal vein and renal venous circulations have been correlated with RV dysfunction and venous congestion [10–17] and there is a strong correlation between femoral venous Doppler and splanchnic solid organ venous Doppler [9].

In the absence of pathology in the venous system of the lower limbs, examination of venous flow at the level of the femoral vein using Doppler may be practical for the evaluation of volume overload, venous congestion, and RV dysfunction [18–20]. Retrograde CFV greater than 10 cm/s is associated with CVP greater than 12 mmHg, with a sensitivity of 80.5% and specificity of 71.2% [9].

Our primary objective was to assess whether there was an association between an abnormal CFV Doppler waveform and ICU mortality in patients with sepsis. The secondary objectives of this study were to evaluate the association of abnormal CFV Doppler waveform with other outcomes (length of stay in the ICU and in-hospital mortality), in addition to verifying, in an exploratory analysis, whether there was an association between abnormal CFV Doppler waveform and RV dysfunction assessed by tricuspid annular plane systolic excursion (TAPSE).

Materials and methods

This prospective cohort study was conducted from August 2021 to December 2022 at the ICU of the Hospital de Clinicas de Porto Alegre, Brazil. This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the Hospital de Clinicas de Porto Alegre. Written informed consent was obtained from the patients or from their next of kin.

Patients admitted to the ICU with a diagnosis of sepsis according to Sepsis-3 criteria were included [21]. Exclusion criteria were age less than 18 years, pregnancy, history of proximal deep vein thrombosis, common femoral or iliac vein thrombosis, and intra-abdominal hypertension. Considering an RR 0f 3.4, a power study of 80%, an alfa-error of 0.05 and a proportion of the outcome in the unexposed group of around 20%, the sample size estimation was 100 patients [8].

At the time of inclusion, data on age, sex, site of infection, SAPS-3, comorbidities, COVID-19, and the origin of the patient were collected. We calculated the volume of fluid administered 6 h prior to the ultrasound (US) examination. At the time the US was performed, we collected the PEEP level for patients on mechanical ventilation (MV) and the vasopressor dose. Patients were followed up to verify the need for MV, vasopressors, and renal replacement therapy (RRT) during the ICU stay. The patients were followed-up until hospital discharge. The primary outcome was ICU mortality. Secondary outcomes were hospital mortality, length of ICU stay, duration of MV, and length of hospital stay.

Doppler ultrasound of the CFV was performed within the first 48 h after ICU admission. All measurements were performed by two trained physicians. Both common femoral veins were scanned with Duplex ultrasound (DUS). Patients were in dorsal decubitus position. A maximum of 20° tilt angle of the upper body was tolerated. DUS imaging was performed using a high-frequency (5–13 MHz) linear-array vascular probe, which is often employed for central venous catheterization. PWD was obtained by examining the CFV in the short axis without angle correction and in the long axis with angle correction. Emission sound beam was positioned as parallel as possible to the flow direction of the vessel. The PWD was obtained at 60° or less. The maximum flow velocity was defined as the peak velocity of the antegrade flow on venous Doppler tracing. The minimum flow velocity was specified as either the lowest value of anterograde flow (when no retrograde venous flow was observed) or the peak reverse flow velocity (Fig. 1). Abnormal CFV Doppler waveform was determined by a retrograde velocity peak (RVP) > 10 cm/s in the long axis or RVP > 50% of the antegrade velocity peak in the short axis [22].

Echocardiograms were performed in 16 patients with a 2.5-MHz phased-array probe within 4 h of DUS of the CFV by an intensivist with experience in echocardiography who was blind to the DUS of the CFV. Three cardiac cycles were analyzed and averaged. The patients were placed in a semi-left lateral position during the examination. TAPSE was obtained by placing the M-mode cursor along the lateral part of the tricuspid valve ring. TAPSE < 17 mm was defined as RV dysfunction [23].

Normal distribution of continuous values was assessed using the Kolmogorov–Smirnov test. Group comparisons were performed using Student's *t*-test, Mann–Whitney *U* test, Chi-squared test, or Fisher's exact test, where appropriate. Multivariate linear regression analysis, including age,

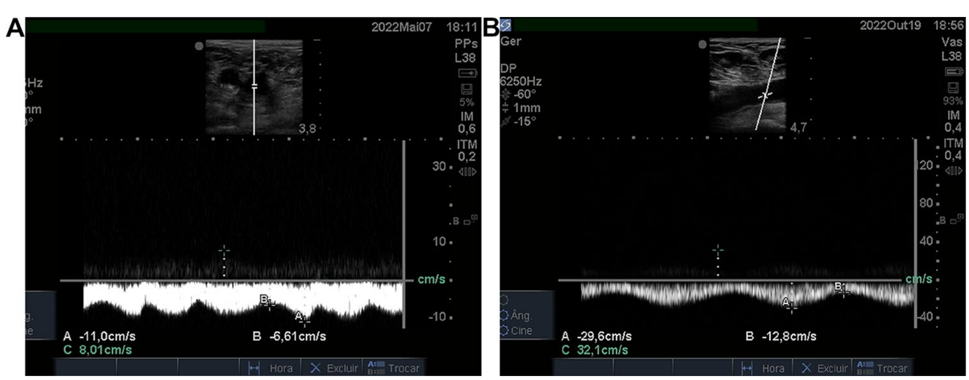


Fig. 1 Two-dimensional ultrasound images of common femoral vein (CVF) demonstrating normal respiratory variation. **A** spectral doppler profile of CVF acquired in short axis. **B** spectral dopplerprofile of CVF acquired in long axis

SAPS 3, septic shock, and abnormal CFV Doppler waveform, was performed to assess the independent associations of these variables with ICU mortality. The diagnostic performance of abnormal CFV doppler waveform for detecting right ventricular dysfunction was evaluated using standard methods such as sensitivity, specificity, positive predictive value, and negative predictive value. All p-values were two-tailed and considered significant at $p < 0.05$. All analyses were performed using IBM SPSS Statistics, version 20.0 (IBM Corp., Armonk, NY, USA).

Results

One hundred and ten patients were included in the study through convenience sampling. The general patient characteristics are shown in Table 1. Most patients required mechanical ventilation and vasopressors, and almost half of them required RRT. Only 13% of patients had a previous diagnosis of heart failure.

Doppler analysis of the CFV

The mean time for performing Doppler ultrasound (DUS) was 15.3 ± 10.2 h from ICU admission, and 90% of the patients were evaluated within the first 24 h. The median fluid received in the 6 h prior to the DUS measurements was 547.5 ml (363.0–840.8 ml). The median PEEP at the time the DUS measurements were taken was 7.0 cmH_2O (5.0–8.0 cmH_2O). There was no significant difference in these values between patients with and without abnormal CFV Doppler waveforms.

In 40 (36.4%) patients we identified an RVP > 10 cm/s in the long axis. In the short axis, we identified an RVP > 50% of antegrade flow in 44 (40.0%) patients. A strong correlation was observed between the RVP assessed on the two axes (rho 0.74; $p < 0.001$).

Association of abnormal CFV Doppler waveform with outcomes

There was no association between abnormal CFV Doppler waveforms, both in the long and short axes, and ICU mortality (Table 2). There was also no association between abnormal CFV Doppler waveforms and the secondary outcomes.

In the multivariate analysis, only SAPS 3 was independently associated with ICU mortality in models that also included age, septic shock, and abnormal CFV Doppler waveform in the short axis (model 1) and in the long axis (model 2).

Table 1 Baseline characteristics of the population

Variables	Normal CFV (*n* = 51)	Abnormal CFV (*n* = 59)	*p*
Age, years	60.8 ± 15.1	59.8 ± 16.6	0.756
Sex, Male, *n* (%)	63 (57.3)		
Pre-existing conditions			
Chronic hypertension	28 (54.9)	40 (67.8)	0.165
Diabetes mellitus	12 (23.5)	20 (33.9)	0.232
Peripheral vascular disease	5 (9.8)	1 (1.7)	0.094
Chronic kidney disease	11 (21.6)	9 (15.3)	0.392
COPD	8 (15.7)	12 (20.3)	0.528
Chronic heart failure	5 (9.8)	10 (16.9)	0.404
Cirrhosis	2 (3.9)	3 (5.1)	1.000
Solid neoplasm	11 (21.6)	9 (15.3)	0.392
Hematologic neoplasm	5 (9.8)	9 (15.3)	0.568
Location before ICU admission			
Emergency	14 (27.5)	16 (27.1)	0.969
Ward	23 (45.1)	25 (42.4)	
Operating room	11 (21.6)	15 (25.4)	
Other hospital	3 (5.9)	3 (5.1)	
COVID-19	8 (15.7)	4 (6.8)	0.219
SAPS 3	79.6 ± 17.2	74.1 ± 19.1	0.134
Site of infection			
Pulmonary	24 (47.1)	29 (49.2)	0.827
Abdominal	17 (33.3)	23 (39.0)	0.539
Urinary	7 (13.7)	3 (5.1)	0.183
Bloodstream	1 (2.0)	5 (8.5)	0.213
Cutaneous	4 (7.8)	2 (3.4)	0.413
Central nervous system	1 (2.0)	1 (1.7)	1.000
Skeletal muscle	4 (7.8)	2 (3.4)	0.413
Other	1 (2.0)	–	0.464
Septic shock	31 (62.0)	29 (50.0)	0.211
MV			
On admission	40 (78.4)	39 (66.1)	0.152
During ICU stay	46 (92.0)	48 (82.8)	0.250
RRT	25 (53.2)	23 (41.1)	0.219

Data are median (IQR), mean (SD), or *n* (%)

COPD chronic obstructive pulmonary disease, *ICU* intensive care unit, *MV* mechanical ventilation, *RRT* renal replacement therapy

Association of abnormal CFV Doppler waveform with TAPSE

The TAPSE measurements were performed in 16 patients. RV dysfunction was identified in 8 (50.0%) patients.

There was no association between the diagnosis of RV dysfunction based on the TAPSE measurement and the

Table 2 Primary and secondary outcomes

	Long axis		p	Short axis		p
	Abnormal ($n=40$)	Normal ($n=70$)		Abnormal ($n=44$)	Normal ($n=66$)	
Primary outcome						
ICU mortality	14 (35.0)	27 (38.6)	0.709	13 (29.5)	28 (42.4)	0.171
Secondary outcomes						
Duration of mechanical ventilation, days	6.0 (3.0–17.0)	6.0 (2.0–14.0)	0.613	6.0 (3.0–17.0)	7.5 (2.0–13.3)	0.474
ICU length of stay, days	9.0 (5.0–20.0)	10.0 (4.0–15.0)	0.701	7.5 (5.0–17.0)	10.0 (4.0–14.8)	0.849
In-hospital mortality	16 (40.0)	34 (48.6)	0.385	18 (40.9)	32 (48.5)	0.434

Data are median (IQR) or *n* (%)

identification of abnormal CFV Doppler waveforms in the long axis ($p=1.000$) and in the short axis ($p=1.000$). Of the eight patients with TAPSE < 17 mm, there was an abnormal CFV Doppler waveform in only three (37.5%) patients in the short axis and in only two (25.0%) patients in the long axis.

Abnormal CFV Doppler waveform in the long axis for detecting RV dysfunction had a sensitivity of 25%, specificity of 62.5%, positive predictive value (PPV) of 40%, and negative predictive value (NPV) of 45.5%. In the short axis, an abnormal CFV Doppler waveform had a sensitivity of 37.5%, specificity of 62.5%, PPV of 50%, and NPV of 50%.

Discussion

Our findings indicate that there is no association between abnormal CFV Doppler waveforms and adverse outcomes in septic patients. Notably, to the best of our knowledge, our study represents the largest investigation assessing the prognostic significance of CFV Doppler waveform in individuals with sepsis.

Reverse flow in the CFV has been described in RV dysfunction, tricuspid regurgitation, venous insufficiency, pulmonary embolism, and venous obstruction [24–28]. The CFV has high specificity for right atrial pressure (RAP) estimation [27]. As RAP rise, causing venous congestion, the normal continuous venous outflow of CFV is transformed into pulsatile venous outflow [9]. Recently, Croquette et al. found a good correlation between CFV Doppler and RAP (measured with a venous catheter with the distal tip in the right atrium) in patients with pulmonary hypertension [29]. However, the CFV Doppler association with more specific measures of RV dysfunction is more uncertain [24, 30, 31]. Despite this, some authors suggest that examination of the femoral vein in the ICU could represent an easy and reliable way to assess venous congestion and RV dysfunction, in addition to monitoring the response to treatment for these conditions [18, 22].

Considering the prevalence and prognostic value of venous congestion and RV dysfunction in patients with sepsis, identifying them using an easy and reproducible tool is highly desirable. In a recent meta-analysis, RV dysfunction was associated with an increased risk of short-term and long-term mortality in patients with sepsis and septic shock [7]. Lanspa et al. also verified an association between RV dysfunction and higher mortality in patients with sepsis, in addition to verifying that almost half of the population had this condition [8]. Associated or not with RV dysfunction, more positive fluid balance and higher central venous pressure (CVP) were also associated with higher mortality in patients with septic shock [32]. Thus, CFV Doppler could be useful in identifying RV dysfunction and/or venous congestion in these patients and identifying a subgroup with a higher risk of mortality. However, our findings do not support this hypothesis.

Most studies assessed the association between CFV Doppler and RAP measured with venous catheter, indirectly inferring RV function [10, 25–27, 29]. Zhang et al. found no correlation between TAPSE and RAP in patients with preserved ejection fraction [33]. This finding suggests that more specific measures of RV function rather than RAP should be used. In an exploratory analysis, we evaluated the association of an abnormal CFV Doppler waveform with TAPSE measurement, a recommended measure for estimating RV systolic function [34]. Our findings do not suggest that CFV Doppler can be used as an indicator of RV dysfunction.

We acknowledge several limitations of our study. First, the sample size was small, and data were collected from a single center, which may limit the generalizability of our findings to broader populations. Additionally, our evaluation of an abnormal CFV Doppler waveform was solely based on the RVP, disregarding alternative metrics such as the femoral venous stasis index, which Croquette et al. found to be more accurate in estimating right atrial pressure (RAP). Moreover, we did not assess inter-observer reliability in the interpretation of CFV Doppler waveforms, as only two physicians performed the DUS evaluations. This limited assessment of inter-observer agreement may introduce potential bias and restrict the variability of interpretations. Finally, the absence of LV function assessment prevents us from determining whether the results differ based on the presence or absence of LV dysfunction. These limitations should be considered when interpreting our results and highlight the need for larger, multicenter studies with comprehensive evaluations of inter-observer reliability to enhance the generalizability and reliability of future research in this area.

Conclusions

Our findings indicate that abnormal CFV Doppler waveforms were not associated with ICU mortality in sepsis patients. However, further studies are warranted to evaluate the potential utility of CFV Doppler changes in identifying more severe patients within other critically ill populations.

Author contributions ND and MB conceived of the presented idea, developed the theory and performed the computations. MB encouraged ND to investigate TAPSE and supervised the findings of this work. AO performs a workshop on doppler ultrasound and revised the first exams made from ND and DG. ND and DG performed the exams on the sample and wrote the manuscript with support from MB. JP performs echocardiograms on the sample. All authors provided critical feedback and helped shape the research, analysis and manuscript.

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Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest. Financial disclosure: The authors declares that they have no relevant or material financial interests that relate to the research described in this paper.

Ethical approval This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the Hospital de Clinicas de Porto Alegre.

Consent to participate Written informed consent was obtained from participants included in the study (or from legal guardians).

Consent to publish Not applicable.

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