Critical Care

CORRESPONDENCE

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Lack of preload responsiveness may determine poor clinical outcomes in mechanically ventilated patients with ARDS

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Trial registration: NCT03763773. Registered 3 December 2018.

Keywords Preload responsiveness, Fluid responsiveness, Acute respiratory distress syndrome, ARDS, Superior vena cava, Transesophageal echocardiography, Intensive care, Prognosis, Mechanical ventilation

Joseph et al. recently reported that hypovolemia was associated with ICU mortality in mechanically ventilated patients with ARDS and shock [1]. We aimed to investigate whether an opposite condition, such as preload unresponsiveness during the initial phase of hospitalization for ARDS, could also be a risk factor for impaired ventilatory outcomes and 28-day mortality.

We conducted a single-center, prospective pilot study at the University Hospital Center (CHU) in Lille, France, between April 2019, and April 2021. The study received approval from the Northwest ethics committee (2018A0146352). Eligible for inclusion were adult patients hospitalized in the intensive care units (ICUs) at Roger Salengro Hospital in CHU Lille, presenting with moderate or severe ARDS of less than 24 h duration, and who were treated with both tracheal intubation and mechanical ventilation in controlled assisted ventilation mode in the absence of spontaneous ventilation cycle triggering. Non-inclusion and exclusion criteria are detailed in the Supplementary file.

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Patients included in the study underwent the placement of a ClariTEE™ miniaturized transesophageal echocardiography (TEE) probe (CLT0110-1, IMACOR, New York NY, USA) within the first 24 h of mechanical ventilation. The probe remained in place for a maximum of 72 h. Preload responsiveness was sequentially assessed by measuring the superior vena cava (SVC) diameters and the respiratory collapse index (cSVC), as described in Figure S1. The mean cSVC (cSVC-mean) was obtained by calculating the average over the monitoring duration. The cSVC was calculated using the following formula: cSVC = (maximal diameter—minimal diameter)/maximal diameter [2]. Detailed methods of the study can be found in the Supplementary file.

Fifty patients were studied with a median age of 64 years (57–69). Fifteen (30%) patients died by 28 days after ICU admission. The main patients' characteristics at the time of enrollment and outcomes are described in Table S1. As shown in Fig. 1, there was a significant correlation between cSVC-mean value and the number of days spent alive without mechanical ventilation on day-28 ($\rho = 0.33$; 95%CI 0.05 to 0.56; $p = 0.018$). Median cSVC values assessed at baseline, day-1 (cSVC-d1), day-2 (cSVC-d2) and day-3 (cSVC-d3) according to 28 day-survival status are depicted in Figure S2. In univariate, logistic regression analysis, cSVC-mean, cSVC-d1 and cSVC-d3 were inversely associated with 28 day-mortality

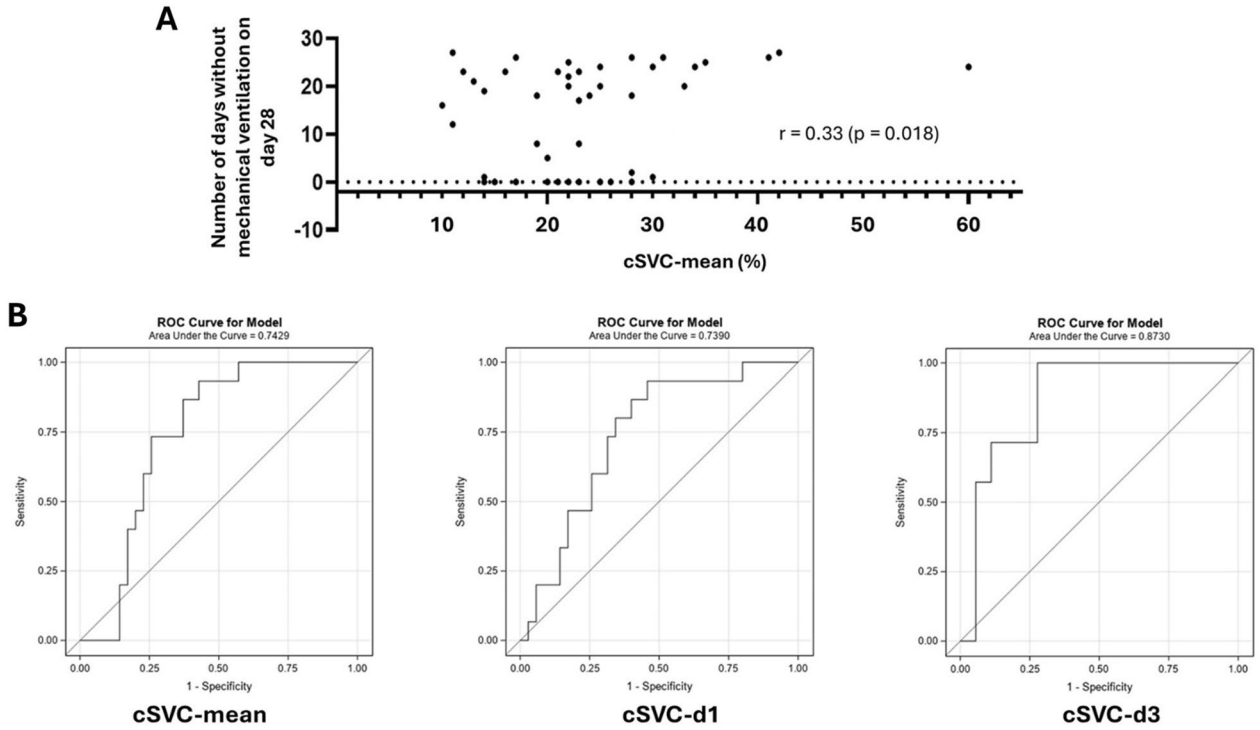

Fig. 1 Associations between cSVC and outcomes. Scatterplot of cSVC-mean value and the number of days without mechanical ventilation at day 28 (**A**). Areas under the receiver operating characteristics (ROC) curve for predicting 28 day-mortality with cSVC-mean, cSVC-d1 and cSVC-d3 (**B**). cSVC, collapsibility index of the superior vena cava; cSVC-d1 and d3, cSVC value on day-1 and day-3; cSVC-mean, average cSVC over the monitoring duration (maximum of 3 days)

with an odd ratio (OR) per one standard deviation increase of 0.27 (95%CI 0.10 to 0.78; p = 0.02), 0.29 (95%CI 0.09 to 0.89; p = 0.03) and 0.20 (95%CI 0.05 to 0.86; p = 0.03), respectively. A similar but non-significant negative association with cSVC-d2 was also noted (OR = 0.39, 95%CI 0.14 to 1.10; p = 0.07). The areas under the ROC curves for predicting 28 day-mortality with cSVC-mean, cSVC-d1 and cSVC-d3 were 0.74 (95%CI 0.61 to 0.88), 0.74 (95%CI 0.60 to 0.88) and 0.87 (95%CI 0.73 to 1.00), respectively (Fig. 1). The optimal thresholds for prediction of 28 day-mortality were 21%, 23% and 21% for cSVC-mean (Sensitivity = 93%, Specificity = 57%), cSVC-d1 (Sensitivity = 93%, Specificity = 54%) and cSVC-d3 (Sensitivity = 100%, Specificity = 72%), respectively (Figure S3). Patients' characteristics on day-1 and day-3 are shown in Table S2, and their associations with cSVC values are reported in Figures S4 and S5.

Our results suggest that a lack of preload responsiveness (cSVC < 21%) may be a determinant of poor outcomes in mechanically ventilated patients admitted to the ICU for moderate to severe ARDS. Conversely, Joseph et al. demonstrated that hypovolemia (cSVC > 60%) could also be clinically detrimental in this context [1]. Therefore, targeting a cSVC between 21 and 60% may represent a pragmatic safety goal in future clinical trials. Furthermore, the clinical implications of fluid responsiveness have been emphasized by Castro et al., who proposed that a fluid removal strategy aimed at optimizing preload dependence is feasible, safe, and may facilitate weaning from mechanical ventilation in critically ill patients with fluid overload [3].

A lack of preload dependence may indicate RV systolic dysfunction, RV dilation, and even the presence of paradoxical septal motion in patients with ARDS [1]. Moreover, a lack of fluid responsiveness has been shown to parallel impaired cardiovascular function, a known predictor or poor weaning from mechanical ventilation and increased mortality in ARDS. In the same line, our patients with RV systolic dysfunction tended to have lower cSVC values compared to those without RV systolic dysfunction on day-1 and day-3: standardized mean differences of − 0.41 and − 0.92, respectively. However, this association remains inconclusive due to the wide CIs of standardized mean differences overlapping zero. Therapeutic strategies aimed at improving RV function may help restore preload dependence, reduce venous congestion, and potentially enhance survival in this clinical context [4, 5]. Given the monocentric nature

of this work, it seems important to confirm our results in a prospective, multicenter study, which may also provide a more precise pathophysiological explanation for these findings.

Abbreviations

ACP	Acute cor pulmonale
ARDS	Acute respiratory distress syndrome
cSVC	Collapsibility index of the superior vena-cava
cSVC-d1, d2 or d3	Average cSVC during the first, the second or the third day after study enrollment.
cSVC-mean	Average cSVC over the monitoring duration (1 to 3 days)
CVP	Central venous pressure
DAP	Diastolic arterial pressure
FiO2	Fraction of inspired oxygen
ICU	Intensive care unit
MAP	Mean arterial pressure
PaCO2	Partial pressure of carbon dioxide
PaO2	Partial pressure of oxygen
PEEP	Positive end-expiratory pressure
ROC	Receiver operating characteristics
RV	Right ventricle
SAP	Systolic arterial pressure
SAPS 2	Simplified acute physiology score 2
SARS-COV-2	Severe acute respiratory syndrome coronavirus 2
SEM	Standard error of the mean
SOFA	Sequential organ failure assessment
SVC	Superior vena cava
TAPSE	Tricuspid annular plane systolic excursion
TEE	Transesophageal echocardiography

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-025-05409-4.

Additional file1 (DOCX 1004 KB)

Acknowledgements
We would like to thank Dr. Julien GOUTAY for his significant help with screening and recruiting patients. We also would like to thank Dr. Younes BENZIDI for his significant help with getting the funds to finance the miniaturized TEE probes used in the study.

Author contributions
All authors met authorship criteria and participated significantly to the study. SP, AP, LC, JL, CB, AD and RF: conception and design. SP, OP, ME, AD, CB, TO: patients' screening and enrollment. SP, OP and ME: echocardiography acquisitions of video loops. OP and ME: acquisition of data. SP, RF, AP, MH, LC and JL: analysis and interpretation of data. SP, OP, ME, LC and JL: writing the article. AP, MH: critical revisions of the manuscript. All authors read and approved the final manuscript.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on request.

Declarations

Ethics approval and consent to participate
The study received approval from the Northwest ethics committee (protocol number 2018 A014 63 52). Each inclusion required oral and written informed consent from a representative (spouse, close relative, or friend) and then from the patient as soon as they were able to provide it.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no conflict of interest. SP has received payments from AOP Orphan and Viatris for lectures.

Received: 1 February 2025 Accepted: 8 April 2025
Published online: 01 May 2025

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