Critical Care

RESEARCH LETTER

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Variation in central venous oxygen saturation to assess volume responsiveness in hemodynamically unstable patients under mechanical ventilation: a prospective cohort study

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Intravenous fluid administration is a cornerstone of hemodynamic resuscitation. Its goal is to restore effective circulating blood volume and correct tissue perfusion as quickly as possible to avoid multi-organ failure [1]. In extreme clinical situations, the diagnosis of hypovolemia is easy; the problem arises when hypovolemia is latent or when associated with a patent left ventricular dysfunction. It is often the case with critically ill patients, for whom the diagnosis of hypovolemia is rarely possible without the use of accurate hemodynamic indicators [2, 3]. The use of central venous oxygen saturation ($ScvO_2$) measurement has been proposed to guide fluid therapy [4]. The rationale behind assessing fluid responsiveness by $ScvO_2$ is to identify patients on the ascending portion of the Frank-Starling curve who would likely to be fluid-responsive [5]. We studied the ability of $SCVO_2$ variation ($\Delta ScvO_2$) to define fluid responsiveness in critically ill emergency department (ED) patients needing volume expansion (VE). Here, we present a comprehensive summary of 88 adult patients under mechanical ventilation who required VE. VE consisted of 500 ml normal saline infused within 10 min. Cardiac output (CO) was measured by thermodilution method before and after VE. Fluid responsiveness was defined as increase in $CO \geq 15\%$ after VE, while fluid non-responsiveness was defined as no increase or increase in $CO < 15\%$. Hemodynamic assessment and blood gases measurements were performed at baseline and immediately after the end of VE. It included heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), central venous pressure (CVP), $ScvO_2$, CO, cardiac index (CI), oxygen delivery (DO_2), oxygen consumption (VO_2) and blood lactate. The most common underlying clinical condition was septic shock. All patients received catecholamine and 46 patients (52.3%) died during hospitalization. Overall, 61 patients (69.3%) responded to VE. Before VE, $ScvO_2$ did not differ between responders and non-responders. Patients' characteristics and hemodynamic variables before VE are summarized in Table1. The increase in SBP, DBP and CI after VE was significantly higher in responders compared to non-responders. CI increased significantly from 2.62 ± 0.75 to 3.47 ± 0.8 L/min/m^2 ($p < 0.001$) and $ScvO_2$ from $70.5 \pm 6.8\%$ to $75.2 \pm 6.6\%$ ($p < 0.001$) in

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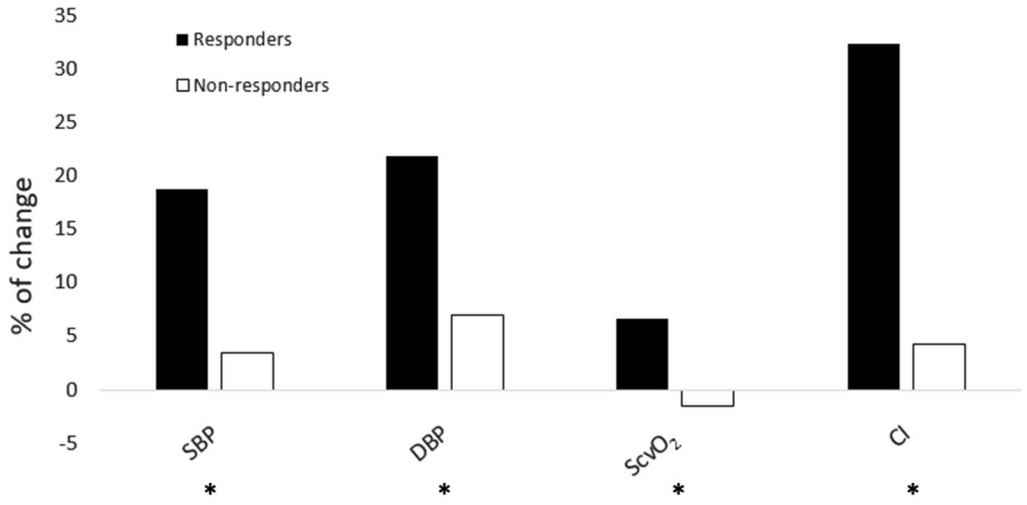
Table 1 Baseline characteristics and hemodynamic variables before volume expansion in the responders and the non-responders groups

	Overall population ***N*** **= 88**	**Responders** ***n*** **= 61**	**Non-responders** ***n*** **= 27**	***p***
Age (SD)	70 ± 13	71 ± 14	67 ± 11	0.14
Male (%)	65 (73.9)	46(75.4)	19 (70.4)	0.61
Underlying diseases n (%)				
Heart failure	19 (21.6)	12 (25)	5(19.2)	0.77
Arterial hypertension	47 (53.4)	24 (50)	16 (61.5)	0.46
Diabetes	72 (81.8)	42 (87.5)	18 (69.2)	0.06
Coronary artery disease	27 (30.7)	13 (27.1)	8 (30.8)	0.79
SOFA score mean (SD)	15 ± 3	15 ± 3	15 ± 3	0.75
SAPS II score mean (SD)	75 ± 25	75 ± 24	76 ± 25	0.85
Type of shock				
Septic (%)	34 (38.6)	26 (42.6)	8 (29.6)	0.34
Hypovolemic (%)	11 (12.5)	7 (11.5)	4(14.8)	0.73
Cardiogenic (%)	10 (11.4)	6 (9.8)	4 (14.8)	0.48
Combined (%)	33 (37.5)	22 (36.1)	11 (40.7)	0.81
Death (%)	46 (52.3)	31(50.8)	15 (55.6)	0.82
Heart rate (bpm)	110 ± 19	109 ± 18	111 ± 22	0.61
Systolic arterial pressure mmHg, mean (SD)	91.3 ± 10	91.3 ± 8	91.3 ± 12	0.99
Diastolic arterial pressure mmHg, mean(SD)	54.2 ± 9	51.2 ± 8	61.1 ± 8	< 0.001
Central venous pressure cmH_2O mean (SD)	7.95 ± 2.38	6.8 ± 1.48	10.6 ± 1.88	< 0.001
Cardiac output (L/min)	4.88 ± 1.52	4.97 ± 1.42	4.67 ± 1.75	0.39
Cardiac index (L/min/m^2) mean (SD)	2.57 ± 0.8	2.6 ± 0.74	2.46 ± 0.92	0.39
Oxygen delivery (ml/kg/min) mean (SD)	446.2 ± 150	497.5 ± 131	330.5 ± 126	< 0.001
Oxygen consumption (ml/kg/min) mean (SD)	120.5 ± 51	137.3 ± 54	95.5 ± 44	0.001
Lactate (mmol/l) mean(SD)	3.6 ± 2.58	3.5 ± 2.31	3.9 ± 3.05	0.53
$ScvO_2$ (%)	70.8 ± 7	70.5 ± 7	71.5 ± 8	0.51

SOFA, Sequential Organ Failure Assessment, SAPS, Simplified acute physiology Score, $ScvO_2$, central venous oxygen saturation

responders. CI and $ScvO_2$ did not change significantly in non-responders after VE. Figure 1 shows the relative changes from baseline of hemodynamic variables after VE. Relative changes of $ScvO_2$ were 7 ± 8.4% in responders and − 1.4 ± 9.6% in non-responders. The difference was statistically significant between the two groups ($p < 0.001$). $\Delta ScvO_2$ was positively and significantly correlated with CO variation after VE ($r = 0.46$, $p < 0.001$). When analyzed using multivariate logistic regression, $\Delta ScvO_2$ was the only factor associated with fluid responsiveness [OR: 1.44 (95% CI: 1.15–1.79)]. Diagnostic performance of $\Delta ScvO_2$ and ΔCVP after VE showed areas under ROC curves of 0.84 (95% CI; 0.72–0.96) and 0.56 (95% CI; 0.43–0.68), respectively. The AUC of $\Delta ScvO_2$ was significantly greater than that of ΔCVP (z statistic = 3.033, $p = 0.0024$). The best cut-off value found was 4%, allowing discrimination between responders and non-responders with a sensitivity of 78.7%, a specificity of 81.5% and a percentage of correct classification of 61.1%. It is important to mention that our results would work when $ScvO_2$ is low and when there is no significant change in VO_2 and haemoglobin. However, changes depend on the amount of fluid administered. Also, $ScvO_2$ may not change if VO_2 is dependent on DO_2. We concluded that in patients with acute circulatory failure, $\Delta ScvO_2$ has an adequate correlation with ΔCI and could be very helpful alternative tool when CO measurement or surrogates aren't possible or not applicable. Further studies with larger populations are required to confirm these results on the role of $ScvO_2$ monitoring in assessing fluid responsiveness instead of a cardiac output measurement during a fluid challenge.



SBP: systolic blood pressure, DBP: diastolic blood pressure, $ScvO_2$: central venous oxygen saturation, CI: cardiac index. * : $p<0.001$ percentage of change of systolic blood pressure, diastolic blood pressure, central venous oxygen saturation and cardiac index varied significantly between responders and non responders group after volume expansion.

Fig. 1 Relative changes from baseline of hemodynamic variables after volume expansion

Abbreviations
$ScvO_2$: Central venous oxygen saturation; $\Delta ScvO_2$: $ScvO_2$ variation; CO: Cardiac output; CI: Cardiac index; ΔCI: Cardiac index variation; ED: Emergency department; VE: Volume expansion; VO_2: Oxygen consumption; DO_2: Oxygen delivery; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CI: Cardiac index; CVP: Central venous pressure; ΔCVP: CVP variation.

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Authors' contributions
MHK and SN conceived of the study and participated in its design and coordination and helped to revise the manuscript. AS participated in the design of the study and revised the manuscript. MHK and WZ collected the data and wrote the first draft of the manuscript. AZ and HBS collected the data. MHK and WZ participated in the design of the study and performed the statistical analysis. All authors read and approved the final manuscript.

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Availability of data and materials
The data are fully available, please contact the corresponding author.

Declarations

Ethics approval and consent to participate
All patients and/or their surrogates received written information about the study and provided their verbal consent to participate. The study's objectives and procedures were approved by the independent Ethics Committee of the Medical University of Monastir.

Consent for publication
Not applicable.

Competing interests
None.

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