



Cardiac Critical Care Original Article

## Functional Evaluation of Microcirculation in Response to Fluid Resuscitation in Hypovolemic Adult Post-cardiac Surgical Patients

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### ABSTRACT

**Objectives:** Microcirculation is bound to be altered during cardiac surgery due to multiple factors, mainly the intense systemic inflammatory response syndrome which peaks in the first 24-h postoperatively. Decreased microvascular flow associated with increased postoperative morbidity has been reported. The literature suggests a potential independence of macrocirculation and microcirculation during fluid loading. The present study was conducted to assess the thenar muscle tissue oxygen saturation (StO<sub>2</sub>) changes during vascular occlusion test (VOT) in response to hypovolemia and to assess the dynamic responses of the StO<sub>2</sub> variables post-volume expansion (VE).

**Material and Methods:** Thirty-five adult post-cardiac surgical patients, with stroke volume (SV) variation >12% were included in the study. Fifty-two fluid challenges were studied. Functional evaluation of microcirculation using VOT and near infrared spectroscopy (NIRS) variables along with monitoring of macrocirculatory indices was performed before and after VE. Statistical analysis was done using Student *t*-test.

**Results:** Post-VE, 34 were responders with increase in SV ≥15% and 18 were non-responders (SV <15%). Rate of resaturation was significantly faster in responders compared to non-responders after VE (*P* = 0.0293 vs. *P* = 0.1480). However, macrocirculatory indices including cardiac output, SV, and delivery of oxygen showed significant improvement in both responders and non-responders.

**Conclusion:** Preload dependence is associated with significant change in the StO<sub>2</sub> recovery slope measured at the thenar eminence in volume responders. Functional evaluation of microcirculation using VOT and StO<sub>2</sub> can be a useful complimentary tool along with the macrocirculatory indices for optimal fluid resuscitation in adult post-cardiac surgical patients.

**Keywords:** Fluid responsiveness, Microcirculation, Macrocirculation, Near infrared spectroscopy variables, Vascular occlusion test, Cardiac surgery

### INTRODUCTION

Goal directed therapy has been used for nearly 30 years, being one of the most prevalent strategy in fluid resuscitation which has shown to improve both short-term and long-term outcome.<sup>[1,2]</sup> Early goal directed therapy (EGDT) has been extensively studied in septic shock

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patients when fluid is administered within 6 h of presentation to the emergency department. Evidence supporting the use of EGDT in sepsis was found by the landmark Rivers trial, which showed a 16% of mortality reduction.<sup>[3]</sup> The literature shows that EGDT has also been beneficial when employed postoperatively after major high risk surgeries.<sup>[4,5]</sup>

Correct assessment of hypovolemia and fluid responsiveness is critically important in patients with compromised cardiac and pulmonary function. Microcirculation has been found to be altered during cardiac surgery due to multiple factors such as anesthesia, surgery, hypothermia, microemboli,<sup>[6,7]</sup> and the intense systemic inflammatory response syndrome which peaks in the first 24-h postoperatively.<sup>[8]</sup>

Fluid therapy guided by functional hemodynamic indices of volume responsiveness such as pulse pressure variation and stroke volume variation (SVV), instead of static measures such as central venous pressure, pulmonary artery pressure, or mean arterial pressure (MAP) reported a better outcome.<sup>[9]</sup> However, the previous reports have suggested a potential independence of macrocirculation and microcirculation during fluid loading.<sup>[10,11]</sup> Thus, fluid administration may correct macrocirculatory hemodynamic variables with or without improvement in microcirculation.

Decreased microvascular flow associated with increased postoperative morbidity has been reported.<sup>[12]</sup> The operative and post-operative mortality in cardiac surgery has decreased significantly in the recent years due to improved care and advanced monitoring of the macrocirculatory indices.<sup>[13-15]</sup> The post-operative morbidity is still significantly high,<sup>[13]</sup> as a result of which 10% of patients require a prolonged post-operative care.<sup>[16]</sup> The alterations in microcirculation leading to inadequate tissue oxygen delivery have been recognized as an independent marker for prolonged intensive care unit (ICU) stay.<sup>[17]</sup>

Hence, there is a need to correlate macrocirculatory variables like increase in SV with change in microcirculation, especially in critically ill cardiac surgical patients for effective fluid resuscitation.

Microcirculatory hemoglobin and oxygen availability can be measured by the use of near infrared spectroscopy (NIRS),<sup>[18]</sup> a non-invasive technique that can be performed at the bedside. Differential absorption of infrared light at two specific wavelengths (680 and 800 nm) by deoxyhemoglobin is used to define the hemoglobin saturation level in vessels located in the tissue volume that is illuminated by the probe.<sup>[19]</sup>

Tissue oxygen saturation (StO<sub>2</sub>) values were shown to have a large overlap between healthy subjects and septic shock patients which largely limits the interest of this parameter for individual care. In this respect, a vascular occlusion test (VOT) combined with StO<sub>2</sub> measurement is proposed.<sup>[20]</sup>

The dynamic response of the StO<sub>2</sub> recovery slope, during a standardized VOT, is assumed to reflect the recruitment of microvessels in response to a local hypoxic stimulus.<sup>[21]</sup>

In view of the limited literature to guide optimal fluid therapy in correlation with improvement in microcirculatory parameters in cardiac surgical patients, the present study was conducted to assess thenar muscle StO<sub>2</sub> changes during VOT in response to hypovolemia and to assess the dynamic responses of the StO<sub>2</sub> recovery slope post-volume expansion (VE).<sup>[22,23]</sup>

## MATERIAL AND METHODS

### Methodology

After obtaining the Institutional Ethical Committee clearance, the prospective, observational, and clinical study was performed at a tertiary care cardiac center.

### Study population

Patients shifted to post-operative ICU with >18 years of age, post-elective cardiac surgery with SVV >12% were included in the study.

Patients on extracorporeal circulatory support, intracardiac shunts, left ventricular ejection fraction <35%, inotrope score of >20, emergency surgery, patients with arrhythmias, and history of peripheral vascular disease were excluded from the study.

### Study protocol

In the post-operative ICU, NIRS (Equano × 7600) optode was attached to the thenar eminence and Flotrac vigileo cardiac output monitor was connected to the femoral artery. Sphygmomanometer cuff was applied around the same arm as NIRS optode.

Post-operative management was standardized for all the patients, including ventilation protocol (tidal volume of 6–8 mL/kg, positive end expiratory pressure of 5 cm of water, respiratory rate of 12–16/min). Ventilatory parameters were not altered throughout the procedure. All patients received intravenous fentanyl (1 mcg/kg) bolus before commencement of VOT.

Thenar StO<sub>2</sub> was measured using NIRS. StO<sub>2</sub> stability was defined as variation <2% over 30 s (pre-VOT StO<sub>2</sub>).<sup>[24]</sup>

Macrocirculatory variables were measured using Flotrac vigileo monitor.

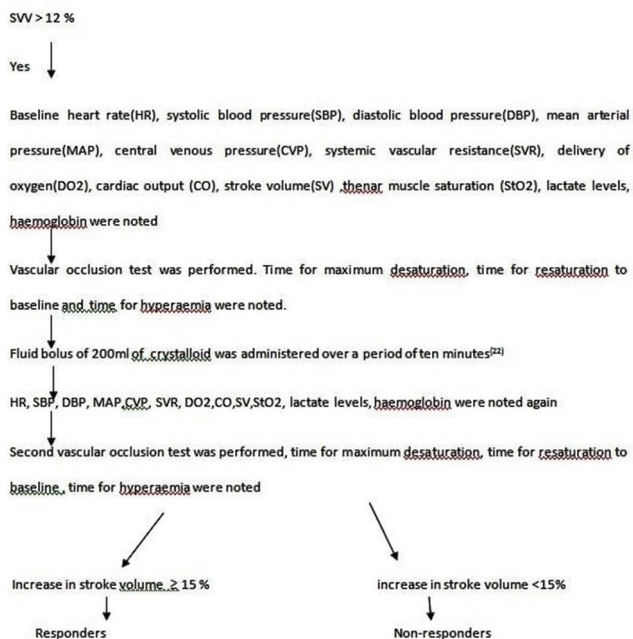
Normal saline was used for fluid bolus.

### VOT procedure

VOT involved rapidly inflating a sphygmomanometer cuff (< 3 s) until 50 mmHg above the systolic blood pressure (SBP). The cuff

was released rapidly (< 2 s) after 3 min of occlusion. The StO<sub>2</sub> occlusion slope is shown to relate to tissue oxygen consumption and the StO<sub>2</sub> reperfusion slope is proposed to evaluate tissue flow reperfusion and vascular recruitment [Study flow diagram].<sup>[25]</sup>

**Study flow diagram**



**Statistical analysis**

Statistical analysis was performed using MedCalc version 12.2.1.0. Categorical data were analyzed with Chi-square test. Paired Student *t*-test was used to compare data at two different time points. Unpaired student *t*-test was used to compare data between two different groups. The results were tested for normality using the one-sample Kolmogorov–Smirnov goodness of fit test. Normally distributed data were presented as mean ± standard deviation. *P* ≤ 0.05 was considered statistically significant.

The study population was grouped into responders and non-responders, based on the percentage increase in SV after intravascular VE. Responders were defined when an increase in SV was ≥15% to fluid challenge, Non-responders were defined when an increase in SV was <15%.

**RESULTS**

A total of 52 fluid challenges were studied in 35 patients who satisfied the inclusion criteria. [Table 1] summarizes the demographic profile. Study population was grouped into responders and non-responders based on the percentage increase in SV. Patients with increase in SV by ≥15% were grouped into responders and those with <15% were grouped into non-responders. [Table 2] represents the clinical

**Table 1:** Demographic profile.

Variable	Value
Age (yrs)	52.06±12
Sex (m/f)	38/14
Height (cm)	163±6.5
Weight (kg)	65.6±11
BMI	24.1±3.5
Comorbidities	
Hypertension	26
Diabetes	10
Smokers	5
Hypothyroidism	1
Euro score 2	0.8±0.1
Type of Surgeries	
OPCAB	30
DVR	2
AVR	3

BMI: Body mass index, OPCAB: Off pump coronary artery bypass, DVR: Double valve replacement, AVR: Aortic valve replacement, m: Male, f: female

parameters between the responders and non-responders which were recorded in all the patients before fluid bolus. Clinical parameters were comparable between the two groups. [Table 3] shows the changes in microcirculatory and macrocirculatory variables recorded before and after fluid bolus.

Administration of fluid bolus resulted in significant improvement in macrocirculatory variables such as SV and cardiac output in both the groups.

In responders, the SV (mL) increased from 54.3 ± 14.8 to 73.2 ± 17.0 (*P* ≤ 0.0001). Similarly, cardiac output (L/min) increased from 5.0 ± 1.2 to 6.2 ± 1.1 (*P* ≤ 0.0001) which was statistically significant.

In non-responders, there was a statistically significant increase in SV and cardiac output after fluid bolus. Stroke volume (mL) increased from 58.6 ± 17.8 to 63.2 ± 18.6 (*P* = 0.0002), cardiac output (L/min) increased from 5.2 ± 1.4 to 5.7 ± 1.5 (*P* = 0.0005). However, the change was >15% [Figure 1].

The rate of resaturation [Graph 1a] was significantly faster after fluid administration in responders (52.1 ± 38.9–64.5 ± 34.1, *P* = 0.0293) compared to non-responders who did not show any significant change in the rate of resaturation (77.5 ± 38.6–67.0 ± 27.7, *P* = 0.1480).

However, the rate of desaturation [Graph 1b] did not show any significant change in both responders and non-responders after administration of fluid bolus. (*P* = 0.5197 vs. *P* = 0.3499 in responders and non-responders, respectively). The time required for maximum hyperemia was significantly less in responders compared to non-responders after fluid bolus (*P* = 0.028 vs. *P* = 0.950 in responders and non-responders, respectively).

**Table 2:** Clinical profile of two groups.

Variables	Responders Mean±SD	Non-responders Mean±SD	P-value
Urine output (mL/h)	101±20	105±21	0.51
SpO <sub>2</sub>	99.12±0.91	99.44±0.51	0.17
Inotrope score	3.11±1	3.3±1.7	0.62
Vasodilator (SNP/NTG)	1.08±0.45	1.2±0.2	0.131
Temperature (nasopharyngeal) (°C)	36.2±0.5	36.3±0.32	0.59

SD: Standard deviation, SNP: Sodium nitroprusside, NTG: Nitroglycerine

**Table 3:** Changes in macrocirculatory and microcirculatory variables recorded before and after fluid boluses in responders and non-responders.

Variables	Responders (n=34)		“P”-value	Non-responders (n=18)		“P”-value
	Before VE	After VE		Before VE	After VE	
SBP (mmHg)	114.6±18.6	136.5±13.2	< 0.0001	115.3±15.4	115.7±15.4	0.8427
DBP (mmHg)	66.7±13.5	76.2±11.0	0.0001	68.0±7.1	67.8±8.6	0.9337
MAP (mmHg)	82.5±13.3	96.1±10.9	0.0001	83.3±10.0	84.7±11.1	0.3335
HR (beats/min)	90.7±21.2	89.5±19.5	0.3126	93.2±16.3	92.2±17.2	0.1287
SV (mL)	54.3±14.8	73.2±17.0	< 0.0001	58.6±17.8	63.2±18.6	0.0002
SVV (%)	18.1±4.3	14.2±4.0	0.0001	16.3±2.3	13.3±3.3	<0.0001
CO (L/min)	5.0±1.2	6.2±1.1	< 0.0001	5.2±1.4	5.7±1.5	0.0005
Des StO <sub>2</sub> (absolute) (s)	148.2±33.6	162.8±21.1	0.0044	167.4±13.8	160.5±40.7	0.3874
Des StO <sub>2</sub> (%/s)	7.7±3.0	7.5±3.5	0.5197	8.4±3.0	9.5±3.2	0.3499
Res StO <sub>2</sub> (absolute) (s)	35±24.2	21.8±13.4	0.0024	21.8±11.2	27.1±14.8	0.0034
Res StO <sub>2</sub> (%/s)	52.1±38.9	64.5±34.1	0.0293	77.5±38.6	67.0±27.7	0.1480
Hyperaemia (s)	61.0±31.05	46.0±20.0	0.028	46.25±12.8	46.00±11.9	0.950
DO <sub>2</sub> (mL O <sub>2</sub> /min)	901.6±285.0	1101.1±280.5	< 0.0001	937.9±3 13.2	1049.8±330.2	0.0020
Systemic vascular resistance (dynes.sec.cm <sup>-5</sup> )	1313±491	1246±309	0.5019	1231±311	1132±197	0.2654
Hemoglobin (g/dL)	12.7±2.0	12.5±2.1	0.783	12.7±1.9	12.6±1.9	0.861
Blood lactate (mmol/L)	2.4±1.2	2.1±1.1	0.189	3.3±1.6	3.0±1.2	0.499
Baseline StO <sub>2</sub> (%)	71.8±6.8	73.8±9.1	0.317	79.7±10.3	80±10.3	0.934

Des StO<sub>2</sub> (absolute): Time to maximum desaturation in seconds, Des StO<sub>2</sub> (%/s): Rate of desaturation, Res StO<sub>2</sub> (absolute): Time to resaturation till baseline in seconds, Res StO<sub>2</sub> (%/s): Rate of resaturation, StO<sub>2</sub>: Thenar muscle saturation, VE: Volume expansion, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, HR: Heart rate, SV: Stroke volume, SSV: Stroke volume variation

SBP, diastolic blood pressure, and MAP demonstrated a significant increase after fluid bolus administration in responders; however, there was no significant change in non-responders.

Delivery of oxygen showed a significant increase in both the groups ( $P \leq 0.0001$  in responders and  $P = 0.0020$  in non-responders). However, the increase in DO<sub>2</sub> was more in responders.

With regard to VE, there was a statistically significant difference in SVV in both the responders and non-responders (SVV 18.1 ± 4.3 vs. 14.2 ± 4.0,  $P \leq 0.0001$  and 16.3±2.3 vs. 13.3±3.3,  $P < 0.0001$  for responders and non-responders, respectively)

Heart rate did not show any significant change after fluid administration in both responders ( $P = 0.3126$ ) and non-responders ( $P = 0.1287$ ). The change in hemoglobin concentration before and after fluid bolus in both the groups was not significant as shown in [Table 3].

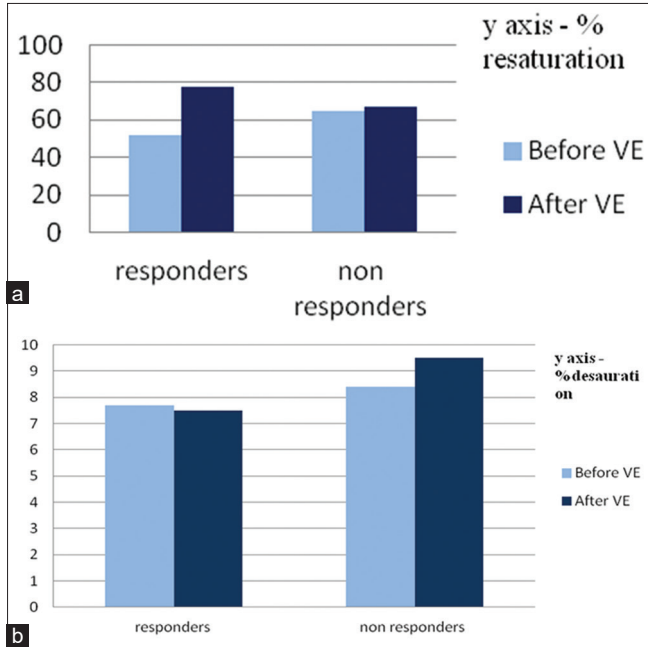
## DISCUSSION

Adequate fluid resuscitation remains the “holy grail” of critical care medicine. This is complicated by the fact that both under and over resuscitation is associated with increased morbidity and mortality. Therefore, the patient should receive sufficient fluid to restore adequate organ perfusion. The ideal volume replacement strategy should also improve microcirculation perfusion and tissue oxygenation.

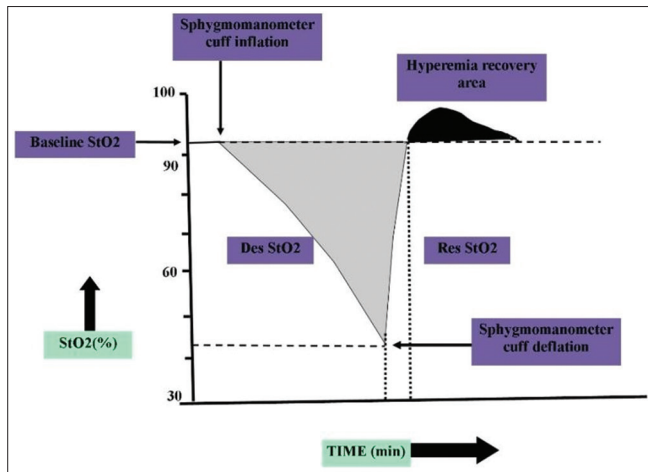
The present study was done to assess the efficacy of fluid resuscitation in improving the microcirculation in immediate post-cardiac surgical patients. The literature reports using thenar StO<sub>2</sub> (NIRS) have been proposed as a surrogate and non-invasive indicator of tissue oxygenation.<sup>[23,24]</sup>

In the present study, a significant improvement in resaturation rate was observed in responders in contrast to non-responders post-fluid resuscitation. These findings are





**Graph 1:** (a) Percentage resaturation between responders and non-responders before and after volume expansion (b) Percentage desaturation between responders and non-responders before and after volume expansion.



**Figure 1:** Response to tissue oxygen saturation during a vascular occlusion test, StO<sub>2</sub>: Tissue oxygen saturation, Des StO<sub>2</sub>: StO<sub>2</sub> desaturation slope, Res StO<sub>2</sub>: StO<sub>2</sub> resaturation slope.

in accordance with the previous study done by Tripodaki *et al.*<sup>[25]</sup> who assessed microcirculation with NIRS and the VOT performed at thenar eminence in 23 patients undergoing open cardiac surgery. They demonstrated that resaturation rate correlated with cardiac index and DO<sub>2</sub> and were higher in survivors compared to non-survivors.

The previous research shows that dynamic indices are useful for predicting individualized fluid responsiveness.<sup>[26]</sup>

SVV >12% was used to predict fluid responsiveness during mechanical ventilation with a tidal volume of 8 mL/kg.<sup>[27]</sup> A similar protocol was adopted in the present study. This indicates that such patients with SVV >12% will be on the ascending portion of the Frank-Starling curve and has recruitable cardiac output.

In the present study, patients with an increase in the SV ≥15% after fluid bolus were considered as responders similar to the previous study done by Futier *et al.*<sup>[28]</sup> They enrolled 24 patients undergoing major abdominal surgery with evidence of hypovolemia, defined as SVV >12%. They evaluated 42 fluid challenges and found that VE leads to significant improvement in the recovery slope in both responders and non-responders without any apparent change in systemic hemodynamics. In contrast, the present study demonstrated significant faster rate of resaturation in responders ( $P \leq 0.029$ ) compared to non-responders ( $P \leq 0.148$ ).

Payen *et al.*,<sup>[20]</sup> studied 43 critically ill patients with septic shock, evaluated microcirculation using VOT, a significant relationship was found between cardiac output and the reperfusion slope regardless of fluid responsiveness. They suggested that an increase in cardiac output leads to an increase in the regional perfusion and subsequent improvement of microcirculatory indices. These findings are similar to the present study as the rate of resaturation was significantly faster in responders compared to non-responders. This suggests better recruitment of microvasculature with effective fluid replacement in responders compared to non-responders who probably required further fluid administration. This finding may have important clinical implications, because the ultimate goal of resuscitation should be improvement of tissue oxygenation and perfusion.<sup>[22]</sup>

There was no significant change in the hemoglobin levels before and after VE, so it is unlikely that changes in the StO<sub>2</sub> recovery slope with VE were due to changes in rheologic factors. This finding is in support of the study done by Creteur *et al.*<sup>[29]</sup> who performed VOT before and after red blood cell transfusion and found no difference despite the difference in hemoglobin levels.

It must be stressed that in non-responders, though there was a statistically significant improvement in macrocirculatory indices such as cardiac output, SV, and delivery of oxygen, the recovery slope remained statistically insignificant. This suggests that the increase in SV <15% was clinically insignificant as microcirculation and tissue oxygenation remain uncorrected.

### Limitations

The present study did not determine whether faster rate of resaturation after effective fluid bolus was associated with

reduced morbidity such as decreased duration of ventilation, ICU stay, and reduced organ failure. The present study is a pilot study with a small sample size.

## CONCLUSION

Preload dependence is associated with significant change in the StO<sub>2</sub> recovery slope measured at the thenar eminence in volume responders. Functional evaluation of microcirculation using VOT and StO<sub>2</sub> can be a useful complementary tool along with the macrocirculatory indices for optimal fluid resuscitation in adult post-cardiac surgical patients.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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