Original Article

Role of Central Venous - Arterial pCO2 Difference in Determining Microcirculatory Hypoperfusion in Off-Pump Coronary Artery Bypass Grafting Surgery

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Abstract

Background: Cardiac surgery is frequently associated with macro and microcirculatory hypoperfusion. Patients with normal central venous oxygen saturation (Scvo2) also suffer from hypoperfusion. We hypothesized that monitoring central venous-arterial pco2 difference (dCO_2) could also serve as additional marker in detecting hypoperfusion in cardiac surgery patient. **Methods:** This is a prospective observational study. Patients undergoing off-pump coronary artery bypass grafting included in this study. The dCO2 was measured postoperatively. The patients with a ScvO2 ≥70% were divided in to 2 groups, the high-dCO2 group (≥8 mmHg) and the low-dCO2 group (<8 mmHg). **Results:** The 65 patient had $scvO_2$ ≥70%. Out of these, 20 patients were assigned to the high dCO_2 group and 45 patients to the low dCO_2 group. Patients with high dco2 had higher lactate levels after ICU admission. They also had significantly prolonged need for mechanical ventilation (14.90 ± 10.33 vs 10 ± 9.65, P = 0.0402), ICU stay (5.05 ± 2.52 d vs 3.75 ± 2.36 d, P = 0.049) and hospital stay (12.25 ± 5.90 d vs 8.57 ± 5.55 d P = 0.018). The overall rate of post-operative complications was similar in both the group. **Conclusion:** The present study demonstrates dCO_2 as an easy to assess and routinely available tool to detect global and microcirculatory hypoperfusion in off-pump CABG patients, with assumed adequate fluid status and $ScvO_2$ as a hemodynamic goal. We observed that high dCO_2 (>8 mmHg) was associated with decreased DO_2I, increased oxygen extraction ratio, the longer need for mechanical ventilation and longer ICU stay.

Keywords: *Central venous-arterial pco2 difference, microcirculatory hypoperfusion, off-pump coronary artery bypass*

Introduction

Goal-directed therapy is the basis of any hemodynamic intervention in intensive care medicine to improve postoperative outcome.[1,2] This approach is based on optimizing parameters such as stroke volume, cardiac output (CO), cardiac index (CI), and/or perfusion parameters such as stroke volume variation, central venous oxygen saturation ($ScvO_2$), mixed venous oxygen saturation (SvO_2), and arterial lactate.[1]

SvO_2 is a measurement of global tissue oxygenation and it reflects matching between arterial oxygen delivery (DO_2) and O_2 consumption (VO_2).[3] A low SvO_2 indicates high oxygen extraction ratio (OER) to maintain aerobic metabolism with constant O_2 consumption in response to an acute fall in DO_2. But when DO_2 is below critical level, OER is no longer capable of upholding O_2 consumption, and global tissue hypoxia ensues, as indicated by the high lactate levels.[4,5]

$ScvO_2$ can be obtained easily and trends in $ScvO_2$ closely mirrors SvO_2.[6] Cardiac surgery induces ischemia-reperfusion injury along with systemic inflammatory response leading to capillary shunting and mitochondrial damage.[7] These changes cause disturbances in tissue oxygen extraction and leads to normal/high $ScvO_2$ values. $ScvO_2$ is measured downstream from the tissues, So, Low venous O_2 saturation from tissue with inadequate DO_2 is masked by highly saturated blood from tissue with better perfusion resulting overall normal or high $ScvO_2$ and remaining blind to local perfusion disturbances.[8]

Impaired tissue oxygenation leads to increased anaerobic metabolism and

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production of pyruvate, which is subsequently converted to lactate. Serum lactate is a marker of global tissue hypoxia in circulatory shock. Hyperlactatemia in cardiac surgery may be due to other mechanisms such as stress response to surgery, use of βadrenergic agonist, sepsis, hyperglycaemia etc.[9,10] Therefore, after cardiac surgery, hyperlactatemia may not be a reliable means of judging the adequacy of tissue oxygenation.

According to the modified Fick equation central venous-arterial pCO_2 difference (dCO_2) is related to CO_2 production (VCO_2) and inversely linked to cardiac output.[11] As per Ariza *et al*.,[12] better approximation of $PaCO_2$ under normal condition of cardiac output and arterial oxygen saturation is $PaCO_2$ = 0.8 $PvCO_2$. The major determinant of increased dCO_2 is decreased tissue perfusion. So dCO_2 can be considered as an indicator of adequate blood flow to remove CO_2. Its usefulness has already been described in septic shock, high risk surgical patients and on pump cardiac surgical procedures.[1,2] The aim of this study was to evaluate the patient outcome and clinical parameters in correlation with central venous-arterial PCO_2 difference (dCO_2) in cardiac surgery patients with assumed adequate circulatory status according to existing guidelines (i.e., $ScvO_2$ ≥70%).

Methods

After getting ethical committee approval and preoperative written and informed consent, 100 patients scheduled for elective off-pump CABG surgery were included in the study. In this prospective observational study, we evaluated the central venous to arterial PCO_2 difference (dCO_2) in patients with a central venous saturation ($ScvO_2$) ≥70% and its relationship to the postoperative hemodynamic profile, outcome and complications.

Inclusion criteria were written informed consent, age >18 and <75 years, elective off-pump coronary artery bypass graft surgery, preoperative hemoglobin ≥10 g/dl and American Society of Anaesthesiology (ASA) Grade 1 and 2. Exclusion criteria were left ventricular ejection fraction of less than 35%, unstable angina pectoris, heart failure with New York Heart Association class III-IV, acute myocardial infarction within the last 2 weeks, previous CABG surgery, peripheral arterial occlusive disease and Patients with chronic obstructive pulmonary disease.

Perioperative patient management was standard, based on institutional protocol. Induction and maintenance of anesthesia was done with midazolam, fentanyl, propofol, vecuronium and sevoflurane. The right internal jugular vein was cannulated with 8.5 F Introducer sheath (IntroFlex, Edwards Lifesciences, Irvine, CA). A Swan-Ganz Thermodilution Venous Infusion Port Catheter, 7.5 F×110 CM (Edwards Lifesciences, Irvine, CA) inserted through the sheath and guided to the pulmonary artery before starting the operation. During surgery, the patients were mechanically ventilated and $ETCO_2$ was maintained between 35-40 mmHg. Intraoperative fluid management was done according to goal directed fluid therapy targeting goal of maintaining mean arterial pressure ≥65 mmhg and $ScvO_2$ ≥70%.

All hemodynamic and laboratory parameters were measured after surgery at 1, 6, and 18 hours after admission to the ICU. At these time points, arterial and central venous, and mixed venous blood samples were taken. The blood gas analysis was performed. We collected $ScvO_2$, SvO_2, PO_2, SaO_2, PCO_2 and lactate from this analysis. Oxygen delivery index (DO_2I), oxygen consumption index (VO_2I), arterial oxygen content (CaO_2), venous oxygen content (CvO_2) and oxygen extraction ratio (OER) were calculated using standard formulae (ANNEXURE).

The dCO_2 was calculated as the difference between the PCO_2 of central venous and arterial blood. Based on the first measurement of dCO_2, the patients were divided in to two groups, the high dCO_2 group (Group A, dCO_2 >8 mmHg) and the low dCO_2 group (Group B, dCO_2 ≤8 mmhg).

Cardiovascular complications were defined as new arrhythmias or a newly diagnosed myocardial ischemia detected in the electrocardiogram (new Q-wave, ST-elevations >2 mm), or a ratio of creatine kinase (CK) and its myocardial subtype (CK-MB) >10%. Neurologic complications were defined as transitory ischemic attack and postoperative delirium; pulmonary complications defined as respiratory failure and the need for reintubation, prolonged Respiratory support (>48 h) or the need for continuous positive airway pressure breathing; renal complications were defined as patients requiring renal replacement therapy and continuous intravenous loop diuretics or patients with an increase of creatinine >2.0 mg/dl. Additional outcome parameters like hours of mechanical ventilation, length of ICU stay, length of hospital stay and any morbidity or mortality were recorded.

Statistics

Statistical analysis was performed using SPSS, Version 20.0 (Chicago, IL, USA).

The Chi-square test was used to compare the categorial variable. The independent sample *t*-test was used to compare continuous variables. Mann-Whitney U test was used where the assumptions of the *t*-test were not met. Data were presented as mean ± SD or proportion as appropriate. The "*P*" value less than 0.05 was considered to be significant.

Results

A total of 100 patient undergoing elective coronary artery bypass grafting without cardiopulmonary bypass were included in our study. On admission to ICU, central venous and arterial blood gas samples were collected in all patients and analyzed. From those 100 patients,

65 patients had $ScvO_2$ ≥70%. From those 65 patients, as per the first postoperative dCO_2 measurement, 20 patients were assigned to the high dCO_2 group (Group A, dCO_2 >8 mmHg) and 45 patients were assigned to low dCO_2 group (Group B, dCO_2 ≤8).

Demographic and clinical data of both the groups are summarized in Table 1. There were no differences between the basic characteristics of patients with high dCO_2 and low dCO_2 group. Surgery duration was comparable in both the groups. Pre-operative ejection fraction was lower in group A but the difference was not significant.

Comparison of hemodynamic parameters is shown in Tables 2a and 2b. Heart rate (HR), mean arterial pressure (MAP), mean pulmonary artery pressure (MPA), central venous pressure (CVP), lactate, cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) were observed at 1st, 6th and 18th hours of ICU stay in both the groups. After ICU admission, patients in group A showed an initial tendency towards lower CO, but it was not significant. However, group A had higher HR at 6th and 18th hour duration and were statistically significant. Patients had comparable inotropic scores at 1st hour after admission to the intensive care unit. However, these values were higher at 6th and 18th hour in the high dCO_2 group.

MAP was higher on admission in group B, but this difference was narrowed at the end of 18th hour. Both CVP and MPA were significantly higher in group A at all points of measurements. SVR was higher in group B on admission to ICU whereas PVR was higher in group A which was statistically significant. Lactate levels were higher in group A and remained elevated at 6th and 18th hour time period as compared to group B.

Oximetry parameters are listed in Table 3. We did the arterial, venous and mixed venous blood gas analysis and calculated arterial oxygen content (CaO_2), mixed venous oxygen content (CvO_2), oxygen delivery index (DO_2I), oxygen consumption index (VO_2I) and oxygen extraction rate (OER) at 1st, 6th and 18th hours of ICU stay in both the groups. The CaO_2 1st hour after ICU admission was significantly lower in group A, but was within physiological limit ($P < 0.05$). Gradually CaO_2 improved over time and showed no difference at 18th hour after ICU admission. Similarly, DO_2I was also lower in group A on admission and remained lower than group B at all point of time but the difference was not significant. While comparing the CvO_2, it was significantly lower in group A at 1st hour after ICU admission and remained lower at 18th hour. OER was significantly higher in group A as compared to group B at 1st hour. VO_2I did not show a significant difference.

Post-operative outcome parameters are listed in Table 4. The observed hemodynamic, oximetric and laboratory alterations were associated with a significantly prolonged need for mechanical ventilation (14.90 ± 10.33 vs

Table 1: Demographic data

	Group A (*n*=20)	Group B (*n*=45)	*P*
Age	62.2±7.31	62.4±7.17	0.9182
Sex (M/F)	11/9	26/19	
Height	162.95±7.40	163.93±8.36	0.6525
Weight	66.4±10.32	66.84±11.20	0.881
BSA	1.71±0.13	1.72±0.14	0.7860
BMI	25.13±4.36	24.98±4.54	0.9010
preop_pco2	33.95±6.83	35.73±4.43	0.2101
preop_po2	82.95±9.25	85.17±8.36	0.3413
surgery duration	290.25±70.97	298.33±61.72	0.6433
EF	50.50±6.66	53.3±6.82	0.1289
DM (n)	8	10	0.1402
HTN (n)	4	06	0.4901

Table 2a: Comparision of hemodynamic parameters in patients with $ScvO_2$ ≥70%

Parameters	Time	Group A (*n*=20)	Group B (*n*=45)	*P*
HR	1st hr ICU	91.35±17.76	89.77±13.11	0.6914
	6th hr ICU	85.15±9.83	78.53±12.80	0.0441
	18th hr ICU	92.85±12.35	70.42±11.86	0.001
MAP	1st hr ICU	73.5±12.23	77.75±12.23	0.2001
	6th hr ICU	70.35±9.91	83±8.85	0.001
	18th hr ICU	78.4±11.05	78.51±7.53	0.9624
MPA	1St hr ICU	35.55±6.34	27.26±4.51	0.001
	6th hr ICU	32.65±5.40	22.86±4.78	0.001
	18th hr ICU	29±4.88	18.4±3.91	0.001
CVP	1st hr ICU	12.6±1.95	9.11±1.41	0.001
	6th hr ICU	10.65±2.27	7.51±1.84	0.001
	18th hr ICU	9.2±2.74	4.24±1.89	0.001
LACTATE	1st hr ICU	3.63±2.26	2.78±1.16	0.04
	6th hr ICU	3.46±2.21	2.41±1.20	0.015
	18th hr ICU	2.48±1.02	1.64±1.08	0.004
INOTROPIC SCORE	1st hr ICU	4.93±3.38	3.11±3.93	0.077
	6th hr ICU	4.55±2.43	1.93±2.12	0.001
	18th hr ICU	2.25±2.29	0.8±1.54	0.004

Table 2b: Comparision of hemodynamic parameters in patients with $ScvO_2$ ≥70%

Parameters	Time	Group A (*n*=20)	Group B (*n*=45)	*P*
CO	1st hr ICU	3.85±0.61	4.04±0.58	0.2462
	6th hr ICU	3.93±0.53	3.96±0.54	0.8279
	18th hr ICU	4±0.36	4.02±0.60	0.8942
CI	1st hr ICU	2.27±0.45	2.36±0.43	0.4427
	6th hr ICU	2.31±0.41	2.30±0.32	0.9197
	18th hr ICU	2.34±0.30	2.35±0.38	0.9123
SVR	1st hr ICU	1290.65±310.02	1387.6±325.09	0.03062
	6th hr ICU	1230.2±217.9	1552.24±290.20	<0.001
	18th hr ICU	1379±222.5	1513.11±301.3	0.0794
PVR	1st hr ICU	323.1±174.4	247.8±65.27	0.0135
	6th hr ICU	302.75±122.18	252.42±61.79	0.0306
	18th hr ICU	228.1±77.64	197.95±51.51	0.0688

Table 3: Comparision of oximetry parameters in patients with $ScvO_2$ ≥70%

Parameters	Time	Group A (*n*=20)	Group B (*n*=45)	*P*
$ScvO_2$	1st hr ICU	75.3±3.55	74.84±3.64	0.6409
	6th hr ICU	71.35±4.86	72.35±4.04	0.3883
	18th hr ICU	70.6±4.61	71.4±3.51	0.4456
SvO_2	1st hr ICU	67.3±7.16	72.86±4.71	<0.001
	6th hr ICU	66.65±6.82	68.02±4.91	0.3619
	18th hr ICU	67.45±6.10	69.2±4.19	0.1842
CaO_2	1st hr ICU	13.32±1.67	15.05±2.09	0.0017
	6th hr ICU	13.48±0.89	13.62±1.92	0.7513
	18th hr ICU	13.47±1.42	13.56±1.18	0.791
CvO_2	1st hr ICU	9.1±1.61	10.95±1.63	<0.001
	6th hr ICU	9.35±1.26	9.48±1.68	0.7435
	18th hr ICU	9.34±1.17	9.73±0.98	0.1654
DO_2I	1st hr ICU	299.76±72.36	355.84±78.9	0.0082
	6th hr ICU	309.28±64.13	315.75±68.29	0.7201
	18th hr ICU	317.98±65.84	318.95±60.8	0.950
VO_2I	1st hr ICU	98.35±31.71	95.48±27.13	0.7109
	6th hr ICU	102.15±39.2	95.3±26.0	0.4124
	18th hr ICU	101.1±32.12	92.55±26.08	0.2612
OER	1st hr ICU	0.323±0.07	0.269±0.049	<0.001
	6th hr ICU	0.314±0.075	0.302±0.05	0.4495
	18th hr ICU	0.304±0.065	0.287±0.047	0.2378

Table 4: Comparison of outcome parameters in patients with $ScvO_2$ ≥70%

	Group A (*n*=20)	Group B (*n*=45)	*P*
Duration of mechanical ventilation	14.90±10.33	10±9.65	0.0402
ICU STAY	5.05±2.52	3.75±2.36	0.049
HOSPITAL STAY	12.25±5.90	8.57±5.55	0.018
REEXPLORATION (*n*)	1	1	0.54
COMPLICATIONS (*n*)	1	1	0.54

10 ± 9.65 hrs, *P* = 0.04) and ICU stay (5.05 ± 2.52 vs 3.75 ± 2.36 days, *P* = 0.049) in group A. Incidence of re-exploration was similar in both the groups. The total duration of hospital stay was significantly higher in group A. In the high dCO_2 group, out of 20 patients, one patient died due to multi-organ failure and septic shock, while in the low dCO_2 group, out of 45 patients, one patient died due to respiratory failure and sepsis.

Discussion

After cardiac surgery, the patient might be subjected to undetected tissue hypoperfusion even when circulation and oxygen supply/demand ratio is considered adequate by $ScvO_2$ ≥70%. Here in our study, we found that in cardiac surgery patients, dCO_2 may be used as an additional, readily available tool to identify clinically relevant hypoperfusion. Current techniques for monitoring tissue perfusion have largely focused on systemic blood flow and the balance between oxygen demand and supply.[13] An early hemodynamic optimization that targets central venous oxygen saturation ($ScvO_2$) and systemic hemodynamic parameters improves outcomes in severe sepsis and septic shock, reinforcing the idea that tissue perfusion abnormalities are flow dependent at least during the very early stages.[14] A $ScvO_2$ ≥70% is considered a goal for optimal hemodynamic resuscitation after cardiac surgery according to the S3 guidelines for postoperative intensive care in cardiac surgery patients, and also in the Surviving Sepsis Guidelines.[2] However, normalizing systemic hemodynamic parameters does not guarantee adequate tissue perfusion, and in fact a substantial number of patients still progress to multiorgan dysfunction and death despite meeting $ScvO_2$ targets.[14]

In our study, we found low CI, low MAP and higher HR in the high dCO_2 group. These findings are in line with the study done by Futier *et al*.[15] They concluded that $ScvO_2$ reflects important changes in O_2 delivery in relation to O_2 needs during the perioperative period. A dCO_2 <5 mmHg might serve as a complementary target to $ScvO_2$ during goal-directed therapy to identify persistent inadequacy of the circulatory response in face of metabolic requirements when a $ScvO_2$ ≥70% is achieved. A recently published study reported a higher prevalence of circulatory shock in patients with a pre-operatively increased dCO_2.[16]

We found higher lactate levels in the high dCO_2 group on admission to ICU and this difference persisted at 6th and 18th after ICU admission also. Similar results were observed by Vallee *et al*.[17] The study reported that the low dCO_2 group had a lower (Simplified Acute Physiology Score) SOFA score after 24 hours, despite the fact that they had a higher score at admission to the ICU. Furthermore, a significantly lower lactate level was described for the low dCO_2 group. The authors concluded that a high dCO_2 can identify patients who are still under-resuscitated, even when they are resuscitated to a $ScvO_2$ ≥70 according to the surviving sepsis campaign guideline.[17] In another study by Bakker *et al*.,[18] septic patients showed that a high dCO_2 was associated with poor outcome and higher lactate levels.

There are many reasons for a high dCO_2. It has been shown that dCO_2 was related linearly to CO_2 production and inversely related to cardiac output.[19] Several studies showed that if global or regional blood flow was critically reduced or unevenly distributed as in shock, venous blood carbon dioxide increased.[20,21] Therefore, dCO_2 may increase after hypoperfusion because of a decreased washout.[22] Thus, dCO_2 also has been proposed as a marker of tissue hypoxia.[23] Durkin *et al*.[24] described 2 different mechanisms for increased dCO_2 in patients suffering from shock. The first mechanism was related to the lower blood flow in shock patients. A longer blood transit time in the microcirculation because of decreased microcirculatory flow causes more carbon dioxide to diffuse in to venous blood. Secondly, because of the increased ventilation-to-perfusion

ratio, arterial partial pressure of carbon dioxide decreases as well. Another possible mechanism is a relative increase in carbon dioxide production by ischemic cells through anaerobic metabolism, which would explain the relative increase of venous-to-arterial partial pressure of carbon dioxide.[24,25]

In our study, CI and DO_2 were lower in the high dCO_2 group. We also found that OER was significantly higher in the high dCO_2 group. This was in line with the results described by Durkin *et al*.,[24] for example, related to microcirculatory hypoperfusion in the hepatosplanchnic region. Therefore, the results could be interpreted as insufficient tissue perfusion with lactic acidosis due to anaerobic metabolism. A relationship between a high dCO_2 (9 mmHg ± 0.5 mmHg) and lactate levels was described in an earlier investigation in postoperative cardiac surgical patients.[12] Other studies reported a correlation between dCO_2 and CI.[26,27]

Our study showed high VO_2I and high OER in the high dCO_2 group. These results in low SvO2 values as compare to ScvO2 potentially because of splanchnic hypoperfusion. This was also in line with data from Nygren *et al*.,[28] who showed that patients with intestinal vasoconstriction and hypoperfusion had significantly lower SvO_2 compared to patients with normal intestinal perfusion after cardiac surgery. This was supported by the finding that after hemodynamic deterioration mesenteric blood flow decreased, resulting in venous desaturation of the lower body.[29] Therefore, it seemed quite reasonable to assume splanchnic hypoperfusion in the patients with a high dCO_2 gap. Splanchnic hypoperfusion in the high dCO_2 group also was supported by the increase of the aspartate transaminase (SGOT) on day 1 pointing towards structural liver damage.

Clinically, patients with high dCO_2 required longer ICU stay, mechanical ventilation, and had a higher incidence of cardiovascular complications in the postoperative setting. Therefore, we believe that a substantial cohort of cardiac surgical patients in the postoperative period might have been under-resuscitated if $ScvO_2 \geq 70\%$ alone was used as the goal to assess the adequacy of global and microcirculatory perfusion. Du *et al*. had also confirmed these findings.[30] Thus, from a physiologic point of view, it seemed reasonable to assume that hemodynamic optimization strategies minimizing dCO_2 aiming at individualized increases of global and regional/splanchnic blood flow to adjust for individual carbon dioxide production might have been more sufficient compared to strategies aiming solely at $ScvO_2 \geq 70\%$.

Conclusion

The present study demonstrates dCO_2 as an easy to assess and routinely available tool to detect global and microcirculatory hypoperfusion in post-operative off-pump CABG patients, with assumed adequate fluid status and $ScvO_2$ as a hemodynamic goal. We observed that high dCO_2 (>8 mmHg) was associated with decreased DO_2I, increased oxygen extraction ratio, increased postoperative complication rate, the longer need for mechanical ventilation and longer ICU stay. This suggest that a high dCO_2 is associated with microcirculatory hypoperfusion and might be a useful marker to detect patients who remain insufficiently resuscitated and it can better guide volume management in the post off-pump CABG patients and decrease the mechanical ventilation time and length of ICU stay. However, we admit that more prospective studies testing this hypothesis and the finding reported here are needed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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ANNEXURE

Calculation formulas

Cardiac index (L/min/m^2)

$CI = CO/ BSA(m^2)$

CI, cardiac index; CO, cardiac output

Oxygen delivery (mL/min/m^2)

$DO_2I = CaO_2 \times CI \times 10$

DO_2I, oxygen delivery; CaO_2, arterial oxygen content; CI, cardiac index

Oxygen consumption (mL/min/m^2)

$VO_2I = (CaO_2 - CvO_2) \times CI \times 10$

VO_2I, oxygen consumption; CaO_2, arterial oxygen content; CvO_2, oxygen content; CI cardiac index

Arterial oxygen content (mL/dL)

$CaO_2 = (Hb \times 1.39 \times SaO_2) + (0.0031 \times paO_2)$

CaO_2, arterial oxygen content; Hb, hemoglobin concentration; SaO_2, arterial oxygen saturation; paO_2, arterial partial pressure of oxygen: 1.39 is the oxygen-carrying capacity of hemoglobin (mL O_2/ gram Hb); 0.0031 is the solubility coefficient of oxygen in plasma (mL O_2/mmHg pO_2)

Mixed venous oxygen content (mL/dL)

$CvO_2 = (Hb \times 1.39 \times SvO_2) + (0.0031 \times pvO_2)$

CvO_2, mixed venous oxygen content; Hb, hemoglobin concentration; SvO_2, mixed venous oxygen saturation; pvO_2, mixed venous partial pressure of oxygen

Oxygen extraction rate (%)

$OER = VO_2I/DO_2I$

VO_2I, oxygen consumption; DO_2I, oxygen delivery