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Original Research Article

A Hospital Based Assessment of the Significance of the Central Venous - Arterial Pco2 Difference in Identifying Microcirculatory Hypoperfusion After Off-Pump Coronary Artery Bypass Grafting Surgery

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Abstract

Aim: To determine the significance of the Central Venous - Arterial pCO2 Difference in identifying Microcirculatory Hypoperfusion after Off-Pump Coronary Artery Bypass Grafting Surgery.

Material and methods: This study was conducted in Indira Gandhi institute of cardiology, Patna, Bihar, India for one year, 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 haemoglobin ≥10 g/dl and American Society of Anaesthesiology (ASA) Grade 1 and 2.

Results: The observed hemodynamic, oximetric and laboratory alterations were associated with a significantly prolonged need for mechanical ventilation (14.90 ± 10.33 vs 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.

Conclusion

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.

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

Introduction

Off-pump coronary artery bypass grafting (OPCAB) surgery has gained prominence as a preferred technique for myocardial revascularization, primarily due to its potential to reduce complications associated with cardiopulmonary bypass. Despite its advantages, OPCAB surgery is not without challenges, particularly in ensuring adequate tissue perfusion and oxygenation during the procedure. One critical aspect of perioperative management in OPCAB is the assessment of microcirculatory perfusion, which plays a crucial role in patient outcomes. [1-5] The central venous to arterial carbon dioxide difference (ΔpCO2) has emerged as a valuable parameter for evaluating microcirculatory perfusion. ΔpCO2 reflects the balance between tissue CO2 production and its clearance by blood flow, making it an indirect marker of the adequacy of tissue perfusion. [6-9] An increased ΔpCO2 can indicate microcirculatory hypoperfusion, even when microcirculatory parameters such as blood pressure and cardiac output appear normal. Therefore, monitoring ΔpCO2 during OPCAB surgery can provide vital information about the patient's microcirculatory status, enabling timely interventions to optimize perfusion and oxygen delivery. [10-13] In OPCAB surgery, maintaining optimal microcirculatory perfusion is crucial, as inadequate perfusion can lead to organ dysfunction and adverse postoperative outcomes. Traditional hemodynamic parameters may not always

accurately reflect the microcirculatory state, necessitating the use of more sensitive indicators like ΔpCO2. By assessing the central venous to arterial pCO2 difference, clinicians can gain insights into the effectiveness of perfusion strategies and make informed decisions to ensure adequate tissue oxygenation throughout the surgical procedure. [14-16] This study aims to explore the role of the central venous to arterial pCO2 difference in determining microcirculatory hypoperfusion during OPCAB surgery. By analysing the relationship between ΔpCO2 and microcirculatory perfusion, we seek to enhance our understanding of how this parameter can be utilized to improve patient outcomes. Furthermore, this research intends to establish ΔpCO2 as a reliable and practical tool for monitoring microcirculatory perfusion in the clinical setting of OPCAB surgery, potentially leading to better perioperative management and reduced complications.

Material and Methods

This study was conducted in the Indira Gandhi institute of cardiology, Patna, Bihar, India for one year. 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 haemoglobin ≥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 anaesthesia was done with midazolam, fentanyl, propofol, vecuronium and sevoflurane. The right internal jugular vein was cannulated with 8.5 F Introducer sheath (Introflexion, 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. 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 analysis

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 analysed. 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.

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

Comparison of hemodynamic parameters is shown in Tables Tables2a2a and and2b.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.

Table 2a: Comparison 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: Comparison 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

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.

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

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 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.

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

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 dCO2 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 DO2 were lower in the high dCO2 group. We also found that OER was significantly higher in the high dCO2 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 SvO2 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

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.

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