SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Behera *et al.*, 2025
doi: 10.21276/SSR-IIJLS.2025.11.6.41

Original Article

open access

Evaluation of Central Venous-to-Arterial Carbon Dioxide Difference (DCO_2)-Guided Goal-Directed Therapy in Cardiac Surgery: A Randomized Controlled Study

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Received: 19 Jun 2025/ Revised: 03 Sep 2025/ Accepted: 17 Oct 2025

ABSTRACT
Background: Goal-directed therapy (GDT) aims to optimize hemodynamic parameters and tissue perfusion in perioperative care. The central venous-to-arterial carbon dioxide difference (DCO_2) is an emerging marker of tissue hypoperfusion and may complement conventional parameters such as central venous oxygen saturation ($ScvO_2$). This study evaluated the effectiveness of DCO_2-guided GDT in improving perioperative outcomes in patients undergoing elective cardiac surgery.
Methods: A prospective, randomized, controlled, single-blind study was conducted at S.C.B. Medical College and Hospital, Cuttack, Odisha, from August 2024 to January 2025. One hundred ASA I–II patients aged >18 years undergoing elective cardiac surgery were randomized into control (conventional management) and intervention (goal-directed DCO_2 <6 mmHg, $ScvO_2$ >70%) groups, 50 each. Intraoperative and postoperative parameters, including hemoglobin, DCO_2, $ScvO_2$, lactate, fluids, urine output, and outcomes, were recorded. Data were analyzed using SPSS v25.0; p<0.05 was considered significant.
Results: Baseline characteristics were comparable between groups. Intraoperative DCO_2 was significantly lower in the intervention group (5.93±1.96 mmHg) than controls (8.46±3.05 mmHg, p<0.001) and remained lower postoperatively (5.6±1.64 vs. 8.59±2.8 mmHg, p<0.001), while $ScvO_2$ was higher (74.39±5.76% vs. 67.51±6.45%, p<0.001). ICU stay was shorter in the GDT group (1.48±0.85 vs. 2.46±1.06 days, p=0.002), with similar hospital stay and complications.
Conclusion: Goal-directed therapy guided by DCO_2 and $ScvO_2$ significantly improved perioperative hemodynamic optimization and reduced ICU stay in patients undergoing cardiac surgery, without increasing complications or hospital stay. Incorporating DCO_2 into GDT protocols may enhance perioperative management and align with the principles of enhanced recovery after surgery (ERAS).

Key-words: Cardiac surgery; Goal-directed therapy; DCO_2 gap; Central venous-to-arterial carbon dioxide difference; Tissue perfusion; Hemodynamic optimization; Enhanced recovery after surgery

INTRODUCTION
Goal-directed therapy (GDT) in hemodynamic management has emerged as a key strategy to optimize peri-operative outcomes in high-risk surgical and critically ill patients.

How to cite this article
Behera CS, Subudhi BSK, Singh S. Evaluation of Central Venous-to-Arterial Carbon Dioxide Difference (DCO_2)-Guided Goal-Directed Therapy in Cardiac Surgery: A Randomized Controlled Study . SSR Inst Int J Life Sci., 2025; 11(6): 8891-8897.

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This approach involves structured monitoring and individualized correction of hemodynamic parameters, including mean arterial pressure (MAP), central venous pressure (CVP), central venous oxygen saturation ($ScvO_2$), urine output (UO), arterial oxygen saturation (SaO_2), and cardiac index. By maintaining these physiological targets within optimal ranges, GDT aims to ensure adequate tissue perfusion and oxygen delivery, thereby reducing morbidity and mortality in the peri-operative period [1–3].
Several studies have explored the benefits of GDT; however, its clinical effectiveness and the choice of guiding parameters remain debated [4,5]. Recent research

doi: 10.21276/SSR-IIJLS.2025.11.6.41

suggests that incorporating additional resuscitation endpoints such as the central venous-to-arterial carbon dioxide difference (ΔCO_2 or DCO_2) may enhance the precision of GDT protocols [6,7]. In cardiac surgery patients—who are particularly vulnerable to complications such as significant blood loss, prolonged ICU stay, and sepsis—DCO_2 has been proposed as a sensitive marker of tissue hypoperfusion and circulatory adequacy [8]. A DCO_2 gap of <6 mmHg is generally considered optimal during fluid resuscitation, indicating effective cardiac output and tissue perfusion [9,10].

Integrating DCO_2 into the hemodynamic optimization algorithm provides additional insight beyond traditional oxygen-derived parameters. Both $ScvO_2$ and DCO_2 have been identified as valuable complementary markers for guiding intra-operative and post-operative resuscitation [11,12]. Any major surgical procedure represents a physiological insult, increasing catabolic activity, oxygen consumption, and CO_2 production. $ScvO_2$ reflects the balance between systemic oxygen delivery and utilization and serves as an indirect indicator of tissue oxygenation [13]. However, $ScvO_2$ alone may not reliably detect tissue hypoxia, as normal values can persist even in the presence of regional underperfusion [14].

In contrast, DCO_2, which measures the difference between central venous and arterial CO_2 partial pressures, rises when tissue perfusion is inadequate. This occurs because CO_2, being approximately 20 times more soluble than oxygen, accumulates more readily in hypoperfused tissues [15]. Thus, a normal $ScvO_2$ combined with an elevated DCO_2 suggests impaired microcirculatory flow despite adequate oxygen delivery. Monitoring DCO_2 is both practical and cost-effective, as it requires only routine arterial and central venous blood gas analyses—tools already available in most operating rooms and intensive care units [16].

By integrating DCO_2 into GDT protocols, clinicians can better identify and correct tissue hypoperfusion, potentially reducing post-operative organ dysfunction and improving recovery. This study, therefore, aims to assess whether goal-directed therapy guided by DCO_2, an adjunct marker of tissue perfusion, can reduce perioperative complications compared with conventional hemodynamic management in patients undergoing cardiac surgery.

MATERIALS AND METHODS

Study Setting- This prospective, randomized, controlled, single-blind clinical study was conducted after obtaining approval from the Institutional Ethics Committee of Srirama Chandra Bhanja (S.C.B.) Medical College and Hospital, Cuttack, Odisha. The study was carried out jointly by the Departments of Surgery and Cardiothoracic and Vascular Surgery over six months (August 2024 to January 2025). A total of 100 adult patients of either sex, aged over 18 years, belonging to ASA physical status I or II, and scheduled to undergo elective cardiac surgeries under general anesthesia were enrolled. Written informed consent was obtained from all participants before inclusion in the study.

Randomization and Blinding- Participants were randomly allocated into two equal groups (n=50 each):

Group C (Control group)– Conventional hemodynamic management

Group I (Intervention group)– Goal-directed therapy (GDT) guided by DCO_2 and $ScvO_2$

Randomization was performed using computer-generated random numbers, and allocation concealment was ensured using sealed opaque envelopes. The treating anesthesiologist was blinded to the central venous blood gas parameters to maintain the single-blind design.

Inclusion Criteria

1. Adult patients aged >18 years.
2. ASA physical status I and II.
3. Patients scheduled for elective cardiac surgeries under general anesthesia.

Exclusion Criteria

1. Refusal to provide written informed consent.
2. History of end-organ failure (renal, hepatic, or cardiac).
3. Preoperative evidence of sepsis.
4. Emergency surgical procedures.

All patients were counseled and prepared in accordance with institutional pre-anesthetic protocols. Following induction, arterial and central venous catheters were inserted for continuous hemodynamic monitoring and blood sampling.

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Parameters monitored and optimized included:

- Hemoglobin concentration
- Fraction of inspired oxygen (FiO_2) and positive end-expiratory pressure (PEEP)
- Central venous oxygen saturation ($ScvO_2$)
- Central venous-to-arterial CO_2 difference (DCO_2)
- Requirement of dobutamine infusion

Control Group (Conventional Management)- Patients in the control group were managed according to standard institutional anesthesia and hemodynamic protocols at the discretion of the treating anesthesiologist. Arterial and central venous blood samples were obtained every two hours intraoperatively for blood gas analysis. The anesthesiologist was blinded to venous sample results, while arterial values were available for standard management.

Postoperatively, both arterial and central venous blood samples were analyzed every four hours. Patients were transferred to the Intensive Care Unit (ICU) following surgery for standard postoperative care. Weaning, extubation, and ICU discharge decisions were made by the ICU team in accordance with established hospital protocols. Sedation and analgesia were standardized for all patients.

Intervention Group (Goal-Directed Therapy Guided by DCO_2 and $ScvO_2$)- In the intervention group, intraoperative management was guided by goal-directed principles based on DCO_2 (<6 mmHg) and $ScvO_2$ (>70%) as primary endpoints of tissue perfusion. A fluid bolus of 4 mL/kg (maximum 250 mL) of crystalloid solution was administered whenever DCO_2 exceeded 6 mmHg or $ScvO_2$ fell below 70%. Before recording pulse pressure variation (PPV), tidal volume was standardized to 10 mL/kg. If DCO_2 remained elevated despite fluid optimization, dobutamine infusion was titrated to improve cardiac output and reduce the CO_2 gap. Serial hemodynamic and gas parameters were recorded every two hours intraoperatively and every four hours postoperatively until stabilization. Patients were then transferred to the ICU for postoperative monitoring and managed according to the same sedation, analgesia, and ventilation protocols as the control group.

Primary Outcome

- Incidence of postoperative organ dysfunction between the two groups.

Secondary Outcomes

- Duration of mechanical ventilation.
- Length of ICU stay.
- Total postoperative hospital stays.
- Intraoperative fluid requirements & vasopressor use.
- Incidence of perioperative complications.

Statistical Analysis- All data were entered into a secure database and analyzed using SPSS software (Version 25.0, IBM Corp., Armonk, NY, USA). Categorical variables such as gender and ASA physical status were analyzed using the Chi-square test, while continuous variables such as age were compared using the unpaired Student's t-test. Parametric data, including hemoglobin, $ScvO_2$, DCO_2, lactate levels, total fluid input, urine output, ICU stay, and hospital stay, were analyzed using the unpaired t-test. The incidence of perioperative complications between groups was compared using the Chi-square test. $p<0.05$ was considered statistically significant.

Ethical Considerations- Ethical approval was obtained from the Institutional Ethics Committee, S.C.B. Medical College and Hospital, Cuttack. Written informed consent was obtained from all participants or their representatives. Confidentiality was ensured, and all data were anonymized for analysis.

RESULTS

A total of 100 patients were included in the study and equally randomized into two groups — the Control group (n=50) and the Intervention group (n=50). Baseline demographic and clinical variables were statistically comparable between the two groups (Table 1). The mean age of patients was 53.72±14.39 years in the control group and 49.38±15.26 years in the interventional group (*p*=0.38). The gender distribution was identical (Male: Female= 25:25 in both groups). Most patients were in ASA physical status II (52% in the control vs. 36% in the intervention, *p*=0.62). The mean surgical duration was also similar between the two groups (5.4±0.8 hours in the control group vs. 5.3±0.6 hours in the intervention group; *p*=0.48). No statistically significant differences were observed, indicating effective randomization and baseline homogeneity.

doi: 10.21276/SSR-IIJLS.2025.11.6.41

Table 1: Comparison of baseline characteristics between the intervention and control groups

Variable	Control Group (n=50)	Intervention Group (n=50)	p-value
Age (years)	53.72±14.39	49.38±15.26	0.38
Gender (M/F)	25/25	25/25	1
ASA I / II	24 (48%) / 26 (52%)	32 (64%) / 18 (36%)	0.62
Duration of surgery (hours)	5.4±0.8	5.3±0.6	0.48

Intraoperative parameters, including hemoglobin, $ScvO_2$, lactate levels, total fluid input, and urine output, were comparable between the two groups (Table 2). The mean intraoperative hemoglobin was 12.4±5.7 g/dL in the control group and 11.1±3.7 g/dL in the intervention group (p=0.24). Similarly, mean $ScvO_2$ values were 80.46±6.48% and 81.05±4.27% (p=0.54), respectively. However, a statistically significant difference in DCO_2 levels was observed, with lower levels in the intervention group (5.93±1.96 mmHg) compared to the control group (8.46±3.05 mmHg; p<0.001). This demonstrates that goal-directed measures effectively reduced the CO_2 gap, suggesting better tissue perfusion in the intervention group.

Table 2: Comparison of intraoperative parameters between the intervention and control groups

Variable (Mean±SD)	Control Group (n=50)	Intervention Group (n=50)	p-value
Hemoglobin (g/dL)	12.4±5.7	11.1±3.7	0.24
$ScvO_2$ (%)	80.46±6.48	81.05±4.27	0.54
DCO_2 (mmHg)	8.46±3.05	5.93±1.96	<0.001*
Lactate (mmol/L)	2.32±1.6	1.89±0.9	0.17
Fluid input (mL)	2045±583	1972±753	0.59
Urine output (mL)	429±189	378±263	0.78

**Statistically significant (p<0.05)*

Postoperative parameters, including hemoglobin, lactate, fluid input, urine output, and blood transfusion requirements, were similar between groups (Table 3). The postoperative DCO_2 was significantly lower in the intervention group (5.6±1.64 mmHg) compared to the control group (8.59±2.8 mmHg) (p<0.001). Conversely, postoperative $ScvO_2$ was significantly higher in the intervention group (74.39±5.76%) than in the control group (67.51±6.45%, p<0.001), indicating improved oxygen delivery and tissue perfusion with goal-directed therapy.

Table 3: Comparison of postoperative parameters between the intervention and control groups

Variable (Mean±SD)	Control Group (n=50)	Intervention Group (n=50)	p-value
Hemoglobin (g/dL)	11.6±2.84	11.8±2.1	0.28
$ScvO_2$ (%)	67.51±6.45	74.39±5.76	<0.001*
DCO_2 (mmHg)	8.59±2.8	5.6±1.64	<0.001*
Lactate (mmol/L)	7.6±5.9	6.1±3.3	0.14
Fluid input (mL)	1285±362	1361±316	0.45
Urine output (mL)	796±214	849±346	0.53
Blood transfusion (units)	0.37±0.6	0.58±0.8	0.24

**Statistically significant (p<0.05)*

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Outcome measures, including postoperative complications, ICU stay, and hospital stay, were analyzed and compared (Table 4). Complications were assessed using the Sequential Organ Failure Assessment (SOFA) score, where a score >1 indicated the presence of postoperative complications. The incidence of complications on POD 0, 1, and 2 did not differ significantly between the two groups. However, a significant reduction in ICU length of stay was observed: 1.48±0.85 days in the interventional group compared with 2.46±1.06 days in the control group (p=0.002). The mean hospital stay was slightly shorter in the interventional group (9.46±4 days) than in the control group (10.29±4.32 days), although the difference was not statistically significant (p=0.30).

Table 4: Comparison of outcome measures between the intervention and control groups

Variable	Control Group (n=50)	Intervention Group (n=50)	p-value
Postoperative Complications (SOFA >1)			
POD 0	40 (80%)	33 (66%)	0.24
POD 1	26 (52%)	24 (48%)	0.69
POD 2	22 (44%)	22 (44%)	0.89
Length of ICU stay (days)	2.46±1.06	1.48±0.85	0.002*
Length of hospital stay (days)	10.29±4.32	9.46±4.00	0.3

**Statistically significant (p<0.05)*

DISCUSSION

The central venous-to-arterial carbon dioxide difference (DCO_2) has emerged as a sensitive marker of tissue hypoperfusion and microcirculatory compromise, particularly in the perioperative and critical care settings. It reflects the adequacy of blood flow relative to metabolic demand and provides valuable insight into the balance between oxygen delivery and consumption. When cardiac output decreases or tissue perfusion is impaired, CO_2 clearance is reduced, resulting in an elevated DCO_2.

Previous studies have established the physiological relevance of this parameter. Rhodes *et al.* [16] reported that elevated DCO_2 levels correlated with low cardiac output and increased mortality in infants following cardiac surgery, emphasizing its prognostic utility. Similarly, Pearse *et al.* [17], in a meta-analysis of goal-directed cardiac output–guided therapy during major abdominal surgeries, found that while overall mortality was unaffected, perioperative complications were significantly reduced, highlighting the importance of dynamic perfusion-guided management.

To the best of our knowledge, this study is the first randomized controlled trial to evaluate DCO_2-guided GDT for fluid and inotrope optimization in elective cardiac surgery. In contrast to $ScvO_2$, which may remain within normal limits despite regional hypoperfusion, DCO_2 provides an earlier and more sensitive indication of circulatory inadequacy. As $ScvO_2$ can be influenced by factors such as hemoglobin concentration, oxygen extraction, and microvascular shunting, its interpretation alone may not fully capture tissue-level perfusion deficits [18].

Our findings demonstrated that intraoperative DCO_2 values were significantly lower in the intervention group than in controls, indicating improved perfusion and oxygen delivery with DCO_2-guided GDT. Moreover, postoperative $ScvO_2$ was significantly higher in the interventional group, suggesting improved systemic oxygenation and reduced oxygen debt. Although total hospital stays and complication rates were similar between groups, the ICU stay was markedly shorter in the DCO_2-guided group, signifying more rapid physiological stabilization and recovery.

The results are consistent with the theoretical framework of goal-directed therapy, where individualized hemodynamic optimization improves organ perfusion, mitigates tissue hypoxia, and enhances recovery. DCO_2's integration into perioperative monitoring offers a simple, inexpensive, and reproducible tool that complements conventional parameters such as lactate and $ScvO_2$ [1,8]. In addition, its routine assessment is feasible in cardiac anesthesia and

doi: 10.21276/SSR-IIJLS.2025.11.6.41

critical care environments where arterial and central venous lines are already in place.

Therefore, this study highlights the potential of DCO_2 as an adjunctive endpoint in hemodynamic management, capable of refining intraoperative decision-making and contributing to enhanced recovery strategies after cardiac surgery [3-5]. This prospective randomized controlled trial evaluated the efficacy of a GDT protocol guided by the DCO_2 in optimizing hemodynamics during elective cardiac surgeries.

CONCLUSIONS

In the present study, goal-directed hemodynamic management using DCO_2 as an adjunct marker significantly reduced ICU stay duration without increasing complications or hospital stay in patients undergoing elective cardiac surgery. The findings indicate that DCO_2, when incorporated into a structured GDT algorithm, can effectively guide fluid and inotrope therapy, improve tissue perfusion and accelerate postoperative recovery. Given its low cost, ease of measurement, and physiological relevance, DCO_2 may serve as a valuable addition to perioperative monitoring protocols, particularly in high-risk surgical populations. However, as this study was limited to cardiac surgical patients, the results should be interpreted cautiously. Future multicentric trials with larger sample sizes and inclusion of diverse surgical populations are needed to confirm its broader utility. Overall, DCO_2-guided GDT aligns with the modern principles of precision medicine and enhanced recovery after surgery (ERAS), offering a feasible and impactful tool for improving perioperative outcomes.

CONTRIBUTION OF AUTHORS

Research concept– Dr Chandra Sekhar Behera, Dr B Swagat Kumar Subudhi
Research design– Dr Chandra Sekhar Behera, Dr Suryast Singh
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