ORIGINAL RESEARCH ARTICLE

Effect of Goal-directed Hemodynamic Therapy in Postcardiac Surgery Patients

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Abstract

Background and aims: Early goal-directed therapy (EGDT) provides preset goals to be achieved by intravenous fluid therapy and inotropic therapy with earliest detection of change in the hemodynamic profile. Improved outcome in cardiac surgery patients has been shown by perioperative volume optimization, while postoperative intensive care unit (ICU) stay can be decreased by improving oxygen delivery. Our aim of this study was to study the outcome of EGDT in patients undergoing elective cardiac surgery.

Materials and methods: This is a prospective single institute study involving a total of 478 patients. Patients were divided into group I, who received standard hospital care, and group II, who received EGDT. Postoperatively, patients were observed in ICU for 72 hours. Hemodynamics, laboratory data, fluid bolus, inotrope score, complication, ventilatory time, and mortality data were collected.

Results: Postoperative ventilatory period (11.12 ± 10.11 vs 9.45 ± 8.87, $p = 0.0719$) and frequency of change in inotropes (1.900 ± 0.9 vs 1.19 ± 0.61, $p = 0.0717$) were lower in group II. Frequency of crystalloid boluses (1.33 ± 0.65 vs 1.75 ± 1.09, $p = 0.0126$), and quantity of packed cell volume (PCV) used (1.63 ± 1.03 vs 2.04 ± 1.42, $p = 0.0364$) were highly significant in group II. Use of colloids was higher in group II and was statistically significant (1.98 ± 1.99 vs 3.05 ± 2.17, $p = 0.0012$). The acute kidney injury (AKI) rate was (58 (23.10%) vs 30 (13.21%), $p = 0.007$) lower and statistically significant ($p = 0.007$) in group II.

Conclusion: Early goal-directed therapy reduces the postoperative ventilatory period, frequency of changes in inotropes, and incidence of AKI, and decreases ventilation hours, number of times inotropes changed, and AKI.

Keywords: Acute kidney injury, Cardiopulmonary bypass, Early goal-directed therapy.

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Introduction

Among patients undergoing cardiac surgery, approximately 10% require prolong postoperative care because of hemodynamic instability, organ dysfunction, and multi-organ failure.[1] Perioperative complications, in addition to being distressing to patients and healthcare delivery teams, dramatically increase healthcare costs. This increased cost is due to an increased use of expensive resources [intensive care unit (ICU) and hospital beds, diagnostic tests, medical and surgical therapies]. Limited cardiovascular resources and an inadequate hemodynamic response to the postoperative surgical stress have recently been shown to be independent predictors of prolonging the ICU stay.[2]

Nowadays, cardiac surgery can be performed in high-risk patients due to high-quality supportive care and improved surgical techniques.[3] These high-risk patients undergoing cardiac surgery carry higher risk of morbidity and mortality. Consistently higher postoperative cardiac output and oxygen delivery are important factors in determining survival after cardiac surgery.[4]

It has been suggested that the mortality rate in high-risk surgical patients may be reduced if the hemodynamic parameters noted in the survivors were used as goals in high-risk patients. Global tissue hypoxia is an important marker of serious illness or low cardiac output.[5] The recognition and treatment of low cardiac output, in the immediate postcardiac surgery period, produces improvement in terms of outcome.[6] Early goal-directed therapy (EGDT) provides preset goals to be achieved by intravenous fluid therapy and inotropic therapy with earliest detection of change in the hemodynamic profile.[7]

Improved outcome in cardiac surgery patients has been shown by perioperative volume optimization, while postoperative ICU stay can be decreased by improving oxygen delivery.[8] The aim and objective of our study was to compare patients outcome in terms of ventilation duration, ICU stay, hospital stay, use of PCV, use of colloids, organ dysfunctions, and mortality with EGDT compared to conventional hemodynamic management in elective cardiac surgery.

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Materials and Methods

The EGDT study was prospective, single-blind, conducted from May 2015 to December 2015 at U N Mehta Institute of Cardiology and Research Centre (UNMICRC), Ahmedabad, Gujarat, India. The protocol was approved by UNMICRC Ethics Committee (UNMICRC/C. ANESTHE/2015/21) in accordance with Helsinki Declaration of the

World Medical Association. Patients with elective cardiac surgery (both on-pump and off-pump) of both sex and age more than 18 years were enrolled in the study. Patients with emergency cardiac surgery, age less than or equal to 18 years, and patients on intra-aortic balloon pump (IABP) before surgery were excluded.

Patients were divided into group I as control and group II as study group. Group I patients received standard hospital care as per the institutional protocol from May 2015 to August 2015. All patients received 2 mL/kg/hour of crystalloid solution. Central venous pressure (CVP) was maintained between 6 mm Hg and 8 mm Hg. Mean arterial pressure (MAP) was maintained between 65 mm Hg and 90 mm Hg by altering the dosage of the inotropic agent if already being infused and initiating or adding other inotropic agents. Arterial blood gas (ABG) at 4 hours interval and urinary output hourly were monitored, and the biochemical abnormalities were corrected as necessary. The hematocrit value was maintained at or above 30% with packed cell transfusions, if necessary. Heart rate (HR), MAP, oxygen saturation (SpO_2), CVP, and laboratory investigations were monitored continuously and recorded for 72 hours or till the patient was shifted from ICU (Flowchart 1). Flowchart 1 Please show IVF 2 mL/kg/hour in study group as well. U/O target is higher in group II why?

After providing training of the EGDT protocol to all anesthesiologists who manage postcardiac surgery patients in ICU, patients data from group II were collected from September 2015 to December 2015. Predefined goals for group II were to maintain CVP between 6 mm Hg and 8 mm Hg, MAP at 65–90 mm Hg, serum lactate concentration ≤2 mmol/L, hematocrit value more than 30%, central venous oxygen saturation ($ScVO_2$) ≥70%, and urine output ≥0.5 mL/kg/hour.

The protocol was as follows (Flowchart 2). A 250 mL crystalloid/colloid bolus was given every 30 minutes to maintain CVP between 6 mm Hg and 8 mm Hg. If MAP was less than 65 mm Hg, then vasopressors were given to maintain MAP at least 65 mm Hg. Vasodilators were used to keep MAP 90 mm Hg or below. If $ScVO_2$ was less than 70%, red blood cells were transfused to keep hematocrit 30% or above. In spite of optimizing CVP, MAP, and hematocrit, if the $ScVO_2$ was still less than 70%, inotrope infusion was started or increased in the dose of existing inotrope. The choice of inotropic agent selection was determined by MAP, HR, $ScVO_2$, and CVP. All parameters were recorded at specific time intervals (T1–12).

The duration of ventilation (hours), frequency of bolus infusions (250 mL) used, number of PCV and colloid used, frequency of change of inotropes, length of stay (LOS) in the ICU (hours), occurrence of organ dysfunction, and mortality were noted. Acute kidney injury (AKI) was defined as per KIDIGO guidelines: increase in serum creatinine by ≥0.3 mg/dL within 48 hours of surgery.[9]

As per calculation done by the Raosoft software, we estimated minimum sample size (was with 95% confidence interval and 85% power of the study and type I error of 0.05) to be 450 patients, so we decided to include 250 patients in each group. The results were analyzed with the SPSS software for windows (SPSS Inc., version 20, Chicago, Illinois, USA). The Student's *t* test or Mann–Whitney tests were used as appropriate to analyze the data. The two-way ANOVA test was used to analyze the data within the same group at various time intervals. All the values are reported as mean ± SD.

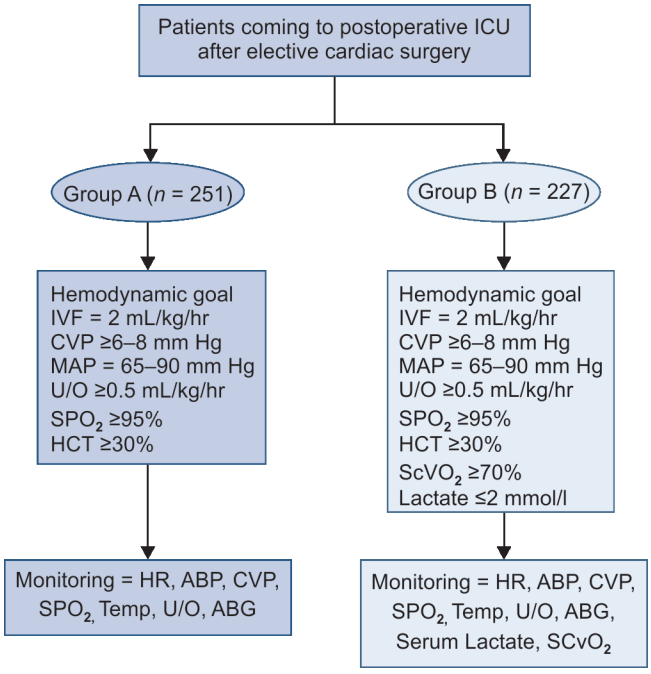
Results

We enrolled total 478 patients in our study, 251 patients were in group I while 227 patients were in the study group. Group demographic data and Euro SCORE, ejection fraction (EF), cardiopulmonary bypass (CPB) time, aortic cross clamp (AOX) time, and vasoactive inotrope score were comparable as per Table 1. Types of surgery in both groups were as per Figure 1.

Ventilator hours (11.12 ± 10.11 vs 9.45 ± 8.87, $p = 0.0719$) and number of times inotropes changed (1.900 ± 0.9 vs 1.19 ± 0.61, $p = 0.0717$) were lower in group II, but not significant. The HR, MAP, CVP, and UO measured at various time intervals as per Table 2.

Number of crystalloid bolus use (1.33 ± 0.65 vs 1.75 ± 1.09, $p = 0.0126$) and number of PCV used (1.63 ± 1.03 vs 2.04 ± 1.42,

Flowchart 1: Study design



Flowchart 2: Group II EGDT protocol

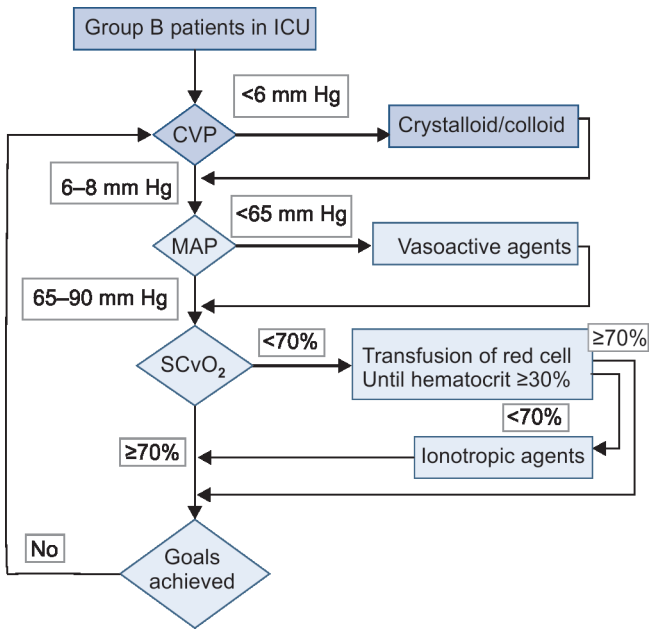


Table 1: Demographic data

	Control group (n = 251)	*Study group (n = 227)*	*p value*
Age (years)	49.94 ± 13.19	49.81 ± 13.02	0.909
Male:female ratio	145:106	149:78	—
Weight (kg)	56.20 ± 12.46	56.97 ± 12.57	0.504
EuroSCORE additive	4.23 ± 2.82	4.18 ± 2.63	0.829
Logistic	0.051 ± 0.06	0.047 ± 0.050	0.485
EF (%)	48.45 ± 12.91	48.26 ± 11.56	0.87
CPB time (minutes)	111.55 ± 47.89	102.77 ± 63.02	0.2
AOX time (minutes)	84.44 ± 42.57	79.45 ± 40.37	0.19
Vasoactive ionotrop score	7.38 ± 9.59	6.32 ± 7.23	0.175

EF, ejection fraction; CPB, cardiopulmonary bypass; AOX, aortic cross clamp

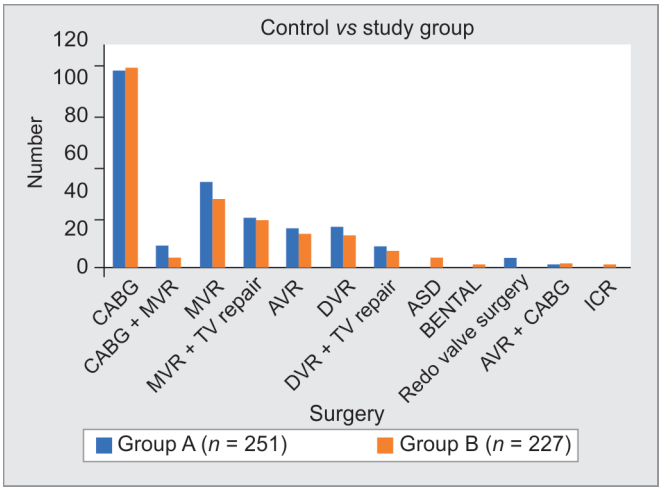


Fig. 1: Types of surgery in two groups

p = 0.0364) were higher and statistically significant in group II. Number of colloids used (1.98 ± 1.99 vs 3.05 ± 2.17, p = 0.0012) were higher in group II, which was also statistically significant. Need of intensive care for >72 hours was required in 51 patients, out of that 22 were from group I and 29 from group II (Table 3).

Five patients from group I and four patients from group II died within 28 days post cardiac surgery. All these patients had more than 3 Euro SCORE, and two patients had 20% EF. The overall 28 days' hospital mortality rate was 1.99% in group I and 1.76% in group II, which was statistically not significant. The AKI rate was [58 (23.10%) vs 30 (13.21%) p = 0.007] lower and statistically significant (p = 0.007) in group II. Two patients from group I and one patient from group II developed central nervous system complications. All three patients had cardiac surgery on CPB. Small areas of infarction were detected in computerized tomography (CT) head evaluation. Six patients in group I and four patients in group II developed acute respiratory distress syndrome (ARDS). Total four patients, three in group I and one in group II, required reexploration due to high drain output and fall in hemoglobin. One patient from group II had reexploration following cardiac arrest (Table 4). The $ScVO_2$ and lactate level in group II were as per Figures 2 and 3, respectively.

Discussion

There was no difference in HR, MAP, CVP, and urine output between the two groups at various time intervals, except CVP was higher in group I during first 6 hours in ICU (p = <0.001). In group II, bolus fluids were administered if CVP was <6 mm Hg. We found requirement of bolus crystalloid and colloid as well as PCV were higher and statistically significant in group II. The dose of inotropic agents and inodilators was changed to maintain the values of MAP, CVP, and urine output.

Table 2: Heart rate, MAP, CVP, and urine output in two groups

Parameter	*Time*	*Control group (n = 251)*	*Study group (n = 227)*	*p value*
HR	POD1 HR after 2 hours	95.04 ± 20.03	92.35 ± 18.82	0.137
	POD1 HR after 4 hours	96.09 ± 19.26	94.36 ± 18.01	0.322
	POD1 HR after 6 hours	95.15 ± 19.24	96.35 ± 17.67	0.488
	POD1 HR after 12 hours	93.16 ± 16.99	92.70 ± 16.85	0.767
	POD1 HR after 18 hours	94.74 ± 17.71	93.29 ± 17.21	0.372
	POD1 HR after 24 hours	93.63 ± 16.34	92.11 ± 15.05	0.304
	POD2 HR after 6 hours	94.86 ± 17.76	91.82 ± 16.37	0.08
	POD2 HR after 12 hours	95.98 ± 16.98	91.72 ± 15.80	0.011
	POD2 HR after 18 hours	95.73 ± 16.64	92.36 ± 16.03	0.0486
	POD2 HR after 24 hours	95.65 ± 16.40	92.43 ± 15.45	0.071
	POD3 HR after 12 hours	93.56 ± 18.57	90.04 ± 16.81	0.2009
	POD3 HR after 24 hours	94.43 ± 12.89	90.12 ± 18.04	0.1183
MAP	POD1 MAP after 2 hours	88.56 ± 16.78	88.13 ± 18.12	0.791
	POD1 MAP after 4 hours	85.76 ± 15.12	83.29 ± 14.24	0.072
	POD1 MAP after 6 hours	83.99 ± 12.90	81.79 ± 13.60	0.075
	POD1 MAP after 12 hours	83.22 ± 13.40	82.80 ± 12.43	0.728
	POD1 MAP after 18 hours	84.02 ± 12.10	81.17 ± 11.44	0.009
	POD1 MAP after 24 hours	81.90 ± 11.16	80.28 ± 11.88	0.131
	POD2 MAP after 6 hours	88 ± 63.06	79.20 ± 11.57	0.062
	POD2 MAP after 12 hours	80.75 ± 13.36	79.42 ± 11.11	0.292
	POD2 MAP after 18 hours	80.68 ± 12.12	78.98 ± 11.65	0.1732
	POD2 MAP after 24 hours	80 ± 11.42	78.99 ± 11.62	0.4323
	POD3 MAP after 12 hours	75.73 ± 13.38	78.34 ± 13.01	0.2046
	POD3 MAP after 24 hours	79.05 ± 14.66	80.29 ± 11.73	0.6014

Contd…

Contd…

Parameter	*Time*	*Control group (n = 251)*	*Study group (n = 227)*	*p value*
CVP	POD1 CVP after 2 hours	7.44 ± 11.59	4.36 ± 2.83	0.0016
	POD1 CVP after 4 hours	7.34 ± 7.06	4.81 ± 2.67	<0.001
	POD1 CVP after 6 hours	6.48 ± 5.06	4.55 ± 2.94	<0.001
	POD1 CVP after 12 hours	6.29 ± 5.01	5.40 ± 3.46	0.0739
	POD1 CVP after 18 hours	6.90 ± 4.87	5.86 ± 3.61	0.0373
	POD1 CVP after 24 hours	7.08 ± 4.41	6.84 ± 3.6	0.6184
	POD2 CVP after 6 hours	6.97 ± 4.38	6.21 ± 3.06	0.0905
	POD2 CVP after 12 hours	7.21 ± 4.37	6.61 ± 2.97	0.1846
	POD2 CVP after 18 hours	7.19 ± 4.04	6.46 ± 3.20	0.1036
	POD2 CVP after 24 hours	7.38 ± 5.29	6.40 ± 2.91	0.0983
	POD3 CVP after 12 hours	11.6 ± 14.54	7.02 ± 3.57	0.0498
	POD3 CVP after 24 hours	10.22 ± 8.10	6.58 ± 3.60	0.048
Urine output	POD1 U/O after 2 hours	145.96 ± 81.04	140.63 ± 180.32	5.199
	POD1 U/O after 4 hours	100.94 ± 60.81	95.56 ± 58.51	3.909
	POD1 U/O after 6 hours	96.81 ± 62.93	87.02 ± 50.06	4.045
	POD1 U/O after 12 hours	92.65 ± 52.20	80.89 ± 46.38	3.349
	POD1 U/O after 18 hours	92.94 ± 55.63	84.28 ± 47.82	3.569
	POD1 U/O after 24 hours	82.26 ± 39.93	76.79 ± 39.74	2.561
	POD2 U/O after 6 hours	82.88 ± 78.49	78.81 ± 43.12	0.536
	POD2 U/O after 12 hours	77.05 ± 43.97	79.83 ± 46.19	0.548
	POD2 U/O after 18 hours	75.4 ± 43.92	84.27 ± 49.11	0.072
	POD3 UO after 12 hours	90.45 ± 69.81	80.62 ± 47.20	0.3013
	POD3 UO after 24 hours	95.94 ± 60.70	113.02 ± 70.75	0.1948

POD, postoperative day; MAP, mean arterial pressure; HR, heart rate; CVP, central venous pressure; U/O, urine output

Table 3: Outcome comparison between two groups

	Control group (n = 251)	*Study group (n = 227)*	*p value*
MVT (hours)	11.12 ± 10.11	9.45 ± 8.87	0.0719
No. of PCV	1.63 ± 1.03	2.04 ± 1.42	0.0364
No. of colloids	1.98 ± 1.99	3.05 ± 2.17	0.0012
Bolus crystalloid (250 mL)	1.33 ± 0.65	1.75 ± 1.09	0.0126
Number of times change of support	1.900 ± 0.9	1.19 ± 0.61	0.0717
ICU stay >72 hours	22 (8.76%)	29 (12.77)	0.7635

MVT, mechanical ventilation time; PCV, packed cell volume

Table 4: Comparison of complications between two groups

Complications	*Control group (n = 251)*	*Study group (n = 227)*	*p value*
AKI	58 (23.10%)	30 (13.21%)	0.0076
CNS complications	2 (0.79%)	1 (0.44%)	0.9304
Reexploration	3 (1.19%)	1 (0.44%)	0.6879
IABP	1 (0.39%)	1 (0.44%)	0.5233
ARDS	6 (2.39%)	4 (1.76%)	0.8834
Mortality	5 (1.99%)	4 (1.76%)	0.879

AKI, acute kidney injury; CNS, central nervous system; IABP, intra-aortic balloon pump; ARDS, acute respiratory distress syndrome

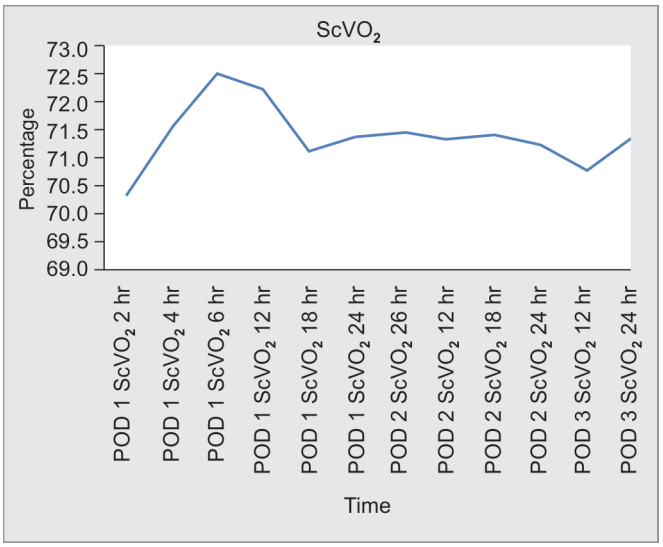


Fig. 2: Central venous saturation in group II

One patient from each group required >72 hours of ventilation. The patient from group I was succumbed to death due to ARDS while another one from group II was successfully extubated and discharged from the hospital later on. One patient from each group required insertion on IABP in view of persistent low cardiac output.

The average number of times the inotropic agent adjusted during the study period was 1.900 ± 0.9 and 1.19 ± 0.61 in the group I and group II, respectively, which was statistically not significant

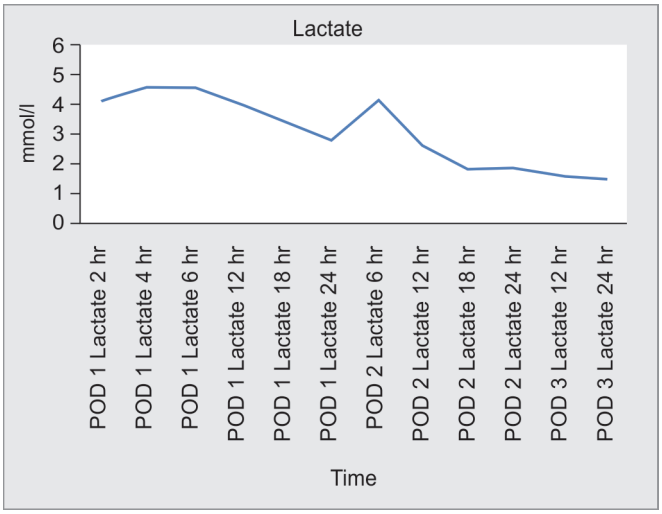


Fig. 3: Serum lactate in group II

($p = 0.0717$). Longer duration of ventilation, use of inotropic agent, ICU, and hospital stay were noted in patients with complications. Acute kidney injury within 48 hours of cardiac surgery was lower and statistically significant ($p = 0.007$) in group II.

For assessment of patient outcome after heart surgery, EuroSCORE is a simple, objective, and up-to-date system.[10] In our study, we used EuroSCORE additive and logistic, which were comparable between two groups (Table 1).

Organ dysfunction and multiple organ failure are the main causes of prolonged hospital stay after cardiac surgery.[1] Patient outcome can be improved with increase in oxygen delivery and utilization.[11] Because of exposure to extracorporeal circulation and limited cardiovascular reserve, patients undergoing cardiac surgery are at risk of inadequate perioperative oxygen delivery.[12]

A study including 403 elective cardiac surgery patients by Polonen et al. concluded that by maintaining mixed venous oxygen saturation (SVO_2) more than 70%, LOS decreases in ICU as well as hospital.[11] A meta-analysis by Aya et al. concluded that gold-directed hemodynamic therapy reduces hospital stay and postoperative complication after cardiac surgery.[13] A recent study concluded that gold-directed therapy decreases duration of inotropic support in high-risk cardiac patients undergoing off-pump coronary artery bypass.[14]

Mixed venous oxygen saturation can be measured by withdrawing blood from the pulmonary artery through the pulmonary artery catheter (PAC). Goldman et al. studied the $ScVO_2$ in 31 patients with myocardial infarction and concluded that the serial measurements of $ScVO_2$ appear a useful method for monitoring changes in myocardial function in patients with myocardial infarction.[15] Although $ScVO_2$ is not similar to SVO_2 but it correlates well with SVO_2. The mixed venous oxygen saturation estimated from the superior vena cava was found to be 5–13% lower than that estimated from the pulmonary artery.[15] In our study, we used $ScVO_2$ measurement.

Many uses the esophageal Doppler probe, a noninvasive method, for EGDT in immediate postoperative period after cardiac surgery, and demonstrated a decrease in length of hospital stay.[16,17] A PAC is invasive with its own set of complications, and the esophageal Doppler probe is not easily tolerated by patients who are on ventilator and conscious following cardiac surgery.[7]

The Vigileo system has been validated by a few studies.[18–20] These studies showed that the cardiac index (CI) obtained by FloTrac and PAC are interchangeable. However, a study by Opdam et al. performed the cardiac output (CO) measurements in six patients and concluded with limited correlation between CO measurements obtained by using the FloTrac and PAC.[21] They suggested that further evaluation is required before recommending this device for use in the clinical setting.

Early goal-directed therapy provides early intervention to correct hyperlactemia, which has direct correlation with AKI. By keeping $ScVO_2$ target ≥70%, we prevent prolong episodes of low oxygen delivery. By monitoring of serum lactate and SvO_2, a clinician can initiate early intervention and provide better outcome.[11] The PAC provides intermittent monitoring of SvO_2, while other minimally invasive monitors provide continuous monitoring.

As this was a single-center study and patients were operated by center-specific surgeons, results may have limited external validity. We detected and corrected abnormal hemodynamic earliest by using EGDT. It decreased incident of AKI and ventilation duration. In future trials, various biomarkers and multimodal monitoring can provide early detection of organ failure.

Conclusion

Perioperative goal-directed therapy decreases ventilation duration, number of times inotropes changed, and AKI. It provides guide for early initiation of intervention. As our study was performed in single center, a multicentric study involving large number of patients is required to support the outcome.

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