Original article

A prospective randomized study of goal oriented hemodynamic therapy in cardiac surgical patients

Shrestha KR[1], Pradhan B[2], Koirala B[3]

Department of Cardiothoracic and vascular surgery (CTVS), Manmohan Cardiothoracic Vascular and Trasplant Center (MCVTC), Maharajgunj Medical Campus (MMC), Institute of Medicine (IOM),

Correspondence: Kajan Raj Shrestha,

Email: kajanrs@gmail.com

Abstract

Introduction: Approximately 10% of patients require prolonged care after cardiac surgery because of hemodynamic instability, organ dysfunction or multi organ failure. Increased levels of oxygen delivery and consumption in early postoperative period are associated with improved outcome and early recovery. The aim of the study was to evaluate early post-operative outcome in cardiac surgery patients with adoption of goal oriented hemodynamic therapy.

Methods: This is a prospective randomized controlled trial of 12 months period, of adult patients undergoing cardiac surgery in a tertiary level teaching hospital. In the control group, standard postoperative monitoring was done, while in the study group FloTrac™ cardiac output sensor with Vigileo monitor and central venous oxygen saturation monitoring was done to reach a set goal within 8 hrs postoperatively. Findings were analysed using SPSS software version 17.

Results: 100 patients were enrolled in the study with 50 in each group. Both groups were comparable by baseline characteristics, body surface area (BSA) and duration of surgery, cardiopulmonary bypass (CPB) and aortic cross-clamp (AoX) time. But the average age was statistically higher in study group. Yet, the ventilator time and duration of use of ionotropes were significantly less in study group. The duration of intensive care unit (ICU) and hospital stay were less in study group but did not reach statistical significance.

Conclusion: This study has shown that the use of goal oriented hemodynamic therapy in cardiac surgical patients improves immediate outcome. Mortality, ICU and hospital stay also tend to be lower.

Key words: Cardiac surgery, Goal oriented hemodynamic therapy, FloTrac system™, hemodynamic monitoring

Introduction

Approximately 10% of patients require prolonged postoperative care after cardiac surgery because of hemodynamic instability, organ dysfunction or multi organ failure.[1] One of the factors for prolonged hospital stay is inadequate hemodynamic response to postoperative surgical stress. This in turn leads to increased hospital resource utilization.[2] Randomized studies in high-risk surgical or trauma patients, with intervention started perioperatively, have shown a marked decrease in mortality and morbidity rates.[3,4]

Types of surgery and patients' condition usually carry high risk of morbidity and mortality in cardiac surgery. Various studies concluded that limited cardiovascular resources, inadequate oxygen (O_2) delivery after cardiac surgery and inadequate hemodynamic response to post operative stress are independent predictors of prolonged ICU stay. Some studies have reported increased levels of oxygen delivery and consumption in postoperative period to be associated with improved outcome and early recovery after cardiac surgery. Increased oxygen extraction immediately after

cardiac surgery was found to be an independent predictor of prolonged ICU stay.[5]

The high risk individuals who survived major operations demonstrate persistent higher cardiac output and oxygen delivery than those who did not survive.[6] Increasing oxygen delivery to supranormal values perioperatively is associated with improved outcome in high risk surgical patients.[7] Early recognition and treatment of low cardiac output states and prevention of tissue hypoxia is the focus of present day post operative care. Goal oriented manipulation of cardiac preload, afterload and contractility to achieve a balance between the systemic oxygen delivery and demand by guiding fluid and ionotrope therapy improves outcome in cardiac surgery patients.[8, 9]

The aim of the study was to evaluate the early post operative outcome in cardiac surgery patient with adoption of early goal directed hemodynamic therapy. The outcome indicators were mortality, duration of ICU stay, use of mechanical ventilator and use of ionotropes, length of hospital stay, organ dysfunctions, need for hemodialysis and wound complication.

Materials and method

This is a prospective randomized clinical trial conducted in patients undergoing open cardiac surgery at a tertiary level cardiothoracic teaching hospital during February 1st 2012 to January 31st 2013 after taking ethical clearance from Institutional Review Board (IRB) and informed consent from patients and patients' party. Estimated sample size was 100 with 90% power at $\alpha = 0.05$.

The patients were divided into study and control using sealed envelope technique with 50 patients in each group. All patients between 15 to 75 years attending for cardiac surgery were included. Patients not giving consent, those with significant cardiac dysrhythmias preoperatively or postoperatively and those on intraaortic balloon pump (IABP) were excluded.

Control group received standard care during and after cardiac surgery according to hospital protocol. Study group ie goal oriented hemodynamic therapy (GOT) group received extra monitoring with FloTrac™ device (Edward Lifesciences, CA, USA) to measure cardiac output (CO), cardiac index (CI), stroke volume index (SVI), stroke volume variation (SVV), systemic vascular resistance (SVR) and central venous oxygen saturation ($ScVO_2$) from blood sample taken from central venous catheter. Oxygen tension was measured by clinical blood gas analyzer (Stat profile 4®; NOVA Biomedical, Waltham, MA).

After randomization, study group was monitored to maintain CI 2.2 -4.2 l/min/m^2; SVI 30 -65 ml/beat/m^2; $ScVO_2$ >70%; SVV <10%, SVR 800- 1500 dynes*sec/cm^5 till study period ie from opening of sternum till 8 hrs in the postoperative period. Other parameters maintained in both groups were central venous pressure (CVP) 6 -10 mmHg; mean arterial pressure (MAP) 60 -90 mmHg; pulse oximetry (SpO_2) > 90%; arterial blood gas (ABG) values pH 7.35- 7.45, PaO_2 >100mmHg, $PaCO_2$ 35 -45 mmHg, hematocrit (Hct) >30%, hemoglobin (Hb) > 10 gm% and urine output >1 ml/kg/hr. Ventilator parameters set were respiratory rate (RR) 8-16 breaths/min, tidal volume (Vt) 8 -10 ml/kg, FiO_2 0.4 - 0.6 in pressure regulated volume control mode of ventilation. Since FloTrac™ cardiac output sensor was kept in study group the care givers were aware of randomization.

In the study group, CI, SVV, SVI, SVR, $ScVO_2$ and blood lactate level were recorded after opening of the sternum and before going on pump (T1). Another set of parameters were recorded at the time of the closure of the sternum after coming off bypass (T2). All patients were mechanically ventilated at arrival in ICU and gradually weaned off ventilator according to hemodynamic and other parameters.

Postoperative management

In the control group, postoperative management was carried out according to institutional protocol. CVP – 6-10 mmHg and MAP – 60 - 90 mmHg was maintained with crystalloid 1000 ml/m^2/day and ionotropes or vasodilators as needed. ABG and urine output were monitored hourly. Hematocrit (Hct) was maintained above 30%. Temperature was maintained at 97.8ºF to 98.6 ºF. Hemodynamic parameters were recorded at arrival in ICU (T3), and after 2hrs (T4), 4hrs (T5), 6hrs (T6) and 8hrs (T7).

In study group, if CI < 2.2 l/min/m^2, CVP < 6 mmHg or SVV >10%, fluid was given in aliquot of 100ml and response was reassessed. Depending on MAP, SV, CO, blood lactate level and $ScVO_2$ ionotropes were used. (Chart 1) If $ScVO_2$ <70% and Hct <30% then packed cell transfusion was given and if $ScVO_2$ <70% and Hct >30% then higher level of CI, SVI was maintained. Dopamine (DA) was used as initial ionotrope, followed by adrenaline and nor-adrenaline as indicated. Milrinone was added in study group if patient had high pulmonary artery pressure, high systemic vascular resistance or low blood pressure despite other inotropes. Glyceryl trinitrate (GTN) was used in patients with arterial graft and high blood pressure. All the parameters were recorded in same time interval.

The number of times the ionotropes were adjusted and total additional amount of fluid given was recorded. After study period, postoperative management was continued till the patient was in ICU with standard protocols. Patients were also monitored in wards for organ functions till the patient

was discharged from the hospital.

Dysfunction of organ systems were defined as follows:

(a) Central nervous system: hemiplegia, stroke or GCS <10 in the absence of sedation

(b) Circulatory: need for vasoactive medication to treat hypotension (DA, NA) or decreased cardiac output (DA, Db, Adr) for more than 48 hrs.

(c) Respiratory: need for mechanical or assisted ventilation for more than 48 hrs

(d) Renal: urine output < 750 ml/24 h or increase of serum creatinine >150 mmol/L

(e) Hepatic: ALT > 40 IU/L and bilirubin >40 mmol/L

(f) Gastrointestinal: macroscopic bleeding or paralytic ileus

(g) Hematological: leukocyte count <3.5 x 10^9/L and platelet count <80 x 10^9/L.

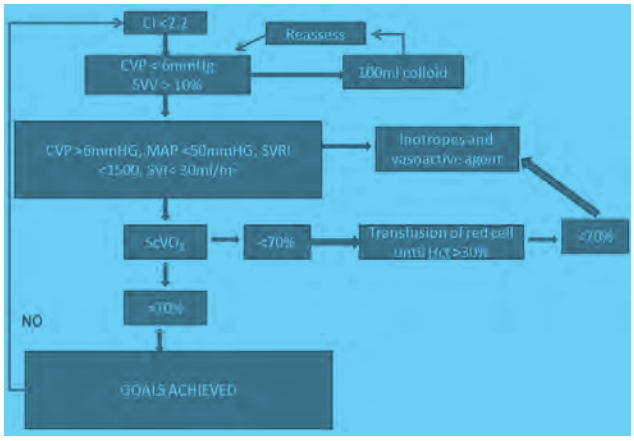

Chart 1 Flowchart of management guideline for early goal oriented therapy [8]

Patients were discharged from hospital once they were fit for the same.

Statistical analysis

All data were entered in the Microsoft excel program and was analyzed by using SPSS software version 17 (Chicago, Illinois, USA) and internet based graphical analysis calculators. Data collected were compared by student unpaired t test, for means of normally distributed variables and standard deviation of means between the two groups and chi square test to compare proportion of two groups. One way ANOVA test was used to analyze data within same group to calculate significance between interventions in same group. P value less than 0.05 was considered significant. Wherever required 95% confidence interval (95% CI) was calculated and expressed.

Results

Age in study group ranged from 19 years to 70 years with mean age of 52.98 ± 13.083 years while in control group age range from 15 years to 70 years (42.60 ± 14.82 years) (p = 0.0003).

All the preoperative and intraoperative variables in two groups were comparable (Table 1). Temperature, heart rate, mean arterial pressure & CVP were also comparable at all the times (Table 2).

Table 1 Preoperative and Intraoperative patient parameters

	Study (mean ± SD)	Control (mean ± SD)	p value	95% CI
BSA (mean ± SD)	1.578 ± 0.18	1.558 ± 0.184	0.584	-0.052 to 0.092
Duration of surgery (mins)	159.54 ± 54.21	158.23 ± 44.78	0.896	-18.423 to 21.043
Duration of CPB (mins)	98.25 ± 16.89	94.65 ± 8.96	0.186	-1.766 to 8.966
Duration of AoX (mins)	75.51 ± 11.48	74.21 ± 5.68	0.475	-2.2946 to 4.895

BSA - Body Surface Area; CPB - Cardiopulmonary Bypass; AoX - Aortic Cross Clamp (p < 0.05 significant)

Table 2 Types of surgeries

Parameters	Study (no of patients)	Control (no of patients)
CABG	20	15
CABG + Valve Surgery	2	2
CABG + CEA	1	0
OPCABG	5	0
MVR	2	0
MVR + TV Repair	11	22
AVR	4	0
AVR + Aortoplasty	1	1
AVR + Other Valve Repair	1	2
DVR	3	14

CABG - Coronary Artery Bypass Graft; CEA - Carotid Endarterectomy; OPCABG - Off-pump CABG; MVR - Mitral Valve Replacement; TV repair - Tricuspid Valve repair; AVR - Aortic Valve Replacement; DVR - Double Valve Replacement.

In study group, hemoglobin and blood lactate level changed with statistical significance within 2hrs post operatively. Statistical significance was noted in SVV, SVR and ScVO2 at various time intervals (Table 3).

Table 3 CO, CI at different times

Parameter	T1	T2	T3	T4	T5	T6	T7	P value*
CO (l/min)	4.422 ± 0.961	4.8 ± 1.255	5.089 ± 1.494	5.125 ± 1.237	5.949 ± 0.997	4.993 ± 0.945	4.975 ± 0.735	0.437
CI (l/min/m^2)	2.912 ± 1.131	2.9 78 ± 1.535	3.140 ± 2.798	3.192 ± 0.777	3.777 ± 0.632	3.134 ± 1.286	3.112 ± 1.155	0.260
SVV (%)	13.322 ± 5.691	18.276 ± 8.452	18.021 ± 8.570	15.84 ± 6.513	13.044 ± 9.803	12.240 ± 9.043	11.960 ± 8.362	**0.001**
SVR (dyn·s/cm^5)	1100.44 ± 190.076	1156 ± 219.942	1085.17 ± 216.446	1085.67 ± 181.26	1112.48 ± 147.728	1184.87 ± 217.157	1220.93 ± 235.372	**0.001**
SVI (ml/beat/m^2)	53.341 ± 11.592	45.3 ± 11.844	46.314 ± 13.597	46.872 ± 11.313	52.184 ± 8.746	46.577 ± 8.815	46.283 ± 6.838	0.022
ScVO2 (%)	82.284 ± 5.224	74.672 ± 7.759	70.032 ± 9.861	69.128 ± 7.984	69.29 ± 6.316	67.776 ± 5.526	69.134 ± 6.177	**0.001**

*One way ANOVA applied

On analyses the outcome variables (Table 4). Other Parameters were also favorable in study group, though not statically significant.

Postoperatively ventilator time and duration of use of inotropes were found to be significantly different.

Table 4 Outcome analyses in study and control group

Parameters	Study (mean ± SD)	Control (mean ± SD)	P value	95% CI
No of times inotropes changed	5.7 ± 3.307	4.94 ± 2.583	0.203	-0.418 to 1.938
Ventilator time (hrs)	10.48 ± 7.640	16.429 ± 11.801	**0.041**	-11.64 to -0.254
Length of ICU stay (hrs)	53.82 ± 29.727	76.3 ± 37.768	0.089	-48.486 to 3.526
Duration of use of inotropes (hrs)	23.2 ± 17.870	39.12 ± 18.615	**0.032**	-30.456 to -1.384
Duration of hospital stay (days)	7.64 ± 3.001	9.10 ± 5.389	0.097	-3.191 to 0.271
Additional amount of fluid given (ml)	1199.04 ± 638.701	938.32 ± 736.151	0.062	-12.8 to 534.24
Mortality	2	3	0.653	0.104 to 4.085
No of organ dysfunction (mean)	0.44 (0- 4; total 15)	0.66 (0- 4; total 21)	0.592	0.259 to 1.351
Dialysis	3	6	0.468	0.110 to 1.987
Post op USG	2	6	0.299	0.057 to 1.559
Post operative Echo	13	15	0.820	0.342 to 1.966
Re-operation	4	6	0.638	0.169 to 2.414
Wound complication	4	8	0.457	0.128 to 1.627
Other complication	8	14	0.490	0.185 to 1.300

Complication

Two patients in study group and 3 patients in control group died. All 5 mortalities were of patients undergoing MVR with TV repair for rheumatic heart disease with severe mitral stenosis with regurgitation and severe tricuspid regurgitation. 2 patients in study group (1 MVR with TV repair and 1 CABG) and 1 patient in control group (CABG with CEA) developed hemiplegia who recovered partially by discharge. No other organ dysfunctions were evident in either of the group.

Table 5 Complications in both groups

Complications	Study (no of patients)	Control (no of patients)
CVA	2	1
Sternal instability	2	1
Major wound infection	2	2
LCOS	0	1
Pneumonia	0	2
Jaundice	0	2
Arrhythmia	0	2

Discussion

Cardiac surgery is one of the most difficult and challenging endeavor of medical field. To achieve this goal, various improvements in surgical techniques, preoperative optimization, intraoperative modification and postoperative management have been suggested which has certainly improved the outcome. Among these management options, early goal-directed therapy (EGDT) introduced by Emanuel P. Rivers in 2001, for critical care medicine involving intensive monitoring and aggressive management of perioperative hemodynamics in high risk patients is one of the most successful options.[10] In cardiac surgery, EGDT has proved effective when commenced after surgery and has demonstrated a marked decrease in mortality.[11] This approach involves adjustments of cardiac preload, afterload, and contractility to balance oxygen delivery with an increased oxygen demand before surgery.[10, 12]

In our study we have included all patients above 15 years and below 75 years because FloTrac - Vigileo™ (Edwards Lifesciences, Irvine, CA, USA) system has not been approved in children and in patients with congenital heart disease due to their varied pathophysiology. [13]

As FloTrac system is based on arterial waveform contour, patients with significant arrhythmia like frequent VPCs, short run ventricular tachycardia and ventricular fibrillation preoperatively or those present till 8hrs postoperatively were excluded as it gave false recording of cardiac output. Very high risk patients like those on IABP were also excluded for similar reasons.

In this study mean age group was significantly higher in study group. This could have some impact in outcome. But generally we would expect worse outcome in higher age group, which was not the case in our study. This goes in favour of early goal directed therapy in in cardiac surgical patients. In a study of 40 patients undergoing total hip arthroplasty Cecconi et al had patients of similar ages in EGDT group.[14]

Gender distribution in our study resembled as in the studies of Kapoor et al, Polonen et al and Cecconi et al.[8,9,14] Female category in cardiac surgery is considered to be poor risk group and is included in different scoring systems.

This study also compared parameter like body surface area (BSA), duration of surgery, duration of total bypass time and duration of aortic cross clamp time. Kapoor et al added height, weight, EURO score and number of anastomosis to compare two groups.[8] Similarly Polonen et al included LVEF, diabetes, New York Heart Association (NYHA) grading, type of surgery and preoperative TIA/ stroke to compare two groups.[9] Cecconi et al used median age, height, weight and ASA grading to compare two groups.[14] Monnet et al compared age, gender, Simplified Acute Physiologic Score, ARDS, source of infection and vasopressor as baseline parameters to compare two groups in 80 patients with circulatory failure.[15]

Studies have found EGDT to be effective when commenced before surgery and even in the intra-operative period.[16] In cardiac surgery, EGDT was proved to be effective even when started immediately in the post operative period.[8,9]

Increasing the oxygen delivery to critically ill patients has been shown to result in an increase in the $ScvO_2$ which is a useful marker of CI. Some argue that $ScvO_2$ does not accurately reflect the mixed venous oxygen saturations (SVO_2) and that pulmonary artery catheterization is preferable.[17] However Reinhart et al and Ladakis et al suggested SVO_2 approximates $ScVO_2$ values and are interchangeable for initial management.[18,19]

Goldman et al also found that $ScVO_2$ correlated well with the myocardial function and patient's clinical course.[20].

Intermittent sampling from the central line for $ScvO_2$ provides adequate information. As $ScVO_2$ from superior vena cava is 5-13% lower than the pulmonary artery, a higher target was selected.[21, 22]

Some have also used an oesophageal Doppler probe for EGDT, demonstrating a decrease in the length of hospital stay instead of the pulmonary artery catheter.[23] Unlike the FloTrac™, doppler probe is not readily tolerated by conscious patients.

Sakka et al also concluded that the placement of a pulmonary artery catheter (PAC) solely for the measurement of CO is no longer justified, unless continuous CO measurements are needed.[31]

Chakravarthy et al. have validated the Vigileo™ system and values obtained are interchangeable with the measurement obtained by using the pulmonary artery catheter. [25] Opdam et al found that CO measurements obtained using the FloTrac™ system correlated well with intermittent technique rather than continuous technique for CO measurement using PAC. [26]

Our study group had significant less duration of use of inotropes and less ventilator time. Study group, however had more number of inotropes changed and increased amount of additional fluid required. This suggests that most of post cardiac surgical patient could have been volume depleted. Complication rates were also less in study group. Dialysis, echocardiogram, ultrasonogram and reoperation rates were less in study group though it was not statistically significant. Hospital stay was lower in study group but did not reach statistical significance.

Kapoor et al showed that by actively adjusting the ionotropic agent in the early recovery period, recovery can be hastened and the duration of use of ionotropic agent can be reduced. They concluded that monitoring of CI, SVRI, SVI, SvO2 and oxygen delivery (DO_2) helps in initiating therapy early in the postoperative period.[8]

In a systematic review and meta-analysis, Dalfino et al found out that perioperative GDT significantly reduced surgical site infections ($p < 0.0001$), pneumonia ($p = 0.009$), and urinary tract infections ($p = 0.02$). They concluded that EGDT must be strongly encouraged, particularly in the high-risk surgical population.[27]

Rhodes et al found that long-term survival was improved in the GDT group, possibly due to decreased complications in the immediate postoperative period. [28]

Michard in a letter to editor estimated that around 860,000 lives could potentially be saved every year (the equivalent of one life every 37 seconds) if EGDT strategy becomes the standard of care around the world.[29] Meta-analysis by Hamilton and colleagues suggest that the post-operative complication rate could be reduced from 29.8% to 18.0% with goal-directed strategies. So it may be time for health-care systems to consider perioperative goal-directed strategies as part of quality improvement programs and as national priorities.[30]

Limitations of the study

This is not a multicentric study and blinding was not possible. Using a risk scoring system to stratify cardiac surgical patients to identify those at high risk could have been more beneficial. Inclusion of different types of surgeries (coronary and valvular surgeries) may have confounded the findings.

Conclusion

It may be concluded that the use of goal oriented hemodynamic therapy in cardiac surgical patients improves immediate outcome. It reduces duration of use of ionotropes and ventilatory support. ICU and hospital stay tended to be lower in study group but did not reach statistical significance.

Conflict of interest: None declared.

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