Modified ultrafiltration & postoperative course in patients undergoing repair of Tetralogy of Fallot

Running Head: Modified ultrafiltration

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ABSTRACT

Background: Expected benefits of modified ultrafiltration(MUF) include increased hematocrit, reduction of total body water & inflammatory mediators, improved left ventricular systolic function, & improved systolic blood pressure and cardiac index following cardiopulmonary bypass(CPB). This prospective randomized trial tested this hypothesis.

Methods: 79 patients undergoing intracardiac repair of Tetralogy of Fallot(TOF) were randomized to MUF group(Group-M, n=39) or only conventional ultrafiltration(CUF) group(Group-C, n=40). Primary outcome was change in hematocrit. Secondary outcomes were changes in peak airway pressures, ventilatory support, blood transfusions, time to peripheral rewarming, mean arterial pressure, central venous pressure, inotrope score(IS) and cardiac index. Serum inflammatory markers were measured.

Results: Following MUF, Group-M had higher hematocrit(44.3±0.98 g/dl) compared to Group-C(37.8±1.37g/dl),P=<0.001. Central venous pressure(mmHg) immediately following sternal closure was 9.27±3.12mmHg in Group-M & 10.52±2.2mmHg in Group- C(P=0.04). In the ICU, they were 11.52±2.20mmHg in Group-C and 10.84±2.78mmHg in Group-M(P=0.02). Time to peripheral rewarming was 6.30±3.91 hours in Group-M and 13.67±3.91hours in Group-C(P=0.06).

Peak airway pressures in ICU were 17±2mmHg in Group-M & 20.55±2.97mmHg in Group-C, P<0.001. Duration of mechanical ventilation

was 6.3±2.7 hours in Group-M compared to 14.7±3.5 hours in Group-C(P=0.002). IS was 11.52±2.20 in Group-C compared to 10.84±2.78 in Group-M. 8/39(20.5%) patients in Group-M had IS>10 compared to 22/40(55%) patients in Group-C(P=0.02). Serum Troponin-T and Interleukin-6 levels were lower in Group-M; TNF-α and CPK-MB were similar. ICU & hospital stay were similar.

Conclusion: MUF group had higher post-operative hematocrit, decreased duration of mechanical ventilation, lower need for inotropes & lower Interleukin-6 & Troponin-T levels. MUF group had better post-operative outcomes.

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This study was registered with the Clinical trials registry of India (CTRI/2017/11/010512) prior to commencement.

Introduction

Complexity of cardiac malformations, immaturity of tissues and the overall small size of the equipment make pediatric cardiopulmonary bypass (CPB) challenging with special attention to haemodilution and inflammatory response[1]. The practices of conducting CPB have been variable at different centers and it is difficult to define the optimal CPB strategy in these subsets of patients. Common practices include circuit miniaturization to reduce the systemic inflammatory response and conventional ultrafiltration (CUF) to reduce hemodilution. However, CUF is thought to have limited efficiency, prompting the development of modified ultrafiltration (MUF) by Naik et al in 1991[2]. In this, following termination of CPB, the residual contents of the extracorporeal circuit are ultrafiltered and transfused while the patients are still cannulated and attached to the extracorporeal circuit[2]. MUF has since gained widespread popularity[3-5] and it has been claimed to remove excess fluid with greater efficiency than CUF[3-8]. Expected benefits include reduction of total body water, removal of inflammatory mediators, reduction of myocardial water, restoration of normal organ function and improved ventricular systolic function resulting in increased systolic blood pressure and cardiac index[6]. It is claimed that it increases blood viscosity and systemic vascular resistance, allows for removal of anaesthetic agents and/or vasodilators, removes myocardial depression factors, or stimulate sympathetic reflex by removing water from the aorta[4]. A combination of all of these probably contributes

greatly to improved outcomes[4,6].

In a randomized trial involving 46 patients, Ziyaeifard et al[7] concluded that MUF leads to improved outcomes within 48 hours of surgery. In another randomized trial involving 80 patients, Singh et al[8] showed that a combination MUF & CUF decreased the need for homologous blood transfusion, reduced requirement of inotropes, and shortened the duration of ventilatory support compared to only CUF. However in a cohort of 98 patients, Milovanovic et al[9] demonstrated that only CUF is adequate & MUF confers no additional advantage. Another study by McRobb demonstrated reported that a simple strategy of miniaturization of the CPB circuit is enough to deliver equally good results compared to CUF plus MUF[10]. Similar results have been reported by Mejak e al[11] who concluded that eliminating MUF reduces costs, prevents MUF-related errors and does not have any negative impact on outcomes (reduced transfusion rates, chest tube output, inotrope use, and time from weaning off CPB to chest closure). They inferred that in the present era, there is no justification for conducting further prospective randomized studies for comparing CUF alone with CUT & MUF.

To further answer these questions, this double blinded randomized controlled trial compared the post-operative outcomes in pediatric patients undergoing intra-cardiac repair of Tetralogy of Fallot (TOF). We studied the effect of intra-operative MUF on post-operative hematocrit, cardiac index, amount of blood transfused and duration of mechanical ventilation.

Patients and methods

84 patients (<20 Kg) undergoing intracardiac repair of TOF between November 2017 and May 2019 in the Department of Cardiothoracic and Vascular Surgery at All India Institute of Medical Sciences, New Delhi, India were recruited in this study.

The study protocol was reviewed and approved by the institutional ethics committee (IECPG/385/8/2017) and was registered with the Clinical trials registry of India (CTRI/2017/11/010512) prior to commencement of the study. Informed consent was obtained from the legally assigned guardians of all patients.

The study population comprised of patients less than 20Kg undergoing routine intracardiac repair of TOF that was repaired via the pure right atrial or a trans right-atrial-trans-right ventricular approach with or without the need for a transannular patch. A large chunk of our surgical practice comprises patients undergoing repair of TOF and these patients are typically 5-7 years of age. They usually weigh less 20 Kg and choosing them ensures a uniform patient population. The 20 Kg limit is therefore, based on our experience rather than and based on evidence in the literature. In older patients, multiple factors such as effects of chronic hypoxia, major aorto-pulmonary collateral arteries and multiple organ dysfunction in response to CPB become important factors. Additionally, higher hematocrit in the older population weighing more makes assessment of the effects of strategies of ultrafiltration difficult. We do not perform intracardiac repair of TOF in patients weighing <5Kg.

Exclusion criteria included patients with discontinuous pulmonary arteries,

those requiring extensive pulmonary artery plasty, patients with known coagulopathies, preoperative respiratory compromise, re-operations and those requiring re-exploration for surgical causes of bleeding.

Sample size and randomization

We used data from a previous publication[12] to calculate the sample size. Assuming a similar baseline hematocrit and the difference in hematocrit between the test and the control groups at termination of CPB as 4.9 ± 5.5% with a statistical power of 80%, alpha error of 0.05 with equal variance and effect size similar to that reported for improvement of hematocrit, we required a total of 38 patients, i.e. 19 patients in each group. In order to further increase the power of the study to 90%, we required 40 patients in each group. Of 84 patients undergoing repair of TOF in this period, five patients were excluded as they did not meet the selection criteria; thus, a total of 79 patients were randomized to either the MUF group (n=39) or the control group (n=40).

Randomization list was generated using nQuery advisor version 7.0 with a block size of 10. This sequence was transferred to sealed envelopes which were opened by the circulating nurse. These were handed over to the perfusionists and the patients were assigned to either CUF only group (control group i.e. Group-C) or MUF group (study group i.e. Group-M). The operating surgeon was however always aware of either group for unavoidable reasons.

Anaesthesia, Surgery and CPB

Routine protocols were followed for induction & maintenance of anaesthesia. Anticoagulation was established using bovine heparin at 4mg/kg to achieve a

celite based activated clotting time of 480 seconds before initiating CPB.

In all patients, the Terumo ATS machine with the CAPIOX FX10R (Ann Arbor, USA) oxygenator and standardized CPB circuit were used. The priming volume was 800 ml comprising of Mannitol (1g/kg), Sodium bicarbonate (25ml), Heparin (5000 units) and Plasmalyte-A with blood as needed. The volume of bank blood to be added was calculated using standard formulae to achieve a pre-operative prime hemoglobin of 8g/dl (hematocrit 25%) after ultrafiltration of the prime, with the purpose of adjusting the prime hematocrit, maintaining potassium below 4mmol/L and to and to remove the thrombolytic enzymes from the bank blood.

CPB was carried out as per standard protocols at 28°Celsius. We used Sorin DHF-02 haemofilter (Sorin Group Italia, Mirandola Modena, Italy) for ultrafiltration. The inlet and outlet parts of this hemofilter were connected to the arterial line and venous reservoir, respectively. Flow rate through the hemofilter was adjusted to 10 ml/kg/min (maximum 400 ml/min) and while on CPB, hematocrit of the circulating volume was maintained around 30%. The techniques of CUF and MUF at our center have been described in our prior publication[13]. The ultrafiltration process (CUF) was begun during the rewarming phase (0.25ºC/min or 4 min for each 1ºC up to 35º C) and was performed until the end of CPB. During CUF, the target was to achieve a hematocrit around 25-30%, following which the CPB was terminated. In patients assigned to the MUF group, arteriovenous MUF was performed after termination of CPB as described previously[13]. The aim was to remove

ultrafiltrate of a minimum of 10 ml/kg to a maximum of up to 50 ml/kg over a period of 20–30 minutes to achieve a hematocrit not less than 35–40% or hemoglobin > 10g/dl[13]. Infusion rates were adjusted to maintain a minimum CVP of 4 mm Hg. In both groups, the primary surgeon waited in the operating room till MUF was completed and the sternum and skin incision were closed.

Routine inotropic support at the time of weaning off CPB was Dopamine (5 microgarms/Kg/min), Dobutamine (5 microgarms/Kg/min) and Sodium nitroprusside (0.5 microgarms/Kg/min). Additional inotropes were added as needed.

Care in the Intensive care unit

Critical care physicians and the nursing staff managing the patients in the intensive care unit (ICU) were blinded to the two groups. In the absence of features of low cardiac output (LCOS) (defined as delayed time to peripheral warming, non-palpable lower limb distal pulses, urine output <0.5 ml/kg/hr >3 hours, increasing acidosis and lactate levels or a combination of these), and after complete reversal from anesthesia with hemodynamic stability, no bleeding from chest drains and adequate respiratory efforts, the patients were weaned off mechanical ventilation.

Data Collection

Primary outcome was change in hematocrit between Group-M and Group-C.

Secondary outcomes were (a) peak air way pressures in post-operative period (b) duration of mechanical ventilation (c) amount of blood transfusion (d) central venous pressures (e) cardiac index (CI) (f) inotropic score (IS) (g)

mortality and (h) morbidity. The latter was defined as elevated peak air way pressures, higher duration of mechanical ventilation, more blood transfusion, higher central venous pressures, higher IS and lower CI necessitating prolonged ICU stay.

Biochemical markers of myocardial injury: Troponin-T, CPK-MB, and the level of inflammatory parameters:Interleukin-6 and TNF-α were measured on day-0 and day-1 of surgery. Duration of ICU stay, hospital stay, and 30-day mortality were recorded.

CI Measurement

CI was measured using the non-invasive ICON electrical cardiometry device (ICON Osypka Medical, Berlin, Germany) as detailed by others & us earlier[14]. First reading of CI was obtained before surgery (CI-0), immediately after skin closure in the operating room (CI-I), 12 hours later (CI-II), and 24 hours later (CI-III).

The need for inotropes was assessed as under[15]:

IS = dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/ min) + (100 x epinephrine dose (mcg/kg/min)) + (10 x milrinone dose (mcg/kg/min)) + (10,000 x vasopressin dose (U/kg/min)) + (100 x norepinephrine dose (mcg/kg/ min)[15].

Biochemical Analysis

Two venous blood samples were collected, first 30 minutes after termination of CPB, second in the ICU, 24-hours after termination of CPB. These were analysed for IL-6, TNF-α, CPK-MB and troponin-T using assay kits by a

laboratory technician blinded to the group.

Statistical analysis

This was performed using Stata 14.0 software (StataCorp LP, College station, TX, US). Continuous variables were expressed as mean ± standard deviation and were analysed by the Student-t test or ANOVA. Non-normally distributed data were analysed using Wilcoxon ranksum test. Detailed sub-analysis of the entire patient groups was performed according to weight. Clinical outcomes including LCOS, mechanical ventilation >24 hours, and death were compared between the groups by Fisher's exact test. P value<0.05 was considered statistically significant.

Results (Tables 1-4)

Table-1 shows that age, sex, weight, body surface area, pre-operative hematocrit, pre-operative coagulation profile and CI were similar in both groups. CPB and aortic-cross clamp times, priming volume, cardioplegia volume, incidence of arrhythmias post-aortic clamp release and patients requiring transannular patch was similar. Post-operative echocardiography demonstrated normal biventricular function and no residual defects following surgery an all patients. Two patients in Group-M and four in Group-C underwent re-exploration for bleeding. In all these, bleeding was from suture lines and not from medical causes. These were excluded from analysis as fall in haematocrit is expected in patients with surgical causes and is independent of CUF/MUF.

Overall, patients in Group-M had improved hematocrit (44.3±0.98 g/dl) in

Group-M than Group-C (37.8±1.37g/dl),P=<0.001. As is apparent from sub-analysis according to weight (Table-2), patients in Group-M had higher hematocrit irrespective of weight(P<0.001). Similarly, patients in Group-M had higher hemoglobin(15.06±0.98 g/dl) compared to Group-C (11.65±1.37g/dl). Time to peripheral rewarming was 6.30±3.91 hours in Group-M compared to 13.67±3.91 hours in Group-C ,P=0.06.

Peak airway pressures in the ICU were lower in Group-M(17±2 mm Hg) compared to Group-C(20.55±2.97mmHg),P<0.001). Mean mechanical ventilation time(hours) was 6.3±2.7 hours in Group-M compared to 14.7±3.5 hours in Group-C(P=0.002)(Table-3). CVP following sternal closure in the operating room was lower in Group-M(9.27±3.12mmHg) compared to Group-C(10.52±2.2mmHg), P=0.04. CI was similar at all time-points between two groups. Mean arterial pressures and CVP in the ICU were similar.

Mean IS in the ICU was 11.52±2.20 in Group-C compared to 10.84±2.78 in Group-M,P=0.04. 8/39(20.5%) patients in Group-M had IS>than 10 compared to 22/40(55%) patients in Group-C(P=0.02). Amount of blood transfused in the two groups was similar(P=0.59).

Interleukin-6 levels were lower in Group-M compared to Group-C on post-operative day-0(P=0.04). These were however similar on post-operative day-1(P=0.98). Serum Troponin-T was lower in Group-M compared to Group-C on postoperative day-0,P=0.02. &day-1,P=0.004. CPK-MB & TNF-α levels were similar (Table-4).

ICU stay(P=0.88) and hospital stay(P=0.43) were also similar. One patient in

Group-M and three in Group-C died due to ventilator associated pneumonia, while another in Group-C succumbed to sepsis secondary to deep seated surgical site infection. 30-day mortality between groups was comparable (P=0.17).

Discussion

This trial tested the hypothesis that patients undergoing intracardiac repair of TOF undergoing MUF have higher hematocrit, lesser need for mechanical ventilation, better hemodynamics and decreased morbidity and mortality. This study demonstrated that although patients between the two groups had no statistically significant differences in parameters of hemodynamic status and morbidity, patients in MUF group had significantly higher hematocrit, lower peak airway pressures and lower need for mechanical ventilation.

There is evidence that MUF reduces postoperative morbidity following cardiac operations[16]. Possibly it decreases total body water, reduces post-operative blood loss and blood product use, increases arterial blood pressure, and improves left ventricular systolic function. In the experience of many[5-7], it improves the alveolar–arterial oxygen gradient and pulmonary compliance, decreases the frequency of pulmonary hypertensive episodes and reduces the duration of post-operative mechanical ventilation.

Votaries of mechanisms advocate that MUF reduces tissue edema, produces hemoconcentration[21], and removes inflammatory mediators. We observed increased hematocrit in Group-M in the operating room (OR). This persisted in Group-M in the ICU, even 6-hours following surgery.

Contrary to previous experience[16-18], mean arterial pressures (MAP) in the OR & ICU were identical. CVP was significantly lower (P=0.04) in Group-M in OR and immediate post-operative period, and this persisted in ICU and 6-hours later. CI was similar at all time points. Although statistically insignificant, patients in Group-M had shorter time to peripheral rewarming(P=0.06).

Studies by Sever[17], Alizadehasi[18] and Bando[12] have documented decreased post-operative blood transfusion in patients undergoing MUF. We observed this to be similar (P=0.59). As critical care physicians were blinded to both groups, any transient hypotension during peripheral rewarming was managed by blood transfusions for maintaining MAP. Also, an effort was made by the critical care physician to maintain a post-operative hemoglobin >14g/dl, as cyanotic patients are used to higher preoperative hemoglobin levels.

Patients in Group-M had lower peak airway pressures(P<0.001) reflecting better lung compliance leading to faster extubation. Time to peripheral rewarming was one of our extubation criteria; quicker rewarming could have contributed to faster extubation in Group-M. Fewer patients in Group-M (8/39) had IS >10 than Group-C (22/40),P=0.02, indicating that patients in MUF group required lesser inotropes.

TNF-alpha levels 6-hours after surgery (P=0.36) and 24-hours later(P=0.72) were no different. IL-6 levels were lower at 6-hours following surgery in MUF group(P=0.04) but similar 24-hours later(P=0.98). Chew et al[6] observed no differences in TNF-α and IL-1 levels in MUF versus controls. They claimed that beneficial effects of MUF resulted from reduced extracellular fluid and less likely due to reduced inflammatory mediators.

Serum Troponin-T and CPK –MB were measured on post-operative day-0 and day-1 to estimate ongoing myocardial injury. Serum Troponin-T levels were significantly lower in Group-M on post-operative day-1 indicating lower myocardial injury in Group-M. These differences may be responsible for accelerated recovery in MUF group. However, ICU stay was similar in both groups as this is decided by multiple factors such as prolonged need for inotropes, low CI & transient arrhythmias which were similar in both groups.

Zero Balance Ultrafiltration (ZBUF) has been described as an alternative to ultrafiltration[19]. This resembles CUF except that the filtered volume is replaced with equal amounts of crystalloids. Some claim better extraction of inflammatory mediators since larger volumes of blood are filtered[,20], albeit negative fluid balance is not achieved[21]. ZBUF may be effective as MUF, but we have not studied this. In a randomized trial on ZBUF, Journois[19] showed decreased levels of TNF-α, IL-10, IL-6, IL-8, C3a and myeloperoxidase in patients undergoing ZBUF. They demonstrated better clinical outcomes & concluded that removal of pro-inflammatory mediators led to better outcomes in these patients.

As differences in the values of higher hematocrit, CI, IS & serum enzymes are temporary, an alternative conclusion may be that some benefits of MUF may be temporary/minimal or that there is no positive effect on clinical outcomes as noted by hemodynamic and morbidity parameters in our study.

Although risks associated with MUF such as entrainment of air in the aortic cannula, hemodynamic instability, high ultrafiltration rates causing cerebral

steal and prolongation of exposure to non-endothelialized structures do exist[22], we observed that MUF in experienced hands can improve post-operative lung compliance and reduces duration of mechanical ventilatory support.

Study limitations

Our study includes only TOF patients and does not include complex cardiac diagnoses that may respond differently. Our patients are older in whom benefits of MUF are doubtful. Due to financial constraints in a resource limited environment we did not use a cell saver.

Williams[22] considered chest drain output as a surrogate marker of adequacy of coagulation. We did not consider this as a parameter in our study. We did not measure serum clotting factors after ultrafiltration to assess any changes following MUF, nor did we quantify myocardial edema. Instead we used surrogate markers like CI, MAP and CVP to estimate myocardial dysfunction consequent to edema. We used impedance cardiometry to measure CI, although we acknowledge that invasive monitoring of CI is the gold standard. Lack of equipment for invasive monitoring led us to use ICON monitor which requires further validation.

Conclusions

MUF increases post-operative hematocrit, decreases duration of mechanical ventilation and reduces need for inotropes. Interleukin -6 levels were lower on the day of surgery in patients undergoing MUF. MUF did not impact ICU and hospital stay between groups.

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Table 1. Baseline characteristics of the patient population

Variable	**Group-C (n=40)** Mean ± SD	**Group-M (n=39)** Mean ± SD	**P value**
Age (years)	5.12± 3.46	4.25± 2.76	0.22
Sex *			0.24
Male	26(65%)	30(76.9%)	
Female	14(35%)	9(23.1%)	
Body weight(kg)	15.13 ±6.54	13.48 ± 4.31	0.19
Body surface area(m^2)	0.70 ±0.28	0.63 ± 0.22	0.22
Pre-operative haematocrit (gm/dl)	50.6±10.02	43.9±5.55	0.36
Pre-operative cardiac Index(L/min/ $m^{2)}$	3.26±1.27	3.28±0.96	0.93
Cardiopulmonary bypass time(min)	100.85 ± 31.56	105.4±40.59	0.57
Aortic cross clamp time(min)	65.72 ±25.93	65.15 ± 28.29	0.92
Priming Volume(ml)	897.5± 309	872.05±244	0.68
DelNido cardioplegia(ml)	482 ± 190.76	444.61 ± 195	0.39
Ventricular Tachycardia/Ventricular fibrillation post-clamp release*	6(15%)	9(23.1%)	0.83

Table 2: Sub-analysis of changes in haematocrit (Primary outcome) in patients undergoing TOF Repair in the CUF only (Controls group) versus MUF+ CUF (Study) group based on body weight.

	Group-C (n=40) Mean ± SD	Group-M(n=39) Mean ± SD	P-Value
5-9.9 Kg	**n = 6**	**n = 7**	
Pre-Operative	48.9 ± 7.15	47.4 ± 3.36	**0.627**
Immediate Post-Operative	34.4 ± 3.87	46.5 ± 4.17	**0.001**
6hrs Post-Operative	37.1 ± 3.21	46.5 ± 3.58	**0.001**
Diff (Post-Operative - Pre-Operative)	-14.5 ± 10.57	-0.9 ± 5.42	**0.001**
Diff (6hrs Postoperative - Preoperative)	-11.5 ± 9.76	0.9 ± 4.69	**0.021**
10-14.9 Kg	**n = 18**	**n = 21**	
Pre-Operative	47.5 ± 10.63	42.3 ± 4.39	**0.049**
Immediate Post-Operative	35.1 ± 4.48	44.5 ± 2.69	**0.001**
6hrs Post-Operative	37.0 ± 3.21	44.3 ± 3.19	**<0.001**
Diff (Post-Operative - Pre-Operative)	-12.5 ± 13.89	2.2± 4.75	**<0.001**
Diff (6hrs Postoperative - Preoperative)	-10.5±11.13	2.8 ± 5.05	**<0.001**
15-20 Kg	**n = 16**	**n = 11**	
Pre-Operative	54.8±3.87	44.7 ± 7.55	**0.005**
Immediate Post-Operative	35.0±4.04	45.7 ± 2.47	**0.001**
6hrs Post-Operative	37.8 ± 2.61	44.3 ± 3.83	**0.001**
Diff (Post-Operative - Pre-Operative)	-19.8 ± 10.0	0.95 ±8 .20	**<0.001**
Diff (6hrs Postoperative - Preoperative)	-17.2±8.82	0.4.9 ± 9.28	**<0.001**

Table 3. Description of Secondary Outcome parameters in patients undergoing COF alone or those undergoing CUF +MUF.

Variable	**Group C (n=40)** Mean ± SD	**Group M (n=39)** Mean ± SD	**P value**
Peak airway pressures (mm Hg)	20.55± 2.97	17.17 ± 2.05	**<0.001**
Duration of Mechanical ventilation (hours)	14.7±3.5	6.3±2.7	**0.002**
Duration of Mechanical ventilation > 10 hours	22 (55%)	8(20.5%)	**0.002**
Blood transfusion(ml)	430.25 ± 148	448.58 ± 124	0.59
Time to peripheral Rewarming (hours)	13.67 ± 3.91	6.30±2.98	0.06
Mean arterial Pressures (mm Hg) in OT	63.8±4.1	65.3±3.26	0.07
Mean arterial pressures (mm Hg)in ICU	62.6 ± 4.97	64.4±4.84	0.10
Central venous pressures (mm Hg)in OT	10.52±2.2	9.27±3.12	**0.04**
Central venous pressures (mm Hg) in ICU	11.52 ± 2.20	10.84 ± 2.78	0.23
Mean Inotropic Score	11.52 ± 2.20	10.84 ± 2.78	**0.04**
Inotrope score >10 on Day 0 of surgery	22(55%)	8(20.5%)	**0.02**
Baseline CI	3.26 ± 1.27	3.28± 0.96	0.93
CI after termination of CPB (mean (± SD)	3.16±0.91	3.17 ±1.03	0.97
CI -12 hours in ICU	3.14±0.87	3.26 ± 0.86	0.51
CI -24 hours in ICU	3.28 ± 0.99	3.46 ± 0.87	0.51

Table 4. Biochemical parameters

Variable	**Group C (n=40)** Median (IQR)	**Group M (n=39)** Median (IQR)	**P value**
Lactate (mg/dl) at 24 hours	3.2 (1.8, 4.5)	3.1(1.96 , 4.3)	0.51
Troponin-T(ng/ml) Post op Day 0 Post op Day 1	 5057 (3461.5 , 8770) 5431 (3316.5 - 7036.5)	 231 (2737 , 5634) 3241 (2500-4734)	 **0.02** **0.004**
CPK-MB(units/L) Post op Day 0 Post op Day 1	 178 (125 , 239.5) 126.5(8 6 , 230)	 210 (120 , 312) 178 (91-312)	 0.22 0.10
TNF-alpha(microgram/ml) Post op Day 0 Post op Day 1	 4.1(2.0 , 5.85) 10.5(5.9 , 17.9)	 4.3 (3.2 , 5.5) 6.2 (3.6 , 16.3)	 0.36 0.72
IL-6(pg/ml) Post op Day 0 Post op Day 1	 4.8 (4.1 , 8.6) 9.5 (4.6 , 12.2)	 4.6(3.4 , 6.2) 5.8(4.2 , 10.1)	 **0.04** 0.98