Euvolemic off Pump Coronary Surgery Further Improves Early Postoperative Outcomes

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ABSTRACT

Background: Fluid resuscitation during Off-Pump Coronary Surgery (OPCABG) is still not protocolized and depends on multiple variables. We are exploring in this study whether a restrictive or euvolemic approach has any impact on short term surgical outcomes following OPCABG.

Methods: It is a retrospective study of 300 patients analyzed based on the intraoperative fluid requirement with 150 patients in each group (Group I: Fluid <2 Litres, Group II: Fluid >2 Litres).

Results: Multivariable analysis showed echocardiography variables such as E/e ratio, LA volume index, and atrial fibrillation (AF). LA volume index is related to the higher fluid requirement. Group II had significantly higher ventilation time ($P < 0.05$), drain output ($P = 0.05$), drain removal time (<0.05), inotropic requirement, and diuretic use.

Conclusion: The requirement of the intraoperative fluid was associated with various factors including diastolic dysfunction (left atrial volume index, left ventricle mass index, E/e ratio) and preoperative dual antiplatelet use. Group II patients had longer ventilation time, diuretics use, high drain output, and required drains for a longer period of time. Although there was no statistical difference among two groups as far as postoperative AF concerned, a reversal of AF to sinus rhythm was delayed in group II patients.

Keywords: Angina, congestive cardiac failure, low cardiac output

INTRODUCTION

Off Pump Coronary Bypass Grafting (OPCABG) has been reported to have better short-term outcomes in comparison to the On Pump Coronary Artery Bypass Grafting surgery (ONCABG), and especially in certain groups of high-risk patients.[1] The reasons stated for the improved results are, less systemic inflammatory response and global myocardial ischemia, minimal aortic manipulation. Haemodilution and volume overload are the by-product of cardiopulmonary bypass circuit and this fluid overload may lead to the pulmonary complications, slow recovery of the patient, atrial fibrillation (AF), anaemia, longer stay in critical care unit, and acute renal failure.[2,3] These studies have shown that volume management and fluid overload can have detrimental effects on the postoperative outcomes, even then often judging fluid adequacy can be a hardest decision for the anaesthetist in cardiac operating room. In this study, we are analysing relation of the intraoperative fluid infusion and short-term outcomes following OPCABG surgery.

METHODS

Our study is a retrospective analysis of the 300 patients who underwent OPCABG surgery from January 2017 to April
2020 at our institute. Two groups were made retrospectively based on intraoperative fluid requirement with 150 patients in each group (Group I: Less than 2 litres fluid, Group II: more than 2 litres fluid). Patients in both groups received a balanced crystalloid solution (Hartmann’s solution, compound sodium lactate) and plasma-derived colloid (4% Human Albumin) for fluid resuscitation. When required, patients were transfused using pack blood cells, platelets, plasma and cryo-precipitate.

Our approach is of “conservative fluid resuscitation” and 2 L was kept as cutoff because majority of the cases needed nearly 2 L of the fluid replacement in the operating room.

General anaesthesia induction was done using balanced Fentanyl and Propofol with an intermediate acting neuromuscular blocking agent (usually vecuronium). Maintenance of the general anaesthesia was done using Sevoflurane and Fentanyl. Decision of fluid replacement was based on the combination of pulse pressure variation (PPV), clinical indication and trans-oesophageal echocardiogram (TOE) findings.

Patients and data collection
Our study was approved by the hospital quality improvement and ethical committee and requirement for individual patient consent was waived. Inclusion criteria’s were, routine, early and emergency OPCABG surgery cases requiring two or more coronary artery bypass grafts. Exclusion criteria were, single vessel OPCABG, chronic Atrial Fibrillation (AF), redo surgeries, significant other medical history such as hypothyroidism, Rheumatoid arthritis, long term steroid use, additional procedures such as left atrial occlusion and total arterial OPCABG cases. Data were collected from the patient records and it was annually submitted to the Australia and New Zealand Society of Cardiac and Thoracic Surgeons National database (ANZSCCTS).

Outcomes
Primary outcomes analysed in this study were diuretics use, ventilation time, new-onset atrial fibrillation (NOAF), chest tube removal day and blood transfusion rate while secondary outcomes were all-cause mortality and myocardial infarction.

Statistics
Statistical calculations were performed using NCSS 10 (NCSS 10 Statistical Software (2015, NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/ncss)). Continuous variables were described as mean with the standard deviation. Normally distributed continuous variables are compared using one-way ANOVA, nonparametric variables with Kruskall–Wallis test corrected for ties, and 2 × 2 categorical variables are compared with Fisher’s exact test. Propensity matching was performed by using logistic regression with postoperative AF as the dependent variable, and age, sex and LA volume index as the independent variables. Matching was performed using nearest available Mahalanobis matching with a calliper of 0.25. Statistical significance was assessed at $P < 0.05$. The Odds Ratio (OR) calculated conventionally while the confidence intervals (CI) were calculated using conditional exact method.

DEFINITIONS

Diastolic dysfunction (DD)
DD was defined on the findings of E/e ratio, and LA volume index and LV mass index as these are most accurate and relatively preload independent non-invasive predictors of Left Ventricle (LV) filling pressures.\(^{10}\) E/e is an indicator of diastolic function that correlates well with LV filling pressure and is relatively independent of systolic function and rhythm abnormalities. E/e ratio was classified into three groups respectively: Normal E/e <8, Undetermined E/e 8 to 15, and severely elevated >15.\(^{16}\) Left Atrial Volume Index (LAVI): It was described in four groups: <26 mL/m\(^2\): normal, 27 to 33 mL/m\(^2\): mild; 34 to 39 mL/m\(^2\): moderate; and 40 mL/m\(^2\): high or severe.\(^{7}\) Normal Left Ventricle Mass index (LVMI) range is 70 ± 9 gm/m\(^2\) in men and 61 ± 8 gm/m\(^2\) in females respectively.\(^{18}\)

Inotrope/vasoconstrictors requirement
In the majority of the cases mean arterial pressures (MAP) were maintained at >65 mm Hg with or without vasoconstrictors infusion. Central venous pressure line (CVP) and pulmonary sheath were inserted in all the cases and Pulmonary Catheter was floated in sick cases. Vasoconstrictors were used according to the Vasoactive-Inotropic Scoring (VIS) system.\(^{19}\) Maximum VIS (VISmax) was calculated at the end of the first 24 h in the intensive care unit (ICU). Noradrenaline infusion was started at 0.04 mcg/kg/min and was escalated up to 0.5 mcg/kg/min if patient remains hypotensive. Dobutamine and Adrenaline were used rarely and in very low doses.

Definition of post-surgery myocardial Infarction was accepted from the previous reports.\(^{10}\) High sensitivity Troponin I was used to assess postoperative myocardial ischemia (0-10 ng/L in females and 0-20 ng/L in male).

NOAF was defined as any new AF recorded during or after the surgery, which can be either paroxysmal or persistent.
Emergency surgery was defined as operation performed on the day of the referral or next day first list. Early surgery: was defined when patient presented to the cardiology department and cannot be waitlisted because of critical coronary anatomy and need surgery in the same admission within a week.

Patients were transfused if haemoglobin level was $<80$ g L$^{-1}$, fresh frozen plasma and platelets given if International Normalised Ratio (INR) was $>1.5$, and platelet count was $<100 \times 10^{9}$ L$^{-1}$, or if bleeding was because of platelet dysfunction respectively.

All patients stopped angiotensin-converting enzyme Inhibitors (ACE) three days prior to the surgery and continued aspirin till the date of surgery.

Criteria’s used for fluid resuscitation were based on Pulse Pressure Variation (PPV), clinical judgement and Echocardiography (TOE) findings.

**RESULTS**

Both groups had comparable demographic variables and other medical co-morbidities.

**Preoperative variables [Table 1]**

Both groups had comparable age and gender distribution (Group I: 45–82 years, Group II: 50–82 years). Group II had higher number of triple vessel disease cases (OR 0.42, 95% CI 0.16–1, $P = 0.07$) while Group I had higher number of left main stenosis (OR 1.53, 95% CI 0.77–3.07, $P = 0.25$).

Group II had higher numbers of early surgeries, preoperative STEMI, peripheral vascular disease (PVD), but none of these variables were statistically significant except carotid artery disease (OR 0.46, 95% CI 0.21–0.97, $P = 0.039$). The patients in group I had higher NYHA class as compared to the Group II (OR 0.82, 95% CI 0.46–1.48 between NYHA 3,4 vs NYHA 1,2, $P < 0.05$).

A tota of 25% patients in both the groups had Ticagrelor (Brilinta, AstraZeneca, Australia) as second antiplatelet agent at the time of the cardiology admission (Group I: 25.72% and Group II: 30.48%, $P = 0.53$). Our policy is to wait for 72 h after the last dose of Ticagrelor and continue Aspirin till surgery.

**Preoperative transthoracic echocardiography [Table 2]**

The left ventricular ejection fraction (EF) and regional wall motion abnormalities (RWMA) were not significantly different among both groups. Although all three parameters of the Diastolic Dysfunction (LAVI, E/e ratio and LVMI) were higher in Group II, none were found statistically significant. Approximately 31.15% patients in Group II had E/e ratio $>15$, it correlates well with high LAVI and may be a reason of higher fluid requirement (OR 2.43, 95% CI 1.35–4.35, $P < 0.05$). Linear regression analysis showed a positive correlation between the incidence of the AF and LAVI [Figure 1].

Both groups had similar demography and other parameters except that group II had E/e ratio but it was not statistically significant (OR 1.06, 95% CI 0.46-1.95, $P = 0.58$). Similarly, preoperative LAVI and EF findings were comparable in both groups as well.

**Intraoperative findings [Table 3]**

A significant difference was observed among two groups in intraoperative fluid requirement ($P$ value $<0.00001$), and cell saver blood return ($P < 0.00001$). No patient required intraoperative blood transfusion, while two patients in each group needed platelet transfusion before closing the chest. Fluid responsiveness was seen in 60% of the patients during the surgery using PPV criteria. Blood gas parameters were not included as all cases done OPCABG and there were no significant differences in both groups.

**Postoperative Variables [Table 4]**

Both groups had one 30-day mortality each (Group 1: Patient developed heparin-induced thrombocytopenia and complicated by systemic thrombosis, while in Group II patient died because of the multiorgan failure). One patient in Group I and two patients in Group II needed chest tube insertion for left pleural effusion after the surgery.

Patients in Group II had higher ventilation time, drain output, drain removal time, inotropic requirement and diuretic use [Figure 2, 3]. Vasoconstrictor requirement (VISmax) was lesser in restrictive group (Group I) as compared to the liberal group patients (OR 3.8, 95% CI 2.5–5, $P = 0.05$) and overall VISmax was higher in patients requiring high fluid requirement [Table 4].

![Figure 1: Relation between AF and Left atrial size](image)
The linear regression analysis showed a positive correlation between E/e ratio and inotropic requirement [Figure 4]. Use of Ticagrelor (with-in 72 h) before surgery was associated with the higher intraoperative fluid requirement \((P = 0.022)\).

Multivariate analysis showed early surgery, high LVMI, DD, and longer diuretic use are independent risk factors for the NOAF. Although the incidence of the AF was not statistically significant among two groups (OR 0.68, 95% CI 0.24–1.20, \(P = 0.37\)), noticeably reversal to the sinus rhythm was delayed in Group II (OR 0.74, 95% CI 0.56–0.98, \(P < 0.04\)).

### DISCUSSION

Deciding appropriateness of the fluid replacement during cardiac surgery and especially OPCABG can be a challenge for the anaesthetists because of the interaction between factors related to the physiology, pharmacology, and mechanical ventilation. Noticeable hypovolemia can be identified by the systolic pressure variation, TOE findings and CVP measurements, but on many occasions these changes are subtle and subclinical.\[11\] There is a thin line of clinical discretion between managing patient inappropriately with vasoconstrictors leading to systemic hypoperfusion.
versus overzealous volume replacement and exposing patient to the fluid overload.[12]

Infusion of crystalloid or colloid fluid without knowing volume responsiveness can lead to hypervolemia with fluid accumulation in the interstitial spaces.[13] Various techniques have been studied in the literature for determining fluid responsiveness (PPV, systolic pressure variation, stroke volume variation, left ventricular end-diastolic area, pulmonary artery wedge pressures and central venous pressures) and PPV is recounted to be highly predictive of the fluid responsiveness.[11] Our major criteria’s for volume infusion were PPV (cut-off value 13%) and preloading during lifting of the heart.

In our study, we found 60% of cases responded to the volume replacement on the base of PPV criteria as reported previously by others (variation of 13% or more).[14] Balanced crystalloid fluid has advantage of avoiding metabolic acidosis and it also maintains renal blood flow.[15] But 80% of crystalloid fluid is eventually ends up in extravascular compartment, which is a major contributor of myocardial oedema, pulmonary fluid overload and weight gain after surgery. Clinically it manifests in the co-morbidities like AF, anaemia, poor respiratory efforts and low cardiac output. Albumin would appear to offer an advantage in comparison to other colloids and crystalloid fluids but being a human-derived product carries a risk of transmission of prions and most importantly there are no randomized trials supporting advantages of Albumin compared to the balanced crystalloids.[15] Even in our study use of Albumin was <5% during the surgery and around 10% in the immediate postoperative period for the goal-directed resuscitation.

Table 2: Pre-operative echocardiography variables

| Variables                  | Group I       | Group II      | Odds Ratio | P (Fishers Exact test) |
|----------------------------|---------------|---------------|------------|------------------------|
| Ejection Fraction          | 53.50 ± 10.7  | 52.48 ± 10.6  | 0.49 (Kruskal Wallace test) |
| <30%                       | 6.67%         | 1.90%         |            |                        |
| 30-55%                     | 39.05%        | 47.62%        |            |                        |
| >55%                       | 55.24%        | 49.05%        |            |                        |
| Regional Wall Motion Artefact | 54.28%    | 57.14%        | 0.97 (0.67-4.6) | 0.18 (Kruskal Wallace test) |
| LA Volume Index (mL/m²)    | 33.88 mL ± 6.9| 34.74 ± 6.3  | 0.71       | 0.20 (Kruskal Wallace test) |
| <26 mL/m²                  | 12.39%        | 9.53%         |            |                        |
| 27-33 mL/m²                | 41.91%        | 36.20%        |            |                        |
| 34-39 mL/m²                | 19.05%        | 22.86%        |            |                        |
| >40 mL/m²                  | 26.67%        | 31.43%        |            |                        |
| LV Mass Index (gm/m²)      | 85 ± 13.7     | 86.71 ± 14.9  | 0.98       | 0.49 (Kruskal Wallace test) |
| >110 gm/m²                 |               |               |            |                        |
| Aortic Valve disease (AS/AR)| 9.5%          | 12.23%        | 0.59 (0.23-1.46) | 0.29 (Kruskal Wallace test) |
| Mitral Valve disease (MR/MS)| 15%           | 10.47%        | 2.01 (0.86-4.92) | 0.119 (Kruskal Wallace test) |
| E/e Ratio                  | 11.37 ± 3.4   | 11.83 ± 3.7   | 1.06       | 0.58 (Kruskal Wallace test) |
| >15                        | 30.41%        | 37.15%        | OR is for E/e>8 vs <8 (0.46-1.95) |
| 8.1-14.9                   | 49.53%        | 42.86%        |            |                        |
| 8 or <8                    | 20%           | 20%           |            |                        |

Figure 2: Post-operative outcomes: Drain output and Cell saver volume

Figure 3: Post-operative outcomes: Intra-operative fluid, post-operative fluid, drain removal day
Table 3: Intra-operative findings

| Variables                          | Group I        | Group II       | Odds Ratio with 95% CI | P (Fishers Exact test) |
|-----------------------------------|----------------|----------------|------------------------|------------------------|
| Intra op fluid (lit) crystalloid plus colloid | 1.77 ± 0.34 | 3.19 ± 0.60 | 2.43 (1.35-4.35) | 0.00001 (Kruskal Wallace test) |
| Colloid used in patients           | 4.76%          | 6.7%           | 0.85 (0.70-0.90) | 0.90                   |
| Grafts                            | AVERAGE:3.12 | 3.55           | 1.1 (0.8-2.1)    | 1                      |
|                                   | 7.61%:2       | 10.4%:2        |                        |                        |
|                                   | 73.34%:3      | 57.1%:3        |                        |                        |
|                                   | 18.15%:4      | 27.6%:4        |                        |                        |
|                                   | 0.90%:5       | 4.7%:5         |                        |                        |
| Left Internal Mammary artery      | 100%           | 100%           | 1                      | 1                      |
| Saphenous vein                    | 100%           | 100%           | 1                      | 1                      |
| Radial artery                     | 12.38%         | 17.10%         | 0.64 (0.27-1.46) | 0.78                   |
| Mean Urine output (mL)            | 660.52 ± 178.6 | 658.25 ± 152.10 |                        | 0.97                   |
| Cell saver (mL)                   | 228.6 ± 90.3  | 399.25 ± 139.6 | 0.00001 (Kruskal Wallace test) |
| Grafting time (Min)               | 110.24 ± 30.25 | 135.90 ± 40.78 |                        | 0.75                   |

Table 4: Postoperative findings

| Variables                          | Group I            | Group II           | Odds ratio | P (Fishers Exact Test) |
|-----------------------------------|---------------------|--------------------|------------|------------------------|
| Ventilation hours                 | 7.73 ± 4 (6 (median)| 9.25 ± 5.2 (8 (median)) |           | 0.0022 (Kruskal Wallace test) |
| Drain output (mL)                 | 304.58 ± 111.9     | 387.95 ± 173.6    | 0.05       |                        |
| Drain removal day                 | Day 1: 80%         | Day 1: 72%        | 0.31 (0.16-0.59) | 0.0036 |
|                                   | Day 2:17.10%       | Day 2: 17.10%     | 0.85       |                        |
|                                   | Day 3: 2.85%       | Day 3: 1.90%      | 0.85       |                        |
| New onset AF                      | 16.10%             | 20.96%            | 0.68 (0.24-1.20) | 0.37 |
| Amiodarone loading                | 16.10%             | 20.96%            | 0.55 (0.24-1.20) | 0.15 |
| AF reverted hours                 | 81.25%:reverted <24 hrs | 33.34%:reverted in <24 hrs | 0.74 (0.56-0.98) | 0.04 |
|                                   | 18.75%:reverted in 50 hrs | 66.67%:reverted in > 24 hrs |           |                        |
| Blood transfusion                 | 4 (2.67%)          | 8 (5.71%)         | 2.34 (0.71-8.89) | 0.19 |
| Diuretics>3 days                  | 13 (8.67%)         | 44 (29.34%)       | 3.98 (2.2-8.8) | 0.05 |
| Highest Troponin I               | 656 ± 896.3        | 1096 ± 1735.5     | 0.0032     |                        |
|                                   | 450 (median)       | 550 (median)      |            |                        |
| Fluid intake in ICU (lit) 24 hrs  | 1.59 ± 0.63        | 1.67 ± 0.59       | 0.39       |                        |
| New AKI                           |                     |                   |            |                        |
| grade I                           | 0.90%              | 1.90%             | 0.74 (0.11-4.52) | 0.56 |
| grade II                          | 0.90%              | 0.90%             | 0.74 (0.11-4.52) | 0.56 |
| Post Op Urine output 24 h         | 1100.67 ± 232.20   | 1150.45 ± 349.89  | 0.78       | 0.97 |
| TIA / stroke                      | 1.90%              | 1.90%             | 0.81 (0.01-9.68) | 1     |
| Graft failure                     | 0                  | 1 (0.90%)         | 0.19 (0.01-1.77) | 0.21 |
| Pleural Effusion                  | 1 (0.90%)          | 2 (1.90%)         | 0.70 (0.24-2.02) | 0.64 |
| No Inotropes                      | 116 (77.1%)        | 86 (57.34%)       | 0.020 (0.15-0.89) | 0.030 |
| Low Inotropes (VIS<10)            | 34 (22.67%)        | 57 (38%)          | 0.46 (0.30-0.90) | 0.016 |
| Moderate Inotropes (VIS>10)       | 2 (1.34%)          | 10 (6.67%)        | 0.32 (0.27-1.1) | 0.17 |

With the escalating healthcare costs, concept of “Fast Track” cardiac surgery is getting more and more attention. Main factors are reducing mechanical ventilation time and eventually ICU stay to cut down overall cost of the procedure.[16] Good early outcomes of the OPCAB surgery has been well established and OPCAB surgery could be an ideal example of the “Fast Track” cardiac surgery if surgical team could achieve early extubating, less pulmonary complications, minimum blood transfusion with low or no vasoconstrictors support. Liberal fluid infusion might delay in achieving these goals by creating dilutional anaemia requiring transfusion, fluid accumulation in the lungs requiring longer mechanical ventilatory support, splanchnic oedema and slowing gut motility.[17] These facts were supported by our study as Group II cases had significantly high ventilation time, bleeding, vasoconstrictor requirement and drain output.

In multiple large series OPCAB has been associated with reduced rates of transfusions, reoperation for perioperative bleeding, respiratory complications, and acute kidney injury as compared to the ONPUMP. Puskas et al. presented a retrospective analysis and showed that within all Predictive Risk of Mortality (PROM) quartiles;
OPCAB was associated with a significantly reduced risk of death and stroke.\(^\text{[18]}\) Moreover, the magnitude of the apparent risk reduction increased with increasing PROM. Benefits of OPCAB surgery becomes more apparent in high-risk patients, especially those with chronic obstructive pulmonary disease, renal insufficiency, and advanced atheromatous disease of the ascending aorta subject to aortic clamping, manipulation, and cannulation with CPB.

The issue with these surgical reports is that they focus mostly on the surgical aspect of the OPCABG rather than reflecting on anaesthetic and ICU side of the management, including factors like fluid resuscitation, vasoconstrictors choices and number of the cases performed in that unit.

Our hypothesis was that longer intake of diuretics might cause electrolyte imbalance and make patients prone for the rhythm disturbances.\(^\text{[13]}\) But, fluid restriction or liberal fluid intake could not make a difference in the rate of AF and its incidence was similar as previously reported in the literature. It would be interesting to explore these outcomes in the future with larger cohort of patients.

Lately, Diastolic Dysfunction (DD) and high Left Ventricular End Diastolic Pressure have been stated as independent risk factors for poor outcome during and after coronary surgery.\(^\text{[19]}\) DD is directly related to the reduction in early LV relaxation and compromising the effective blood flow from left atrium into the LV cavity. Condition worsens when heart is positioned for lateral and inferior grafts, as atria become dependent chamber and cardiac apex is directed towards the sky. All these changes might increase atrial filling pressures and eventually requires additional volume infusion.

Shim et have reported association between E/e ratio >15 and poor intraoperative haemodynamic tolerance during OPCABG surgery.\(^\text{[20]}\) They have found that in this subset of the patient’s cardiac index and mix venous saturation (Sv02) takes longer to recover and often requires vasoconstrictor support and higher amount of fluid infusion. Similarly in our series, Group II patients had higher E/e ratio and LAVI as compared to the group I (although not statistically significant) and required more fluid replacement during the surgery.

**Study Limitations**

A key issue here would be whether larger volumes of intraoperative fluid in this study constituted only appropriate volume replacement, or whether in retrospect they constituted ‘fluid’ overload.

**CONCLUSION**

Adequacy of the fluid resuscitation during OPCABG surgery depends on the variety of the factors. Euvolemic or restrictive fluid infusion strategy during OPCABG has benefits of preventing haemodilution, lower transfusion rate, short ventilation time, lesser use of diuretics and might expedite early postoperative recovery.

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**Conflicts of interest**

There are no conflicts of interest.

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