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Fluid Overload after Coronary Artery Bypass Grafting Surgery Increases the Incidence of Post-Operative Complications

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Abstract

This study is a prospective trial comparing the incidence of post-operative complications to fluid status in patients undergoing coronary artery bypass grafting (CABG) surgery. One hundred and nine subjects undergoing CABG surgery at the Jewish general hospital were recruited over a 5 months period in the year 2006. All of the patients underwent CABG surgery "on pump". Post operative fluid overload was measured by weight gain. Using logistic regression with complications (major vs. minor only/none) as an outcome and fluid overload as a covariate, the risk of major complications significantly increases for fluid overload ≥5 kg compared to 1 - 5 kg ($p < 0.001$), while the risk for ≤1 kg is not significantly different from 1 - 5 kg. Also, the risk of major complications significantly ($p = 0.012$) increases for days with fluid overload ≥5 days in comparison to ≤1 day.

Keywords: Fluid Overload, Complications, Coronary Artery Bypass Grafting

1. Introduction

Open heart surgery requiring cardio-pulmonary bypass (CPB) has been well known to result in post-operative fluid overload. Several mechanisms have been postulated as possible causes for this hypervolemia: excessive fluid replacement pre and intra-operatively and post-operative crystalloid administration in an effort to correct hypotension and a systemic inflammatory reaction caused by CPB which ultimately results in increased capillary permeability and leakage of fluid in the extra-vascular space. It is believed that fluid overload participates in the pathogenesis of important severe clinical complications [1]. The relation between fluid overload and early post-operative complications has not been studied adequately yet.

Our present proposed study therefore is a prospective trial comparing the frequency of post-operative complications to fluid status in patients undergoing coronary artery bypass grafting (CABG) surgery.

2. Method

One hundred and nine subjects undergoing CABG surgery at the Jewish General Hospital were recruited over a 5 month period in the year 2006. Exclusion criteria included redo CABG surgery, valve surgery, combined procedures (valve + CABG), patients with pre-operative renal failure (documented serum creatinine level of more than 2.0 mg/dl or on dialysis) and pre-operative congestive heart failure. Congestive heart failure diagnosis required at least 3 of the following: presence of dyspnea, rales thought to represent pulmonary congestion, peripheral edema, cardiomegaly on chest x-ray and chest x-ray compatible with interstitial edema.

Eighty-eight patients were male with an average age of 62.1 ± 10.4 years old and 21 patients were female with a mean age of 64.7 ± 11.5 years old. For the entire group of patients, the mean Canadian Cardio-vascular Society Class was 3.8, with a median Parsonnet Score of 7 and a mean left ventricular ejection fraction of 48.6%. All the patients underwent coronary artery bypass grafting surgery "on pump". The median number of grafts per patient was 4, with mainly the use of the left internal mammary artery for the left anterior descending artery and the saphenous vein grafts for the other coronary arteries. The average aortic cross-clamp time and total pump time were respectively 58 minutes and 77 minutes. The average amount of fluids given intra-operatively, including pump prime, cardioplegia, crystalloids, colloids, blood transfusions and blood derived products was 4733.46 mL. The average amount of fluids given post-operatively up to 24 hours, including crystalloids and colloids, blood transfusions and blood derived products was 3240.04 mL. The amount of patients requiring blood transfusions and blood derived products was 64%.

Post-operative fluid overload was measured by weight gain, which was measured on a ScaleTronix electronic scale on each day in the hospital after surgery for eight days and compared to pre-operative weight. The maximum weight gain over eight days was the value used for fluid overload. Arbitrarily, this weight gain was divided into 3 categories: less than 1 kg, 1 to 5 kg and more than 5 kg. The number of days in the hospital until pre-operative weight was also calculated and defined as number of days in the hospital with fluid overload. This variable was categorized arbitrarily into ≤1, 2 to 4, and ≥5 days. The complications were divided into 2 groups: major (death, myocardial infarction, cardiac arrest, low cardiac output syndrome, cardiac tamponade, mediastinal exploration for bleeding, cerebral vascular accident, respiratory failure requiring prolonged intubation, renal failure and deep sternal wound infection) and minor (atrial fibrillation, supra-ventricular tachycardia, new heart block, transient ischemic attack, delirium, pneumonia, leg wound infection, arm wound infection and superficial sternal wound infection). The median hospital length of stay was 5 days.

Statistical analysis to examine the association between type of complication (major, minor only, none) and fluid overload or days with fluid overload groups was performed using Fisher's exact test (because some table cell counts were <5). The association between type of complication and fluid overload was subsequently simplified by dichotomizing complications group into major vs. minor only/none. Two logistic regression models with complications group as the outcome were run: one with fluid overload categories and another with days with fluid overload categories as covariates. Odds ratios, which represent the odds of major complications in one fluid overload group compared to the odds of major complications in the fluid overload reference group, are reported with corresponding 95% confidence intervals and *p*-values. Statistical calculations were carried out using Stata statistical software (Intercooled Stata v8.2, College Station, TX, StataCorp).

3. Results

There was no operative mortality (up to one month post-operatively). The complications and their frequencies are listed in **Table 1**. Twenty-one patients (19%) had a major complication, 36 (33%) had only minor complications, and 52 (48%) had no complications. Looking at the relationship between demographic factors and complications, we found that the median age of patients with major, minor or no complications was similar at 62 years old. The median left ventricular ejection fraction was better (55%) in patients without complications than patients that presented minor or major complications (50%). The body mass index of our population did not influence the frequency or severity of the complications. The gender distribution of major, minor or no complications was respectively 15.91%, 31.82% and 52.27% for males and 33.33%, 38.10%, and 28.57% for females. For patients with major complications, 43.36% were in NYHA class III or IV compared to 0% in NYHA class I or II.

Type of complication (major, minor only, none) was examined in relation to groups of fluid overload post-operative weight gain (≤1 kg, 1-5 kg, ≥5 kg) (**Figure 1**). Among the 20 patients that presented with a post-operative weight gain ≤1 kg, the counts of major, minor and no complications were respectively 1, 7 and 12. Out of 62 patients with a weight gain of 1 to 5 kg, the counts of major, minor and no complications were 7, 21 and 34. In the group of 27 patients with a weight gain of ≥5 kg, the counts of major, minor and no complications were 13, 8 and 6. The association between type of complication and fluid overload weight gain shown in **Figure 1** was statistically significant (Fisher's exact $p = 0.001$).

Using logistic regression with complications (major vs. minor only/none) as an outcome and fluid overload as a covariate (with 1 - 5 kg as the reference group because of small numbers in the ≤1 kg category), the risk of major complications significantly ($p < 0.001$) differed for fluid overload ≥5 kg compared to 1 - 5 kg, while the risk for ≤1 kg was not significantly different from 1 - 5 kg **(Table 2)**.

Type of complication was also examined in relation to number of post-operative days (≤1, 2 to 4, and ≥5 days) where the patient remains overweight. Overall, 39 patients (36%) had fluid overload for ≤1 day, 22 (20%) for 2-4 days, and 48 (44%) for ≥5 days. **Figure 2** illustrates the frequency of type of complications in relationship to the number of days with fluid overload. The association shown in **Figure 2** was statistically significant (Fisher's

Table 1. Subjects in every category of complications.

Complications	Subjects in Category	Results in %
1-Death	0/109	0%
2-MI	2/109	1.83%
3-LCOS	15/109	13.76%
4-A.Fib or SVT	61/109	55.96%
5-Heart block >24 hr	22/109	20.18%
6-Cardiac Arrest	1/109	0.91%
7-Tamponade	1/109	0.91%
8-Re-exploration	3/109	2.75%
9-TIA	0/109	0%
10-RIND	0/109	0%
11-CVA	1/109	0.91%
12-Delirium	4/109	3.66%
13-Pneumonia	0/109	0%
14-Resp. failure + intubation	4/109	3.66%
15-Renal Impairment	8/109	7.33%
16-Leg wound infection	0/109	0%
17-Arm wound infection	0/109	0%
18-Superficial sternal wound	3/109	2.75%
19-Deep sternal wound	1/109	0.91%

exact $p = 0.048$). Using logistic regression with complications (major vs. minor only/none) as an outcome and days with fluid overload as a covariate, the risk of major complications significantly ($p = 0.012$) differed for days with fluid overload ≥5 days in comparison to ≤1 day **(Table 2)**.

4. Discussion

Open heart surgery is associated with a degree of fluid overload. The reason being; during cardio pulmonary bypass (CPB), the patient is exposed to the administration of a significant amount of exogenous fluids. Such fluids include the CPB pumps prime (1200 cc), fluids used for cardioplegia (200 cc) and other fluids given to deal with hypotensive episodes and/or intra-operative fluid redistribution. These fluids can often reach the amount of 3 to 4 litres of combined colloid and crystalloid solutions. Often, the patient undergoes cardiac surgery presenting with conditions such as heart or renal failure and under these circumstances, a degree of fluid overload already exists and is aggravated by CPB. Irrespective of the circumstances, fluid overload often participates in the pathogenesis of post-operative hypoxemia, myocardial oedema and organ oedema. It is also often responsible for a delay in recovery and several clinically important complications [1].

In our cohort of patients, the age and body mass index did not affect the frequency or the severity of the complications. However, as reported in the literature, we have shown that female gender, patients with lower left ventricular ejection fraction, and patients with NYHA class III or IV are at increased risk of complication.

5. Cardiopulmonary Dysfunction

Cardiopulmonary bypass may induce alterations in intra-vascular volume status and extra-vascular body water content [2,3], leading to oedema and cardiopulmonary dysfunction [4,5]. With the onset of CPB, the blood is diluted by the prime volume of the extra-corporeal circuit, resulting in a decreased colloid osmotic pressure [3-5]. CPB causes increased capillary permeability by activating the inflammatory mediators system [6-8]. Fur-

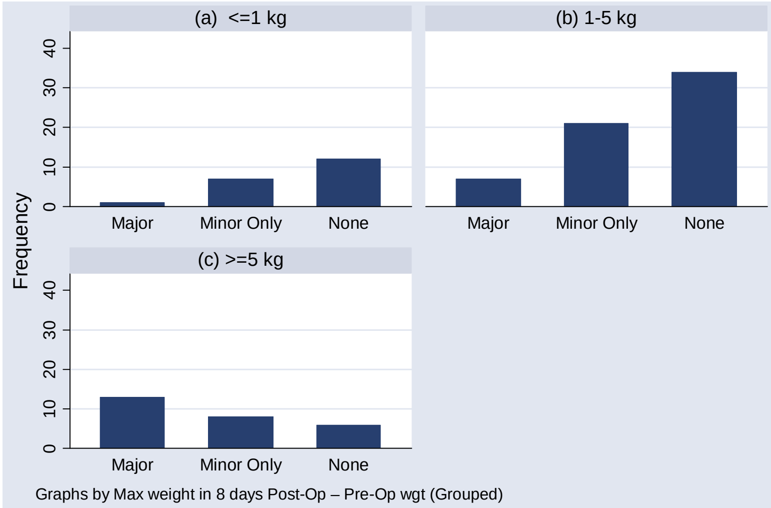

Figure 1. Type of complications by fluid overload group.

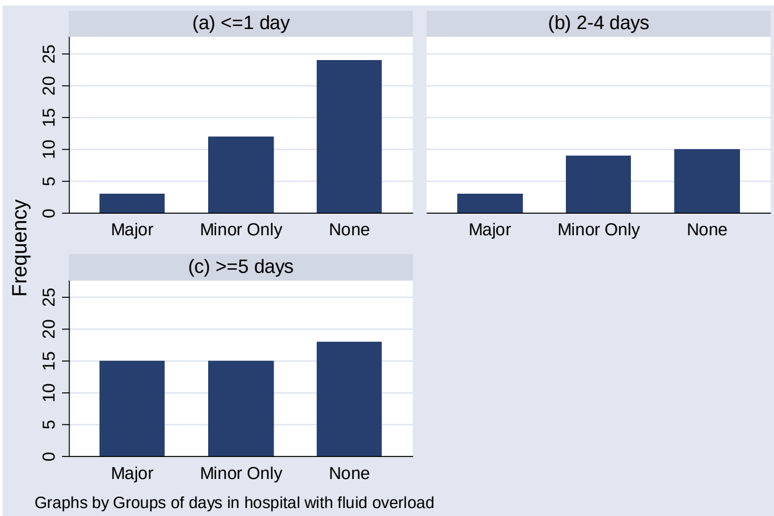

Figure 2. Type of complications by days with fluid overload.

Table 2. Logistic regression results with complication group as the outcome (major vs. minor only/none) and fluid overload and days with fluid overload as covariates (two separate models).

Covariate	Odds ratio (95% confidence interval)	*p*-value
Fluid overload		
≤1 kg	0.414 (0.048, 3.58)	0.423
1 - 5 kg	1 (reference)	-
≥5 kg	7.30 (2.45, 21.70)	<0.001
Days with fluid overload		
≤1 day	1 (reference)	-
2 - 4 days	1.89 (0.35, 10.31)	0.460
≥5 days	5.45 (1.45, 20.55)	0.012

thermore, the hydrostatic pressure within the capillaries is influenced by hypothermia [9] and post-ischemic myocardial dysfunction as a consequence of altered myocardial lymphatic function after cardioplegic arrest [10]. Thus, net filtration of fluid into the interstitium is increased during and after extra-corporeal circulation resulting in elevated extra-vascular lung water content [2, 11] and oedema formation in the myocardial interstitium [12] which can contribute to ventricular dysfunction, which may explain the relatively high (13.07%) incidence of low cardiac output syndrome in our series.

6. Other Complications

Acute reduction in cardiac output early after the operation is the most common and most important risk factor for the development of acute renal failure. Yet the prevalence of acute renal failure varies among patients with low cardiac output in part because of the role played by other risk factors. Despite fluid overload with weight gain post-open heart surgery, the intra-vascular compartment may be depleted leading to renal dysfunction.

Brain embolization and hypo-perfusion with resultant ischemia, have most generally been considered etiologic to these organic changes. The causes of both general neuropsychological subsystem dysfunction and localized subsystem dysfunction (such as strokes) are the same except in degree and/or distribution [13]. Could brain oedema resulting from fluid overload contribute to post-operative delirium?

In 2003, Brandstrup [14] and al. reported the effects of intravenous fluid restriction on post-operative complications after elective colorectal resection surgery. The restricted regimes aimed at maintaining pre-operative body weight; the standard regimen resembled everyday practice. The restricted intravenous fluid regimen significantly reduced post-operative complications both by intention-to-treat (33% vs. 51%, $p = 0.013$) and per-protocol (30% vs. 56%, $p = 0.003$) analyses. The number of both cardiopulmonary (7% vs. 24%, $p = 0.007$) and tissue healing complications (16% vs. 31%, $p = 0.04$) were significantly reduced, no patients died in the restricted group compared to 4 deaths in the standard group (0% vs. 4.7%, $p = 0.12$). The reduction of cardiopulmonary complications in the restricted group was pronounced. Subclinical oedema in lungs and other tissues may cause decreased tissue oxygenation [15], and may explain the findings of significantly increased tissue healing complications in the standard group.

A correlation has been reported between fluid overload, thrombosis [16] and prolongation of intestinal paralysis.

7. Treatment and Prevention of Fluid Overload

The patients in our series received "standard" amounts of fluids (mainly crystalloids) during or immediately after surgery to maintain adequate cardiac output. In the case of a persistent low cardiac output despite optimum intra-vascular compartment measurements (adequate CVP and PCWP), the patient would then be started on inotropic treatments.

Most of our patients received Mannitol while on CPB. Aggressive diuresis is usually started on the first post-operative day and continued until the patients' weight returns to baseline.

Hemofiltration (HF) during CPB in this observational study was not used. We use it for complex procedures requiring prolonged CPB. Many advantages of the hemofiltration during CPB have been mentioned in the literature. Ultrafiltration is effective in reducing the inflammatory response and fluid overload induced by CPB in paediatric patients [17-19]. In adults, Bellomo *et al.* [1] found that post-operative anemia, thrombocytopenia and hypoalbunemia were significantly decreased by the removal of approximately 3.4 litres of fluid with hemofiltration during CPB. One of the possible benefits of such hemoconcentration is improved post-operative haemostasis [20-23]. Preservation of colloidal osmotic pressure may reduce the excessive accumulation of extra-vascular water. In their patients, large pleural effusions were significantly less common when hemofiltration had been used during CPB. Hemofiltration during CPB has also been shown to remove inflammatory mediators [10]. Therefore, hemofiltration may protect against transcapillary loss of albumin hence reducing the accumulation of body water during CPB. Post-operatively, in the intensive care unit, early use of continuous venovenous hemofiltration (CVVHF) has shown similar advantages [1].

In spite of demonstrating an association between fluid overload and post-operative complications, this study is probably underestimating the problem since the patients underwent only non-complex and short procedures. Furthermore, patients with pre-operative renal dysfunction or congestive heart failure were excluded. Based on these results, while performing open heart surgery, our goal should be to administer a minimal amount of fluids to maintain adequate cardiac output. As a future research project we should aim to look at the same fluid overload and complications on patients undergoing CABG surgery with the use of the "mini-pump" or "OFF pump".

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