

# Upper gastrointestinal bleeding after open heart surgery

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## Abstract

**Objective:** The occurrence of digestive complications especially upper gastrointestinal bleeding (UGIB) has increased after cardiac surgery. The aim of this study was to determine the incidence of UGIB and identify the independent risk factors. **Materials and Methods:** We retrospectively analyzed data of 1077 patients undergoing cardiopulmonary bypass (CPB) from 1994 to 2012. The group of patients with UGIB ( $n_1 = 20$ ) was compared with the population group ( $n_2 = 1057$ ). Demographic characteristics, therapeutic management, endoscopic findings, and outcomes were analyzed. Through a regression analysis we identified independent risk factors of UGIB. **Results:** The mean age of the group  $n_1$  was  $58.2 \pm 12.4$  years and  $50.18 \pm 13.5$  years in the group  $n_2$ . UGIB occurred about  $13 \pm 5.5$  days after cardiac surgery. Gastroduodenal ulcer was the most common etiology of hemorrhage ( $n = 13$ , 65%). Renal insufficiency, previous gastric ulcer, increased lactate concentration during CPB, prolonged mechanical ventilation, use of vasopressor drug and pulmonary infection was likely contributing factors in UGIB. **Conclusion:** UGIB following open cardiac surgery is most frequently secondary to gastroduodenal ulceration. Many determinant factors of bleeding are incriminated. Surgeons must be aware of these factors to avoid fatal complications.

## Key words

Gastrointestinal bleeding, open cardiac surgery, postoperative complications, stress ulceration

## Introduction

Cardiac surgery using cardiopulmonary bypass (CPB) is a common major surgical procedure that imposes considerable physiological multi-organ stress despite the recent technological advances.<sup>[1]</sup> Peptic ulcer disease (PUD) and bleeding from the upper gastrointestinal (GI) tract is a rare serious postoperative complication (0.35–0.9%) with significant morbidity.<sup>[2-4]</sup> Blood transfusion, endoscopic or surgical treatment are always required, with an increased hospital costs.<sup>[5]</sup> Many factors were identified as predictive of GI bleeding (GIB). It is, therefore,

important to prevent these factors and this complication since fatal complications are noted in 35%.<sup>[6]</sup>

## Materials and Methods

The 1077 patients who underwent open heart surgery were retrospectively evaluated for GIB. All patients presenting with GIB within 30 days following cardiac surgery were included. GIB was defined as hematemesis, melena, nasogastric tube aspiration of blood material, hematochezia on rectal examination, or the combination of guaiac positive stools on occult blood testing and significant decline in the hemoglobin level ( $<10$  g/l) with transfusion of  $>2$  units of blood.<sup>[7]</sup> Were excluded: patients whose GIB was due to bleeding endoscopic varices, patients with lower intestinal bleeding. All patients underwent either coronary artery bypass grafting (CABG), valve surgery combined valve surgery and CABG, thoracic aortic surgery or surgical correction of adult congenital heart defects. Extracorporeal circulation was conducted between ascending aorta and

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right atrial or bicaval cannulation using a roller pump, and membranous oxygenation. Blood temperature was maintained between 32°C and 34°C range. Before the year 2000 myocardial protection was performed with cold crystalloid intermittent antegrade cardioplegia and antegrade blood cardioplegia since 2000 was daily used. Routine protocol of the cardiovascular surgery department was applied to all patients. Acetyl salicylic acid was not stopped before surgery. All patients received a 40 mg dose of diazepam, and 100 mg of hydroxyzine was administered per os the night before the surgery. Before 2000, patients were received histamine 2 receptor blockers from the first operative day for 1 month. After 2000, all patients received proton pump inhibitors (PPIs) intravenously for 2 days, followed by 20 mg per os for 1 month. Preoperative gastroscopy for patients with a history of gastroduodenal ulcer (GDU) or gastritis was systematic. If the previous ulcer is healed and there are no others lesions, the patient underwent cardiac surgery. Unlike, the therapy is based on the inhibition of gastric acid by PPIs and eradication of *Helicobacter pylori* infection, followed a month after by endoscopic control.

Management of GIB has changed in our institution. Since 2000, endoscopic therapy is generally recommended as the first-line treatment. Medical therapy included after stopping anticoagulation, red blood transfusion and intravenous PPIs until the bleeding control. The demographic, operative and postoperative findings of the patients were recorded.

Statistical analysis was performed with SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean  $\pm$  standard deviation, or median and categorical variable as proportions. Logistic regression with step-wise back and elimination was performed to identify possible predictor factors with the upper GIB (UGIB).

## Results

A total of 1077 adult patients who underwent CPB were included in this study. GIB occurred in 1.83% (20/1077).

### Patient characteristics

Patients with and without GIB were similar when compared for age, smoking, vascular disease, left ventricular function, Canadian Cardiovascular Society angina class, functional class New York Heart Association (NYHA) III-IV [Table 1]. We found significant differences between the groups in male-female ratio, renal dysfunction, peripheral arterial disease, and prior cardiac surgery. GIB was more common in the patients who had a history of PUD and/or gastritis (4% vs. 20%,  $P < 0.0001$ ). On the other hand, no significant differences were observed between the groups in terms of operative parameters (emergency surgery, CPB time, aortic cross-clamp time, and type of surgery). However regarding postoperative parameters, mechanical ventilation and ICU stay were longer

**Table 1: Clinical characteristic of cases and controls**

| Variable   | Controls<br>(n=1057) (%) | Cases<br>(n=20) (%) | P     |
|--|--------------------------|---------------------|-------|
| Age (years)                                      | 50.18 $\pm$ 13.5         | 58.2 $\pm$ 12.4     | 0.42  |
| Sex: Male/female                                 | 718/355                  | 18/2                | 0.027 |
| BMI (kg/m <sup>2</sup> )                         | 24.8 $\pm$ 5.4           | 25.3 $\pm$ 2.9      | 0.3   |
| Smoking  | 455 (41.9)               | 12 (60)             | 0.1   |
| Diabetes mellitus                                | 261 (24.6)               | 7 (35)              | 0.28  |
| Hypertension                                     | 235 (22.1)               | 8 (40)              | 0.09  |
| Chronic obstructive pulmonary                    | 102 (9.6)                | 1 (5)               | 0.48  |
| Renal insufficiency                              | 84 (7.9)                 | 5 (25)              | 0.006 |
| Cerebro-vascular disease                         | 37 (3.5)                 | 0                   | 0.39  |
| Peripheral vascular disease                      | 124 (11.7)               | 4 (20)              | 0.047 |
| History of peptic ulcer disease and/or gastritis | 42 (4)                   | 4 (20)              | 0.000 |
| CCS angine Class III-IV                          | 155 (15.2)               | 10 (50)             | 0.23  |
| Functional class NYHA II-IV                      | 447 (42.7)               | 6 (30)              | 0.3   |
| EF (%)   | 53.3 $\pm$ 14            | 57.2 $\pm$ 12       | 0.39  |
| Pulmonary arterial hypertension mmHg             | 48.9 $\pm$ 20            | 53.8 $\pm$ 26.7     | 0.45  |
| Prior cardiac surgery                            | 192 (18.6)               | 0                   | 0.033 |
| Atrial fibrillation                              | 273 (25)                 | 3 (15)              | 0.53  |
| Mean Euroscore                                   | 3.97 $\pm$ 3.2           | 3.8 $\pm$ 3.9       | 0.1   |

BMI=Body mass index, CCS=Canadian cardiovascular society, NYHA=New York heart association, EF=Ejection fraction

in the GIB group. No significant differences were found between the groups when we compare low cardiac output, use of intra-aortic balloon pump (IABP), and postoperative myocardial infarction. Patients developing renal insufficiency with/without requiring hemodialysis were significantly more likely to experience GI hemorrhage ( $P < 0.0001$ ). Similarly, patients requiring pharmacological support with vasopressor drug and those who developed pulmonary infection were also more likely to experience a GIB. Acute cerebral stroke, multi-organ failure (MOF), and need for chest reexploration were frequent in GIB group. Mean lactate concentration during CPB was higher in GIB group ( $P < 0.0001$ ). Hospital mortality increased more in patients with UGIB (7.3% vs. 25%,  $P = 0.0013$ ). To identify associated factors to UGIB after CPB, logistic regression with step-wise back and elimination was performed [Table 2]. We found seven possible predictor factors of UGIB: Renal insufficiency, previous GDU, increased lactate concentration per CPB, need of vasopressor drug, prolonged mechanical ventilation, pulmonary infection, and MOF. The mean interval between cardiac surgery and onset of GI hemorrhage was  $13 \pm 5.5$  days (range 4–25 days). Symptoms were hematemesis ( $n = 4$ ), melena ( $n = 9$ ), hematemesis-melena ( $n = 7$ ). Five patients had recurrent bleeding [Table 3]. Eighteen patients underwent endoscopic examination. Two patients did not undergo endoscopy because they were hemodynamically unstable. The following endoscopic diagnoses were confirmed: duodenal ulcer ( $n = 6$ ), gastric ulcer ( $n = 4$ ), gastric + duodenal ulcer ( $n = 3$ ), ulcerohemorrhagic oesophagitis ( $n = 2$ ) and erosive gastritis ( $n = 3$ ). Bleeding control required surgery in 2 cases, therapeutic endoscopy in 6 patients and medical therapy in 12 patients.

**Table 2: Perioperative and postoperative data**

| Variable                            | Controls<br>(n=1057)<br>(%) | Cases<br>(n=20)<br>(%) | P     |
|-------------------------------------|-----------------------------|------------------------|-------|
| <b>Operative data</b>               |                             |                        |       |
| Emergency surgery                   | 70 (6.6)                    | 1 (5)                  | 0.77  |
| CPB time (min)                      | 104.8±44                    | 101.2±28.2             | 0.08  |
| Aortic cross clamp time (min)       | 67.6±32.8                   | 59±19.1                | 0.06  |
| Operative time (min)                | 216.5±63.7                  | 226.7±73.1             | 0.5   |
| Mechanical ventilation time (h)     | 9 (6-18)                    | 17 (9-28)              | 0.023 |
| Mechanical ventilation up to 48 h   | 86 (8.3)                    | 7 (35)                 | 0.008 |
| ICU length of stay (h)              | 48 (24-64)                  | 72 (41-174)            | 0.008 |
| Hospital stay (days)                | 13.7±14                     | 19.4±10.4              | 0.008 |
| <b>Postoperative complications</b>  |                             |                        |       |
| Low cardiac output                  | 148 (14.1)                  | (5.25)                 | 0.18  |
| <b>Need for vasopressor drug</b>    |                             |                        |       |
| Inotropics >0.02 µg/kg epinephrine  | 204 (19.4)                  | 8 (40)                 | 0.022 |
| IABP                                | 83 (7.9)                    | 2 (10)                 | 0.98  |
| Chest reexploration for bleeding    | 51 (4.9)                    | 3 (15)                 | 0.041 |
| Pulmonary infection                 | 89 (8.5)                    | 6 (30)                 | 0.001 |
| Acute renal failure                 | 99 (9.5)                    | 6 (30)                 | 0.002 |
| Need for dialysis                   | 23 (2.2)                    | 3 (15)                 | 0.000 |
| Acute cerebrovascular accident      | 17 (1.7)                    | 2 (10)                 | 0.006 |
| Transfusion                         | 424 (41.2)                  | 18 (90)                | 0.000 |
| In-hospital mortality               | 77 (7.3)                    | 5 (25)                 | 0.013 |
| Arythmia                            | 63 (6)                      | 3 (15)                 | 0.098 |
| Postoperative myocardial infarction | 23 (2.2)                    | 1 (5)                  | 0.73  |
| Lactate                             | 2.3±1.3                     | 5.5±6.3                | 0.000 |
| MOF                                 | 52 (5.1)                    | 5 (25)                 | 0.000 |

MOF=Multi-organ failure, ICU=Intensive care unit, IABP=Intra-aortic balloon pump, CPB=Cardiopulmonary bypass

## Discussion

The large use of cardiac surgery has increased the occurrence of digestive complications, especially upper digestive tract bleeding. In this retrospective study, UGIB following open heart surgery showed an overall incidence of 1.85% and was associated with a high mortality of 25% in comparison with literature.<sup>[8,9]</sup> Bleed from upper GI tract was the most common noted complication.<sup>[5,10-13]</sup> van der Voort and Zandstra<sup>[2]</sup> reviewed the available publishing literature before 2000, concerning the incidence of upper GIB and found it occurring in 0.45–2%. The same result was reported by Aljarallah *et al.*<sup>[14]</sup> In numerous published papers, we noted UGIB rate did not decline through the years despite constant improvements in medical management. In general, upper GIB occurs more frequently than lower intestinal bleeding. The site of the bleed is proximal to the ligament of Treitz in more than 90%.<sup>[15]</sup> The two most common etiologies of upper GIB are GI ulceration and gastric erosion.<sup>[3,8,16-18]</sup> In our study, GI ulceration was responsible for bleeding in 13 cases (65%), and erosive gastritis in 3 cases (15%). Our results confirmed the literature data and GIB occurred around 10 days after surgery.<sup>[8,9,16,18,19]</sup>

Delayed diagnosis is frequent because of undiagnosed symptoms particularly in sedated patients. In the absence of hematemesis, a particular attention should be accorded to the

nasogastric tube contents. Gastric endoscopy is the next step in evaluation and treatment of potential digestive bleeding.<sup>[20]</sup> The pathogenesis of mucosal damage and subsequent bleeding is complex and multifactorial including psychological and physiological stress and postoperative complications.<sup>[16]</sup> Upper GI hemorrhage due to stress ulceration is the most commonly identified mechanism.<sup>[21]</sup> According to Bhat *et al.*<sup>[8]</sup> and Amarin *et al.*,<sup>[9]</sup> 85.5% of patients had ulcers on endoscopy. Stress ulceration has been attributed to ischemia and/or reperfusion injury of the splanchnic territory and endotoxemia leading to gastroduodenal mucosa damage.<sup>[21,22]</sup> Rey *et al.*<sup>[23]</sup> have observed some special characteristics in case of bleeding ulceration: first, digestive bleeding is frequent in patients who underwent cardiac surgery for coronary artery bypass grafting than in the case of heart valve replacement. Second, in the case of earlier hemorrhage after surgery (1 after 5 days), endoscopic examination showed multiple superficial gastric and duodenal ulcerations. In Yoshida *et al.* study,<sup>[18]</sup> the onset of UGIB was 13.1 ± 9.3 days and no cases of single peptic ulcer were observed. In our study, gastroscopy found gastric and duodenal ulcer in 13 cases (65%). Third, a second bleeding period occurred during the 3<sup>rd</sup> week following surgery, and they have usually observed in endoscopy a large duodenal bleeding ulcer. There are controversial opinions about the role of preexisting PUD as a cause of postoperative hemorrhage. In some reports, patients with a history of PUD were more exposed to have UGIB.<sup>[24,25]</sup> In other reports, there is no significant evidence that a previous history of PUD would be correlated with increased risk for gastric hemorrhage.<sup>[26]</sup> In a study published by Geissler *et al.*,<sup>[27]</sup> among 41 patients with UGIB, only 2 cases had a history of gastritis or peptic ulcer. In our study, four patients (20%) had a history of GDU disease, and in logistic regression analysis, it predicted UGIB (odds ratio: 6, confidence interval 95%, 1.9–18.8;  $P=0.002$ ) [Table 4]. CPB is known to cause increased systemic inflammation and therefore many have suggested that performing coronary bypass grafting off-pump could substantially minimize the risk of digestive complications. According to the Raja *et al.*<sup>[28]</sup> finding, CPB is the main independent predictor of postoperative GI complications; the risk being seven times higher in the on-pump compared with the off-pump group (Raja *et al.*). In recent prospective randomized study, Croome *et al.* did not find any statistically significant difference in the total number of GI complications between the off-pump and on-pump groups.<sup>[29]</sup> Several studies have examined pharmacological stress prophylaxis in patients undergoing cardiac surgery. The benefit of histamine 2 receptor antagonists (H2RA) to protect the stomach is still discussed. Many investigators demonstrated that H2RA were effective in decreasing surgical stress response and preventing clinical GIB.<sup>[30-32]</sup> In a recent meta-analysis, prophylactic PPIs could reduce hemorrhagic gastritis and hematemesis but was associated with an increased risk of nosocomial pneumonia.<sup>[33]</sup> Therefore, PPI are considered mandatory to prevent the upper GIB after open heart procedure<sup>[30]</sup> particularly in patients with an increased risk of GIB after cardiac surgery. According to the literature, intra-operative factors, such as CPB time and

**Table 3: Diagnosis and treatment in patients developing UGIB**

| Variable                   | Patients (n=20) |
|----------------------------|-----------------|
| Symptoms                   |                 |
| Hematemesis                | 04              |
| Maelena                    | 09              |
| Hematemesis and maelena    | 07              |
| Recurrent GIB              | 05              |
| Endoscopic fundings        |                 |
| Duodenal ulcer             | 06              |
| Gastric ulcer              | 04              |
| Gastric and duodenal ulcer | 03              |
| Erosive gastritis          | 03              |
| Erosive esophagitis        | 02              |
| Unknown                    | 02              |
| Treatment                  |                 |
| Medical therapy            | 12              |
| Endoscopic therapy         | 06              |
| Surgery                    | 02              |
| Onset of UGIB (days)       | 13±5.5          |

UGIB=Upper gastrointestinal bleeding, GIB=Gastrointestinal bleeding

**Table 4: Multivariate predictors of UGIB after cardiac surgery**

| Variable                           | OR  | 95%, CI   | P     |
|------------------------------------|-----|-----------|-------|
| Renal insufficiency                | 3.8 | 1.3, 10.8 | 0.011 |
| Previous gastroduodenal ulcer      | 6   | 1.9, 18.8 | 0.002 |
| Mean lactate concentration per CPB | 1.4 | 1.1, 1.9  | 0.002 |
| Use of vasopressor drug            | 2.7 | 1.1, 6.8  | 0.028 |
| Prolonged mechanical ventilation   | 5.9 | 2.3, 15.3 | 0.000 |
| Pulmonary infection                | 4.6 | 1.7, 12.3 | 0.002 |
| Postoperative renal insufficiency  | 4.1 | 1.5, 10.9 | 0.005 |
| Need for hemodialysis              | 7.8 | 2.1, 28.6 | 0.002 |
| MOF                                | 6.2 | 2.1, 17.8 | 0.001 |

UGIB=Upper gastrointestinal bleeding, CI=Confidence interval, OR=Odds ratio, CPB=Cardiopulmonary bypass, MOF=Multi-organ failure

some postoperative events, such as low output syndrome, necessity of surgery, use of IABP and the development of acute renal failure are good indicators of low output. The relationship between prolonged mechanical ventilation with high positive end-expiratory pressure has been documented in various studies.<sup>[34,35]</sup> In our study, we concluded a higher incidence of UGIB in patients with renal insufficiency, prolonged mechanical ventilation, pulmonary infection and MOF. Previous PUD, increased lactate per CPB or hemodynamic instability requiring vasopressor may also be a determinant for potential upper gastric haemorrhage. On the other hand, some risk factors of UGIB, such as advanced age, NYHA functional Class IV, smoking, diabetes mellitus, left ventricular dysfunction, emergent surgery, blood transfusion are incriminated.<sup>[10,34,36,37]</sup> The first case of UGIB reported in the literature required subtotal or total gastrectomy with a high mortality rate ranging from 20% to 40%.<sup>[16,38]</sup> Nowadays initial treatment consists on rapid correction of coagulation disorders, red blood transfusion followed by endoscopy. Endoscopic treatment achieves control in 98% of patients and many authors consider it a treatment of choice in high risk patients.<sup>[16,39,40]</sup> In our study, endoscopic procedures were successfully practiced by experienced interventional

endoscopists. Surgery was performed only in 2 cases, 1 in 1994 and other 1 in because of recurrent massive GIB.

## Conclusion

Upper GIB is the most clinical problem after open cardiac surgery. Many risk factors were identified. This condition should increase the awareness of physicians to identify susceptible patients, to contribute to early diagnosis, and to prevent fatal consequences.

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