Gastrointestinal complications after cardiopulmonary bypass: Sixteen years of experience

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BACKGROUND: Gastrointestinal (GI) complications are one of the serious complications of cardiac surgery. Although rarely seen, they cause major morbidity and mortality. The aim of the present study was to retrospectively analyze the risk factors acting on the GI complications seen after cardiac operations performed under cardiopulmonary bypass.

METHOD: The present study was designed to retrospectively evaluate 13,544 patients who underwent cardiac surgery under cardiopulmonary bypass, between 1988 and 2004 in the authors' clinic.

RESULTS: The overall mortality was 346 (2.55%) of 13,544 patients. GI complications developed in 128 patients (0.94%). Among those, 18 (14.1%) died because of GI complications, the most common of which was bleeding. Mesenteric ischemia had the highest case-fatality rate at 71.4%. Valve surgery, concomitant valve and coronary artery bypass grafting surgery, preoperative chronic renal dysfunction, postoperative acute renal failure, deep sternal infection, prolonged ventilation, need for intra-aortic balloon pump and ejection fraction less than 30% were found to be risk factors acting on GI complications.

CONCLUSION: GI complications remain a significant concern after cardiac surgery under cardiopulmonary bypass. Higher-risk patients can be identified and treated prophylactically and in the postoperative period.

Key Words: CABG; Cardiopulmonary bypass; GI complications

Gastrointestinal (GI) complications are one of the serious Complications of open-heart surgery. Although rarely seen (0.3% to 2.0%), they cause major morbidity and mortality (1-3). Several retrospective studies (4-7) have reported various GI complications after coronary artery bypass grafting (CABG), including GI bleeding, mesenteric ischemia, pancreatitis, cholecystitis, perforated ulcers and ileus. Indeed, cardiac surgery itself is a risk factor for GI complications. The combined stress of anesthesia, surgery, anticoagulation, hypothermia and cardiopulmonary bypass (CPB) causes a hormonal stress response and a defense reaction, which, as a whole, can lead to organ damage (8). The GI system, like all other organ systems, is exposed to vasoactive substances and microembolism during CPB, but usually few clinical manifestations occur. Most of the GI complications after CPB have been attributed to low

Les complications gastro-intestinales après une circulation extracorporelle : Seize ans d'expérience

HISTORIQUE : Les complications gastro-intestinales (GI) font partie des graves complications des chirurgies cardiaques. Bien qu'elles soient rares, elles provoquent un taux élevé de morbidité et de mortalité. La présente étude vise à analyser rétrospectivement les facteurs de risque agissant sur les complications GI observées après une opération cardiaque avec circulation extracorporelle.

MÉTHODOLOGIE : La présente étude a été conçue pour évaluer rétrospectivement 13 544 patients qui ont subi une chirurgie cardiaque avec circulation extracorporelle entre 1988 et 2004 dans la clinique de l'auteur. **RÉSULTATS :** Au total, 346 (2,55 %) des 13 544 patients sont décédés. Des complications GI se sont manifestées chez 128 patients (0,94 %). De ce nombre, 18 (14,1 %) sont morts par suite de complications GI, la plus courante étant une hémorragie. L'ischémie mésentérique était reliée au taux de létalité le plus élevé, à 71,4 %. On a établi que la chirurgie valvulaire, le pontage aortocoronarien et valvulaire concomitant, une dysfonction rénale chronique préopératoire, une insuffisance rénale aiguë postopératoire, une infection sternale profonde, une ventilation prolongée, le besoin de ballonnet intra-aortique et une fraction d'éjection inférieure à 30 % étaient des facteurs de risque agissant sur les complications GI.

CONCLUSIONS : Les complications GI demeurent une préoccupation considérable après une chirurgie cardiaque avec circulation extracorporelle. Les patients les plus vulnérables peuvent être repérés et traités par prophylaxie ainsi que pendant la période postopératoire.

cardiac output and visceral hypoperfusion resulting in mucosal ischemia and necrosis. Stress ulceration, mucosal atrophy and loss of barrier function with increased permeability may lead to bacterial translocation, sepsis and multiorgan failure (9). The aim of the present study was to retrospectively analyze the risk factors acting on the GI complications seen after cardiac operations performed under CPB.

PATIENTS AND METHODS

The present study was designed to evaluate, retrospectively, 13,544 patients who underwent cardiac surgery under CPB in the authors' clinic between 1988 and 2004. Among these, 8268 had CABG surgery, 2147 had valvular operation, 469 had combined CABG and valvular operation, 718 had aortic operation and 1942 (214 cyanotic) had adult congenital defect repair. GI complications

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were seen in 128 patients. The computer database system in the clinic was used for data collection. The demographic, operative and postoperative findings of the patients were recorded.

GI bleed prophylaxis

The authors routinely administer prophylactic preoperative H_2 receptor blockers to patients with a history of ulcer or GI bleeding. Between 1988 and 1995, patients were medicated with H_2 receptor blockers from the first postoperative day for up to two months. After 1995, all patients received proton pump inhibitors (intravenously) for two days followed by H_2 receptor blockers (orally) for one month. The patients routinely started oral feeding 6 h after extubation. Patients with normal hemodynamic parameters are discharged from the intensive care unit on the first postoperative day and from hospital on the seventh day.

Diagnosis of GI complications and definitions

Low cardiac output syndrome (LOS) was defined when the cardiac index was under 2.5 L/min, when there was hemodynamic instability, and the need for an inotropic agent or intra-aortic balloon pump (IABP) usage for more than 24 h.

Prolonged mechanical ventilation was defined as mechanical ventilatory support for more than 24 h for any reason.

GI complications were defined as GI bleeding, mesenteric ischemia, pancreatitis, cholecystitis, diverticulitis, hepatic dysfunction, perforated ulcers or ileus that developed in the first 30 days after operation. All patients with GI complication were referred to the general surgery and internal medicine departments at the Gulhane Military Academy of Medicine, Ankara, Turkey for consultation, diagnosis and treatment.

Hematemesis or melena which caused a 2 g or more decrease in hemoglobin was defined as GI bleeding. Pancreatitis was diagnosed by abdominal pain, nausea, vomiting and an elevated urinary or serum amylase level.

Acute renal failure (ARF) was defined as anuria which did not respond to volume replacement or diuretics, or increase of creatinine levels greater than 177 µmol/L. Chronic renal failure (CRF) was defined as preoperative serum creatinine level greater than 177 µmol/L. More than a 50% sustained increase in transaminase and bilirubin levels was defined as hepatic dysfunction.

Mesenteric ischemia was considered in patients with abdominal pain, nausea, vomiting, metabolic acidosis and/or leukocytosis, with the diagnosis being made at laparotomy.

Diverticulitis was diagnosed with colonoscopy in patients with lower abdominal pain, fever and leukocytosis. Ulcer perforation was diagnosed with upper GI endoscopy in patients with epigastric pain and positive radiological findings.

Medication, technique of anesthesia and cardioplegia

Routine CABG protocol of the cardiovascular surgery clinic was applied to all patients.

Acetylsalicylic acid was stopped seven days before the scheduled date of operation but antianginal drugs were continued until the operation time. A 10 mg dose of diazepam was administered orally the night before the surgery and 5 mg of morphine sulfate was administered intramuscularly 1 h before surgery, to all patients. Cefazolin sodium was used as a prophylactic antibiotic, 1 g intravenously four times daily for 48 h.

A peripheral venous line, central jugular vein catheters and urethral catheters were inserted. Body temperature was monitored with rectal and esophageal probes. Heparin (400 U/kg) was administered before the institution of CPB. Activated clotting time was maintained over 400 U during CPB. At the end of the CPB, the heparin effect was reversed with protamin sulphate in a 1:1 ratio.

Aortic and two-stage venous cannula were used to institute the CPB using a roller pump, membrane oxygenation and identical priming solution.

The content of the prime solution was 1000 mL Ringer's lactate, 150 mL mannitol, 60 mL bicarbonate and 1 mg/kg heparin. Systemic blood flow was maintained at 2.2 L/m²/min and mean arterial blood pressure at 60 mmHg to 70 mmHg during CPB. Systemic hypothermia (28°C) and hemodilution were applied. For myocardial protection antegrade, 4°C blood cardioplegia (1000 mL blood, 70 mL citrate, 750 mg magnesium sulphate, 3 mEq potassium/100 mL blood and 10 mEq sodium bicarbonate) was given, 10 mL/kg at the beginning of the arrest and then repeated every 20 min. Topical cooling was maintained with cold saline solution.

Postoperatively, pharmacological support was instituted according to hemodynamic requirements. Inotropic support, when necessary, was maintained with adrenaline, dopamine and dobutamine infusion. IABP was inserted in case of LOS.

Statistical analysis

Statistical analysis was performed with SPSS software version 10.0 (SPSS Inc, USA). Clinical data were expressed as mean \pm SD and per cents. Comparisons were made with Wilcoxon signed ranks tests and χ^2 tests, as appropriate. Multivariate analyses using logistical regression were conducted. Forward stepwise selection was used to identify significant risk factors. The effects of the variables were investigated by calculating the odds ratios (ORs) in analyses for all patients. Differences were considered significant at P<0.05.

RESULTS

The overall mortality was 346 (2.55%) among 13,544 patients. GI complications were seen in 128 patients (128 of 13,544; 0.94%). Among these 128 patients, 18 (14.1%) died because of the GI complication. The mortality rate in the rest was 2.4% (328 of 13,416). Table 1 shows the demographic data of patients compared with those who had GI complications.

Mean age, history of peptic ulcers, gastritis and/or GI bleeding, previous gastric surgery, CRF, peripheral vascular disease, three-vessel disease, ejection fraction (EF) less than 30% and emergent cases were found to be factors significantly different in the two groups.

The operative and postoperative findings of the patients are compared in Table 2. Mean duration of cross clamp (CC) and CPB was significantly prolonged in patients who had GI complications. The need for IABP was another factor found to be significantly higher in the same group.

LOS, IABP usage, second look for postoperative bleeding, deep sternal infection, prolonged mechanical ventilation, acute cerebrovascular accident, ARF, valve surgery, concomitant valve and CABG surgery, prolonged hospital stay and mortality were significantly different findings between groups.

Multivariate analysis revealed valve surgery, concomitant valve and CABG surgery, preoperative CRF, postoperative ARF, deep sternal infection, prolonged mechanical ventilation, need for IABP and EF less than 30% as significant risk factors for development of GI complications (Table 3).

Among the 128 patients, the most common GI complication was GI bleeding (n=59; 46.1%; upper GI bleeding 27.4% and lower GI bleeding 18.7%) (Tables 4 and 5). Endoscopy

TABLE 1 Preoperative demographic patient data

		Without GI complications	
	n (%)	n (%)	P
Patients (n)	128 (0.94)	13,416 (99.06)	
Age, years (mean ± SD)	67.2±10.3	63.4±11.1	<0.0001
Sex (male/female)	94/34	9856/3560	
Body mass area (m^2) (mean ± SD) 1.77±1.2	1.79.7±0.8	
Smoking	85/43	8956/4460	
Alcohol abuse	6 (4.6)	645 (4.8)	
Peptic ulcer and/or gastritis	18 (14)	896 (6.6)	<0.0001
Prior GI bleeding	9 (7)	178 (1.3)	<0.0001
Previous gastric surgery	5 (3.9)	21 (0.15)	<0.0001
Diabetes	22 (17.1)	2123 (15.8)	
Hypertension	20 (15.6)	1978 (14.7)	
Hypercholesterolemia	18 (14)	1895 (14.1)	
Anticoagulant/antiplatelet usage	5 (3.9)	456 (3.3)	
COPD	9 (7)	918 (6.8)	
CRF	11 (8.5)	256 (1.9)	<0.0001
PAD	14 (10.9)	768 (5.8)	<0.05
CVA	3 (2.3)	326 (2.4)	
Three-vessel disease	92 (71.8)	8465 (63)	<0.0001
Left main disease	4 (3.1)	403 (3)	
Ejection fraction <30%	13 (10.1)	871 (6.4)	<0.0001
Prior cardiac surgery	3 (2.3)	298 (2.2)	
Emergent procedure	8 (6.2)	524 (3.9)	<0.005

COPD Chronic obstructive pulmonary disease; CRF Chronic renal failure; CVA Cerebrovascular accident; GI Gastrointestinal; PAD Peripheral artery disease

was performed in all patients with GI bleeding. Endoscopic coagulation was successfully performed in eight patients (two with esophageal varices, three with gastritis, two with stress erosions and one with duodenal ulcers). In one patient, GI bleeding due to esophageal varices was controlled with surgical treatment. In the other 27 patients, bleeding was controlled with medical treatment. All of the patients with ulcer perforation underwent surgical treatment. Four of these died postoperatively (two due to respiratory insufficiency and two due to sepsis).

Despite early diagnosis and resection, 10 of the 14 patients (71.4%) with mesenteric ischemia died in the postoperative period (Table 4). Four of these had atrial fibrillation and were not taking any anticoagulant medication. These patients underwent embolectomy of the mesenteric artery, intestinal resection and end-to-end anatomosis. Two of these patients were lost because of ARF and sepsis. In three patients, the whole mesenteric system was found to be necrotic and the patients died perioperatively. Five of the patients who underwent a Hartmann operation died because of respiratory complications, LOS and sepsis.

Medication, including antibiotics, and parenteral feeding were administered in patients with pancreatitis, diverticulitis, cholecystitis and hepatic dysfunction. One patient with pancreatitis and one with diverticulitis died because of ARF and respiratory complications on the seventh and ninth days, respectively. Among the 16 patients with mixed complications, two patients (both older than 75 years of age) died because of respiratory complications (Table 4).

TABLE 2 Operative and postoperative patient data

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	With GI Without GI complications		
	n (%)	n (%)	Р
Perioperative			
CC, min (mean ± SD)	68.9±56.7	61.4±41.2	<0.005
CPB, min (mean ± SD)	103.2±46.5	87.2±41.9	<0.005
Need for inotropic agents	28 (21.8)	1679 (12.5)	<0.0001
Postoperative			
Low cardiac output	31 (24.2)	1432 (10.6)	<0.0001
IABP	29 (22.6)	392 (2.9)	<0.0001
Reexploration of chest	13 (10.1)	196 (1.4)	<0.0001
Deep sternal infection	11 (8.5)	114 (0.8)	<0.0001
Prolonged ventilation (>24 h)	14 (10.9)	145 (1.1)	<0.0001
Postoperative anticoagulant usa	ge 6 (4.6)	598 (4.4)	
Acute cerebrovascular accident	7 (5.4)	148 (1.1)	<0.05
ICU stay, days (mean ± SD)	3.3±2.2	1.9±1.1	
Hospital stay, days (mean ± SD)	16.1±8.6	7.1±2.6	<0.0001
ARF	17 (13.2)	225 (1.6)	<0.0001
Valve surgery	34 (26.5)	2113 (15.7)	<0.005
Concomitant valve and CABG	21 (16.4)	448 (3.3)	<0.005
Mortality	18 (14.06)	328 (2.4)	<0.0001

ARF Acute renal failure; CABG Coronary artery bypass grafting; CC Cross clamp duration; CPB Cardiopulmonary bypass duration; GI Gastrointestinal; IABP Intra-aortic balloon pump usage; ICU Intensive care unit

TABLE 3Multivariate risk factor analysis of 13,544 patients

	OR	95% CI	Р
Valve surgery	2.94	1.32–7.91	0.006
Valve + CABG	3.41	2.45-8.23	<0.05
Preoperative CRF	2.57	1.52-6.12	<0.0001
Postoperative ARF	3.65	2.48-7.19	<0.0001
Deep sternal infection	4.03	2.05-9.92	<0.05
Prolonged ventilation	5.11	3.61-8.43	<0.0001
IABP	2.34	1.76-7.54	0.008
EF <30%	3.61	1.92–5.32	<0.0001

ARF Acute renal failure; CABG Coronary artery bypass grafting; CRF Chronic renal failure; EF Ejection fraction; IABP Intra-aortic balloon pump usage

DISCUSSION

Patients with GI complications after CABG run a high risk of morbidity and mortality (11% to 59%) (10-13). In our series, the incidence was 0.94% and mortality was 14.06%. Unfortunately, GI complications are difficult to identify early in their course. The ability to predict which patients are at greater risk of developing these complications is clinically significant because it allows the surgeon to identify and treat these complications earlier, rendering the interventions more successful (1). In the present study, as with previous studies, the most commonly observed GI complications were GI bleeding and intestinal ischemia (6,10-12). In our series, mesenteric ischemia was the second most commonly seen GI complication but the most serious one, with a mortality of 71.4%. It appears that the cause of GI complications in patients after CABG is ischemia. The CPB machine perfuses the organ systems in a low pressure, nonpulsatile manner. Also,

TABLE 4 The profile of the patients with gastrointestinal (GI) complications

	n	CABG	Valve	Valve + CABG	Aortic surgery	Conge- nital	Case- fatality n (%)
Total patients	13,544	8268	2147	469	718	1942	346 (2.55)
GI complication	128	61	34	21	9	3	18 (14.0)
Upper GI bleed	20	14	1	1	2	2	0
Lower GI bleed	16	11	1	1	2	1	0
Mixed complications	16	10	2	2	2	-	2 (12.5)
Perforated ulcer	15	3	7	5	-	-	4 (26.6)
Mesenteric ischemia	14	3	7	4	-	-	10 (71.4)
Cholecystitis	13	9	2	1	1	-	0
Hepatic dysfunction	11	4	4	2	1	-	0
Pancreatitis	10	4	3	2	1	-	1 (10.0)
lleus	9	2	5	2	-	-	0
Diverticulitis	4	1	2	1	-	-	1 (25.0)

CABG Coronary artery bypass grafting

CPB exposes the blood to abnormal surfaces, causing the release of particulate matter and liberating biologically active substances. These factors combine and clinical disease occurs when the body is no longer able to compensate (6). In another study (5), the major contributing factor for GI complications after cardiac surgery was demonstrated as a low flow state with subsequent hypoperfusion of end organs. Perioperative hypotension, hypovolemia, prolonged CPB, use of vasoconstrictors, postoperative arrhythmias, hemorrhage and preexisting vascular disease play an important role in reducing mucosal injury and organ damage (2,5,14,15). Preoperative, perioperative and postoperative variables may all influence abdominal perfusion. Comorbid conditions, such as low left ventricular EF (3,8,13) and peripheral vascular disease (3), may all cause splanchnic hypoperfusion and have actually been identified as determinants of GI complications in patients undergoing cardiac surgery. Peripheral vascular disease and duration of CBP and CC have been found to be significant in univariate analysis. EF was found to be a significant factor in both univariate and multivariate analysis. During the operation, hypovolemia (8) prolonged CPB (3,13,16) and administration of vasoconstrictors can cause GI hypoperfusion.

CPB is associated with a broad range of systemic complications, including nonpulsatile flow, hemolysis, activation of the inflammatory cascade, anticoagulation, hypothermia and, finally, reduced end-organ perfusion. Furthermore, CPB can increase GI permeability and, as a consequence, enhance the release of cytokines that will lead to mucosal damage and microcirculation problems (17). Zacharias et al (3) and Perugini et al (13) both found a strong relationship between these two variables, with ORs ranging from 1.3 to 1.7. In contrast, Spotnitz et al (16) and Christenson et al (8) did not find any significant relationship on multivariate analysis. Our results revealed CBP and CC as significant risk factors for GI complications in univariate analysis but not in multivariate analysis.

Prolonged mechanical ventilation with high positive endexpiratory pressure (PEEP) can result in decreased cardiac output and hypotension; splanchnic blood flow in these settings decreases

TABLE 5 Source of upper and lower gastrointestinal (GI) bleeding

	n	CABG	Valve	Valve + CABG	Aortic surgery	Congenital
Upper GI bleed	35	12	9	9	4	1
Perforated ulcer	15	3	6	5	-	1
Gastritis	5	3	1	1	-	-
Esophagitis	2	1	-	-	1	-
Esophageal varices	2	-	-	1	1	-
Stress erosions	7	3	2	1	1	-
Duodenal ulcers	4	2	-	1	1	-
Lower GI bleed	24	7	5	6	5	1
Diverticulitis	2	1	-	1	-	-
Mesenteric ischemia	6	2	1	1	2	-
Vascular ectasia	10	3	2	2	2	1
Hemorrhoids	6	1	2	2	1	-

CABG Coronary artery bypass grafting

in parallel with PEEP-induced reductions in cardiac output (18) Furthermore, high PEEP is also associated with increased reninangiotensin-aldosterone activity and elevated catecholamine levels (19). Spotnitz et al (16) first reported the importance of prolonged mechanical ventilation as an independent determinant for GI complications after cardiac surgery, with an OR of 6.6 after nontruncated multivariate analysis. Prolonged mechanical ventilation was found to be a risk factor in our analysis (OR of 5.11).

Perioperative factors such as the use of IABP and the development of ARF are good indicators of a low output state and may, directly or indirectly, be related to GI complications after cardiac surgery. IABP is generally used in patients with ongoing cardiac ischemia or cardiac failure that is unresponsive to medical treatment. These patients are already predisposed to GI hypoperfusion secondary to decreased cardiac output; therefore, the critical need for IABP, rather than the IABP itself, predisposes to GI complications. On the other hand, IABP itself may encourage thrombus formation, embolization and platelet destruction and, thus, potentially contribute to the GI insult (20). Our statistical analysis revealed IABP and EF as risk factors for GI complications in univariate and multivariate analysis (Table 3). D'Ancona et al (20) found IABP and EF significant only in univariate analysis. ARF after cardiac operations is associated with high morbidity and mortality rates and results from generalized organ hypoperfusion during bypass and in the postoperative phases.

The relationship among CRF, ARF and GI complications after cardiac surgery has been emphasized in a limited number of univariate analysis studies (21). Our results revealed both ARF and CRF as risk factors (Table 3). Deep sternal infection was found to be a risk factor in both univariate and multivariate analysis. The complications developed in patients with deep sternal infection were mostly GI bleeding (eight of 11), hepatic dysfunction (two of 11) and pancreatitis (one of 11). This may be explained with the prolonged intensive care unit and hospital stay, infection with resistant microorganisms and medication with broad-spectrum antibiotics.

Among the different perioperative variables that may be related to abdominal complications, valve surgery has been frequently reported in previous univariate analyses (2). Patients after valve surgery may be at higher risk for GI bleeding because of anticoagulant therapy, and upper GI bleeding remains the most common abdominal complication after cardiac surgery with CPB (20). Multi- and univariate analysis of the present study revealed valve surgery and concomitant valve and CABG surgery to be significant risk factors (Table 3). In this regard, advanced age, female sex, preoperative IABP, emergent operation and blood transfusions have all been shown to be more frequent in patients who developed GI complications (3,5,13,16). Age, peptic ulcers and/or gastritis, previous GI bleeding, previous gastric surgery and emergent procedures were significant risk factors found in univariate analysis.

CONCLUSIONS

We evaluated the risk factors for GI complications after cardiac surgery under CPB. Our results showed that GI bleeding was the most common GI complication while mesenteric ischemia had the highest case-fatality rate. Valve surgery, concomitant valve and CABG surgery, preoperative chronic renal dysfunction, postoperative ARF, deep sternal infection, prolonged ventilation, need for IABP and EF less than 30% were found to be risk factors acting on GI complications. In these patients in particular, attention must be paid to appropriate preoperative GI bleed prophylaxis and postoperative monitoring for clinical signs and symptoms of mesenteric ischemia.

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