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Gastrointestinal Ischemia Related Mortality in Patients Undergoing Off- or On-Pump Coronary Artery Bypass Grafting

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ABSTRACT

Objective: Gastrointestinal ischemia (GII) after heart surgery is a rare but devastating condition. The aim of this study was to compare the occurrence of GII after coronary artery bypass grafting (CABG) performed off-pump (OPCAB) vs on-pump (ONCAB).

Methods: We retrospectively evaluated 2625 adult patients who underwent isolated coronary artery surgery during a 6-year period. The OPCAB group included 658 patients and the ONCAB group 1967 patients. Patients were evaluated, and GII, morbidity, and mortality in the 2 groups were compared.

Results: GII developed in 0.4% (7 of 1967) patients in the ONCAB group and in 0.2% (1 of 658) patients in the OPCAB group ($P = .28$). Mortality rates due to GII were 0.2% (4 of 1967) in the ONCAB group, and no deaths occurred in the OPCAB group ($P < .04$). Postoperative atrial fibrillation incidence with GII was 100% (7 of 7) in ONCAB group and 0% (0 of 1) in the OPCAB group ($P < .01$).

Conclusions: Compared to ONCAB, the OPCAB procedure has lower GII related mortality rates, which is an important cause of morbidity and mortality in the postoperative period of CABG surgery.

INTRODUCTION

The incidence of gastrointestinal complications (GIC) after cardiac surgery varies between 0.3% and 3% [Ott 1995; Yilmaz 1996; Akpinar 2000]. Gastrointestinal ischemia (GII) is a type of GIC that is difficult to diagnose, with symptoms that can be masked by sedation and mechanical ventilation in the early postoperative period, causing a delay in diagnosis [Akpinar 2000]. Some risk factors associated with GII after cardiac surgery are low perioperative cardiac output or hypotension, prolonged duration of cardiopulmonary bypass (CPB), advanced age, prolonged ventilation time, valve surgery, reexploration of the chest, and history of peptic ulcer [Yilmaz 1996]. Off-pump coronary artery bypass (OPCAB) surgery has several advantages over on-pump coronary artery bypass (ONCAB) surgery with regard to mortality, morbidity, and cost-effectiveness [Watanabe 1999; Cremer 2000]. The use of OPCAB surgery is becoming increasingly prevalent throughout the world [Hart 2000; Karamanoukian 2000; Puskas 2001]. Coronary surgical procedures are usually delayed until patients reach advanced age because of increasing use of interventional cardiology, so the proportion of higher-risk patients who require complex surgical procedures is likely to increase in the near future [Ulrich 2003]. OPCAB has been reported to reduce the inflammatory response during coronary artery bypass grafting (CABG) [Matata 2000]. In contrast, GII can be caused by altered perfusion and the inflammatory response during ONCAB procedures.

On the basis of this theory, it is believed that OPCAB surgery could reduce subsystem and end-organ damage seen after conventional CABG, leading to less morbidity. Numerous reported studies have compared the outcomes of off-pump and on-pump coronary artery revascularization techniques. To our knowledge, however, there are no data in the literature comparing postoperative GII-related mortality in patients who undergo ONCAB and OPCAB revascularization [Musleh 2003]. The aim of this study was to compare the incidence of GII-related mortality among patients undergoing cardiac surgery with OPCAB or ONCAB revascularization techniques.

METHODS

We retrospectively evaluated a total of 2625 patients who underwent isolated CABG surgery between June 2002 and August 2008. Cases were divided into 2 groups: group 1 included 658 patients who underwent off-pump surgery and group 2 included 1967 patients who underwent on-pump surgery. Cases with concomitant procedures such as valve repair, valve replacement, or resection of left ventricle aneurysm were not included in the study. The identified preoperative variables were age, sex, diabetes mellitus, hypertension, hypercholesterolemia, smoking status, functional capacity (New York Heart Association classification), history of GI events, cerebrovascular accident, carotid artery disease,

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Table 1. Preoperative Patient Data*

	On-Pump Group	Off-Pump Group	*P* value
Age, y	60.1 ± 9.1	66.3 ± 8.3	.01
Female sex	491 (25)	178 (27)	NS
Congestive heart failure	519 (27)	172 (26)	NS
Previous myocardial infarction	773 (39)	244 (37)	NS
Previous cerebrovascular accident	38 (2)	12 (4)	NS
COPD	215 (11)	112 (17)	NS
Diabetes mellitus	474 (24)	162 (25)	NS
Hypertension	1309 (66)	439 (67)	NS
Previous cardiac operation	18 (1)	7 (1)	NS
Ejection fraction	46.75 ± 18.95	45.89 ± 17.75	NS
Previous PCI	713 (36)	243 (37)	NS
Carotid artery disease > 50%	214 (11)	98 (15)	NS
Renal dysfunction	76 (4)	34 (5)	NS
Peripheral artery disease	196 (10)	84 (12)	NS
History of GI event	113 (6)	44 (7)	NS
Smoking	896 (48)	411 (62)	NS
Hypercholesterolemia	758 (38)	271 (41)	NS
NYHA			
Class I	57 (3)	19 (3)	NS
Class II	1091 (55)	398 (60)	NS
Class III	782 (40)	229 (34)	NS
Class IV	27 (2)	12 (3)	NS
Use of FFP	2.32 ± 1.74	1.85 ± 1.52	NS
Use of PRBC	3.77 ± 2.81	2.96 ± 2.84	NS
Mean EuroSCORE	7.4 ± 9.6	9.8 ± 11.6	NS

*Data are mean ± SD or n (%). NS indicates not significant; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; FFP, fresh-frozen plasma; PRBC, packed red blood cells, NYHA New York Heart Association.

peripheral artery disease, renal dysfunction (creatinine > 1.5 mg/dL), chronic obstructive pulmonary disease, previous coronary artery intervention, and history of myocardial infarction. Three operative variables were examined: number of bypasses, duration of CPB (for the on-pump group), and duration of surgery. Postoperative data regarding intensive care unit stay, use of inotropic agents, intraaortic balloon pump, reexploration, blood transfusions, hemodialysis, and atrial fibrillation (AF) were recorded for both groups. The patients were compared according to rates of intestinal resection and mortality and morbidity attributable to GII. Aspirin (150 mg) and oral clopidogrel (75 mg) were administered orally after extubation in both groups. Cefazolin was administered for antibiotic prophylaxis. As prophylaxis for GI bleeding, ranitidine (150 mg) was administered intravenously at the time of anesthesia induction; oral famotidine (40 mg) was maintained during the hospital stay. Patients with a preoperative history of GI bleeding received oral or intravenous omeprazole (40 mg) instead of famotidine.

Surgical Procedures

A median sternotomy was performed in all patients. Standard techniques were used to harvest the left internal mammary artery, radial artery, and saphenous vein. All surgeries were performed by the same surgical team using the same myocardial protection techniques and revascularization strategies.

ONCAB Group. After systemic heparinization, a 2-stage cannula was used to institute CPB between the ascending aorta and the right atrium. Tepid hypothermia (32°C) was maintained during CPB. A membrane oxygenator (Dideco Sorin Group, Mirandola, Italy) was used in all operations. For myocardial protection, cardioplegia using cold blood with a high potassium level was administered in an antegrade and/or retrograde fashion.

OPCAB Group. Partial anticoagulation was accomplished with 1-2 mg/kg body weight of heparin until a target activated clotting time ≥250 seconds was achieved. All patients underwent CABG using the OPCAB technique. An Octopus 4 (Medtronic, Minneapolis, MN, USA) was used as a cardiac stabilizer. After arteriotomy was performed with standard methods and the distal artery was opened, a bloodless anastomotic field in the shunt was obtained by insertion of intracoronary shunts (Clearview; Medtronic) into the coronary artery for each anastomosis. Shunts were 1.5, 2.0, 2.5, or 3.0 mm in size, according to the coronary artery lumen, and were removed after the last suture just before knotting. Hypothermia was avoided by adjustment of the operating room temperature.

In both groups, 8-0 polypropylene suture was used for anastomosis of the left internal mammary artery–left anterior descending artery; 7-0 polypropylene sutures were used for other distal anastomoses. Heparin was neutralized by protamine sulfate at the end of the surgical procedure. A standard method was used to close the thorax.

Statistical Analysis

Statistical analysis was done with SPSS 13.0 statistical software program (SPSS, Chicago, IL, USA). Descriptive analyses were performed. The differences between the groups for nominal data were analyzed with the χ^2 test. In evaluation of continuous variables, the Student *t* test and Mann-Whitney *U* test were used. *P* values less than .05 were considered to be statistically significant. The two-proportions test (Z test) was used for comparing GII between the groups.

RESULTS

A total of 2625 adult patients underwent isolated CABG procedures. Their results were evaluated in 2 groups (ONCAB and OPCAB). The 2 groups were similar (except for age) with respect to sex; presence of hypertension, diabetes mellitus, chronic obstructive pulmonary disease, congestive heart

Table 2. Operative and Postoperative Patient Data*

	On-Pump Group	Off-Pump Group	*P* value
Mean distal anastomoses	2.93 ± 0.74	2.710 ± .69	NS
Duration of operation	177 ± 11.2	148 ± 9.9	.01
Duration of CPB	69.8 ± 19.1	—	
Reexploration for bleeding	9 (2.6)	8 (2.4)	NS
LOS in the ICU, d	1.54 ± 0.53	1.31 ± 0.44	.01
LOS in the hospital, d	6.72 ± 0.86	5.17 ± 0.91	.01
Postoperative renal failure, dialysis	28 (2)	4 (2)	NS
Inotropic support	324 (17)	32 (5)	.01
IABP in ICU and OR	116 (6)	26 (4)	NS
In hospital mortality	37 (2)	7 (1)	NS
Postoperative AF	396 (19)	49 (7)	.01
Postoperative stroke	7	2	NS

*Data are mean ± SD or n (%). NS indicates not significant; CPB, cardiopulmonary bypass; LOS, length of stay; ICU, intensive care unit; IABP, intraaortic balloon pump; AF, atrial fibrillation; OR, operating room.

failure, previous myocardial infarction; and preoperative ejection fraction (Table 1). Patient demographic data for both groups and the distribution of preoperative risk factors are summarized in Table 1. All patients underwent isolated CABG (ONCAB group, n = 1967, 75%; OPCAB, n = 658, 25%). Duration of surgery, occurrence of postoperative AF, length of stay in the intensive care unit, and length of stay in the hospital were significantly higher in the ONCAB group than OPCAB group (Table 2).

Of 2625 total patients, 8 (0.3%) suffered from postoperative GII. A general surgeon reviewed all patients. In the ONCAB group, clinical manifestations included necrosis in the small intestine in 2 patients, in the small intestine/colon in 4 patients, and in the abdominal compartment (abdominal compartment syndrome [ACS]) in 1 patient (Table 3). Because of abdominal distention, patients first underwent minilaparotomy; in these patients, the incision was extended. In 4 patients with bowel necrosis of the small intestine/colon, total occlusion of the superior mesenteric artery was observed by use of colored Doppler ultrasound. These patients then underwent massive small intestine resection and right hemicolectomy. All died during the postoperative period. In another 2 patients who underwent laparotomy but in whom colored Doppler ultrasonography did not show superior mesenteric artery obstruction, small-bowel resections (70 and 130 cm) and end-to-end anastomoses were performed, and these patients were discharged from the hospital in good health. One patient underwent surgery for ACS. This patient also received mechanical ventilation in the intensive care unit. He had a distended abdomen and signs and symptoms consistent with ACS, including oliguria, hypoxia, hypotension, and persistent metabolic acidosis [Deenichin 2008]. Determination of intravesical pressure as an indirect method of measuring intraabdominal pressure was first performed by Kron [1984]. The measured intravesical pressure was 36 cm H_2O. At exploration, dilated small-bowel loops, wall thickening, mesenteric ischemia, intestinal swelling, and gut edema were observed. Necrosis was not observed. Because ischemia was corrected with surgical decompression, the patient's abdomen was not closed primarily, and a Bogota bag was applied without the need for resection. After a 48-hour observation period, intestinal edema had regressed and no ischemia or necrosis was observed, and the abdomen was primarily closed. The patient suffered low cardiac output syndrome and multisystem organ failure and died on postoperative day 6.

Elevated serum lactate levels, persistent metabolic acidosis, increasing lactic acidosis in spite of dialysis, and the use of balloon pumps and enormous doses of inotropes were consistently observed in the majority of patients (n = 5, 71%). Abdominal computed tomographic scans were performed in 7 patients and revealed abnormalities suggestive of ischemic bowel disease in 4 of these patients: dilated small-bowel loops and proximal colon in 3 patients, wall thickening in 3 patients, extraluminal air in 2 patients, and pneumatosis in 1 patient.

In the OPCAB group, gastrointestinal resection (GIR) due to GII was seen in 1 patient. Because of development of abdominal distention, laparotomy was performed on the suspicion of acute mesenteric ischemia in 1 patient. A 110-cm small-bowel resection and end-to-end anastomosis were performed, and the patient was discharged from the hospital in good health.

The incidence of GII was 7 in the ONCAB group vs 1 in the OPCAB group ($P < .28$). The incidence of GIR was 6 in the ONCAB group vs 1 in the OPCAB group. The mortality rate of GIR was 4 (0.2%) in the ONCAB group vs 0 (0%) in the OPCAB group ($P < .01$). The incidence of mortality due to GII was 5 (0.25%) in the ONCAB group vs 0 (0%) in the OPCAB group ($P < .02$). AF incidence was 100%

Table 3. Postoperative GII Patient Data*

	GIC with ONCAB (n = 7)	GIC with OPCAB (n = 1)	*P* value
Smoking	7	1	.28
Colored Doppler USG acute arterial (superior mesenteric artery) occlusion	4	0	.04
Supine direct abdominal radiograph	7	1	.28
On dialysis	6	1	.34
IABP	5	1	.41
Intestinal resection after intestinal ischemia	7	1	.28
Mortality-related GII	4	0	.04
Total mortality incidence–related GII	5	0	.03

* GII indicates gastrointestinal ischemia; GIC, gastrointestinal complication; ONCAB, on-pump coronary artery bypass; OPCAB, off-pump CAB; IABP indicates intraaortic balloon pump; USG, ultrasonography.

(7 of 7) in ONCAB patients with GII and 0% (0 of 1) in OPCAB patients with GII (P = .01).

DISCUSSION

Previous reports on the incidence of and risk factors for GIC have focused on patients undergoing CABG or large cohorts of cardiac surgery patients with predominantly CABG procedures [Akpinar 20002; Musleh 2003]. The profile of patients referred for cardiac surgery has changed during the last decade. Because of advances in interventional cardiology, coronary surgery procedures are usually delayed until patients reach advanced age, and the proportion of higher-risk patients who require complex surgical procedures is likely to increase in the near future. In a study by Filsoufi et al [2007], 53% (17 of 30) of patients with GII died; similarly, in our study 63% (5 of 8) of patients with GIC died.

Hypotension is frequently observed during CPB. Measures to restore aortic pressure during CPB consist of increasing pump flow or administering vasoactive medication. Intestinal tissue perfusion during CPB is primarily dependent on blood flow rather than perfusion pressure [Bastien 2000]. Thus, because vasoconstrictors used for managing hypotension during CPB increase perfusion pressure, they may not improve mesenteric perfusion [O'Dwyer 1997]. Vasoconstrictors may cause selective vasoconstriction of mesenteric vessels and lead to the development of acidosis and mesenteric ischemia [Tofukuji 2000]. It has been demonstrated that significant intestinal mucosal ischemia can occur during CPB despite normal indices of global perfusion.

Factors released during CPB, such as vasopressin, catecholamines, and thromboxane A2 and B2, lead to redistribution of blood flow away from the mucosa because of regional vasoconstriction and may contribute to mucosal ischemia [Tao 1995]. We observed a significantly higher requirement for vasoconstrictors in the on-pump group compared to the off-pump group, a factors that may have contributed to the higher incidence of GIC in our ONCAB group. During off-pump coronary artery surgery, manipulations on the beating heart can depress cardiac functions, and tilting the heart can induce low cardiac output. This situation can be balanced with volume replacement, use of inotropic agents, and Trendelenburg positioning of the patient. The effectiveness of these measures for maintaining adequate distal perfusion to abdominal organs is not clear, however. Avoidance of CPB, on the other hand, can theoretically decrease the risk of distal organ malperfusion by reducing the formation of micro- and macroembolisms associated with cannulation and cross-clamping of the aorta [Kim 2002]. Mangi et al [2005] analyzed 8709 patients undergoing cardiac surgery (ONCAB) and reported an incidence as low as 0.5%. They also reported that the most frequent serious GIC was GII, which developed in 31 patients (67%). Twenty-two (71%) of these patients underwent exploratory surgery for GIC, and 14 (64%) died within 2 days of heart surgery. Of the 9 patients with mesenteric ischemia who did not have exploratory surgery, 7 (78%) died within 3 days of heart surgery. To our knowledge, this is the largest study to investigate GIC complications following heart surgery, and the mortality rate associated with GII was 0.2% (21 of 8709). Similarly, in our study, the incidence of mortality due to GII was 0.19% (5 of 2635). The highest rate of GIC was reported by Christenson et al [1994]. These authors used a broad definition of GIC, including acute cholecystitis, pancreatitis, and medically treated GI bleeding, and they reported an incidence of 2.9% in a series of 3493 patients. In their series, GIC were observed in 73 patients; 8 of these patients developed GII and 5 (0.2%) died. In our series, GII occurred in 7 patients in the ONCAB group, and 0.24% (5 of 1963) died. Spotnitz et al [1995] reported a GIC incidence of 2% in a series of 1831 patients after cardiac surgery. In their series, 46% of patients had upper or lower GI bleeding; only 5% suffered from bowel necrosis, and 0.2% (4 of 1831) died of GII. In our study, the incidence of GIC was 2.6 % (69 of 2625); 52% of patients had upper or lower GI bleeding; only 11% (7 of 2625) had bowel necrosis, and 4 of these 7 patients died.

After CPB, acute mesenteric ischemia leading to massive infarction of the bowel is a serious, life-threatening complication. It is reported to be a rare complication, with an incidence of 0.6%-2% [Zacharias 2000]. The mortality associated with this complication is extremely high, ranging from 70% to 100% [Shutz 1998]. In our study, acute mesenteric ischemia was seen in 0.4% (7 of 1967) of ONCAB-group patients. The rate of acute mesenteric ischemia leading to massive infarction was also high. This complication occurred in 7 patients, and 4 of them died. In our study the rates of GII and GIR were similar to those reported in the literature. To our knowledge this study is the first to compare 2 different surgical techniques (OPCAB vs ONCAB) with regard to GII and GIR and their mortality and morbidity rates.

For patients undergoing open cardiac procedures, the reported incidence of AF is clearly much higher, ranging from 3.1% to 91%, with most large series reporting an incidence of approximately 30% [Creswell 1993; Aranki 1996]. Sedrakyan et al [2006] reported results of a metaanalysis of 19 AF studies involving 2613 patients. These investigators found that off-pump surgery reduced the substantial risk of AF. Postoperative AF has been reported to cause a significant increase in mortality and hospitalization [Banach 2006]. In our study, AF incidence was significantly lower in the OPCAB group. In patients who had GII, a higher rate of AF was seen in the ONCAB group compared to the OPCAB group. These findings indicate that surgeons should be cautious regarding GII in patients who have AF following ONCAB surgery. Additionally, intraaortic balloon pump use and postoperative renal failure were higher in the ONCAB group than the OPCAB group, but the difference was not statistically significant. This may be another reason for the high GII-related mortality in the ONCAB group.

Angelini and colleagues [2002] showed reduced coagulation impairment associated with off-pump CABG. Filsoufi et al [2007] stated that off-pump procedures were performed with an increasing frequency in high-risk patients, in whom they obtained excellent results. In these patients, there was a reduction in postoperative complications, including respiratory failure (P = .013), GIC (P = .017), and stroke (P = .094).

In our study, the risk factors in both groups were similar, but incidences of postoperative AF and GIR were significantly higher in the ONCAB group. In the ONCAB group of patients with GII, AF was seen in 100% (7 of 7) whereas in the OPCAB group of patients with GII, this incidence was 0% (0 of 1). AF was seen in all patients who underwent intestinal resection in the ONCAB group. The high risk of AF incidence in patients with GIC who underwent ONCAB was due to inotropic support and increased coagulation impairment by CPB.

In some studies OPCAB was shown not to reduce incidence of GIC when compared to ONCAB. Musleh et al [2003] suggested in their study that off-pump and on-pump techniques are similar with respect to the rates of GIC. Sanisoglu et al [2004] also stated that the incidence rates of GII were similar in the ONCAB (0.8%) and OPCAB group (0.4%).

In our study, even though preoperative risk factors were similar in the 2 groups (except age and EUROscore, which were significantly higher in the OPCAB patients), postoperative AF and inotropic support were significantly higher in the ONCAB patients compared to OPCAB patients. GII-related mortality was significantly lower in the OPCAB group. All patients who underwent intestinal resection (in ONCAB groups) had AF. Thus we conclude that caution regarding intestinal ischemia is required in patients who have postoperative AF.

Limitations

This study had several limitations: The small number of patients compared in the ONCAB and OPCAB groups decreases the importance of the study. Multicenter studies with a greater number of patients would enhance the results of similar studies. However, our study has the advantage of being a single-center study of procedures performed by the same team of surgeons, thus greatly reducing the effects of various surgical techniques and perioperative or postoperative protocols.

CONCLUSION

In view of the rapid increase in the average age of the CABG surgery population in recent years, OPCAB should be the preferred surgical procedure for reducing GII-related morbidity and mortality.

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