Incidence of Gastrointestinal Complications in Cardiopulmonary Bypass Patients

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Abstract. Gastrointestinal complications after cardiac surgery are associated with a high mortality rate. Because of the absence of early specific clinical signs, diagnosis is often delayed. The present study seeks to determine predictive risk factors for subsequent gastrointestinal complications after cardiosurgical procedures. Within a 1-year period, a total of 1116 patients who had undergone open heart surgery with cardiopulmonary bypass were prospectively studied for gastrointestinal complications. To determine predictive factors, all case histories of the patients were analyzed. Of the 1116 patients, 23 (2.1%) had gastrointestinal complications during the postoperative period, 10 of whom had to undergo subsequent abdominal surgery. Of these 23 patients, 20 died. Early gastrointestinal complications, which occurred mostly on postoperative days 6 or 7, consisted of bowel ischemia or hepatic failure. Late complications were gastrointestinal bleeding, pseudomembranous colitis, cholecystitis, and septic rupture of a spleen. The relative risk for abdominal complications after cardiopulmonary bypass was highly increased in association with (1) a cardiac index less than 2.0 l/min^{-1}/(m^2)$^{-1}$, (2) postoperative onset of atrial fibrillation, (3) emergency surgery, (4) need for vasopressors, (5) need for intraaortic balloon counterpulsation, and (6) need for early redo thoracotomy due to surgical complications. All patients with necrotic bowel disease had elevated serum lactate levels. Furthermore, cardiopulmonary bypass and aortic clamping times were significantly prolonged in patients who developed gastrointestinal complications. A number of predictive factors contribute to the development of gastrointestinal complications after cardiopulmonary bypass surgery. Knowledge of these factors may lead to earlier identification of patients at increased risk and may allow more efficient and earlier interventions to reduce mortality.

Despite intensive therapeutic efforts, the incidence and mortality of gastrointestinal complications after cardiac surgery employing cardiopulmonary bypass (CPB) have not decreased during the last two decades. Gastric bleeding, ischemic bowel disease, gallbladder disease, and pancreatitis are reportedly the most common complications [1–5]. Despite major technologic and medical advances, CBP still imposes considerable physiologic stress on the patient [6, 7]. This holds especially true in the case of severely ill or otherwise compromised patients. However, it has been difficult to define risk factors associated with a significantly increased risk for intraabdominal complications after CBP. The goal of the present study was to determine risk factors predictive of a significantly increased risk for postoperative gastrointestinal complications to identify patients at risk earlier.

Materials and Methods

A total of 1116 patients who had undergone cardiosurgical procedures with extracorporeal circulation at our institution during a 1-year period were studied prospectively. We evaluated all patients for possible risk factors that we believed might contribute to or cause the development of postoperative gastrointestinal complications. Our routine prophylaxis against ulcers was done with ranitidine (4 × 50 mg/day) on the intensive care unit (ICU). A proton channel blocker (omeprazole 2 × 10 mg/day) was only used in patients with a history of ulcers. Ceftriaxone 2 g was given perioperatively to all patients.

Cardiopulmonary Bypass

Cardiopulmonary bypass was performed with membrane oxygenators under mild hypothermia (32°C). A nonpulsatile blood flow rate of not less than 2.4 L/min^{-1}/m^2 was used whenever possible. Buckberg blood cardioplegia was used for myocardial protection. A mean arterial perfusion pressure of 40 mmHg was maintained by application of norepinephrine if necessary. If needed, epinephrine (maximum 0.3 μg/kg^{-1}/min^{-1}) or enoximone (10 μg/kg^{-1}/min^{-1}) was administered. Our guidelines for hemodynamic management were to use dopamine and dobutamine initially up to a maximum dose of 10 μg/kg^{-1}/min^{-1}. If this proved ineffective, we used epinephrine as needed.

Risk Factors

Our definition of preexisting gastrointestinal disease included all patients with a history of gastric or duodenal ulcers and colitis, as well as hepatobiliary disease such as pancreatitis, cholelithiasis, and cholecystitis. Renal insufficiency was considered significant with a serum creatinine level of more than 2.0 mg/dl. All other preoperative risk factors are given in Table 1. Intraoperatively,

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Table 1. Preexisting risk factors and relative risk for development of postoperative gastrointestinal complications.

Risk factor	No gastrointestinal complications ($n = 1,093$)	Gastrointestinal complications ($n = 23$)	p	Relative risk
Hypertension	636 (58.2%)	15 (65.2%)	NS	
History of myocardial infarction	527 (48.2%)	11 (47.8%)	NS	
Diabetes mellitus	348 (31.8%)	6 (26.1%)	NS	
Left ventricular ejection fraction < 50%	199 (18.2%)	6 (26.1%)	NS	
Chronic obstructive pulmonary disease	129 (11.8%)	6 (26.1%)	0.0495	2.565
Atrial fibrillation	103 (9.4%)	5 (21.7%)	NS	
History of abdominal disease	100 (9.1%)	2 (8.7%)	NS	
Emergency surgery	91 (8.3%)	12 (52.2%)	<0.0001	10.729
Redo cardiac surgery	88 (8.1%)	2 (8.7%)	NS	
Renal insufficiency	60 (5.5%)	5 (21.7%)	0.0085	4.491

cardiopulmonary bypass and aortic cross-clamping times were considered potential risk factors. During the postoperative period we looked for postoperative catecholamine support with epinephrine or norepinephrine (or both), loss of sinus rhythm and onset of atrial fibrillation, counterpulsation by intraaortic balloon pump, low cardiac output with a cardiac index of less than 2.0 L/min^{-1}/(m^2)$^{-1}$, and the need for redo thoracotomy within the first 24 postoperative hours.

Gastrointestinal Complications

We defined postoperative gastrointestinal complications as follows: gastrointestinal bleeding confirmed by endoscopy with a decrease in hemoglobin content of at least 2 g/dl, mesenteric ischemia or infarction, cholecystitis, pancreatitis, and hepatic failure confirmed by history and laboratory data.

Statistics

The prevalence of risk factors between the groups with or without gastrointestinal complications was compared in terms of statistical significance with Fisher's exact test, and the relative risk was calculated, providing statistical significance. Demographic data and CPB and aortic clamping times were compared using the Wilcoxon Mann-Whitney test. All statistical calculations were performed with GraphPad InStat Version 3.00 (GraphPad Software, San Diego, CA, USA). Statistical significance was confirmed with a probability of error less than 5% (p < 0.05).

Results

Of the 1116 patients who underwent cardiac surgery with CPB during a 12-month period, 23 (2.1%) developed gastrointestinal complications during their postoperative ICU stay. The two groups were identical in terms of demographic data and the surgical procedure performed. The mortality rate for 1093 patients who did not develop gastrointestinal complications was 2.7% (n = 30). Of the 23 patients with postoperative gastrointestinal complications, 20 (87.0%) died (p < 0.0001), (Table 2). In nine patients with hepatic failure or mesenteric ischemia the actual cause of death was most likely prolonged low cardiac output. One patient died in direct association with gastric bleeding. In the remaining 10 patients who died, it remained unclear whether death was directly related to the gastrointestinal compli-

Table 2. Demographic data and surgical interventions in 1116 patients who underwent cardiac surgery.

Parameter	No gastrointestinal complications ($n = 1093$)	Gastrointestinal complications ($n = 23$)
In-hospital mortality	30 (2.7%)*	20 (87.0%)*
Age (years)	66.1 ± 8.12	64.6 ± 9.71
Gender		
Male	775 (70.9%)	15 (65.2%)
Female	318 (29.1%)	8 (34.8%)
Intervention		
Coronary artery bypass grafting (CABG)	765 (70.0%)	14 (60.9%)
Valve repair or replacement (VR)	169 (15.5%)	3 (13.0%)
CABG and VR	100 (9.1%)	2 (8.7%)
Other	59 (5.4%)	4 (17.4%)

Data are presented as the mean ± SD or number and percent.
*p < 0.0001.

cations or was a result of prolonged hypoperfusion from circulatory failure or prolonged ICU stay.

Altogether, 13 patients received conservative treatment (5 for gastric bleeding, 5 for hepatic failure, 3 for pseudomembranous colitis), and 10 patients underwent laparotomy. Five of these patients had ischemic colitis, and two of them had to undergo repeat laparotomy two and three times, respectively. Two patients had gastric bleeding, and two more had acute cholecystitis. One patient died from rupture of a septic spleen (Table 3).

Preoperative Risk Factors

As shown in Table 1, the most significant risk factors for the development of postoperative gastrointestinal complications were emergency surgery and renal insufficiency. Patients with coexisting chronic obstructive pulmonary disease are also at increased risk for gastrointestinal complications.

Intraoperative Risk Factors

Patients who developed gastrointestinal complications during their ICU stay had significantly prolonged periods of both CPB (205.6 ± 83.16 vs. 114.9 ± 49.08 minutes, p < 0.0001) and aortic cross-clamping (106.3 ± 46.67 vs. 74.0 ± 38.66 minutes, p <

Table 3. Patients with gastrointestinal complications after cardiac surgery.

Complication	Patients (no.)	Survivors (no.)	Days after cardiac surgery the complication manifested
Hepatic failure	5	0	6 (3–8)[a]
Ischemic or necrotic bowel disease	5	1	7 (1–11)
Gastric bleeding	7	1	13 (9–20)
Pseudomembranous colitis	3	0	27 (8–40)
Acute cholecystitis	2	1	45 (30–60)
Septic rupture of the spleen	1	0	43

[a]Data are presented as the median and range

0.0001). There was no clear threshold at which the risk for complications significantly increased.

Postoperative Risk Factors

As listed in Table 4, patients with low cardiac output were at 22-fold increased risk for gastrointestinal complications. Loss of sinus rhythm and onset of atrial fibrillation during the postoperative period increased the risk by almost 17-fold. Another significant risk factor was the postoperative need for vasopressor support with epinephrine or norepinephrine (or both), as was the use of intraaortic balloon counterpulsation. Also, redo thoracotomy within the first postoperative day results in an eightfold increased likelihood of gastrointestinal complications. All patients with necrotic bowel and hepatic failure (n = 10) had reasonably elevated serum lactate levels. In 70% of these patients, serum lactate levels exceeded 10 mmol/L. In all other patients the serum lactate levels were normal, regardless of which gastrointestinal complication occurred.

Discussion

Despite major advances in CPB technology and improved strategies in intensive care medicine, the 1% to 3% incidence of gastrointestinal complications after CPB has remained constant during the last two decades [1–5]. In our study, the incidence of postoperative gastrointestinal complications was 2.1%, which conforms with the low incidence demonstrated by other investigators. Once a gastrointestinal complication occurs, however, the overall mortality ranges from 13.5% to 72.0% [1–5, 8]. In particular, patients with gastric bleeding or cholecystitis are most likely to survive, whereas almost every patient with mesenteric ischemia dies [9, 10]. Because clinical features are often subtle, it is essential to identify patients at risk for early diagnosis and aggressive treatment.

The most severe gastrointestinal complications, ischemic bowel and hepatic failure, occurred in almost half of our patients. None of these patients survived. The diagnosis was most frequently made during the first postoperative week and no later than 11 days after cardiac surgery. These findings suggest an obvious relation of ischemic bowel disease or hepatic failure and previous surgery. Prolonged CPB and aortic clamping result in significant intestinal hypoperfusion and subsequent inflammatory response [7], as does postoperative low cardiac output [10] which often requires application of highly potent vasoactive catecholamines, which further augment intestinal hypoperfusion [11]. Use of intraaortic balloon counterpulsation (which is often also required in these patients) may further aggravate the situation, especially in cases of malposition of the device [12]. We demonstrated that the use of intraaortic balloon counterpulsation increases the risk for gastrointestinal disease by more than eightfold. Intestinal hypoperfusion, which may progress to acute mesenteric infarction, results in an ischemic lesion of the bowel with necrosis and perforation. This, in turn, may lead to sepsis and peritonitis. The occurrence of hepatic failure also seems to be the consequence of a refractory low cardiac output syndrome with prolonged application of vasoactive catecholamines. We believe that both hepatic failure and mesenteric ischemia are complications of prolonged circulatory failure, which was the actual cause of death. Indeed, hepatic failure or mesenteric ischemia due to a state of hypoperfusion from low cardiac output syndrome can rarely be treated sufficiently even if diagnosed early. In contrast, if mesenteric ischemia results from thromboembolic events, which most likely occur in patients who present with postoperative onset of atrial fibrillation, a more timely diagnosis may improve the outcome.

As catecholamine support can rarely be avoided in patients with low cardiac output, risks and benefits must be considered carefully. Because of a 10-fold increased likelihood of gastrointestinal complications, our data demand the restrictive use of vasoactive catecholamines whenever possible, particularly norepinephrine and epinephrine. The use of phosphodiesterase inhibitors may be a better choice. Dopexamine seems to interfere with intestinal perfusion to a lesser degree than norepinephrine and epinephrine [13, 14]. Patients with poor cardiac function who require vasopressors, mechanical support devices such as an intraaortic balloon pump (IABP), or both are at markedly increased risk of gastrointestinal complications; however, hepatic failure or mesenteric ischemia only accelerate the death of most patients who likely would have died from circulatory failure anyway, with or without gastrointestinal complications.

Surprisingly, patients with preexisting atrial fibrillation were not at significantly increased risk for gastrointestinal complications, but those who lost sinus rhythm during the postoperative period were. Of 23 patients with gastrointestinal complications who had been in sinus rhythm preoperatively, 16 developed atrial fibrillation after surgery. If administration of antiarrhythmic drugs proved ineffective, electric cardioversion was performed. Return to and maintenance of sinus rhythm could be achieved in only four patients. Atrial fibrillation represents one of the most common rhythm disturbances after cardiac procedures [15]. The loss of atrial contraction is associated with hemodynamic impairment, reduced stroke volume, and thromboembolic events [16]. The combination of postoperative onset of atrial fibrillation and gastrointestinal symptoms is highly suggestive of a thromboembolic event, which must be confirmed or disproved without delay.

We strongly recommend frequent determinations of serum lactate levels in patients at increased risk for gastrointestinal complications. Serum lactate levels were highly elevated in all our patients with ischemic bowel disease. In contrast, lactate levels in patients with hepatic failure or low cardiac output syndrome virtually always were only moderately elevated. Regardless of the fact that serum lactate levels are not quite specific for ischemic bowel disease, they represent a sensitive diagnostic marker and valuable screening tool. Highly elevated serum lactate levels must be a reason for concern, particularly in patients at risk. If bowel

Table 4. Postoperative risk factors and relative risk for development of gastrointestinal complications.

Risk factor	No gastrointestinal complications ($n = 1093$)	Gastrointestinal complications ($n = 23$)	p	Relative risk
Low cardiac output syndrome	49 (4.5%)	13 (56.5%)	< 0.0001	22.100
Loss of sinus rhythm and onset of atrial fibrillation	119 (10.9%)	16 (69.6%)	< 0.0001	16.610
Vasopressor support with epinephrine and/or norepinephrine	97 (8.9%)	12 (52.2%)	< 0.0001	10.078
Intraaortic balloon counterpulsation	30 (2.7%)	5 (21.7%)	0.0005	8.579
Redo thoracotomy < 24 hours	39 (3.6%)	6 (26.1%)	0.0002	8.400

ischemia is suspected in patients at risk, invasive diagnostic measures such as explorative laparotomy and angiography should follow without delay.

Late gastrointestinal complications consisted of gastric bleeding, pseudomembranous colitis, acute cholecystitis, and septic rupture of the spleen. These complications occurred most frequently during the second postoperative week but were also noted as late as 60 days after cardiac surgery. Despite the routine perioperative use of histamine H_2-blockers and administration of proton channel blockers in patients with a history of ulcers, episodes of gastric bleeding are still the most common gastrointestinal complication after cardiac surgery [4]. In seven patients of our study who had gastric bleeding, bleeding control by endoscopic clipping was successful in five patients, and only two patients had to undergo abdominal surgery. Therefore gastroscopy should be done early if gastric bleeding is suspected in a patient at risk. Regardless of the fact that six of seven patients died, only one died in direct association with gastric bleeding. It can only be speculated to what extent compromised cardiac function and resulting hypoperfusion contributed to the development of gastric bleeding in these patients.

In contrast to other investigators who reported the development of severe, acute pancreatitis after cardiac surgery [4, 5], in our study there was no acute pancreatitis. Acute cholecystitis occurred in two patients. It is speculated that both acute pancreatitis and cholecystitis after cardiac surgery are caused by hypotension and hypoperfusion, which result in inflammation and reperfusion injury. Furthermore, calcium, which is often administered for hemodynamic reasons during separation from CBP, has been described as a significant risk factor for pancreatic injury [17]. Because acute cholecystitis in our patients did not occur earlier than 30 days after cardiac surgery, it can most likely be attributed to the prolonged stay in the ICU rather than to the previous surgical procedure. Similarly, the late complications of septic rupture of the spleen and pseudomembranous colitis are probably also sequelae of prolonged intensive care treatment with steroids and antibiotics or the use of external organ support devices, such as venovenous hemofiltration and aggressive ventilation strategies to support the lungs.

Conclusions

The results of our study show that a number of postoperative complications are associated with a markedly increased risk for the development of gastrointestinal complications after cardiac surgery. Intestinal hypoperfusion as a result of poor cardiac output is likely to result in hepatic failure and ischemic bowel disease early after surgery. Gastric bleeding, cholecystitis, and pseudomembranous colitis are late complications and are probably sequelac of prolonged ICU treatment. The risk factors described allow us to predict who is at increased risk for gastrointestinal complications. Knowledge of these factors and increased awareness of patients at risk may lead to a more timely diagnosis, earlier therapeutic intervention, and therefore a reduction in the alarmingly high mortality rate due to gastrointestinal complications, at least in patients whose gastrointestinal complications are not sequelae of prolonged poor cardiac function and subsequent intestinal hypoperfusion.

Résumé

Objectifs: Les complications gastro-intestinales après chirurgie cardiaque sont associées à un taux de mortalité élevé. Le diagnostic en est souvent retardé en raison de l'absence de signes cliniques spécifiques, précoces. Cette étude cherche à déterminer les facteurs de risque prédictifs de complications gastro-intestinales après chirurgie cardio-vasculaire. Méthodes: Pendant une période d'un an, 1116 patients au total ayant eu une intervention chirurgicale à coeur ouvert avec shunt cardio-pulmonaire ont été étudiés prospectivement danš la recherche de complications gas tro-intestinales. Afin de déterminer les facteurs prédictifs, tous les antécédents ont é té analysés. Résultats: 23 (2.1%) des 1116 patients ont eu des complications gastro-intestinales pendant la période postopératoire, dont 10 qui ont nécessité un acte chirurgical abdominal. Parmi ces 23 patients, 20 sont décédés. Des complications gastro-intestinales précoces sont survenues aux jours postopératoires 6 ou 7, sous forme d'ischémie intestinale ou d'insuffisance hepatique. Les complications tardives ont été l'hémorragie gastro-intestinale, la colite pseudo-membraneuse, la cholécystite et un cas de rupture septique de la rate. Le risque relatif de faire des complications abdominales après shunt cardio-pulmonaire était plus important lorsque le patient: (1) avait un indexe cardiaque inférieur à 2,0 l/min^{-1}/(m^2)$^{-1}$, (2) a prése nté une fibrillation auriculaire postopératoire, (3) a eu besoin d'une intervention en urgence, (4) a eu besoin de vasopresseurs, (5) a nécessité l'utilisation d'un ballonnet à contre-pression, et (6) a eu une re-thoracotomie précoce en raison des complications. Tous les patients ayant une nécrose intestinale avaient des taux de lactates élevés dans le sérum. Les temps de shunt cardio-pulmonaire et de clampage aortique ont été prolongés de façon significative chez les patients qui ont développé des complications gastro-intestinales. Conclusions: Il existe un certain nombre de facteurs prédictifs qui peuvent contribuer au développement des complications gastro-

intestinales après un shunt cardio-pulmonaire. La connaissance de ces facteurs pourrait aider à identifier ces patients à risque et pourrait permettre une intervention plus efficace et plus précoce, réduisant ainsi la mortalité.

Resumen

Objetivo: Las complicaciones gastrointestinales tras cirugía cardiaca conllevan una alta tasa de mortalidad. Debido a la ausencia de signos clinico precoces, el diagnóstico, con frecuencìa, se retrasa. El presente estudio pretende averiguar los factores que permitan predecir el riesgo de padecer complicaciones gastrointestinales tras cirugía cardiaca. Métodos: Durante un año se estudiaron prospectivamente las complicaciones gastrointestinales de 1,116 pacientes intervenidos a corazón abierto con derivación cardio-pulmonar. Se analizaron las historias clínicas de todos los pacientes con objeto de averiguar los factores predictivos. Resultados: En 23 (2.1%) de los 1,116 pacientes se produjeron complicaciones gastrointestinales en el periodo postoperatorio, requiriendo 10 de ellos tratamiento quirúrgico. De los 23 pacientes, 20 fallecieron. Las complicaciones gastrointestinales precoces aparecieron entre el 6, 7 dias del postoperatorio, tratándose de isquemia intestinal o fracaso hepático. Las complicaciones tardias fueron: hemorragia gastrointestinal, colitis pseudo-membranosa, colecistitis y ruptura séptica del bazo. El riesgo de desarrollar complicaciones abdominales, tras derivación cardio-pulmonar se incrementa cuando se producen: (1) índice cardiaco menor a 2.0 l/min^{-1}/(m^2)$^{-1}$, (2) crisis postoperatorias de fibrilación atrial, (3) cirug ía de urgencia, (4) utilización de vasopresores, (5) empleo del balón intraaórtico de contrapulsación y (6) retoracotomía precoz por complicaciones quirúrgicas. Todos los pacientes con afectación necrótica intestinal presentaron niveles altos de la concentración sérica de lactato. Además, en los pacientes que desarrollaron complicaciones gastrointestinales, tanto el tiempo de derivación cardio-pulmonar como el del clampado de aorta fueron significativamente más prolongados. Conclusiones: Se describen diversos factores predictivos que contribuyen al desarrollo de complicaciones gastrointestinales tras cirugía cardiaca con derivación cardio-pulmonar. El conocimiento de los mismos, permitirá la identificación precoz de los pacientes de mayor riesgo, pudiéndose así realizar intervenciones más precoces y eficaces que reduzcan la mortalidad.

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