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ORIGINAL ARTICLE

Risk factors for postoperative complications in patients on maintenance hemodialysis who undergo abdominal surgery

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Summary *Background/Objective:* Patients on hemodialysis (HD) who undergo abdominal surgery for gastrointestinal disease are at increased risk of postoperative complications. In this study, we retrospectively investigated the predictors of postoperative complications among such patients.
Methods: The study group comprised 36 HD patients who underwent abdominal surgery for gastrointestinal disease between 2003 and 2012. The clinicopathological factors of the patients who did and did not suffer postoperative complications were compared.
Results: The overall morbidity and mortality rates were 39% (14/36) and 14% (5/36), respectively. Physical status according to the American Society of Anesthesiologists (ASA) classification ($p = 0.0203$) and intraoperative blood loss ($p = 0.0013$) were found to differ significantly between the groups.
Conclusion: The morbidity and mortality rates of HD patients who underwent abdominal surgery for gastrointestinal disease were high. Physical status according to the ASA classification and intraoperative blood loss were found to be associated with postoperative complications. Therefore, patients with comorbidities, such as heart disease and diabetes mellitus, have to be treated appropriately before surgery. In addition, it is important that surgeons perform operations carefully and avoid excessive blood loss.

Conflicts of interest: None.

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1. Introduction

In 2012, >2.35 million patients received renal replacement therapy around the world.[1] In Japan, >300,000 patients were receiving dialysis treatment at the end of 2011, and the number of patients receiving hemodialysis (HD) is increasing steadily.[2] The mean age of new dialysis patients is 67.84 years, and the mean age of the entire dialysis patient population is 66.55 years.[2] The growing number of patients on long-term HD is likely to lead to an increase in the number of HD patients who require surgery.[3]

Patients receiving HD are at increased risk of postoperative complications such as a tendency to bleed, delayed wound healing, infection, electrolyte imbalances, and hemodynamic instability.[4–7] According to previous studies, the morbidity and mortality rates of HD patients who undergo abdominal surgery range from 39% to 41.8% and from 5.7% to 24%, respectively.[8–10]

It is important to identify the risk factors for morbidity and mortality among HD patients who undergo abdominal surgery to determine the optimal surgical procedures for such patients. In this study, we retrospectively investigated the predictors of complications in HD patients who underwent abdominal surgery for gastrointestinal disease. In addition, we have summarized the findings obtained for the patients who died of diseases related to their postoperative complications.

2. Materials and methods

The study group comprised 36 patients who were on maintenance HD therapy and underwent abdominal surgery for gastrointestinal disease at the Department of Surgery, Juntendo Shizuoka Hospital, between November 2003 and December 2012. Patients who underwent noninvasive surgery were excluded from this study.

The clinical characteristics of the 36 patients who underwent abdominal surgery for gastrointestinal disease are shown in Table 1. There were 28 male and eight female patients. The mean age of the patients was 65.1 years (range 44—82 years) and their clinical diagnoses included colorectal cancer in 14 patients; gastric cancer in eight patients; cholelithiasis in five patients; acute appendicitis in two patients; and remnant gastric cancer combined with hepatocellular carcinoma, gallbladder polyps, a requirement for colostomy due to colorectal perforation, colon perforation, ileus, a perianal abscess, and an intraperitoneal abscess in one patient each. The underlying renal disease was diabetic nephropathy in 11 patients, nephrosclerosis in 10 patients, glomerulonephritis in five patients, nephrectomy in three patients, and polycystic kidney in one patient. Data regarding the underlying renal disease were not available for six cases. All patients underwent HD, and the mean HD duration before the surgery was 7.4 years (range 0.2—31 years). Twenty-five patients had coexisting disorders including hypertension in 14 patients; diabetes mellitus in 12 patients; cerebrovascular disease in seven patients; angina pectoris in five patients; an old myocardial infarction in three patients; chronic heart failure in three patients; arteriosclerosis obliterans in three patients; chronic hepatitis in two patients; and aortic dissection, paroxysmal atrial fibrillation, sick sinus syndrome, and valvular disease in one patient each. Preoperative performance status (PS) was evaluated according to the criteria

Table 1 Patients' characteristics.

Clinical factors		No. of patients
Total		36
Sex	Male	28
	Female	8
Age (y), mean ± SD		65.1 ± 75.2
Clinical diagnosis		
	Colorectal cancer	14
	Gastric cancer	8
	Cholelithiasis	5
	Remnant gastric cancer and Hepatocellular carcinoma	1
	Gallbladder polyps	1
	A requirement for colostomy caused by colorectal perforation	1
	Colon perforation	1
	Ileus	1
	Acute appendicitis	2
	Perianal abscess	1
	Intraperitoneal abscess	1
Reason for hemodialysis		
	Diabetes mellitus	11
	Nephrosclerosis	10
	Glomerulonephritis	5
	Nephrectomy	3
	Polycystic kidney	1
	NA	6
Duration of hemodialysis (y), mean ± SD		7.4 ± 13.1
Comorbidities		
	Hypertension	14
	Diabetes mellitus	12
	Cerebrovascular disease	7
	Angina pectoris	5
	Previous myocardial infarction	3
	Chronic heart failure	3
	Arteriosclerosis obliterans	2
	Aortic dissection	1
	Paroxysmal atrial fibrillation	1
	Chronic hepatitis	2
	Sick sinus syndrome	1
	Valvular disease	1
Performance status		
	0	32
	1	0
	2	4

SD = standard deviation, NA = not available.

Table 2 Type of surgery.

	n
Elective surgery	
Colon resection	11
Distal gastrectomy	6
Laparoscopic cholecystectomy	4
Total gastrectomy	2
Low anterior resection	2
Cholecystectomy	2
Total gastrectomy for remnant gastric cancer	1
Laparoscopic colon resection	1
Bowel resection	1
Emergency surgery	
Appendectomy	2
Hartmann's procedure	1
Drainage with Hartmann's procedure	1
Bowel resection	1
Drainage with bowel resection	1

proposed by the Eastern Cooperative Oncology Group.[11] The operations performed are listed in Table 2. Thirty patients underwent elective surgery, and the remaining six patients underwent emergency surgery. Thirty-one patients received standard laparotomy, whereas the remaining five received laparoscopic surgery. The elective surgical procedures included colon resection in 11 patients; distal gastrectomy in six patients; laparoscopic cholecystectomy in four patients; total gastrectomy in two patients; low anterior resection in two patients; cholecystectomy in two patients; and total gastrectomy for remnant gastric cancer, laparoscopic colon resection, and bowel resection in one patient each. The emergency surgical procedures included appendectomy in two patients and Hartmann's procedure for a perianal abscess, drainage combined with Hartmann's procedure, bowel resection, and drainage combined with bowel resection in one patient each.

We retrospectively investigated the predictors of complications among the 36 HD patients who underwent abdominal surgery for gastrointestinal disease. We divided the patients into two groups as follows: the 14 patients who experienced postoperative complications (the WC group) and the 22 patients who did not (the WOC group). The patients' postoperative complications were assessed according to the Clavien—Dindo classification.[12] In this study, Grade II—V adverse events that occurred within 30 days of the surgery were considered to be postoperative complications. Grade I adverse events were excluded because such complications do not require medical treatment. Operative death was defined as any hospital deaths that occurred within the first 30 postoperative days. By contrast, mortality included all hospital deaths. The postoperative complications suffered by the patients are presented in Table 3, which included sepsis in six patients; severe anemia in two patients; shunt failure in two patients; and surgical wound infection, anastomotic stenosis, ileus, colitis, pneumonitis, heart failure, respiratory failure, cerebral infarction, and subarachnoid hemorrhaging in one patient each. Three of these patients succumbed to operative death. Moreover, five of these patients died of diseases related to their postoperative complications, and thus, the overall mortality rate was 14% (5/36).

Table 3 Postoperative complications (duplicate).

	n
Sepsis	6
Severe anemia	2
Shunt failure	2
Surgical wound infection	1
Anastomotic stenosis	1
Ileus	1
Colitis	1
Pneumonitis	1
Heart failure	1
Respiratory failure	1
Cerebral infarction	1
Subarachnoid hemorrhage	1

2.1. Clinicopathological variables

Clinicopathological factors, such as the patients' background data, preoperative status, and surgical factors, were analyzed. Age, sex, body mass index, the use of anticoagulants and/or antiplatelet drugs, preoperative comorbidities (existence of heart disease and diabetes mellitus), the duration of HD, physical status according to the American Society of Anesthesiologists (ASA) classification, and PS were investigated as patient background factors. Preoperative laboratory test results were used to define the patients' preoperative status. As for surgical factors, the type of surgery (i.e., elective or emergency surgery), operative time, and intraoperative blood loss were investigated. In addition, the effects of intraoperative and postoperative transfusions were analyzed. Furthermore, we have summarized the findings obtained for the five patients who died of diseases related to their postoperative complications.

2.2. Statistical analysis

Data are expressed as the mean $\pm$ standard deviation where appropriate. Comparisons (univariate analysis) between the groups were performed using Fischer exact test and the Mann—Whitney *U* test where appropriate. Differences were considered to be statistically significant at p values < 0.05.

3. Results

The overall morbidity and mortality rates were 39% (14/36) and 14% (5/36), respectively. The morbidity and mortality rates of elective surgery were 36.7% (11/30) and 10% (3/30), respectively, whereas those of emergency surgery were 50% (3/6) and 33.3% (2/6), respectively. The morbidity and mortality rates of the patients who underwent emergency abdominal surgery were not significantly higher than those of the patients who underwent elective surgery.

Table 4 Comparison of clinicopathological factors between patients with and without complications.

		Without complications ($n = 22$)	With complications ($n = 14$)	p
Age (y)		66.3 ± 8.2	63.3 ± 10.6	0.6258
Sex				0.1150
	Male	15	13	
	Female	7	1	
Body mass index		20.6 ± 3.0	19.2 ± 3.9	0.3466
Use of anticoagulants and/or antiplatelet drugs (yes/no)		8/14	3/11	0.4672
Heart disease (yes/no)		5/17	4/10	0.7115
Diabetes mellitus (yes/no)		8/14	4/10	0.7272
Duration of hemodialysis (y)		6.1 ± 6.3	9.4 ± 9.2	0.2483
ASA classification		3.1 ± 0.3	3.4 ± 0.5	0.0203*
Performance status		0.3 ± 0.7	0.1 ± 0.5	0.5713
WBC (/μL)		6155 ± 2448	6307 ± 2464	0.4852
Hb (g/dL)		9.5 ± 1.8	9.7 ± 2.0	0.8201
Hct (%)		29.5 ± 5.1	29.2 ± 6.1	0.9741
Plt ($\times 10^4$/μL)		21.1 ± 5.8	19.8 ± 4.3	0.3808
HbA1c (%)		4.8 ± 0.8	4.7 ± 0.6	0.8292
BUN (mg/dL)		40.2 ± 15.3	38.1 ± 17.0	0.6150
Cr (mg/dL)		7.4 ± 1.6	8.3 ± 1.5	0.1117
TP (g/dL)		6.4 ± 0.7	6.4 ± 0.9	0.5663
Alb (g/dL)		3.5 ± 0.5	3.4 ± 0.7	0.7389
T-cho (mg/dL)		156.2 ± 48.6	137.6 ± 39.5	0.2496
TG (mg/dL)		116.4 ± 65.0	83.3 ± 34.0	0.1839
Type of surgery				0.6582
	Elective	19	11	
	Emergency	3	3	
Operative time (min)		191 ± 74	220 ± 76	0.2552
Blood loss (g)		153 ± 174	638 ± 972	0.0013*
Intraoperative or postoperative transfusion (yes/no)		2/20	5/9	0.0842

Data are presented as mean ± SD unless otherwise indicated.
*Statistically significant at $p < 0.05$.
Alb = albumin; ASA = American Society of Anesthesiologists; BUN = blood urea nitrogen; Cr = creatinine; Hb = hemoglobin; HbA1c = hemoglobin A1c; Hct = hematocrit; Plt = platelet count; SD = standard deviation; T-cho = total cholesterol; TG = triglycerides; TP = total protein, WBC = white blood cell count.

3.1. Comparisons of clinicopathological factors between the WC and WOC groups

There were 14 patients in the WC group and 22 patients in the WOC group (Table 4). In the univariate analyses, significant differences in physical status according to the ASA classification ($p = 0.0203$) and intraoperative blood loss ($p = 0.0013$) were detected between the WC and WOC groups. Physical status score according to the ASA classification was higher in the WC group [95% confidence interval (95% CI) 3.132–3.725] than in the WOC group (95% CI 2.960–3.221, $p = 0.0203$), and the same was true for intraoperative blood loss (WC group: 95% CI 76.33–1199; WOC group: 95% CI 75.24–229.9; $p = 0.0013$).

3.2. Summary of the findings obtained for the five patients who died of diseases related to their postoperative complications

Table 5 summarizes the findings we obtained for the five patients who died of diseases related to their postoperative complications. All five patients were male, and their mean age was 61.8 years. Their clinical diagnoses were colorectal cancer in two patients and remnant gastric cancer combined with hepatocellular carcinoma, colorectal perforation, and an intraperitoneal abscess in one patient each. The underlying renal disease was diabetic nephropathy, glomerulonephritis, nephrectomy, and polycystic kidney in one patient each. Data regarding the underlying renal disease were not available for one case. The mean duration of dialysis before the surgery was 13 years. Four of the five patients had coexisting disorders including chronic heart failure in two patients and diabetes mellitus, cerebrovascular disease, angina pectoris, and aortic dissection in one patient each. As for PS, Patient 1 had a PS of 2, and the other patients had a PS of 0. Concerning physical status according to the ASA classification, all of the patients, except Patient 2, were classified as 4. The patients' mean hematocrit value was 29.8%. All of the patients underwent standard laparotomy. Three of the five patients underwent elective surgery, and two patients underwent emergency surgery. The mean duration of the surgery was 210 minutes (range 65–315 minutes), and the mean intraoperative blood loss was 1304 g

Table 5 Patients who died of diseases related to their postoperative complications.

No.	Sex	Age (y)	Diagnosis	Operation method	Comorbidities	ASA	Reason for hemodialysis	Duration of hemodialysis (y)	PS	Hct (%)	Type of surgery	Operative time (min)	Blood loss (g)	Postoperative complications	Postoperative survival period (d)
1	M	68	Remnant gastric cancer and hepato cellular carcinoma	Total gastrectomy	Diabetes mellitus	4	DM	3	2	28.3	Elective	315	3900	Respiratory failure	17
2	M	45	Rectal cancer	Low anterior resection	None	3	GN	12	0	30.7	Elective	175	390	Subarachnoid hemorrhage	34
3	M	68	Colon cancer	Colon resection	Angina pectoris, chronic heart failure, cerebrovascular disease	4	Nephrectomy for RCC	27	0	30.6	Elective	250	460	Cerebral infarction, sepsis	52
4	M	60	Intra peritoneal abscess	Drainage with bowel resection	Chronic heart failure	4	NA	8	0	21.5	Emergency	245	990	Sepsis, heart failure	2
5	M	68	Colon perforation	Drainage with Hartmann's procedure	Aortic dissection	4	PKD	15	0	38.0	Emergency	65	780	Sepsis, DIC	3
Mean ± SD		61.8 ± 10.0				3.8 ± 0.45		13 ± 9.0	0.4 ± 0.9	29.8 ± 5.9		210 ± 95	1304 ± 1471.4		21.6 ± 21.4

ASA = American Society of Anesthesiologists classification; DIC = disseminated intravascular coagulation; DM = diabetes mellitus; GN = glomerulonephritis; Hct = hematocrit; NA = not available; PKD = polycystic kidney; PS = performance status; RCC = renal cell carcinoma; SD = standard deviation.

(range 390–3900 g). Postoperative complications included sepsis in three patients and respiratory failure, subarachnoid hemorrhage, cerebral infarction, and heart failure in one patient each. The mean postoperative survival period was 21.6 days (range 2–52 days).

Patient 1 was diagnosed with remnant gastric cancer and hepatocellular carcinoma. He underwent total gastrectomy for his remnant gastric cancer, and hepatectomy was attempted for his hepatocellular carcinoma. However, we stopped the hepatectomy because of massive intraoperative bleeding. He suffered respiratory failure and died 17 days after the surgery. Patients 4 and 5 required emergency surgery for pan-peritonitis, which had been caused by an intraperitoneal abscess and colon perforation, respectively. Patient 4 underwent drainage and bowel resection, and Patient 5 underwent drainage and Hartmann's procedure. Both of them had developed severe infections before the surgery. Patients 4 and 5 died of their preoperative diseases at 2 days and 3 days after their surgery, respectively. By contrast, Patients 2 and 3 were diagnosed with rectal cancer and colon cancer and underwent low anterior resection and colon resection as elective surgical procedures, respectively. Both of them had uneventful intraoperative courses; however, Patient 2 suffered a subarachnoid hemorrhage and Patient 3 suffered a cerebral infarction after the surgery. As a result, they died 34 days and 52 days after the surgery, respectively.

4. Discussion

In this study, the overall morbidity and mortality rates were 39% (14/36) and 14% (5/36), respectively. These results are congruent with those reported previously.[8–10] The morbidity and mortality rates of the patients who underwent emergency abdominal surgery were not significantly higher than those of the patients who underwent elective surgery (50% and 33.3% vs. 36.7% and 10%, respectively). However, several studies have reported that the morbidity and mortality rates of patients who undergo emergency surgery are higher than those of patients who undergo elective surgery.[8,9]

Patients on HD are at increased risk of postoperative complications because of the presence of metabolic and coagulopathic disorders and significant medical comorbidities, which can lead to renal failure.[13,14] In this study, 25 patients (69.4%) had comorbidities. Hypertension was the most common comorbidity, followed by diabetes mellitus. Hypertension, diabetes mellitus, and atherosclerosis are associated with renal failure.[5] Therefore, we evaluated the relationships between heart disease or diabetes mellitus and the frequency of postoperative complications. As a result, we found that these conditions were not associated with the risk of postoperative complications. Several studies have reported that patients with heart disease or diabetes exhibit a high morbidity rate.[8,14] Therefore, in this study, patients with these conditions were treated appropriately before the surgery because we found that physical status according to the ASA classification was associated with postoperative complications.

In this study, various postoperative complications were observed, and sepsis exhibited a high postoperative

incidence rate. Three of the five patients who died of diseases related to their postoperative complications developed sepsis. Two of the six patients who developed postoperative sepsis had undergone emergency surgery. The latter two patients underwent emergency abdominal surgery due to an intraperitoneal abscess and colon perforation, respectively; therefore, they had infections before the surgery. Toh et al[15] suggested that bacteremia that develops before emergency surgery can cause postoperative infections and/or disseminated intravascular coagulation. However, four of the six patients who developed sepsis during the postoperative period had undergone elective surgery. Infection is the second most common cause of death in patients with end-stage renal disease (ESRD), following cardiovascular causes. HD patients are at risk of infection due in part to their immunocompromised state.[16] Therefore, it is important to take care of HD patients who undergo elective abdominal surgery as well as those who undergo emergency abdominal surgery.

We also found that intraoperative blood loss was particularly associated with postoperative complications. In addition, a weak correlation was detected between the use of intraoperative and postoperative blood transfusions and the frequency of postoperative complications ($p = 0.0842$). Our results concur with the study by Abe and Mafune,[8] in which it was found that perioperative blood transfusions were associated with high complication rates in abdominal surgery for HD patients. The latter study suggested that anemia, low total protein and albumin levels, and decreased concentrations of coagulation factors caused by intraoperative blood transfusions can lead to postoperative complications.[8] Another study has indicated that operative blood loss might be associated with longer periods of systemic and local hypoperfusion, leading to impaired oxygen delivery to vital organs such as the lungs, liver, and kidneys.[17]

In this study, all of the patients who underwent elective surgery received preoperative HD using nafamostat mesilate. By contrast, all of the patients who underwent emergency surgery received preoperative HD using heparin. There was no significant difference in the frequency of postoperative complications between the elective surgery group and the emergency surgery group [11/30 (37%) and 3/6 (50%), respectively]. However, it was reported that nafamostat mesilate, which is an ultrashort-acting multienzyme inhibitor, is a useful anticoagulant for HD as it decreases the risk of bleeding.[6]

Among the patients who died due to postoperative complications, the mean intraoperative blood loss was 1304 g (range 390–3900 g). Two of the five patients (Patients 4 and 5) underwent emergency surgery. Both of them developed sepsis before the surgery, and their preoperative white blood cell counts were 11,200/μL and 800/μL, respectively. The postoperative survival periods of these patients were 2 days and 3 days, respectively. Conversely, of the three patients who underwent elective surgery (Patients 1–3), two of them (Patients 2 and 3) suffered cerebrovascular conditions (subarachnoid hemorrhage in Patient 2 and cerebral infarction in Patient 3). In addition, Patient 3 had previously suffered a cerebral infarction. Cerebrovascular disease is the fourth most common cause of death among patients with ESRD.[2] HD patients display high incidences of in-hospital ischemic and hemorrhagic strokes, and HD is an independent risk factor for early death after an acute intracerebral hemorrhage because HD patients exhibit increased inflammatory activation and disturbances of the coagulation system.[18,19] One of the three patients who underwent elective surgery (Patient 1) suffered respiratory failure immediately after the surgery. Of all the patients, he suffered the greatest amount of operative blood loss (3900 g). Hemorrhagic shock has been reported to be associated with elevated levels of cytokines, such as interleukin-6, and might increase the risk of adult respiratory distress syndrome and/or multiple organ failure.[20]

It was reported that minimally invasive surgery for patients undergoing emergency operations would assist in lowering the risk of complications because such patients have a poor reserve capacity.[21] We consider that abdominal surgery for HD patients with gastrointestinal disease should be minimally invasive and involve little blood loss. To prevent excessive intraoperative blood loss, it is important to select laparoscopic-assisted surgery, perform the minimal required extent of lymph node dissection for cancer surgery, and select two-stage surgery for synchronous double gastrointestinal cancer.

To summarize, the morbidity and mortality rates of HD patients who underwent abdominal surgery for gastrointestinal disease were high. Physical status according to the ASA classification and intraoperative blood loss were found to be associated with postoperative complications. Therefore, patients with comorbidities such as heart disease and diabetes mellitus have to be treated appropriately before the surgery. In addition, minimally invasive abdominal surgery must to be selected for HD patients, and surgeons should perform such operations carefully to avoid excessive blood loss. However, because the sample size in this study is small, further studies with large numbers of patients are needed to establish guidelines for surgical procedures and perioperative treatment in HD patients who undergo abdominal surgery.

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