Table 3 Postoperative complications according to the Clavien–Dindo classification

Complication	Grade 2		Grade 3a		Grade 3b		Grade 4		Grade 5		≥Grade 3a	
	mD2	D2	mD2	D2	mD2	D2	mD2	D2	mD2	D2	mD2	D2
Surgical												
Pancreas-related abscess	2	0	0	0	0	0	0	0	0	0	4	1
Anastomotic leakage	0	0	0	0	1	0	0	0	0	0		
Ileus	0	0	1	0	0	1	0	0	0	0		
Wound infection	1	1	0	0	2	0	0	0	0	0		
Cholecystitis	0	1	0	0	0	0	0	0	0	0		
Medical												
Pneumonia	1	3	0	0	0	0	0	0	0	1	1	3
Cardiac	0	0	0	0	0	0	0	0	0	1		
Liver	0	0	0	0	0	0	0	0	1	0		
Colitis	0	0	0	0	0	0	0	1	0	0		

mD2 modified D2 lymphadenectomy, *D2* D2 lymphadenectomy

patients, and the mortality rate was 3.6 % (95 % CI 0–7.6 %). Among three patients who developed surgical mortality, one who had liver cirrhosis as a co-morbidity died after surgery owing to hepatic failure; the other two died after surgery owing to cardiac or pulmonary disease even though they had no preoperative co-morbidities.

Discussion

This is the first report to focus on the severity of complications after gastrectomy in elderly patients with gastric cancer. Our results demonstrated that the overall morbidity rate was acceptable but that the rate of severe complications was high, suggesting that surgery for gastric cancer in elderly patients is risky.

In the present study, the overall morbidity rate was 18 %, whereas the rates for patients with ≥grade 3a and ≥grade 3b complications were 8.4 % (7/83) and 7.2 % (6/83), respectively. Previously, morbidity and mortality in nonelderly patients (≤75 years of age) were evaluated in the Japan Clinical Oncology Group (JCOG) 9501 Phase III study [3], which compared D2 with D2 plus paraaortic lymphadenectomy. In that study, the overall morbidity rate was 20.9 % after D2, which is similar to that in the present study. Thus, the safety of D2 for elderly patients may be acceptable when the overall morbidity rate alone is considered. In contrast, the rate of reoperation, which is equal to grade 3b in the Clavien–Dindo classification, was 1.9 % in the Phase III study, so the overall rate of ≥grade 3b complications was considered to be high in elderly patients, as shown in this study. Our results strongly suggest that surgery for gastric cancer was risky when the rate of severe complications was considered. When complications occurred in the elderly patients, they rapidly increased in severity. Moreover, surgical mortality was 3.6 % in the present study, which was also higher than the 0.8 % reported in the JCOG 9501 study. Considering the correlation between preoperative co-morbidities and postoperative mortality, two of three patients died owing to cardiac or pulmonary disease even though they had no preoperative co-morbidities. Thus, elderly patients easily develop severe cardiac or pulmonary morbidity even without the presence of preoperative co-morbidities.

When comparing D2 and modified D2, no significant difference in overall morbidity rate or severity of complications was observed, although the surgical procedures in D2 and modified D2 differ, especially for total gastrectomy. The spleen is resected with total gastrectomy using D2 dissection but is preserved for the modified D2 procedure. Recently, the JCOG 0110 Phase III trial [20] clearly showed a difference in morbidity: 30.3 % after total D2 and 16.7 % after total modified D2, with the difference statistically significant. In the present study, total D2 and total modified D2 were performed in 4 and 14 patients, respectively, being selected according to the physician's preference, the patient's co-morbidities, and tumor status. Only a small number of patients underwent D2 total gastrectomy, which may explain why there was no difference in morbidity between the two procedures. In the patients who underwent D2, rather than modified D2 total gastrectomy, morbidity was greatly increased. In contrast, the difference in morbidity after D2 and modified D2 distal gastrectomy was much smaller. Thus, there was no evidence that D2 increased overall morbidity to a greater extent than modified D2. Among the 65 patients who underwent distal gastrectomy, 41 had the D2 procedure and 24 had the modified D2 operation. Thus, there was no possibility that morbidity and mortality were overestimated.

Because the present study was carried out on a case series from a single center, morbidity may have been affected by surgical indication, and this selection bias is its major limitation. In these cases, the surgical indication was determined by five physicians, including an anesthesiologist, who took into consideration activities of daily living, performance status, medical history, physical examinations, and organ functions, as is done in general community hospitals. However, there is a possibility that only patients with good status were selected because our hospital is a regional cancer center that treats only cancer patients. Elderly patients who have co-morbidities and visit general hospitals often undergo surgery at the same hospital where they were diagnosed with gastric cancer.

Furthermore, surgical skill is an important factor determining surgical morbidity. By reviewing our data of nonelderly patients, overall mortality and morbidity (>grade 2) rates in the nonelderly were 0.3 and 13.0 % (precise data not shown), respectively, which were similar or even low when compared with the data of JCOG-9501 [3], suggesting that our surgical skill seems average for a Japanese high-volume cancer center. Thus, the high severe morbidity rate shown for the elderly patients would not be due to inappropriate surgical skill at our institution but to the patients' ages.

To evaluate the possibility of selection bias in this series, their complications and background characteristics were compared with those in previous reports [4, 5, 7, 8, 10–12, 14] (Table 4). In this study, the rate of co-morbid conditions numbering >1 was 72 % (95 % CI 62.3–81.7 %); and rate of those with an ASA score >3 was 20 % (95 % CI 11.4–29.0 %). The morbidity rate was 18 % (95 % CI 9.7–26.2 %). Among the previous studies, the largest series (sample size 249 patients) was reported by Orsenigo et al. [11]. Their rates of co-morbid conditions >1 and morbidity were both greater than in our series, suggesting that the conditions of their patients were slightly worse than ours. The next largest series (sample size 182 patients) was reported by Eguchi et al. [5]. However, they gave no description of co-morbid conditions or ASA scores. The third largest series (sample size 141 patients) was reported by Katai et al. [7]. In their series, the rate of co-morbid conditions was slightly greater and the morbidity rate higher than our findings; also, their ASA scores were similar to our series, suggesting that the patient conditions were slightly worse than in our series. The fourth largest series (sample size 101 patients) was reported by Jeong et al. [14]. The rate of co-morbid conditions and the morbidity rate were similar to those in our series, whereas their ASA scores were better than in our series, suggesting that the patients conditions were fairly similar in the two series. The other four studies had a sample size of <60. Overall, the background characteristics and morbidity rates in the present series did not differ greatly from those of previous reports [5, 7, 11, 14] with more than 100 patients.

In contrast, mortality ranged from 0 to 17.2 % in previous reports, but some authors [4, 5, 7–12, 14] did not evaluate the severity of surgical morbidity (Table 4). In this study, the mortality rate was 3.6 % and that of severe

Table 4 Comparison for previous studies about postoperative complications and preoperative co-morbidities

Study	Postoperative complications					Preoperative co-morbidities	
	Morbidity rate (%)	Mortality rate (%)	Severe morbidity rate (%)			≥1 Co-morbidity (%)	ASA score ≥3 (%)
			≥Grade 3a	≥Grade 3b	Reoperation		
Our cases ($n = 83$)	18.0 (9.7–26.2)	3.6 (0–7.6)	8.4 (2.4–14.4)	7.2 (1.6–12.8)	4.8 (2.0–9.4)	72.0 (62.3–81.7)	20.0 (11.4–29.0)
Kitamura [4] ($n = 60$)	65.0	1.7	ND	ND	ND	65	ND
Eguchi [5] ($n = 182$)	30.8	2.2	ND	ND	ND	ND	ND
Katai [7] ($n = 141$)	27.0	0	ND	ND	1.4	86.5	19.9
Saidi [8] ($n = 24$)	33.3	8.3	ND	ND	ND	50.0	ND
Gretschel [10] ($n = 48$)	23.0	8.0	ND	ND	10.4	83.0	81.0
Orsenigo [11] ($n = 249$)	20.0	3.0	ND	ND	ND	92.0	ND
Pisanu [12] ($n = 23$)	30.4	17.2	ND	ND	ND	74.0	ND
Jeong [14] ($n = 101$)	23.7	0	ND	ND	ND	65.3	7.9
JCOG9502-D2 [18]	20.9	0.8	ND	ND	1.9	ND	ND

Numbers in parentheses are the 95 % confidence intervals

ND Not described

complications was 8.4 % for ≥grade 3a and 7.2 % for ≥grade 3b. Severe complications easily lead to surgical mortality. Although the point estimate of the mortality rate is important, it is affected by whether patients recover from severe complications. Thus, the proportions of severe complications are more reliable measures to evaluate the safety of surgery with a low mortality rate.

Another limitation is that this was a retrospective study performed in a single hospital. Complications were verified retrospectively and graded by examining patient records. To exclude the possibility of description bias, we did not evaluate grade 1 complications. To include the data of patients with grade 1 complications would have two serious problems. One is reliability. Grade 1 complications were defined as "any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions." In other words, grade 1 complications present a deviation from the normal postoperative course but without any additional treatment. Before the Clavien–Dindo classification was developed, we suspect that grade 1 had not been treated as "complications." Thus, retrospective data of grade 1 complications would be unreliable. The other problem is comparability. All retrospective studies [4, 5, 7, 8, 10–12] had no definition of complications. Moreover, they do not know about the Clavien–Dindo classification. We suspect that all retrospective studies had treated complications as >grade 2. In the prospective study, Jeong et al. [14] defined complications as abnormal findings of radiologic tests that had been performed when a complication was clinically suspected, which should mean complications of >grade 2. Thus, when we compare our data with those from other studies, we should treat complications as >grade 2. Thus, the overall incidence of morbidity could be underestimated. However, it is unlikely that severe complications were underestimated because grade 3 requires surgical, endoscopic, or radiologic intervention. To confirm our results, a prospective multicenter trial is needed.

The changes over a long-term period are another concern. Surgical technique, indications, and postoperative care change over time. However, the morbidity and mortality rates did not change during each 5-year period during 1990–2009 (precise data not shown). Thus, high severe morbidity observed in elderly patients may not be prevented even by sophisticated surgical techniques or updated postoperative care.

Conclusions

The overall morbidity rate in this study was acceptable, but the rate of severe complications was high. The latter finding suggests that surgery for gastric cancer in elderly patients is risky and should be limited.

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Ann Surg Oncol
DOI 10.1245/s10434-012-2720-9

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – GASTROINTESTINAL ONCOLOGY

Poor Survival Rate in Patients with Postoperative Intra-Abdominal Infectious Complications Following Curative Gastrectomy for Gastric Cancer

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ABSTRACT

Background. The impact of postoperative complications on recurrence rate and long-term outcome has been reported in patients with colorectal and esophageal cancer, but not in patients with gastric cancer. This study evaluated the impact of postoperative intra-abdominal infectious complications on long-term survival following curative gastrectomy.

Methods. This study included 765 patients who underwent curative gastrectomy for gastric cancer between 2002 and 2006. Patients were divided into 2 groups: with (C-group, $n = 81$) or without (NC-group, $n = 684$) intra-abdominal infectious complications. Survival curves were compared between the groups, and multivariate analysis was conducted to identify independent prognostic factors.

Results. Male patients were dominant, and total gastrectomy was frequently performed in the C-group. The pathological stage was more advanced and D2 lymph node dissection and splenectomy were preferred in the C-group. The 5-year overall survival (OS) rate was better in the NC-group (86.8 %) than in the C-group (66.4 %; $P < .001$). The 5-year relapse-free survival (RFS) rate was also better in the NC-group (84.5 %) than in the C-group (64.9 %; $P < .001$). This trend was still observed in stage II and III patients after stratification by pathological stage. Multivariate analysis identified intra-abdominal infectious complication as an independent prognostic factor for OS (hazard ratio, 2.448; 95 % confidence interval [95 % CI], 1.475–4.060) and RFS (hazard ratio, 2.219; 95 % CI, 1.330–3.409) in patients with advanced disease.

Conclusions. Postoperative intra-abdominal infectious complications adversely affect OS and RFS. Meticulous surgery is needed to decrease the complication rate and improve the long-term outcome of patients following curative gastrectomy.

The present study was presented in part at 2012 Gastrointestinal Cancers Symposium, San Francisco, California, USA, January 19-21, 2012.

First Received: 14 May 2012

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Published online: 18 October 2012

Gastrectomy with R0 resection is inevitable to cure patients with gastric cancer.[1,2] However, even after R0 resection, a significant number of patients suffer from recurrence, particularly after surgery for advanced gastric cancer.[3–5] Tumor depth and lymph node status are well-known prognostic factors, and patient age and performance status have also been reported as having an impact on the long-term outcome of patients.[1,2, 6,7]

In Japan, gastrectomy with D2 lymph node dissection has been the standard treatment for advanced gastric cancer.[8–11] However, Western randomized trials have failed to prove the efficacy of D2 lymph node dissection, presumably because of the increased incidence of postoperative morbidity, which results in increased in-hospital deaths following D2 lymph node dissection.[12–14] Moreover, postoperative morbidity may adversely affect long-term, as well as short-term outcomes in patients.

Previously, the impact of postoperative complications on recurrence rate and long-term outcome has been reported in patients with colorectal cancer and esophageal or esophagogastric junction cancer.[15–23] In the case of colorectal cancer, anastomotic leakage is generally associated with a high local recurrence rate, as well as a poor long-term survival rate.[15–18] Additionally, a strong correlation between postoperative complications and poor long-term outcome has been reported for esophageal and esophagogastric junction cancer.[19,21,23] However, contradictory studies have also been published. Branagan and Finnis [15] reported that anastomotic leakage does not result in poor survival following colorectal surgery. After esophagogastrectomy, Junemann-Ramirez et al.[22] reported that anastomotic leakage does not correlate with poor survival, and Ancona et al.[20] reported that surgical complications themselves do not affect patients' long-term outcomes although survival of patients with both surgical and medical complications was poor.

In patients with gastric cancer, there have been limited reports assessing the relationship between postoperative complications and long-term outcome. Sierzega et al.[7] reported that anastomotic leakage as well as deeper tumor depth, lymph node metastasis, distant metastasis, and poor performance status were found to be independent prognostic factors following total gastrectomy for gastric adenocarcinoma. Their study included 690 patients from 7 university surgical centers in Poland. However, the impact of other postoperative complications on long-term outcome was not investigated, and their study included patients whose surgery was not curative. Moreover, it is unclear whether their results can be adopted by East-Asian countries where the incidence of gastric cancer is high and the reported incidence of postoperative complications is low compared with Western countries.[13,24–26]

The aim of the present study was to clarify the impact of postoperative intra-abdominal infectious complications on the long-term survival rate of patients undergoing curative gastrectomy in one of the highest-volume centers in Japan.

PATIENTS AND METHODS

A total of 765 patients who underwent curative gastrectomy (R0 resection) for gastric cancer at the Shizuoka Cancer Center between September 2002 and October 2006 were included in the present study. Patients who received neoadjuvant or adjuvant chemotherapy, patients who had other cancers and patients who underwent surgery for gastric stump carcinoma were excluded. Patients were also excluded if the histology of the primary lesion was not adenocarcinoma.

The patients' characteristics and pathological and surgical findings were collected from our database records and individual patient electronic medical records. The postoperative clinical course of each patient, including the incidence and severity of intra-abdominal infectious complications, was collected from individual electronic medical records. The data collection and analysis were approved by the institutional review board of the Shizuoka Cancer Center.

Pathological tumor depth, nodal status, and curability of surgery were assigned according to the International Union Against Cancer (UICC) classification, Seventh edition.[27]

Histological type was classified according to the Japanese Gastric Cancer Association (JGCA) classification system, in which tubular and papillary adenocarcinoma are defined as differentiated adenocarcinoma, while poorly differentiated adenocarcinoma, signet-ring cell carcinoma, and mucinous adenocarcinoma are defined as undifferentiated adenocarcinoma.[28]

Definition of Postoperative Intra-abdominal Complications

In this study, the Clavien–Dindo (CD) classification was adopted to classify each patient's postoperative intra-abdominal complication.[29,30] According to the CD classification, patients were classified as having grade II complications if antibiotics were administered. They were classified as grade IIIa or IIIb if surgical intervention was indicated. If patients required admission to the intensive care unit, they were regarded as having grade IVa or IVb complications. Postoperative mortality was defined as a grade V complication. If multiple complications occurred in a single patient, the highest grade was used.

Comparison Between Patients With and Without Complications

Clinicopathological characteristics were compared between patients with postoperative intra-abdominal infectious complications (C-group, $n = 81$) and those without complications (NC-group, $n = 684$). Overall survival time and relapse-free survival time were also compared between the groups.

Statistical Analyses

All continuous variables are presented as the median (range). Statistical analyses were performed using the Fisher exact test, *t* test, and Mann–Whitney test. The 5-year survival rates were calculated using the Kaplan–Meier method, and the log-rank test was used to compare the groups. Independent prognostic factors were identified using the Cox proportional hazards model. In the analysis, each patient's age, sex, histology, type of surgery, degree of lymph node dissection, intraoperative blood loss, operation time, pathological stage, and postoperative intra-abdominal infectious complication were included as covariates. $P < .05$ was considered significant. All statistical analyses were conducted using R Statistics version 2.13.1.

RESULTS

The clinicopathological characteristics of all the patients are shown in Table 1. There was no difference in age between the C-group and NC-group. Male patients

TABLE 1 Clinicopathological characteristics of patients in both groups

	C-group	NC-group	*P* value
Sex (*n*)			.001
Male	68	452	
Female	13	232	
Age (years)			.061
Median	66	64	
Range	31–83	24–88	
Performance status (ECOG)			.545
0 or 1	80	678	
2 or 3	1	6	
Hemoglobin (g/dL)			.577
Median	13.7	13.7	
Range	7.5–16.4	6.3–17.5	
Albumin (g/dL)			.090
Median	4.3	4.3	
Range	2.4–5.0	1.8–5.3	
Lymphocyte count[a]			.352
Median	1920	1700	
Range	870–3450	620–3960	
Surgical procedure (*n*)			<.001
Total gastrectomy	44	142	
Partial gastrectomy	37	542	
Splenectomy (*n*)			<.001
Performed	38	67	
Not performed	43	617	
Lymph node dissection			<.001
<D2	25	431	
≥D2	56	253	
Operation time (min)			<.001
Median	244	186	
Range	125–733	50–725	
Intraoperative blood loss (mg)			<.001
Median	454	250	
Range	50–2650	0–1800	
Postoperative hospital stay (days)			<.001
Median	23	11	
Range	12–308	7–56	
Histology (*n*)			.347
Differentiated	47	355	
Undifferentiated	34	329	
Tumor depth (*n*)			<.001
T1	29	430	
T2	10	70	
T3	29	150	
T4a	11	31	
T4b	2	3	
Lymph node status (*n*)			.004
N0	39	449	
N1	10	88	
N2	17	77	
N3	15	70	
Pathological stage (*n*)			<.001
I	29	440	
II	27	120	
III	21	115	
IV	4	9	

ECOG Eastern Cooperative Oncology Group

[a] Lymphocyte count was measured in 27 patients in the C-group and 189 patients in the NC-group

predominated in both groups and total gastrectomy was frequently performed in the C-group. Preoperative serum albumin level, hemoglobin level, and lymphocyte count were not different between the groups. D2 lymph node dissection and splenectomy were also preferred in the C-group. Operation time was longer and intraoperative blood loss was higher in the C-group than in the NC-group ($P < .001$). More advanced gastric cancer was observed in the C-group than in the NC-group ($P < .001$).

The type and severity of complications are shown in Table 2. Intra-abdominal infectious complications were observed in 11 % (81 of 765) of patients. Pancreas-related infections were the most frequently observed intra-abdominal infectious complication, followed by intra-abdominal abscess and anastomotic leakage. We found 33 % of patients recovered well with medication (grade II), and surgical intervention with local or general anesthesia was required in 62 and 1 % of patients, respectively. One patient died following deterioration of a postoperative intra-abdominal infectious complication. In every pathological stage, grade IIIa complications were the most frequently observed, followed by grade II complications.

We also investigated the number of patients who required readmission because of postgastrectomy syndromes, which included bowel obstruction, cholecystitis, and insufficient oral intake. If patients had a recurrence, admission after the recurrence was not counted. In the C-group, 7 of 81 patients (9 %) required readmission because of a postgastrectomy syndrome. In the NC-group, readmission was required in 32 of 684 patients (5 %; $P = .174$). The most frequent reason for readmission was bowel obstruction in both groups (4 patients in the C-group, and 20 patients in the NC-group; $P = .308$). We investigated serum albumin levels of patients without recurrence 1 year after the surgery to assess nutritional status. There was no difference in the serum albumin level change between the groups ($P = .330$).

Details of the initial recurrence site following gastrectomy are listed in Table 3. Recurrence was observed in 21 of 81 patients (26 %) in the C-group, and 83 of 684 patients (12 %) in the NC-group ($P = .002$). In the NC-group, peritoneal metastasis was the most frequent recurrence pattern followed by lymph node metastasis and liver metastasis. In the C-group, lymph node metastasis was the most frequently observed site of recurrence. Locoregional recurrence was not observed in any of the patients in the C-group even after anastomotic leakage. The pattern of recurrence was not different between the 2 groups ($P = .401$).

In the median follow-up period of survivors of 63 months, the 5-years overall survival rate was better in the NC-group (86.8 %) than in the C-group (66.4 %; $P < .001$). The 5-years relapse-free survival rate was also better in the NC-group (84.5 %) than in the C-group (64.9 %; $P < .001$).

Overall and relapse-free survival curves stratified by pathological stage were compared between the groups (Figs. 1a, b, 2a, b). In patients with stage I early gastric cancer, there were no differences between the groups. Conversely, in patients with stage II and III gastric cancer, overall and relapse-free survival rates were significantly better in the NC-group than in the C-group, except for relapse-free survival time in patients with stage III gastric cancer. In patients with stage III gastric cancer, the 5-years relapse-free survival rate still tended to be better in the NC-group (55.1 %) than in the C-group (41.3 %); however, the difference did not reach significance ($P = .11$).

Table 4 shows the results of the Cox-proportional hazards model used to identify independent prognostic factors for overall survival. In this analysis, only patients with stage II or more advanced disease were included because the survival analysis did not show a survival difference between the 2 groups in patients with pathological stage I disease. Pathological stage (hazard ratio [HR], 2.564; 95 % CI, 1.681–3.912) and intra-abdominal infectious complications (HR, 2.448; 95 % CI, 1.475–4.060) were found to be independent prognostic factors. The same independent prognostic factors were identified for relapse-free survival (pathological stage [HR, 2.657; 95 % CI, 1.782–3.962], and intra-abdominal infectious complications [HR, 2.219; 95 % CI, 1.330–3.409], Table 5).

Figure 3 shows hazard ratio for death among subgroups. The overall survival was analyzed according to sex, age, type of surgery, splenectomy, degree of lymph node dissection, intraoperative blood loss, operation time, histology, pathological tumor depth, and pathological nodal status.

TABLE 2 Details of postoperative intra-abdominal complications

	Grade of CD classification						Total
	II	IIIa	IIIb	IVa	IVb	V	
Type of complication							
Pancreas-related complication	15	27	0	0	0	0	42
Anastomotic leakage	1	14	1	1	1	0	18
Intra-abdominal abscess	11	9	0	0	0	1	21
Pathological stage							
I	11	17	0	1	0	0	29
II	10	17	0	0	0	0	27
III	6	12	1	0	1	1	21
IV	0	4	0	0	0	0	4
Total	27	50	1	1	1	1	81

CD Clavien–Dindo

TABLE 3 Site of initial recurrence after surgery

	C-group			C-group total	NC-group
	Pancreas-related infection	Anastomotic leakage	Intra-abdominal abscess		
Peritoneal metastasis	4	1	1	6	35
Liver metastasis	5	0	1	6	19
Locoregional recurrence	0	0	0	0	5
Lymph node metastasis	8	1	4	13	31
Lung	1	1	0	2	6
Bone	0	0	0	0	5
Other	0	0	0	0	3
Unknown	0	0	0	0	1
Number of cases with recurrence[a]	12	3	6	21	83

[a] Patients with multiple recurrence sites are included for each recurrence site

DISCUSSION

The present study revealed that postoperative complications were strongly associated with poor overall survival time and relapse-free survival time. This trend was also observed even after stratification by pathological stage.

To investigate the prognostic value of postoperative complications, appropriate assessment of the incidence and severity of complications is mandatory. In 2004, Clavien and Dindo proposed the CD classification, which is a treatment-oriented, objective criteria for postoperative complications.[29,30] Recently, a number of reports, including those concerning postgastrectomy morbidities, have

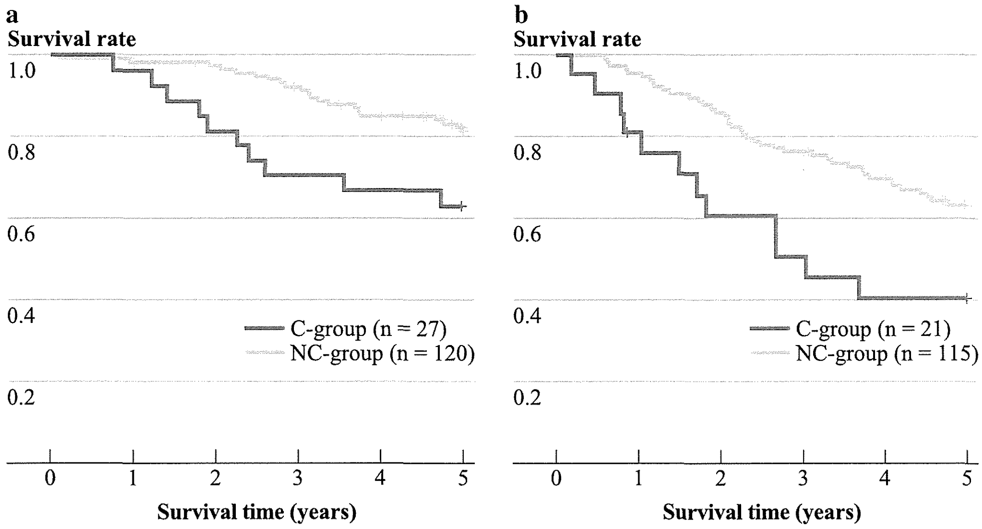

FIG. 1 **a** Overall survival curves of 147 stage II patients who underwent curative gastrectomy for gastric cancer. The 5-year overall survival rate is significantly better in the group of patients without postoperative intra-abdominal infectious complications (NC-group, 81.1 %) than in the group with complications (C-group, 63.0 %; $P = .02$). **b** Overall survival curves of 136 stage III patients who underwent curative gastrectomy for gastric cancer. The 5-year overall survival rate is significantly better in the NC-group (63.3 %) than in the C-group (40.5 %; $P = .03$)

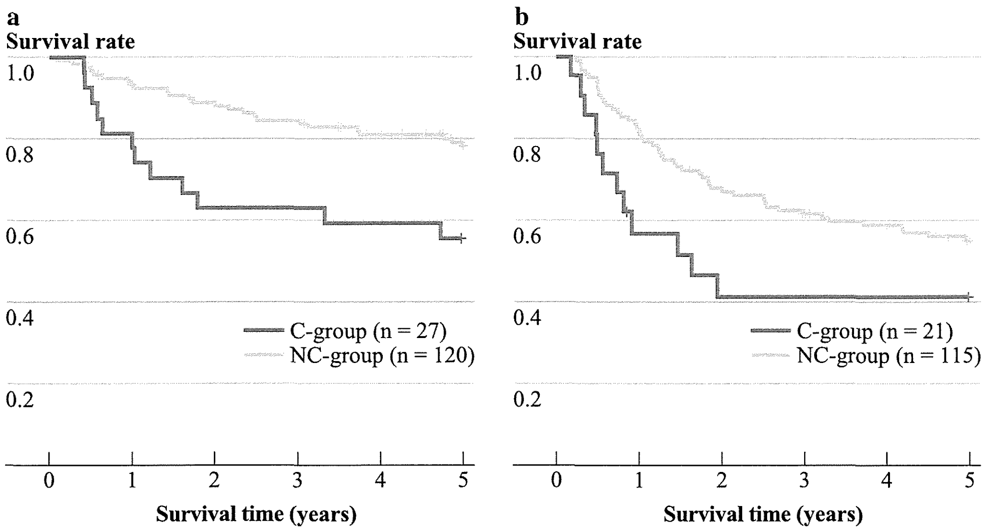

FIG. 2 **a** Relapse-free survival curves of 147 stage II patients who underwent curative gastrectomy for gastric cancer. The 5-year relapse-free survival rate is significantly better in the group of patients without postoperative intra-abdominal infectious complications (NC-group, 78.0 %) than in the group with complications (C-group, 55.6 %; $P = .02$). **b** Relapse-free survival curves of 136 stage III patients who underwent curative gastrectomy for gastric cancer. The 5-year relapse-free survival rate tends to be better in the NC-group (55.1 %) than in the C-group (41.3 %), although the difference is not significant ($P = .11$)

adopted the CD classification to evaluate postoperative problems.[31,32] In contrast, previous studies that investigated the effect of complications on long-term outcomes following surgeries generally used their own criteria to grade the severity of the complications, making it difficult to evaluate the results of the study[15–23] In the present study, to overcome this potential problem, we used the CD classification to assess the severity of complications. In the present study, patients with grade II or more severe intra-abdominal infection were regarded as having complications since we considered these complications to cause systemic inflammatory response syndrome, resulting in excess surgical trauma and tissue damage.

Administration of perioperative chemotherapies has been accepted as it increases the survival rate of patients with advanced gastric cancer.[33–36] In Japan, postoperative administration of S-1 for 1 year after curative surgery has been a standard treatment in patients with advanced gastric cancer since the results of a prospective randomized controlled trial were reported in October 2006.[33] Therefore, in the present study, we only included patients who underwent surgery before 2006 and excluded patients who received neoadjuvant chemotherapy to eliminate the effects of perioperative chemotherapies.

It is unclear why postoperative intra-abdominal infectious complications affect the long-term outcome of

TABLE 4 Results of multivariate analysis to identify independent prognostic factors for overall survival

Covariates	*P* value	Hazard ratio (HR)	95 % CI
Age (≥ 65 vs < 65 years)	.138	1.241	.933–1.651
Sex (male vs female)	.683	1.099	.700–1.725
Surgery (total gastrectomy vs partial gastrectomy)	.496	1.165	.751–1.806
Histology (differentiated vs undifferentiated)	.162	1.340	.889–2.022
pStage (III, IV vs II)	<.001	2.564	1.681–3.912
Duration of surgery (≥ 200 vs < 200 min)	.773	.949	.666–1.353
Intraoperative blood loss (≥ 300 vs < 300 mL)	.057	.726	.523–1.009
Intra-abdominal infectious complications (yes vs no)	<.001	2.448	1.475–4.060
Lymph node dissection (≥ D2 vs < D2)	.248	.761	.478–1.210

CI confidence interval

TABLE 5 Results of multivariate analysis to identify independent prognostic factors for relapse-free survival

Covariates	*P* value	Hazard ratio (HR)	95 % CI
Age (≥ 65 vs < 65 years)	.213	1.187	.906–1.555
Sex (male vs female)	.590	1.127	.729–1.743
Surgery (total gastrectomy vs partial gastrectomy)	.747	.933	.614–1.419
Histology (differentiated vs undifferentiated)	.375	1.191	.810–1.751
pStage (III, IV vs II)	<.001	2.657	1.782–3.962
Duration of surgery (≥ 200 vs < 200 min)	.492	1.123	.807–1.562
Intraoperative blood loss (≥ 300 vs < 300 mL)	.140	.795	.586–.178
Intra-abdominal infectious complications (yes vs no)	.002	2.219	1.330–3.409
Lymph node dissection (≥ D2 vs < D2)	.135	.716	.462–1.110

CI confidence interval

patients. Following colorectal surgery, it was reported that anastomotic leakage increased the rate of local recurrence presumably due to viable colorectal cancer cells being deposited extraluminally into the pelvis.[16–18] However, in the present study the incidence of local recurrence did not increase even after anastomotic leakage; thus, we consider implantation of cancer cells into the abdominal cavity not a contributing factor in the present series.

Another possible factor promoting metastatic growth and early recurrence is immune suppression.[37,38] Specifically, cell-mediated immunity, in particular natural killer cells and cytotoxic T lymphocytes, is compromised, and the degree of suppression is considered to be related to the extent of surgical trauma and tissue damage. Goldfarb et al. reported treatment aimed at perioperative enhancement of cell-mediated immunity with simultaneous inhibition of excessive catecholamine and prostaglandin responses could be successful in limiting postoperative immune suppression and metastatic progression.[38] In the C-group, postoperative intra-abdominal infectious complications increased surgical stress and caused severe tissue damage due to local and generalized inflammatory reactions, resulting in more severe immune suppression than in the NC-group. We consider, therefore, that the difference in the degree of immune suppression between the groups is a possible contributing factor to the survival difference between the groups.

The present retrospective study has limitations. Firstly, backgrounds were different between patients with and without complications. Of different backgrounds, pathological stage is assumed to be the strongest prognostic factor for gastric cancer following curative gastrectomy.[1,2,6] Therefore, we stratified patients by their pathological stage, and multivariate analysis was conducted. Even after stratification, the same trend, better survival outcomes in patients without intra-abdominal infectious complications, was still observed in stage II and III patients. Multivariate analysis also identified intra-abdominal infectious complications as an independent prognostic factor. In addition, we investigated hazard ratio for death among subgroups. In each subgroup, long-term outcome tended to be better in the NC-group than in the C-group. Secondly, the degree of immune suppression was not assessed in this study. This should be examined in a future trial to clarify whether our hypothesis, that patients with intra-abdominal infectious complications have severe immune suppression resulting in high recurrence rates and poor overall and relapse-free survival rates, is correct or not.

D2 lymph node dissection and splenectomy were frequently performed in the C-group, and these procedures were thought to increase the incidence of intra-abdominal infectious complications. We also investigated the effect of D2 lymph node dissection on long-term survival rate by

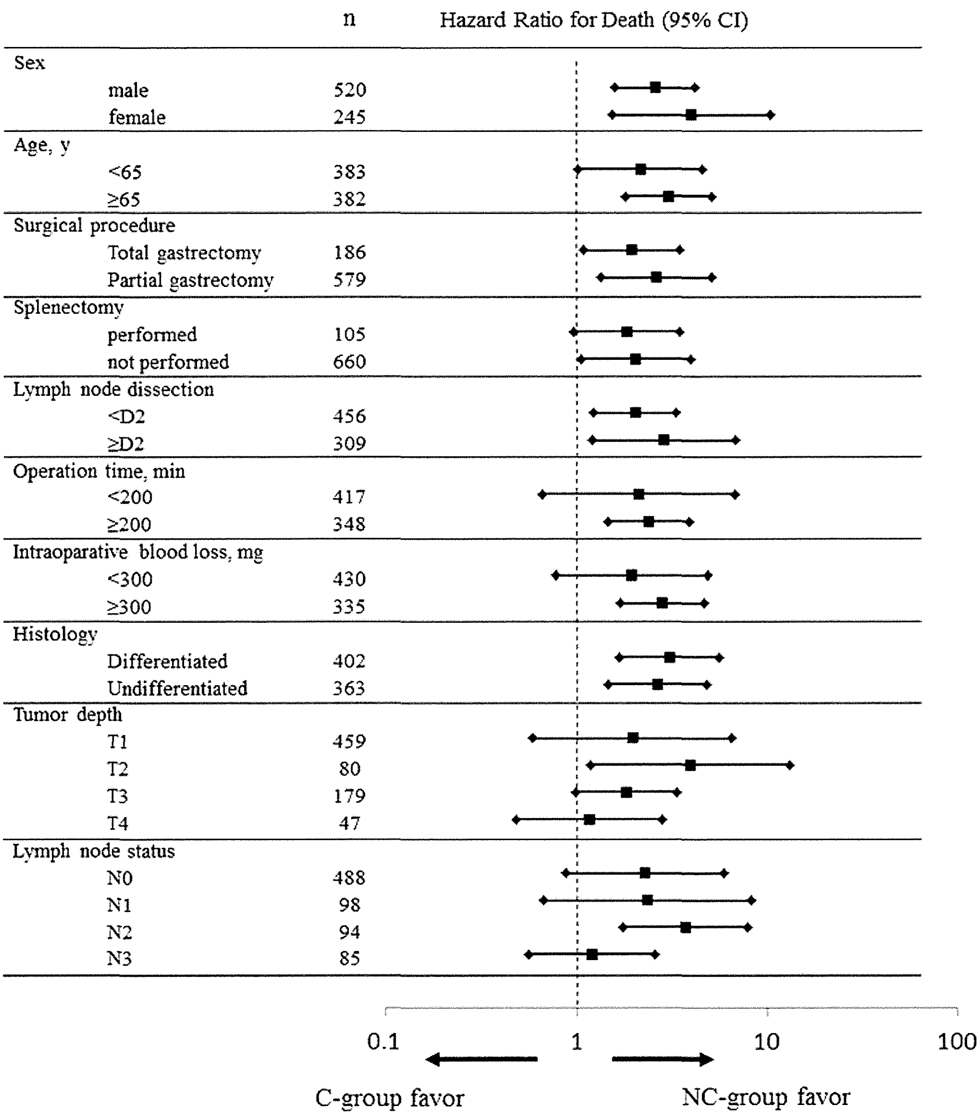

FIG. 3 Hazard ratio for death among subgroups. Long-term survival is better in NC-group than in C-group in most subgroups

multivariate analysis, and it was not identified as an independent prognostic factor. In addition, splenectomy was not identified as an independent prognostic factor even when we included it as a covariate instead of D2 lymph node dissection (data not shown). In Western countries, the most recent European Society for Medical Oncology clinical practice guidelines recommend a D2 gastrectomy as the standard procedure for curable advanced gastric cancer.[39,40] However, in their guidelines, splenectomy is only indicated if there is direct invasion, presumably due to the increased morbidity and mortality seen in 2 European randomized controlled trials.[12–14] In Japan, splenectomy is still a standard treatment for patients with upper-third advanced gastric cancer, although early results from a randomized clinical trial investigating the efficacy of splenectomy showed an increased incidence of postoperative pancreas-related infections. The effect of splenectomy on the long-term survival rate is still unclear even in Japan, and we have to wait for the final results of the randomized clinical trial.[41]

Perhaps surgeons have the urge to decrease postoperative complications in order to improve early surgical outcomes. However, the results of the present study show there are also poor long-term outcomes in patients with postoperative intra-abdominal infections. Therefore, surgeons must perform the surgery with extreme precision, not only to decrease postoperative complications, but also to improve long-term outcomes for patients.

In conclusion, postoperative intra-abdominal infectious complications adversely affect the overall and relapse-free survival of patients with stage II and III advanced gastric cancer. Surgeons have to perform the surgery with meticulous care in order to decrease the complication rate and improve the long-term outcome of patients following curative gastrectomy.

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Gastric Cancer (2012) 15:206–212
DOI 10.1007/s10120-011-0099-0

ORIGINAL ARTICLE

Intra-abdominal infectious complications following gastrectomy in patients with excessive visceral fat

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Received: 15 May 2011 / Accepted: 11 September 2011 / Published online: 13 October 2011

Abstract
Background Excessive visceral fat may be a better predictor of the development of postoperative morbidity after gastrectomy than body mass index (BMI). The aim of the present study was to clarify the most appropriate fat parameter to predict pancreas-related infection and anastomotic leakage following gastrectomy.
Methods The study was performed in 206 patients who underwent curative gastrectomy at the Shizuoka Cancer Center between April 2008 and March 2009. Relationships between fat parameters, including visceral fat area (VFA), and early surgical outcomes were investigated. The risk factors for pancreas-related infection and anastomotic leakage were identified using univariate and multivariate analyses.
Results There was no strong association between any of the fat parameters and operating time, intraoperative blood loss, the number of lymph nodes retrieved, or the duration of the postoperative hospital stay. Pancreas-related infection occurred in 18 patients (8.7%), whereas anastomotic leakage was observed in 10 patients (4.9%). Of all the fat parameters, only VFA was found to be an independent risk factor for both pancreas-related infection and anastomotic leakage, with odds ratios (95% confidence intervals) of 1.015 (1.005–1.025) and 1.010 (1.000–1.021), respectively.
Conclusions Excessive visceral fat, represented by the VFA, was found to be an independent risk factor for both pancreas-related infection and anastomotic leakage following gastrectomy.

Keywords Gastric cancer · Gastrectomy · Visceral fat · Postoperative complication

Introduction

Surgery is the only treatment strategy that offers the hope of a cure for gastric cancer patients. In Japan, in which the rates of gastric cancer are greater than those in Western countries, gastrectomy with D2 lymph node dissection is a well-established and widely accepted procedure [1, 2]. Although two large randomized controlled trials in Europe failed to demonstrate the efficacy of this procedure, due, in part, to increased postoperative morbidity and mortality [3, 4], recent reports suggest that gastrectomy with D2 lymph node dissection may be beneficial in certain patients [3–6]. One of the reasons for the unfavorable outcomes of gastrectomy with D2 lymph node dissection in the European studies may have been the higher proportion of obese patients in those studies.

Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify obesity. In Japan, the median BMI of gastric cancer patients, as well as that of the general population, has increased in recent years [7]. Although a relationship between BMI and postoperative morbidity has been reported previously, it remains contentious whether a high BMI is really associated with an increased rate of postoperative morbidity [8–12]. Recently, several reports have suggested that visceral fat area (VFA) is more strongly associated with postoperative intra-abdominal infectious complications, including pancreas-related infection and anastomotic leakage, than BMI [13, 14]. However, this issue is also contentious.

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Therefore, in the present study we investigated the relationships between various fat parameters, including VFA, and early surgical outcomes following gastrectomy to clarify the most appropriate fat parameter to predict the development of pancreas-related infection and anastomotic leakage.

Methods

Patients

Between April 2008 and March 2009, a total of 217 patients underwent open distal or total gastrectomy with curative intent for primary gastric cancer at Shizuoka Cancer Center, Shizuoka, Japan. Patients who underwent splenectomy, distal pancreatic resection, and cholecystectomy were included in the study, whereas seven patients who underwent combined resection of other organs (liver, colon, and adrenal gland) and four patients who had synchronous cancer in other organs (colon, rectum, and kidney) were excluded from the study. Therefore, data from 206 patients were analyzed in the present study.

Lymph node station number, the degree of lymph node dissection, and pathological stage were determined on the basis of the *Japanese classification of gastric carcinoma* [15] and the *Gastric cancer treatment guidelines in Japan* [16]. Gastrectomy with D2 lymph node dissection was performed in patients with advanced gastric cancer, whereas D1 plus beta lymph node dissection (i.e., D1 + numbers 7, 8a, 9) was performed in patients with early gastric cancer.

Fat measurement

Multidetector computed tomography (MDCT) was performed in all patients prior to surgery. Patients were examined while in the supine position, with their arms stretched above their heads, at the end of inspiration, using a CT scanner (Aquilion; Toshiba Medical Systems, Tokyo, Japan). Parameters for scanning were: tube voltage, 120 kVp; scan time, 0.5 s; and reconstruction slice thickness, 2 mm. The tube current was determined automatically by the CT automatic exposure control system. The images obtained were transferred to a Ziostation workstation (Ziosoft, Tokyo, Japan), which was used to quantify the total fat area (TFA), subcutaneous fat area (SFA), and VFA at the level of the umbilicus. In the present study, relationships between early surgical outcomes following gastrectomy and TFA, VFA, SFA, and BMI, as the fat parameters, were investigated.

Definition of early surgical outcomes

Operating time, intraoperative blood loss, the number of lymph nodes retrieved, postoperative morbidity and mortality, and the duration of the postoperative hospital stay were investigated as early surgical outcomes.

Patients with Grade II or greater complications based on the Clavien-Dindo classification were defined as having postoperative morbidity [17]. In the present study, pancreas-related infection was diagnosed on the basis of the definitions of the International Study Group on Pancreatic Fistula (ISGPF) [18]. Diagnosis of anastomotic leakage was confirmed by radiological examination using contrast media. Postoperative mortality was defined as any death within 30 postoperative days (PODs).

Statistical analysis

Spearman's rank correlation coefficient was used to evaluate relationships between individual fat parameters (BMI, TFA, SFA, and VFA) and early surgical outcomes (operating time, intraoperative blood loss, number of lymph nodes retrieved, postoperative hospital stay). Relationships between individual fat parameters and the categorical variables of pancreas-related infection and anastomotic leakage were evaluated using logistic regression.

To identify independent risk factors for each of the intra-abdominal infectious complications, a multivariate logistic regression model with forward selection was used, with BMI, TFA, SFA, VFA, age, sex, operating time, intraoperative blood loss, number of lymph nodes retrieved, surgical procedure (total or distal gastrectomy), type of lymph node dissection (D2 or D1 plus beta), and splenectomy (yes or no) included as covariates.

All statistical analyses were performed using SPSS version 13.0 (SPSS, Chicago, IL, USA). All continuous data are presented as medians (ranges). $P < 0.05$ was considered significant.

Results

Patients' characteristics

The patients' characteristics are given in Table 1. Total gastrectomy was performed in 48 patients, 29 of whom also underwent splenectomy for the removal of splenic hilar lymph nodes. Additional pancreatosplenectomy was performed in 2 of the 48 patients. The remaining 158 patients underwent distal gastrectomy. D2 lymph node dissection was performed in 111 patients, whereas 95 patients underwent D1 plus beta lymph node dissection.

Table 2 lists the early surgical outcomes of all patients. Postoperative complications were observed in 55 patients (26.7%). The incidence of pancreas-related infection and anastomotic leakage was 8.7% and 4.9%, respectively. Five patients had both pancreas-related infection and

Table 1 Clinocopathological characteristics of patients

Age (years)	65.9 (39–89)
Sex (male/female)	146/60
Diabetes mellitus (*n*)	17
Individual fat parameter	
BMI (kg/m^2)	23 (16.0–32.3)
TFA (cm^2)	198 (6.9–505.8)
SFA (cm^2)	107.4 (3.0–266.9)
VFA (cm^2)	90.5 (3.6–262.5)
Surgical procedure (*n*)	
Total gastrectomy	48
Distal gastrectomy	158
Lymph node dissection (*n*)	
D2	111
D1 plus beta	95
Splenectomy (*n*)	
Yes	29
No	177
Pathological stage (*n*)	
IA	88
IB	48
II	44
IIIA	15
IIIB	9
IV	2

Unless indicated otherwise, values are means, with ranges given in parentheses

BMI body mass index, *TFA* total fat area, *SFA* subcutaneous fat area, *VFA* visceral fat area

Table 2 Early surgical outcomes of 206 patients

Operating time (min)	194 (103–489)
Intraoperative blood loss (mL)	265 (13–2606)
No. of lymph nodes retrieved	37 (8–109)
Postoperative complications	55 (26.7%)
Pancreas-related infection	18 (8.7%)
Anastomotic leakage	10 (4.9%)
Postoperative hospital deaths	1 (0.5%)
Duration of postoperative hospital stay (days)	11 (7–87)

Values are presented as either median with ranges in parentheses or as the number of patients in each group, with percentages in parentheses

anastomotic leakage. Both of the two patients who underwent distal pancreatectomy had pancreas-related infection. Postoperative mortality was observed in one patient (0.5%). This patient had undergone distal gastrectomy with D2 lymph node dissection, and anastomotic leakage developed on POD 7. This patient died suddenly on POD 9 due to a pulmonary embolism.

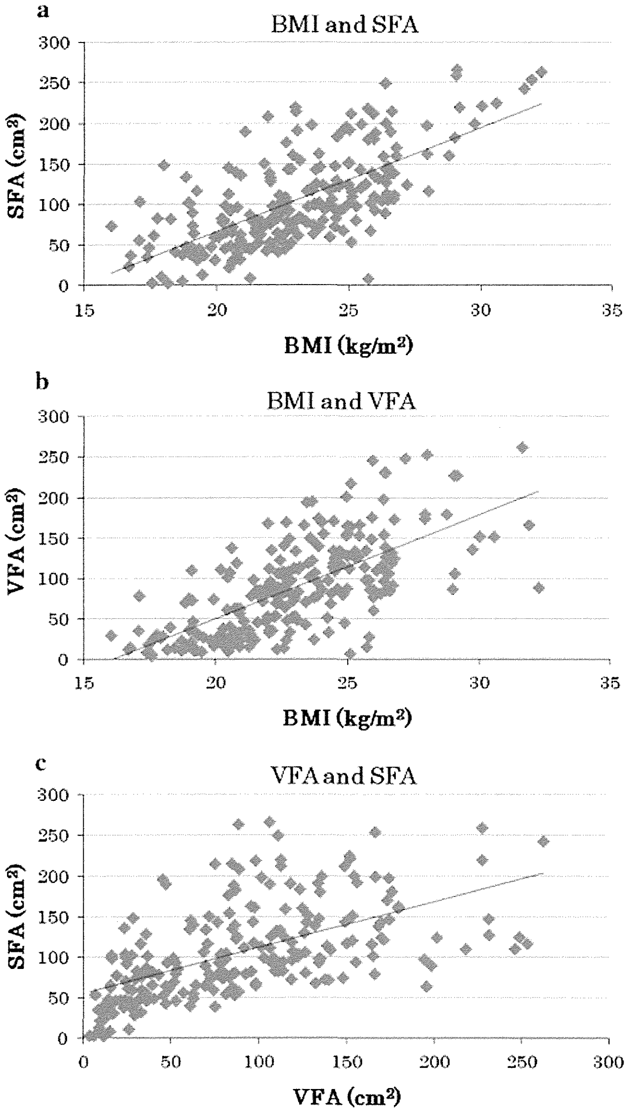

Fig. 1 Correlations between **a** superficial fat area (*SFA*) and body mass index (*BMI*); $R = 0.672$, $P < 0.001$, **b** visceral fat area (*VFA*) and BMI; $R = 0.683$, $P < 0.001$, and **c** SFA and VFA; $R = 0.555$, $P < 0.001$. Significant associations were observed for all comparisons

Relationships between fat parameters and early surgical outcomes

Figure 1 shows the correlations between SFA, VFA, and BMI. Significant correlations were found between SFA and both BMI and VFA, as well as between VFA and BMI. Correlation coefficients for each of the fat parameters and operating time, intraoperative blood loss, number of lymph nodes retrieved, and postoperative hospital stay are given in Table 3. Although VFA was weakly associated with prolonged operating time (correlation coefficient 0.304) and increased intraoperative blood loss (correlation coefficient 0.371), no significant relationships were observed for any of the fat parameters and operation time,

Table 3 Relationship between fat parameters and early surgical outcome data

	Intraoperative blood loss	Operating time	No. of lymph nodes retrieved	Postoperative hospital stay
BMI	0.295 (<0.001)	0.235 (0.001)	−0.196 (0.005)	0.011 (0.872)
TFA	0.322 (<0.001)	0.250 (<0.001)	−0.134 (0.055)	0.103 (0.139)
SFA	0.199 (0.004)	0.153 (0.028)	−0.022 (0.756)	0.025 (0.726)
VFA	0.371 (<0.001)	0.304 (<0.001)	−0.197 (0.005)	0.155 (0.026)

Values are the correlation coefficients, with *P* values given in parentheses

BMI body mass index, *TFA* total fat area, *SFA* subcutaneous fat area, *VFA* visceral fat area

Table 4 Identification of risk factors for the development of pancreas-related infection and anastomotic leakage, determined using univariate analysis

	Pancreas-related infection			Anastomotic leakage		
	Odds ratio	95% CI	*P*	Odds ratio	95% CI	*P*
BMI (kg/m^2)	1.318	1.121–1.548	0.001	1.156	0.946–1.411	0.156
TFA (cm^2)	1.009	1.004–1.014	0.001	1.003	0.997–1.009	0.291
SFA (cm^2)	1.008	1.001–1.016	0.035	0.999	0.987–1.010	0.802
VFA (cm^2)	1.016	1.008–1.025	0.001	1.010	1.000–1.021	0.042
Age (years)	0.978	0.934–1.023	0.332	0.997	0.937–1.061	0.923
Sex (male or female)	2.335	0.655–8.323	0.191	1.681	0.346–8.158	0.519
Intraoperative blood loss (mL)	1.002	1.001–1.003	0.001	1.001	1.000–1.002	0.227
Operating time (min)	1.010	1.003–1.018	0.007	1.006	0.996–1.016	0.234
No. of lymph nodes retrieved	0.987	0.954–1.021	0.458	0.961	0.912–1.012	0.133
Surgical procedure (total or distal)	5.574	2.094–14.841	0.001	2.303	0.622–8.526	0.212
Lymph node dissection (D2 or D1)	3.555	1.137–11.110	0.029	1.300	0.356–4.751	0.692
Splenectomy (yes or no)	7.515	2.729–20.694	0.001	0.667	0.081–5.468	0.706

CI confidence interval, *BMI* body mass index, *TFA* total fat area, *SFA* subcutaneous fat area, *VFA* visceral fat area

intraoperative blood loss, the number of lymph nodes retrieved, or the duration of the postoperative hospital stay.

Risk factors for intra-abdominal infectious complications

Tables 4 and 5 list the results of univariate and multivariate analyses used to identify risk factors for intra-abdominal infectious complications. On the basis of the univariate analysis, all fat parameters, operating time, intraoperative blood loss, surgical procedure, type of lymph node dissection, and splenectomy affected the development of pancreas-related infection. Multivariate analysis revealed that VFA, intraoperative blood loss, and splenectomy were independent risk factors for pancreas-related infection, with odds ratios (95% confidence intervals) of 1.015 (1.005–1.025), 1.001 (1.000–1.003), and 7.125 (2.083–24.372), respectively. With regard to anastomotic leakage, both univariate and multivariate analyses revealed VFA as a risk factor for the development of anastomotic leakage, with an odds ratio (95% confidence interval) on multivariate analysis of 1.010 (1.000–1.021).

Table 5 Multivariate analysis identification of independent risk factors for the development of pancreas-related infection

	Odds ratio	95% CI	*P*
VFA (cm^2)	1.015	1.005–1.025	0.004
Intraoperative blood loss (mL)	1.001	1.000–1.003	0.009
Splenectomy (yes or no)	7.125	2.083–24.372	0.002

CI confidence interval, *VFA* visceral fat area

In order to justify the use of correlation analysis to find risk factors for the surgical complications, it was mandatory to prove that the fat components did not relate to outcomes in binomial fashion. To do so, we divided the patients into 4 groups according to the VFA (<35.8, 35.8–85.6, 85.6–126.5, and >126.5 cm^2), and looked at the incidence of surgical complications in each group. Pancreas-related complications were observed in 0, 2, 8, and 8 patients, respectively, in these 4 groups, showing that the relationship between VFA and surgical complications was not binomial.

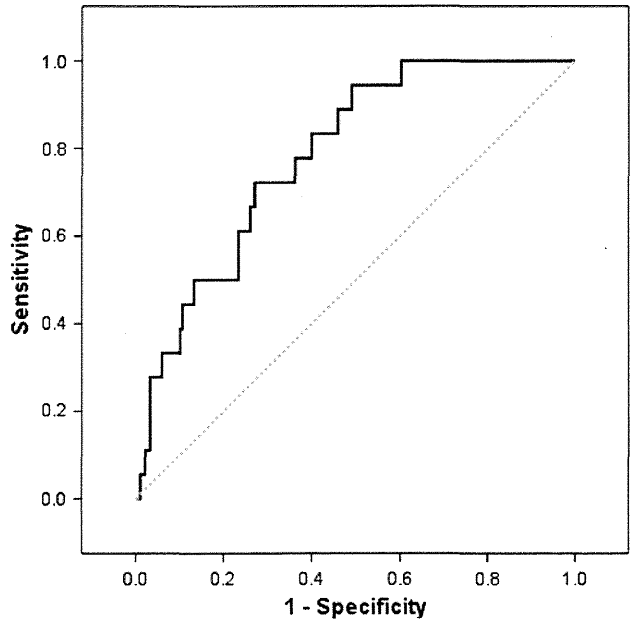

Fig. 2 Receiver operating characteristic (ROC) curve to identify the appropriate cut-off value of VFA to predict pancreas-related infection. The area under the curve (AUC) was 0.787 and the threshold of VFA was 113.6 cm^3 with sensitivity of 72.2% and specificity of 62.9%

The cut-off value for VFA as an indicator of pancreas-related infection

Figure 2 shows the receiver operating characteristic (ROC) curve used to identify the appropriate cut-off value of VFA to predict pancreas-related infection. The area under the curve (AUC) was 0.787 and the threshold of VFA was 113.6 cm^2 with sensitivity of 72.2% and specificity of 62.9%.

Discussion

The incidence of postoperative morbidity following gastrectomy with lymph node dissection (D2 or more) has been reported to be 17–21% in eastern Asia [19, 20] and 21–46% in Europe [3, 4, 21–25]. Previous studies of the risk factors for postoperative morbidity indicate that obesity, defined as BMI > 25 kg/m^2, is one of the most important [8–10]. The recent development of specific computer software has enabled the easy calculation of the amount of visceral fat, and some authors have suggested that the VFA may be a better predictor of the development of postoperative morbidity than the BMI [13, 14].

Of all morbidities, intra-abdominal infectious complications, including pancreas-related infection and anastomotic leakage, are potentially fatal complications; thus, in the present study, we investigated independent risk factors for both of these complications. Although Tokunaga et al. [13] have reported that excessive visceral fat is a risk factor for postoperative intra-abdominal infectious complications and Tanaka et al. [14] have reported that the amount of visceral fat affects the development of pancreas-related infection, independent risk factors for both complications had not been investigated simultaneously in previous studies. In the present study, we determined the factors affecting the development of both pancreas-related infection and anastomotic leakage.

The results of the present study indicate that a high VFA is associated with the development of both pancreas-related infection and anastomotic leakage following gastrectomy. To date, the risk factors for anastomotic leakage after gastrectomy have not been completely clarified [26]. Both Ser et al. [27] and Kang et al. [28] have reported that anastomotic leakage may occur in cases in which there is excess tension and pressure on the anastomotic site and that these conditions are more frequently observed in patients with excessive visceral fat because the thick mesentery creates tension on the anastomosis. In addition, a deeper surgical field in these patients, and preoperative comorbidities, such as cardiovascular disease or diabetes mellitus, which are frequently seen in obese patients, may affect the development of anastomotic leakage [29–31].

In the present study, pancreas-related infections were observed in 18 patients (8.7%), with splenectomy, intraoperative blood loss, and VFA identified as independent risk factors. Splenectomy is a well-known and widely accepted risk factor, because manipulation of the tail of the pancreas during the procedure increases the risk of pancreas-related infection [6, 14, 31]. In Europe, the final results of the Dutch D1D2 trial recommended D2 gastrectomy. However, they also recommended that the spleen should be preserved, because of increased morbidity and mortality after splenectomy [32]. In Japan, though the current standard treatment for upper-third gastric cancer is a total gastrectomy with splenectomy, a recent randomized controlled trial revealed a high incidence of postoperative complications after splenectomy [33]. We should await final survival analysis of this study before we conclude whether or not the spleen has to be preserved. Distal pancreatectomy has been thought to be correlated with pancreas-related complications. In the present study, actually, both of the two patients with pancreatectomy had this complication. However, the number was so small that further analysis could not be done.

In the present study, excessive visceral fat also increased the incidence of pancreas-related infection. It has been proposed that excessive visceral fat makes it difficult to find the border between the pancreas and lymph nodes, which may result in intraoperative pancreatic injury [13, 14]. Our ROC analysis revealed that a VFA of 113.6 cm^2

was an appropriate cut-off value. Careful surgery will be required particularly in these patients having a VFA of 113.6 cm^2 or more.

Although the present study identified a significant relationship between intraoperative blood loss and pancreas-related infection, others have reported that increased bleeding does not affect the incidence of pancreas-related infection [34, 35]. We believe that increased bleeding may have created difficulties in identifying the border between the pancreas and lymph nodes, as occurs in patients with excessive visceral fat, thus contributing to an increased incidence of pancreas-related infection.

Preoperative co-morbidities have also been considered to affect the incidence of postoperative complications. Also, poor nutritional status due to advanced primary gastric cancer may be associated with a high incidence of postoperative complications. However, in the present study, the patients' preoperative nutritional status (performance status, serum albumin level) and co-morbidities (diabetes mellitus, hypertension) were not associated with the incidence of intra-abdominal infectious complications (data not shown).

In conclusion, excessive visceral fat, represented by the VFA, was found to be an independent risk factor for both pancreas-related infection and anastomotic leakage following gastrectomy. Greater diligence during surgery is necessary for patients with excessive visceral fat, particularly if splenectomy has to be performed simultaneously.

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