

Original Article

Identification of frequency, severity and risk factors of complications after open gastrectomy: Retrospective analysis of prospectively collected database using the Clavien-Dindo classification

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Introduction

The purpose of this study was to identify the frequency, severity, and risk factors of complications after open gastrectomy using the Clavien-Dindo classification because institution-specific criteria were mostly used in the previous articles.

Materials and Methods

All complication data were obtained from our prospectively collected database of open gastrectomy from January 1999 to December 2012 ($n=539$). Complications were classified into either major surgical complications such as pancreatic fistula, abdominal abscess, and anastomotic leakage, or others. Frequency and severity were graded retrospectively according to the Clavien-Dindo classification for subsequent analysis of risk factors.

Results

There were 222 events occurred in 156 patients (28.9%). Complications of grade IIIa or greater were 8.3% for major surgical complications and 10.6% for all complications. The mortality rate was 1.1%. Blood loss was the only independent risk factor for major surgical complications of grade IIIa or greater (odds ratio 1.923, 95% Confidence Interval

0.320–0.786, $p=0.003$). Total gastrectomy was the only independent risk factor for all complications of grade IIIa or greater (Odds ratio 2.075, 95% Confidence Interval 0.260–0.896, $p=0.021$).

Discussion

The present study provided the objective overview regarding complications after open gastrectomy. Blood loss and total gastrectomy were revealed as the significant risk factors for complications.

Key Words: Open gastrectomy, Complication, Risk factor, Clavien-Dindo Classification, Blood loss.

Introduction

Although the mortality of gastric cancer has been decreasing in recent years, it is still the main cause of cancer-related deaths, and, in Japan in particular, it is the second leading cause of cancer-related deaths^{1, 2}. Chemotherapy and molecular targeted therapy have made progress^{3, 4}, but the most effective treatment is still gastrectomy with adequate lymph node dissection, and the standard procedure in many countries such as Japan and Korea is gastrectomy with D2 lymph node dissection⁵.

In surgical treatment, the frequency and severity of complications strongly affect patient's postoperative hospital stay, increased medical expenses, and delayed adjuvant chemotherapy. The complications of open gastrectomy seems to have been well investigated to date, but the complications in the most of the articles have been assessed according to the criteria of each institution, because there had been no standard criterion

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for evaluating complications in the past. Therefore, it is quite difficult to compare the results among the previous reports. Even certain reliable reports also use the criteria of each institution^{6, 7}. Thus, the actual frequency and severity of complications after open gastrectomy are not fully recognized in terms of objective and unified criteria.

In 2004, Dindo *et al.* put forward the Clavien-Dindo classification, which defines the severity according to the treatment for each complication⁸. This classification system is objective, simple, reproducible, and easy to understand, making the results easy to understand and compare among different reports. Thus in the present study, frequency, severity, and risk factors

of complications after open gastrectomy for primary gastric cancer were evaluated using the Clavien-Dindo classification.

Materials and Methods

Data collection

From January 1999 to December 2012, 623 patients underwent open gastrectomy in the department of Gastric Surgery, Tokyo Medical and Dental University, Tokyo, Japan. The cases of total and distal gastrectomy with lymphadenectomy for primary gastric cancer were included, and 84 cases were excluded due to other types of operations and non-primary gastric cancer. As

Table 1. Patients' clinicopathological characteristics

Variables	N	%
Age (median, range) (years)	66 (27–93)	
Body Mass Index (median, range) (kg/m ²)	22.1 (13.6–38.3)	
Sex		
Male	399	74.1
Female	140	25.9
Comorbidity		
Yes	65	12.1
No	474	87.9
Operation time (median, range) (min)	244 (93–796)	
Blood loss (median, range) (ml)	450 (0–4500)	
Combined resection		
Yes	137	25.4
No	402	74.6
Tumor size (median, range) (mm)	60 (3–230)	
Histology		
Differentiated	266	49.4
Undifferentiated	273	50.6
Type of operation		
Distal gastrectomy	301	55.8
Total gastrectomy	238	44.2
Extent of lymphadenectomy		
≤D1	97	18.0
D1+	190	35.3
≥D2	252	46.8
Curability		
R0	464	86.1
R1	16	3.0
R2	59	10.9

Variables	N	%
Reconstruction for distal gastrectomy		
Billroth-I	124	41.2
Billroth-II	21	7.0
Roux-en-Y	156	51.8
Reconstruction for total gastrectomy		
Roux-en-Y	225	94.5
Other methods	13	5.5
Depth of invasion		
T1a (mucosa)	56	10.4
T1b (submucosa)	82	15.2
T2 (muscle proper)	49	9.1
T3 (subserosa)	138	25.6
T4a (serosa)	189	35.1
T4b (involvement of adjacent organ)	25	4.6
Nodal classification		
N0	199	36.9
N1	90	16.7
N2	95	17.6
N3a	95	17.6
N3b	60	11.1
Stage		
IA	113	21.0
IB	39	7.2
IIA	55	10.2
IIB	61	11.3
IIIA	52	9.6
IIIB	75	13.9
IIIC	70	13.0
IV	74	13.7

a result, 539 cases were enrolled in the present study.

The TMN Classification 7th edition was used for staging⁹. The extent of lymphadenectomy was decided according to the Guideline of the Japan Gastric Cancer Association⁵. All patients were given a sufficient explanation about the surgical procedure and perioperative management, and written, informed consent was obtained from all of them. This study was approved by the Institutional Review Board of Tokyo Medical and Dental University (Approval number: M2016-028, Approved date:)

Complication evaluation

All complication data were graded retrospectively according to the Clavien-Dindo classification from our prospectively acquired database. Clavien-Dindo classification classifies complications from Grade 1 to Grade 5, including subgroups a and b in Grade 3 and 4. Each grade is defined according to the treatment to the patients. (Supplementary Table 1)⁸ Each patient's medical chart was also carefully reviewed so that the classification would be as accurate as possible. Complications were classified into major surgical complications (MSCs) and other complications. MSCs included pancreatic fistula, abdominal abscess, and anastomotic leakage. (Please insert Supplementary Table 1 (single column) here)

Statistical analysis

Risk factors for complications were analysed using the χ^2 test or Fisher's exact test for the univariate analysis. Factors that were deemed of potential importance on univariate analysis were included in the multivariate analysis, which was performed using multiple logistic regression analysis. In all analyses, the Statistical Package for Social Science (SPSS), version 19.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used, and a p -value less than 0.05 was considered significant.

Results

Clinicopathological data of the patients

The clinicopathological characteristics of the patients are summarized in Table 1. The median age was 66 years (range, 27–93 years), the body mass index (BMI) was 22.1 kg/m² (range, 13.6–38.3 kg/m²), and 65 patients (12.1%) had comorbidities. The median operation time and blood loss were 244 minutes (range, 93–796 minutes) and 450 mL (range, 0–4,500 mL), respectively. Combined resection was performed in 137 cases (25.4%) (spleen 111 cases, spleen+pancreas 11cases,

transverse colon 7 cases, spleen+transverse colon 3 cases, spleen+pancreas+transverse colon 3 cases, liver 2 cases). Overall, 138 cases (25.6%) were early gastric cancer, and 113 cases (21.0%) were Stage IA. Lymph node metastasis was found in 340 cases (63.1%). Total gastrectomy was performed in 238 cases (44.2%), and Roux-en-Y reconstruction was performed for the reconstruction of distal gastrectomy in 156 cases (51.8%). D2 lymphadenectomy was performed in 252 cases (46.8%), and R0 resection was accomplished in 464 cases (86.1%). (Please insert Table 1 (single column) here)

The mortality rate was 1.1% (6/539) (anastomotic leakage in 3 cases, cardiac failure in 2 cases, abdominal abscess leading to disseminated intravascular coagulation in 1 case.), and 222 events were occurred in 156 patients (28.9%). Complications of grade IIIa or greater were 8.3% (45/539) for MSCs and 10.6% (58/539) for all complications. (Table 2) (Please insert Table 2 (single column) here)

Table 2. Actual number and frequency of each complication.

Complications	Total	Grade≥IIIa
Major Surgical Complications		
Pancreatic fistula	25 (4.6%)	13 (2.4%)
Abdominal abscess	36 (6.7%)	27 (5.0%)
Anastomotic leakage	22 (4.1%)	16 (3.0%)
Other Complications		
Anastomotic stenosis	15 (2.8%)	9 (1.7%)
Postoperative bleeding	8 (1.5%)	2 (0.4%)
Bowel obstruction	11 (2.0%)	1 (0.2%)
Wound problem	29 (5.4%)	0
Cardiac	14 (2.6%)	2 (0.4%)
Pulmonary	46 (8.5%)	0
Hepatic	8 (1.5%)	0
Renal	6 (1.1%)	0
Cholecystitis	2 (0.4%)	0

*There were some patients who suffered more than one complication category. The total number of the complications were greater than that of the patients who suffered complications.

Table 3. Univariate and multivariate analyses of risk factors for major surgical complications of grade IIIa or greater

Variables		Univariate analysis		Multivariate analysis	
		<i>p</i> -value	<i>p</i> -value	Odds ratio	95% Confidence Interval
Sex	Female vs. Male	0.739			
Age (years)	<60 vs. ≥60	0.841			
Body Mass Index (kg/m ²)	<25 vs. ≥25	0.124			
Comorbidity	No vs. Yes	0.424			
Type of operation	DG vs. TG	0.006	0.145	1.370	0.478–1.114
Lymphadenectomy	<D2 vs. ≥D2	0.279			
Operation time (min)	<240 vs. ≥240	0.007	0.071	1.560	0.395–1.039
Blood loss (ml)	<500 vs. ≥500	<0.001	0.003	1.923	0.320–0.786
Combined resection	No vs. Yes	0.817			
Tumor size (cm)	<5 vs. ≥5	0.099			
Histology	Diff. vs. Undiff.	0.037	0.389	1.190	0.801–1.770
Tumor depth	T1 vs. T2 or more	0.311			
Lymph node classification	N0 vs. N1 or more	0.866			
Stage	IA vs. IB or more	0.476			
Curability	R0 vs. R1 or R2	0.619			

DG: distal gastrectomy, TG: total gastrectomy, Diff: differentiated, Undiff: undifferentiated

Table 4. Univariate and multivariate analyses of risk factors for all complications of grade IIIa or greater

Variables		Univariate analysis		Multivariate analysis	
		<i>p</i> -value	<i>p</i> -value	Odds ratio	95% Confidence Interval
Sex	Female vs. Male	0.736			
Age (years)	<60 vs. ≥60	0.886			
Body Mass Index (kg/m ²)	<25 vs. ≥25	0.047	0.088	1.745	0.302–1.086
Comorbidity	No vs. Yes	0.596			
Type of operation	DG vs. TG	0.001	0.021	2.075	0.260–0.896
Lymphadenectomy	<D2 vs. ≥D2	0.174			
Operation time (min)	<240 vs. ≥240	0.004	0.711	1.136	0.578–2.234
Blood loss (ml)	<500 vs. ≥500	0.003	0.089	1.767	0.294–1.090
Combined resection	No vs. Yes	0.796			
Tumor size (cm)	<5 vs. ≥5	0.097			
Histology	Diff. vs. Undiff.	0.106			
Tumor depth	T1 vs. T2 or more	0.556			
Lymph node classification	N0 vs. N1 or more	0.905			
Stage	IA vs. IB or more	0.692			
Curability	R0 vs. R1 or R2	0.743			

DG: distal gastrectomy, TG: total gastrectomy, Diff: differentiated, Undiff: undifferentiated

Univariate and multivariate analyses for risk factors

Univariate analysis revealed that the risk factors for MSCs of grade IIIa or greater were total gastrectomy, operation time ≥ 240 min, blood loss ≥ 500 ml, and undifferentiated histology. Of these, multivariate analysis showed that only blood loss ≥ 500 ml was an independent risk factor (Odds ratio 1.923, 95% Confidence Interval 0.320–0.786, $p=0.003$). (Table 3) (Please insert Table 3 (single column) here)

Univariate analysis revealed that the risk factors for all complications of grade IIIa or greater were obese patients, total gastrectomy, operation time ≥ 240 min, and blood loss ≥ 500 ml. Of these, multivariate analysis showed that only total gastrectomy was an independent risk factor (Odds ratio 2.075, 95% Confidence Interval 0.260–0.896, $p=0.021$). (Table 4) (Please insert Table 4 (single column) here)

Discussion

The morbidity of open gastrectomy has been reported to be between 17.4% and 43%^{6, 7, 10}. In the present study, overall morbidity was 28.9%, and the incidences of MSCs and all complications of grade IIIa or greater were 8.3% and 10.6%, respectively according to the Clavien-Dindo classification. Previous reports included patients with different characteristics, and they were written years ago. Therefore, it is not possible to compare directly the present results to those of others, and it is natural that each result was different.

However, there is one issue that makes us confused most when understanding these results. That is, the assessment standards of complications are different, and institution-specific standards were used in each report. Different standards make the detailed results, such as frequency, severity, and risk factors, different. Nowadays most of the surgeons started to assess complications using the Clavien-Dindo classification. But most of the reports included not only open cases but also minimally invasive ones, and the article which focused only on open surgery is rare¹¹⁻¹⁵. In that sense, the present study can provide some reliable and objective overview although the issue regarding complications of open gastrectomy seems somewhat outdated.

Blood loss was the only independent risk factor for MSCs of grade IIIa or greater, and it was also a significant risk factor for all complications of grade IIIa or greater in univariate analysis. There have been several reports that blood loss is the risk factor for complications after open gastrectomy^{16, 17}. Ives *et al.* reported, in their article, that lower oxygen saturation of surgical site led to higher incidence of surgical site infection in abdominal or groin bypass surgery¹⁸.

Furthermore, recently complication prediction system called Surgical Apgar Score (SAS), which consists of intraoperative blood loss, lowest intraoperative mean arterial pressure, and lowest intraoperative heart rate, was proposed to several types of surgery such as colorectal surgery, vascular surgery, urology and so on¹⁹⁻²². This surgical score reflects intraoperative hemodynamic stability, and is influenced by various

Supplementary Table 1 Clavien-Dindo classification

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic, or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient

*Brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks.
CNS, central nervous system; IC, intermediate care; ICU, intensive care unit

factors such as the quality of surgery and anaesthesia, and the patient's pre— and intra —operative condition. In gastric cancer field, Miki *et al.* reported that modified SAS can be applied to gastrectomy, and it was associated with complication rate in their article²³.

Total gastrectomy was an only independent risk factor for all complications of grade IIIa or greater, and it was also a significant risk factor for MSCs of grade IIIa or greater in univariate analysis. Morbidity have already been reported higher after total gastrectomy than after distal gastrectomy^{6,24}. Our results were compatible with previous reports.

The present study has some limitations. First, it was a retrospective analysis, although our database was collected prospectively, and medical charts were also carefully reviewed. Second, the number of cases was not large enough to obtain conclusive data. Third, the proportion of patients with early gastric cancer in the present study is relatively low due to laparoscopic surgery for some early gastric cancer patients in the same period.

In conclusion, we showed the objective evaluation of complications after open gastrectomy according to the Clavien-Dindo classification. The mortality rate was 1.1%. The overall complication rate was 28.9%, and the incidences of MSCs and all complications of grade IIIa or greater were 8.3% and 10.6%, respectively. Blood loss and total gastrectomy were the only significant risk factors for complications. It is hoped that these findings are informative for surgeons who work on gastric cancer treatment.

Conflict of interest

Authors Masatoshi Nakagawa, Kazuyuki Kojima, Mikito Inokuchi, Keiji Kato, Hirofumi Sugita, Sho Otsuki, Kenichi Sugihara have no conflicts of interest or financial ties to disclose.

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