

# Risk factors for postoperative complications after gastrectomy in gastric cancer patients with comorbidities

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## Abstract

**Purpose** We conducted this retrospective cohort study to evaluate which preoperative comorbidities and their combinations are most strongly associated with postoperative complications after gastrectomy.

**Methods** We collected data on 214 consecutive patients who underwent gastrectomy for gastric cancer. Preoperative comorbidities were placed into one of ten categories: cardiac, pulmonary, liver, renal, central nervous system, hypertension, diabetes, endocrine/metabolic, vascular, and immune/hematological. The relationship between the number of comorbidities and the incidence of postoperative complications was evaluated.

**Results** Among 120 patients (56.1 %) with comorbidities, 48 had a single comorbidity and 72 had multiple ( $\geq 2$ ) comorbidities. The incidence of postoperative complications was 45.8 % (33/72) for patients with multiple comorbidities and 23.9 % (34/142) for those with 0 or 1 comorbidity ( $P = 0.001$ ). Among the ten types of comorbidities, only pulmonary ( $P = 0.019$ ) and vascular diseases ( $P = 0.007$ ) were significantly associated with the occurrence of postoperative complications.

**Conclusion** Patients with multiple comorbidities had a significantly higher incidence of postoperative complications after gastrectomy. Among the comorbidities studied, pulmonary and vascular diseases had the strongest association with postoperative complications.

**Keywords** Comorbidity · Complication · Gastric cancer

## Introduction

Gastric cancer is the fourth most common cancer and the second leading cause of cancer-related death in the world [1, 2]. Surgical resection is the only curative treatment for gastric cancer, but postoperative complications are not uncommon, even in the high-volume hospitals, and their occurrence is influenced by various clinicopathological factors. According to previous studies, the risk factors for postoperative complications after gastrectomy include advanced age, male sex, high body mass index, poor nutritional status, total gastrectomy, extended lymph node dissection, and advanced tumor stage [3–10]. With the increasing life expectancy in many countries [11], the proportion of elderly patients diagnosed with gastric cancer is also increasing [12]. Elderly patients are likely to have more comorbidities, such as hypertension, diabetes, cardiovascular diseases, and pulmonary disorders, and the presence of a comorbid condition is considered to be associated with a higher risk of postoperative complications. Although several studies have shown that comorbidity is a risk factor for postoperative complications [13–16], there are few details on the risks associated with preoperative comorbidity. Thus, we conducted a retrospective cohort study to evaluate the relationship between the number of preoperative comorbidities and postoperative complications in patients undergoing gastrectomy for gastric cancer. The secondary aim of this study was to clarify what kinds of preoperative comorbidities are significantly related to postoperative complications after gastrectomy.

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**Table 1** Categories of preoperative comorbidities

Category	Contents
Cardiac	Coronary artery disease, cardiomyopathy, arrhythmia, past history of cardiac surgery or catheter intervention
Pulmonary	Chronic obstructive pulmonary disorder, interstitial pneumonia, asthma, spirometry abnormality (%VC <80 % or FEV1.0 % <70 %)
Liver	Chronic hepatitis B/C, liver cirrhosis, hepatocellular carcinoma
Renal	Chronic renal disease
Central nervous system	Brain infarction, neurodegenerative disease
Hypertension	Controlled by medication
Diabetes	Controlled by medication or insulin
Endocrine/metabolic	Hyperlipidemia, hyperuricemia, hypothyroidism
Vascular	Aortic aneurysm, arteriosclerosis obliterance, carotid artery stenosis, deep venous thrombosis
Immune/hematological	Rheumatoid arthritis, Sjogren syndrome, malignant lymphoma, aplastic anemia

VC vital capacity, FEV1.0 % forced expiratory volume % in one second

**Table 2** Number of patients with preoperative comorbidities

Comorbidity	<i>N</i> (%)
None	94 (43.9 %)
Hypertension	57 (26.6 %)
Cardiac	30 (14.0 %)
Pulmonary	29 (13.6 %)
Endocrine/metabolic	29 (13.6 %)
Diabetes	27 (12.6 %)
Central nervous system	20 (9.3 %)
Vascular	13 (6.1 %)
Renal	11 (5.1 %)
Liver	10 (4.7 %)
Immune/hematological	9 (4.2 %)

The number of patients with each comorbidity can be duplicated

## Materials and methods

We collected data retrospectively on 214 consecutive patients who underwent curative gastrectomy for histologically confirmed gastric cancer at Osaka University Hospital between January 2010 and December 2011. Patients who underwent concurrent procedures for synchronous malignant tumors were excluded. We used the 14th edition of the Japanese classification of gastric carcinoma to establish pT and pN stage [17]. We collected the data of preoperative comorbidities from the preoperative summary sheet. This sheet included preoperative risk factors based on history, preoperative examinations such as blood tests, electrocardiogram, and spirometry, and preoperative consultation with other specialists, such as a cardiologist. The prognostic nutrition index (PNI) was calculated as follows:  $10 \times$  serum albumin level +  $0.05 \times$  total lymphocyte count [18].

We divided the comorbid diseases into ten categories: cardiac, pulmonary, liver, renal, central nervous system,

hypertension, diabetes, endocrine/metabolic, vascular, and immune/hematological (Table 1). The severity of each disease was not assessed. We counted the number of preoperative comorbidities for each patient. All postoperative events were evaluated according to the Clavien–Dindo classification system [19], and we considered complications of grade II or higher as postoperative complications in this study. We evaluated the relationship between clinicopathological factors, including the number of preoperative comorbidities, and the occurrence of postoperative complications, using the Chi-squared test for categorical variables and the Mann–Whitney *U* test for continuous variables. We also evaluated which kinds of comorbidities were associated with the highest risk of postoperative complications, using univariate and multivariate logistic regression.  $P < 0.05$  was considered significant. All statistical analyses were performed with the SPSS statistics software package, version 20 (IBM Corp., Armonk, NY, USA).

## Results

Of the 214 patients, 120 (56.1 %) had preoperative comorbidities. The most common comorbidity was hypertension (26.6 %), followed by cardiac (14.0 %), pulmonary (13.6 %), and endocrine/metabolic disorders (13.6 %), respectively (Table 2). Among the 120 patients with preoperative comorbidities, 48 (40.0 %) had one comorbidity, 37 (30.8 %) had two comorbidities, 24 (20.0 %) had three comorbidities, and 11 (9.2 %) had four or more comorbidities.

There were 67 patients (31.3 %) who experienced postoperative complications. Major complications included anastomotic leakage (5.1 %), pancreatic fistula (4.7 %), postoperative bleeding (4.2 %), abdominal abscess (3.7 %), food stasis (3.7 %), anastomotic stenosis

**Table 3** Relationship between clinicopathological factors and the occurrence of postoperative complications after gastrectomy

	Patients with postoperative complication ( <i>N</i> = 67)	Patients without postoperative complication ( <i>N</i> = 147)	<i>P</i> value
Age			0.034
Median (range)	71 (38–89)	65 (29–88)	
Sex			0.12
Male	55	106	
Female	12	41	
Body mass index			0.54
Median (range)	22.3 (16.9–31.3)	21.9 (14.3–30.1)	
PNI			0.043
Median (range)	44.8 (25.0–58.5)	47.1 (25.8–60.5)	
Approach			0.011
Open	32	44	
Laparoscopic	35	103	
Gastrectomy			0.053
Distal or proximal	43	113	
Total	24	34	
Lymph node dissection			0.002
<D2	30	99	
≥D2	37	48	
pT*			<0.001
pT1	25	99	
pT2–4	42	48	
pN*			0.29
pN0	47	113	
pN1–3	20	34	
Number of comorbidities			0.003
0	22	72	
1	12	36	
2	19	18	
3	7	17	
4 or more	7	4	

pT and pN stage were according to the 14th edition of Japanese classification of gastric carcinoma  
*PNI* prognostic nutrition index

(1.9 %), cholecystitis (1.9 %), and ascites (1.9 %). We evaluated the relationship between clinicopathological factors and the occurrence of postoperative complications (Table 3). Among the ten clinicopathological factors studied, age ( $P = 0.034$ ), PNI ( $P = 0.043$ ), surgical approach ( $P = 0.011$ ), extent of lymph node dissection ( $P = 0.002$ ), pT stage ( $P < 0.001$ ), and the number of comorbidities ( $P = 0.003$ ) were significantly associated with postoperative complications. When we dichotomized the number of comorbidities, two groupings 0 vs.  $\geq 1$  and 0 or 1 vs.  $\geq 2$  showed a significant relationship with postoperative complications ( $P = 0.028$  and  $P = 0.001$ , respectively), but 0 or 1 vs.  $\geq 2$  had a higher odds ratio (2.69; 95 % confidential interval, 1.47–4.91) than 0 vs.  $\geq 1$  (1.96; 95 % confidential interval, 1.07–3.59). When the number of comorbidities was grouped as 0–2 vs.  $\geq 3$ , there was no

significant relationship ( $P = 0.23$ ). The incidence of postoperative complications among patients who had multiple ( $\geq 2$ ) comorbidities vs. those who had no or one comorbidity was 45.8 % (33/72) vs. 23.9 % (34/142), respectively. In the multivariate logistic regression model with all ten clinicopathological factors, only pT2–4 ( $P = 0.006$ ) and multiple comorbidities ( $P = 0.014$ ) were identified as significant risk factors for postoperative complications.

The incidence of each intra-abdominal complication in patients with multiple comorbidities vs. those with no or one comorbidity was as follows: anastomotic leakage, 4.2 vs. 5.6 %; pancreatic fistula, 4.2 vs. 4.9 %; postoperative bleeding, 5.6 vs. 3.5 %; abdominal abscess, 6.9 vs. 2.1 %; and food stasis, 5.6 vs. 5.6 %. Although there was no significant difference in the incidence of any intra-abdominal complication between the groups, extra-abdominal

**Table 4** Univariate and multivariate logistic analysis of risk factor for postoperative complications after gastrectomy

	Univariate		Multivariate	
	Odds ratio (95 % CI)	<i>P</i> value	Odds ratio (95 % CI)	<i>P</i> value
Cardiac	1.32 (0.59–2.96)	0.50		
Pulmonary	2.74 (1.24–6.07)	0.013	2.69 (1.18–6.16)	0.019
Liver	1.86 (0.67–5.14)	0.23		
Renal	1.29 (0.47–3.50)	0.62		
Central nervous system	1.53 (0.59–3.93)	0.38		
Hypertension	1.27 (0.67–2.41)	0.47		
Diabetes	1.59 (0.83–3.06)	0.17	1.20 (0.59–2.43)	0.62
Endocrine/metabolic	0.99 (0.42–2.30)	0.97		
Vascular	5.55 (1.64–18.73)	0.006	5.46 (1.58–18.90)	0.007
Immune/hematological	1.80 (0.47–6.94)	0.39		

*CI* confidential interval

complications such as pneumonia, delirium, cerebral infarction, and pulmonary embolism occurred more frequently in patients with multiple comorbidities than in patients with no or one comorbidity [11.1 % (8/72) vs. 1.4 % (2/142),  $P = 0.003$ ].

Next, we evaluated which preoperative comorbidities were significantly related to postoperative complications. Among the ten types of comorbidities evaluated, only pulmonary ( $P = 0.019$ ) and vascular diseases ( $P = 0.007$ ) were significantly associated with postoperative complications according to both the univariate and multivariate analyses (Table 4). The risk of postoperative complications among patients with multiple comorbidities that included either pulmonary or vascular disease was 55.9 % (19/34), whereas the risk among those with multiple comorbidities excluding pulmonary and vascular diseases was 36.8 % (14/38).

## Discussion

In the present study, we categorized preoperative comorbidities into ten categories and analyzed whether the number of preoperative comorbidities, and which kinds, could effectively predict postoperative complications after gastrectomy. Patients who had multiple ( $\geq 2$ ) comorbidities had a significantly higher risk of postoperative complications than those who had no or one comorbidity. Among the comorbidities, pulmonary and vascular diseases were the most strongly associated with postoperative complications. The risk of postoperative complications among patients with multiple comorbidities that included either pulmonary or vascular disease exceeded 50 %; therefore, careful perioperative management is needed for this patient population.

Preoperative comorbidity is generally considered to be associated with a higher risk of postoperative complications

for any type of surgery. In the field of gastric cancer surgery, some studies have found that comorbidity and old age are important risk factors for complications [13, 14]. The importance of comorbidity as a risk factor was recently demonstrated in patients who underwent laparoscopic gastrectomy [15, 20]. In these studies, patients were divided into two groups according to whether they had preoperative comorbidities or not. However, considering that elderly patients who require gastrectomy often have at least one comorbid disease, the presence of a single comorbidity may not be as relevant for predicting postoperative complications. Indeed, patients with well-controlled hypertension usually experience relatively few complications after gastrectomy. Jeong et al. [21] reported that multiple comorbidities were associated with postoperative complications in elderly patients. Similarly, our study revealed that the existence of multiple comorbidities was a more reliable indicator of postoperative complications than that of single comorbidity. Furthermore, patients with multiple comorbidities had a higher incidence of extra-abdominal complications but not intra-abdominal complications. Since the number of comorbidities is probably a reflection of a patient's systemic condition, this may be a reliable predictor, especially of extra-abdominal complications.

Hypertension, cardiopulmonary disease, and liver disease have already been reported as risk factors for postoperative complications after gastrectomy [20, 22, 23]. Jeong et al. [24] reported that gastric cancer patients with abnormal pulmonary function had a significantly higher incidence of local and systemic complications than other patients. They found that anastomotic leakage and wound complications were more common in patients with abnormal pulmonary function. Our study also revealed pulmonary and vascular diseases as significant risk factors for postoperative complications. In patients with abnormal pulmonary function, hypoxia and malnutrition may result

in poor wound healing. Regarding vascular disease, as most studies combined vascular disease with cardiac disease into a single category of cardiovascular disease, we could not find any studies that specifically analyzed the relationship between vascular disease and postoperative complications. Although cardiac and vascular disorders have some causes in common, we considered cardiac and vascular diseases as having different impacts on postoperative outcome. For example, cardiac diseases such as decreased pump function may be compensated for with medications, whereas vascular diseases such as arteriosclerosis usually involve irreversible damage to blood vessels that cannot easily be compensated for with medications. The most common vascular disease was arteriosclerosis-related disease, which is associated with poor oxygen supply to peripheral tissues and may cause chronic changes in the functioning of multiple organs. Indeed, all patients with vascular disease in our study had two or more comorbidities.

This study did not evaluate the effect of the severity of each comorbidity on the occurrence of postoperative complications because there is no standard method to evaluate the severity of comorbidities. Instead, we evaluated the number of comorbidities, because this may reflect the overall disease burden for each patient. Patients with severe dysfunction of one organ system tend to have disorders involving multiple organ systems. A good example of this is the patient with chronic renal failure, who usually has secondary hypertension as well. A large-scale prospective study using the same criteria for classifying preoperative comorbidities is needed to confirm our conclusions.

**Conflict of interest** We have no conflicts of interest to declare.

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