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ORIGINAL ARTICLE

Significance of Preoperative Pulmonary Function on Short- and Long-Term Outcomes Following Gastrectomy for Gastric Cancer

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Abstract

Background Preoperative pulmonary function assessment is useful for selecting surgical candidates and operative methods and assessing the risk of postoperative pulmonary complications. However, few studies have investigated the relationship between preoperative pulmonary function and short- and long-term outcomes in patients who underwent gastrectomy for gastric cancer.

Methods Of the 1040 patients with gastric cancer (stages I–III) who had undergone R0 gastrectomy between 2009 and 2020, 750 who underwent preoperative spirometry were included. Restrictive ventilatory impairment was defined as a vital capacity of the predicted value (%VC) < 80%, while obstructive ventilatory impairment was defined as forced expiratory volume in one second (FEV1%) < 70%. Postoperative complications were assessed using the Clavien–Dindo (CD) classification. The relationship between clinical factors, including %VC, FEV1%, severe postoperative complications (CD ≥ 3b), overall survival (OS), and relapse-free survival, were assessed.

Results The mean age of the 750 patients was 68 ± 10.5 years. Severe postoperative complications were observed in 25 (3.3%) patients and were significantly associated with FEV1% < 70% in the univariate analysis. The 5-year OS was 72.5%. Multivariate analysis showed that the cancer stage, age > 75 years, preoperative comorbidities, %VC < 80%, total gastrectomy, severe postoperative complications, and postoperative adjuvant chemotherapy were the significant independent factors affecting OS. Pneumonia was significantly associated with %VC < 80%.

Conclusions FEV1% < 70%was associated with the development of severe postoperative complications, while %VC < 80% was associated with poor OS independent of the cancer stage because of death from pneumonia. Spirometry helps surgeons and patients discuss the risks and benefits of surgery.

Keywords Gastric cancer · Pulmonary function · Prognosis · FEV1% · %VC

Introduction

Gastric cancer (GC) is the fifth-most common cancer and the third-most common cause of cancer-related deaths worldwide[1]. Curative resection is the gold standard treatment for non-metastatic GC. It is widely performed for older patients and those with multiple comorbidities; however, major concerns regarding its safety and efficacy exist in the elderly, and it is associated with increased mortality and morbidity, or decreased long-term survival.[2–9]

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Preoperative pulmonary function tests have been performed for the risk assessment for thoracic surgery.[10,11] Spirometry, the most readily available pulmonary function test, measures the total exhaled volume, or the forced vital capacity (FVC), the volume exhaled in the first second (FEV1) being the most important variable.[12] Spirometry is used to predict postoperative pulmonary complication risks in high-risk situations, including chronic obstructive pulmonary disease or asthma, current smoking, and indicated surgery.[13] However, it can promote coughing and aerosol generation, leading to the spread of coronavirus disease (COVID-19). Screening for active COVID-19 is challenging, particularly in patients with underlying respiratory symptoms. Furthermore, asymptomatic patients can shed the virus. The American Thoracic Society recommends limiting spirometry to patients whose results are essential for immediate management decisions[14] Therefore, the clinical significance of spirometry requires reevaluation.

Aging is becoming a global public health concern, and the incidence of GC in the elderly seems to be rising owing to recent increases in life expectancy.[15,16] Elderly patients are vulnerable to and affected by various physiological dysfunctions, with an age-dependent decline in pulmonary function. Older age is associated with high complication rates and severity after gastrectomy.[17] Radical resection is feasible in selected elderly patients with resectable GC, whereas less invasive palliative resection may be beneficial for vulnerable patients. Therefore, the preoperative risk assessment and the estimation of the benefits of gastrectomy are important.

Few studies have investigated the relationship between preoperative pulmonary function and short- and long-term outcomes in patients who underwent abdominal surgeries for GC and colorectal cancer.[18–23] This study aimed to test the hypothesis that preoperative pulmonary function is related to short- and long-term outcomes in patients who underwent gastrectomy for GC.

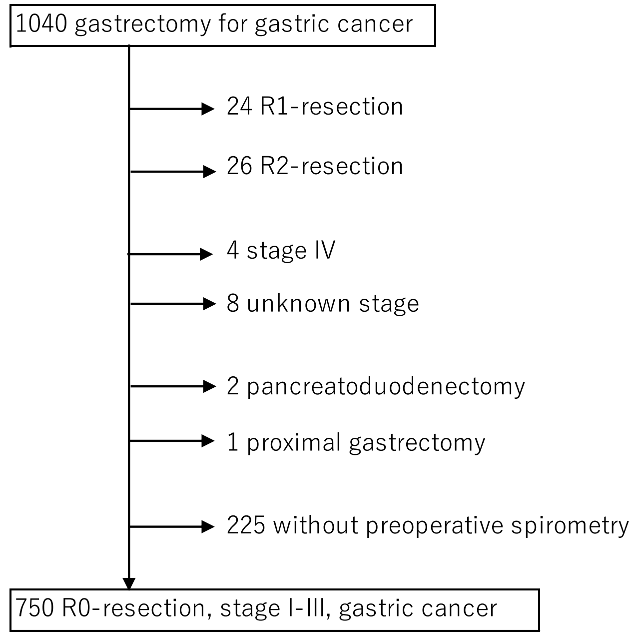

Fig. 1 Flowchart for selecting the study participants

Materials and Methods

Patients

Of the 1040 patients with GC (stages I–III) who underwent R0 gastrectomy at our hospital between 2009 and 2020, those with R1/R2 resection ($n = 50$), stage IV ($n = 4$), and an unknown cancer stage ($n = 8$) were excluded. Patients who underwent surgical procedures other than distal or total gastrectomy ($n = 3$) or did not undergo preoperative spirometry ($n = 225$) were excluded. Finally, 750 patients who underwent preoperative spirometry were included in the study (Fig. 1). At the final follow-up in December 2020, the median follow-up period for the surviving patients was 62 (interquartile range [IQR]: 40–91) months. We investigated the relationship between clinical factors, including preoperative lung function and postoperative complications, and overall survival (OS) and relapse-free survival (RFS). Age was stratified to < 75 and ≧ 75 years according to the Japan Geriatrics Society.[24] This retrospective study was approved by the institutional review board of the Japanese Red Cross Aichi Medical Center Nagoya Daiichi Hospital (approval number: 2022–004).

Study Criteria

Preoperative lung function was assessed by spirometry using CHEST AC-8900 (CHEST, Tokyo, Japan). Restrictive ventilatory impairment was defined as a vital capacity percentage (%VC) < 80%, and obstructive ventilatory impairment was defined as a percent forced expiratory volume in one second (FEV1%) < 70%. Pathological staging was determined according to the 15th edition of the Japanese Classification of Gastric Carcinoma.[25] The extent of gastric resection and lymph node dissection was determined in accordance with the Japanese Gastric Cancer Treatment Guidelines 2018.[26] The reconstruction methods were determined by the surgeons who had performed the gastrectomy. Preoperative comorbidities were classified into 15 categories using the Charlson comorbidity index as a reference: myocardial, hypertension, cerebrovascular, vascular, pulmonary, dementia, neurologic, diabetes, endocrine, renal, gastroenterological, immune, musculoskeletal, hematological disease, and anemia.[27] Postoperative complications were evaluated using the Clavien–Dindo (CD) classification.[28] Severe postoperative complications were defined as CD ≥ 3b, considering the complications that required treatment by surgery, endoscopy, or interventional radiology under general anesthesia to be serious. Postoperative surveillance was performed in accordance with the Japanese Gastric Cancer Treatment Guidelines 2018.[26] Blood tests and computed tomography were performed every 6 months, and upper gastrointestinal endoscopy was performed annually. S-1 monotherapy was administered as postoperative adjuvant chemotherapy for stage II/III GC based on the patients' consent and general condition.[26]

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median (IQR) and were compared using Student's t-test, Mann–Whitney U test, or Kruskal–Wallis

Table 1 Patient background

Age	68.3 ± 10.5		
	< 75 years	514	(68.5%)
	≧ 75	236	(31.5%)
Sex	Male	494	(65.9%)
	Female	256	(34.1%)
Body mass index (BMI)	< 18.5	90	(12.0%)
	18.5 < BMI < 25	501	(66.8%)
	> 25	159	(21.2%)
Preoperative comorbidity	Absent	285	(38.0%)
	Present	465	(62.0%)
%VC	< 80 (%)	41	(5.5%)
	≧ 80	709	(94.5%)
FEV1%	< 70 (%)	223	(29.7%)
	≧ 70	527	(70.3%)
Preoperative blood data			
Albumin	< 3.5 (g/dL)	141	(18.8%)
	≧ 3.5	608	(81.1%)
Hemoglobin	< 10 (g/dL)	103	(13.7%)
	≧ 10	646	(86.1%)
Platelets count	< 15 (× 10^4/μL)	79	(10.5%)
	≧ 15	670	(89.3%)
Lymphocyte	< 1000 (/μL)	81	(10.8%)
	≧ 1000	653	(87.1%)
Mean corpuscular volume (MCV)	< 100 (fl)	670	(89.3%)
	≧ 100	80	(10.7%)
Neutrophil-to-lymphocyte ratio (NLR)	< 4	621	(82.8%)
	≧ 4	124	(16.5%)
Surgical approach	Laparotomy	597	(79.6%)
	Laparoscopy	153	(20.4%)
Surgical procedure	Distal gastrectomy	509	(67.9%)
	Total gastrectomy	241	(32.1%)
Stage	I	413	(55.1%)
	II	141	(18.8%)
	III	196	(26.1%)
Clavien–Dindo classification*	0	556	(74.1%)
	1	11	(1.5%)
	2	77	(10.3%)
	3a	81	(10.8%)
	3b	12	(1.6%)
	4a	6	(0.8%)
	4b	1	(0.1%)
	5	6	(0.8%)
Postoperative adjuvant chemotherapy	done	220	(29.3%)
	not done	530	(70.7%)

*Higher degree when a patient had multiple complications

test, as appropriate. Categorical variables were compared using Pearson's chi-square or Fisher's exact test. Correlations between continuous variables were analyzed using Pearson's correlation coefficient. Correlations between continuous and ordinal variables were analyzed using Spearman's rank correlation test. The OS and RFS were calculated from the date of surgery to that of the last follow-up. A survival curve was drawn using the

Table 2 Severe postoperative complications (Clavien–Dindo ≧ 3b)

Organ/space surgical site infection	5	(0.7%)
Pneumonia	5	(0.7%)
Intra-abdominal bleeding	4	(0.5%)
Anastomotic passage disturbance	4	(0.5%)
Bile leakage	2	(0.3%)
Sepsis	2	(0.3%)
Pulmonary injury	2	(0.3%)
Gastrointestinal bleeding	2	(0.3%)
Acute renal failure	2	(0.3%)
Interstitial pneumonia	1	(0.1%)
Respiratory failure	1	(0.1%)
Diffuse peritonitis	1	(0.1%)
Multiple organ failure	1	(0.1%)
Small intestinal perforation	1	(0.1%)
Incarcerated inguinal hernia	1	(0.1%)
Subdural hematoma	1	(0.1%)
Disseminated intravascular coagulation	1	(0.1%)

Kaplan–Meier method, and comparisons between the groups were performed using the log-rank test. Considering the statistical significance and clinical implications of the univariate analysis, variables were entered into multivariate analyses via logistic regression analysis or a Cox proportional hazards model. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using the JMP software program (version 13.2.0) for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the patients' backgrounds. The average age of the patients was 68 ± 10.5 years. There were 494 males (65.9%) and 256 females (34.1%). Preoperative comorbidities were observed in 465 (62.0%) patients. Hypertension, diabetes, myocardial disease, anemia, and pulmonary disease were more frequently (Supplementary Table 1). The mean %VC and FEV1% were 106.1% ± 17.3% and 74.0% ± 13.0%, respectively. The number of patients who had %VC < 80% and FEV1% < 70% were 41 (5.5%) and 223 (29.7%), respectively. Diabetes, myocardial disease, anemia, and renal disease were significantly related to %VC < 80%, while vascular and neurologic diseases were significantly related to FEV1% < 70% (Supplementary Table 1).

The number of patients with postoperative complications classified as CD 1, 2, 3a, 3b, 4a, 4b, and 5 were 11, 77, 81, 12, 6, 1, and 6, respectively. Thirty-six severe postoperative complications (CD ≥ 3b) were observed in 25 patients (3.3%; median, 2; IQR, 1–4 in a patient; Table 2). Organ/space surgical site infection, pneumonia, intra-abdominal bleeding, and anastomotic passage disturbance were the most frequent complications. Univariate analysis of the clinical factors related to severe postoperative complications showed that age ≥ 75 years, FEV1% < 70%, serum albumin level < 3.5 g/dL, hemoglobin level < 10 g/dL, and platelet count $< 15 \times 10^4$ μ/L were significant. Multivariate analysis revealed that FEV1% < 70% and serum albumin level < 3.5 g/dL approached, but were not statistically significant ($p = 0.0833$ and $p = 0.0690$, respectively; Table 3).

The correlation between FEV1% and %VC was weak and significant ($\gamma = 0.171$, $p < 0.0001$, Supplementary Fig. 1). Reduced FEV1% was associated with the frequent incidence of severe postoperative complications (< 70% vs. ≧ 70%, 12/223 (5.4%) vs. 13/527 (2.5%), $p = 0.0421$), whereas reduced %VC and severe postoperative complications showed no significant association (< 80% vs. ≧ 80%, 2/41 (4.9%) vs. 23/709 (3.2%), $p = 0.6416$).

An investigation of the relationship between clinical factors and pulmonary function showed that %VC < 80% was significantly related to age ≧ 75 years, preoperative comorbidity, serum albumin < 3.5 g/dL, hemoglobin < 10 g/dL, neutrophil-to-lymphocyte ratio (NLR) ≧ 4, and less postoperative adjuvant chemotherapy, and FEV1% < 70% was significantly related to age ≧ 75, male, and preoperative comorbidity (Table 4). Figure 2a shows the correlation between age and %VC in terms of severe postoperative complications. The correlation was weak and significant ($\gamma = 0.280$, $p < 0.0001$). Severe postoperative complications were frequent in patients aged ≥ 75 years and with a %VC of 80–100%. Figure 2b shows the correlation between age and FEV1% in terms of severe postoperative complications. The correlation was weak and significant ($\gamma = 0.206$, $p < 0.0001$). Severe postoperative complications were frequent in patients aged ≥ 70 years and those with FEV1% < 85%. Pneumonia and anastomotic passage disturbance were more frequent in patients with FEV1% < 70% than in those with FEV1% ≥ 70% (3/223 [1.3%] vs. 2/527 [0.9%] and 3/223 [1.3%] vs. 1/527 [0.2%], respectively). The correlations between the number of comorbidities and %VC and FEV1% were weak and significant (Supplementary Fig. 2a and b).

Postoperative adjuvant chemotherapy was administered to 220 (29.3%) patients. The 5-year OS was 74.9% during a median follow-up period of 61 months (IQR: 27–82 months). Table 5 shows the results of the univariate and multivariate analyses for OS. Univariate analysis showed that age ≥ 75 years, preoperative comorbidities, %VC < 80%, preoperative serum albumin level < 3.5 g/dL, hemoglobin level < 10 g/dL, and platelet count $< 15 \times 10^4$ μ/L, neutrophil-to-lymphocyte ratio ≥ 4, laparotomy, total gastrectomy, the cancer stage, severe postoperative complications, and the presence of postoperative adjuvant chemotherapy were significantly associated with unfavorable OS. Multivariate analysis revealed that age ≥ 75 years, preoperative comorbidities, %VC < 80%, total gastrectomy, the cancer stage, severe postoperative complications, and the absence of postoperative adjuvant chemotherapy were significantly associated with unfavorable OS. The hazard ratio of OS in patients with %VC < 80% was 1.95 compared to that in patients with %VC ≥ 80%. Figure 3a–d show the OS curves of all patients and those with stages I–III disease according to the %VC. The OS of patients with %VC < 80% was consistently lower than those with %VC ≥ 80% in stages I–III. The number of comorbidities was the lowest in stage I (Supplementary Fig. 3).

During the follow-up period (median, 27 months, IQR: 15–45 months), 192 patients (25.6%) died. Table 6 shows the relationship between the cause of death and %VC. The incidence of death from non-malignant diseases and pneumonia was significantly higher in patients with %VC < 80% than in those with %VC ≥ 80%.

Relapse occurred in 160 (21.3%) patients during the follow-up period (median: 14 months, IQR: 7–26 months), and the 5-year RFS was 76.6%. Univariate and multivariate analyses of RFS showed that %VC < 80% or FEV1% < 70% were not associated with RFS (Supplementary Table 2).

Table 3 Univariate and Multivariate analysis for factors related to severe postoperative complications (Clavien–Dindo ≧ 3b)

		Univariate analysis					Multivariate analysis		
		CD < 3b (*n* = 725)		CV ≧ 3b (*n* = 25)		*p*	OR	95%CI	*p*
Age	< 75	502	(69.2%)	12	(48.0%)	**0.0245**	1		
	≧ 75	223	(30.8%)	13	(52.0%)		1.60	0.68–3.74	0.2801
Sex	Male	473	(65.2%)	21	(84.0%)	0.0551			
	Female	252	(34.8%)	4	(16.0%)				
Body mass index (BMI)	< 18.5	88	(12.1%)	2	(8.0%)	0.8001			
	18.5–25	484	(66.8%)	17	(68.0%)				
	> 25	153	(21.1%)	6	(24.0%)				
Preoperative comorbidity	Absent	280	(38.6%)	5	(20.0%)	0.0593			
	Present	445	(61.4%)	20	(80.0%)				
%VC	< 80 (%)	39	(5.4%)	2	(8.0%)	0.6416	1.05	0.22–4.86	0.9500
	≧ 80	686	(94.6%)	23	(92.0%)		1		
FEV1%	< 70 (%)	211	(29.1%)	12	(48.0%)	**0.0421**	2.08	0.91–4.77	0.0833
	≧ 70	514	(70.9%)	13	(52.0%)		1		
Preoperative blood data			(0.0%)		(0.0%)				
Albumin	< 3.5 (g/dL)	130	(17.9%)	11	(44.0%)	**0.0011**	2.48	0.93–6.60	0.0690
	≧ 3.5	594	(81.9%)	14	(56.0%)		1		
Hemoglobin	< 10 (g/dL)	96	(13.2%)	7	(28.0%)	**0.0354**	1.36	0.47–3.96	0.5653
	≧ 10	628	(86.6%)	18	(72.0%)		1		
Platelets count	< 15 (×10^4/μL)	73	(10.1%)	6	(24.0%)	**0.0259**	2.19	0.82–5.90	0.1198
	≧ 15	651	(89.8%)	19	(76.0%)		1		
Lymphocyte	< 1000 (/μL)	76	(10.5%)	5	(20.0%)	0.1455			
	≧ 1000	633	(87.3%)	20	(80.0%)				
MCV	< 100 (fl)	648	(89.4%)	22	(88.0%)	0.7425			
	≧ 100	77	(10.6%)	3	(12.0%)				
NLR	< 4	594	(81.9%)	18	(72.0%)	0.1247			
	≧ 4	116	(16.0%)	7	(28.0%)				
Surgical approach	Laparotomy	575	(79.3%)	22	(88.0%)	0.4475			
	Laparoscopy	150	(20.7%)	3	(12.0%)				
Surgical procedure	Distal gastrectomy	496	(68.4%)	13	(52.0%)	0.0840			
	Total gastrectomy	229	(31.6%)	12	(48.0%)				

Bold values indicate significant difference ($p < 0.05$)

Discussion

In this study, FEV1% < 70% was significantly correlated with severe postoperative complications. OS was consistently lower in patients with %VC < 80% than in those with %VC ≥ 80% in stages I–III due to frequent pneumonia-related deaths.

Univariate analysis revealed FEV1% < 70% as a significant factor associated with severe postoperative complications, whereas multivariate analysis revealed FEV1% < 70% as an independent factor that approached, but was not statistically significant. These results were partially supported by previous studies. Miki Y et al. showed that %VC < 80% or FEV1% < 70% was associated with postoperative pneumonia after gastrectomy.[20] Jeong O et al. reported that FEV1/VC < 0.7 was associated with local and systemic complications after gastrectomy.[18] Similar results were reported by a previous study investigating postoperative complications after colorectal resection.[22] Reduced airway clearance may explain the frequent occurrence of pneumonia in patients with low FEV1%. Pneumonia and anastomotic passage disturbances were more frequent in patients with FEV1% < 70% than in those with FEV1% ≥ 70%, possibly because of hypoxia due to reduced airway clearance.[29] Additionally, severe postoperative complications were more common in elderly patients and those with multiple comorbidities (Table 3 and Supplementary Fig. 2), suggesting an association between decreased FEV with older age and multiple comorbidities.

Table 4 Relation between clinical factors and pulmonary function

		%VC < 80% (n = 41)		%VC ≥ 80% (n = 709)		p	FEV1% < 70% (n = 223)		FEV1% ≥ 70% (n = 527)		p
Age	< 75 years	19	(46.3%)	495	(69.8%)	**0.0016**	127	(57.0%)	387	(73.4%)	**< 0.0001**
	≧ 75	22	(53.7%)	214	(30.2%)		96	(43.0%)	140	(26.6%)	
Sex	Male	31	(75.6%)	463	(65.3%)	0.1760	159	(71.3%)	335	(63.6%)	**0.0412**
	Female	10	(24.4%)	246	(34.7%)		64	(28.7%)	192	(36.4%)	
Body mass index (BMI)	< 18.5	6	(14.6%)	84	(11.8%)	0.5398	28	(12.6%)	62	(11.8%)	0.8007
	18.5 < BMI < 25	29	(70.7%)	472	(66.6%)		151	(67.7%)	350	(66.4%)	
	> 25	6	(14.6%)	153	(21.6%)		44	(19.7%)	115	(21.8%)	
Preoperative comorbidity	Absent	8	(19.5%)	277	(39.1%)	**0.0121**	64	(28.7%)	221	(41.9%)	**0.0006**
	Present	33	(80.5%)	432	(60.9%)		159	(71.3%)	306	(58.1%)	
Preoperative blood data								(0.0%)		(0.0%)	
Albumin	< 3.5 (g/dL)	13	(31.7%)	128	(18.1%)	**0.0300**	48	(21.5%)	93	(17.6%)	0.2185
	≧ 3.5	28	(68.3%)	580	(81.8%)		175	(78.5%)	433	(82.2%)	
Hemoglobin	< 10 (g/dL)	11	(26.8%)	92	(13.0%)	**0.0124**	31	(13.9%)	72	(13.7%)	0.9383
	≧ 10	30	(73.2%)	616	(86.9%)		192	(86.1%)	454	(86.1%)	
Platelets count	< 15 (× 10^4/μL)	3	(7.3%)	76	(10.7%)	0.4886	23	(10.3%)	56	(10.6%)	0.8922
	≧ 15	38	(92.7%)	632	(89.1%)		200	(89.7%)	470	(89.2%)	
Lymphocyte	< 1000 (/μL)	4	(9.8%)	77	(10.9%)	0.7879	26	(11.7%)	55	(10.4%)	0.7216
	≧ 1000	37	(90.2%)	616	(86.9%)		197	(88.3%)	456	(86.5%)	
Mean corpuscular volume (MCV)	< 100 (fl)	34	(82.9%)	636	(89.7%)	0.1717	200	(89.7%)	470	(89.2%)	0.8387
	≧ 100	7	(17.1%)	73	(10.3%)		23	(10.3%)	57	(10.8%)	
Neutrophil-to-lymphocyte ratio (NLR)	< 4	27	(65.9%)	585	(82.5%)	**0.0021**	183	(82.1%)	429	(81.4%)	0.5664
	≧ 4	14	(34.1%)	109	(15.4%)		40	(17.9%)	83	(15.7%)	
Stage	I	24	(58.5%)	389	(54.9%)	0.8985	122	(54.7%)	291	(55.2%)	0.0622
	II	7	(17.1%)	134	(18.9%)		52	(23.3%)	89	(16.9%)	
	III	10	(24.4%)	186	(26.2%)		49	(22.0%)	147	(27.9%)	
Clavien–Dindo classification*	0	29	(70.7%)	527	(74.3%)	0.5160	153	(68.6%)	403	(76.5%)	0.0653
	1	2	(4.9%)	9	(1.3%)		3	(1.3%)	8	(1.5%)	
	2	5	(12.2%)	72	(10.2%)		26	(11.7%)	51	(9.7%)	
	3a	3	(7.3%)	78	(11.0%)		29	(13.0%)	52	(9.9%)	
	3b	1	(2.4%)	11	(1.6%)		8	(3.6%)	4	(0.8%)	
	4a	1	(2.4%)	5	(0.7%)		3	(1.3%)	3	(0.6%)	
	4b	0	(0.0%)	1	(0.1%)		0	(0.0%)	1	(0.2%)	
	5	0	(0.0%)	6	(0.8%)		1	(0.4%)	5	(0.9%)	
Postoperative adjuvant chemotherapy	done	5	(12.2%)	215	(30.3%)	**0.0132**	60	(26.9%)	160	(30.4%)	0.3422
	not done	36	(87.8%)	494	(69.7%)		163	(73.1%)	367	(69.6%)	

Bold values indicate significant difference ($p < 0.05$)

In this study, OS did not significantly differ between patients with FEV1% < 70% and ≥ 70%, consistent with a previous study. Sugawara K et al. reported that the OS of patients with stages I–III GC was similar to those with FEV1% < 70% and ≥ 70%.[19] The relationship between low FEV1% and mortality is controversial in various populations.[30–31] FEV1% is reportedly unrelated to muscle mass and muscularity,[33,34] while Bellelli G et al. reported that decreasing FEV1% was a predictor of 3-year mortality in outpatients with bronchiectasis.[35]

In this study, %VC and FEV1% decreased with aging (Fig. 2a and b). In the elderly, the airspace expands, and the elastic contractile force of the lungs decreases without inflammatory changes or alveolar wall rupture. Moreover, the thorax stiffens, and the respiratory muscle strength decreases; therefore, FEV1%, %VC, and lung diffusivity decrease.[36] Skeletal muscle loss correlates better with %VC < 80%.[37] In our study, OS was lower in patients with %VC < 80% than in those with %VC ≥ 80% because of frequent deaths from non-malignant diseases (particularly pneumonia), whereas RFS was not different, consistent with previous studies.[19,21] The incidence of %VC < 80% is reportedly 7–13% in various populations.[32,38] %VC < 80% is associated with cardiovascular disease, diabetes, stroke, systemic inflammation, metabolic syndrome, deficits in the physical quality of life, and mortality.[32,38–41] Accordingly, it can be used as a surrogate marker for decreased systemic function. Many patients with %VC < 80% are asymptomatic or have no interstitial lung disease. Therefore, %VC < 80% cannot be detected without a pulmonary function test. Spirometry is useful in predicting severe postoperative complications and long-term outcomes. These results can offer important information to surgeons and help patients make serious decisions before gastrectomy for GC.

In this study, RFS was slightly lower in patients aged ≥ 75 years than in those aged < 75 years (73.3% vs. 77.9%); however, OS was significantly lower in patients aged ≥ 75 years than in those aged < 75 years (62.9 vs. 79.3%, $p < 0.0001$), probably because of death from non-malignant disease. Several studies have assessed disease-specific survival rather than OS to compare the long-term outcomes of elderly patients who underwent gastrectomy for GC.[2,5] We believe that OS is preferable for primary outcome of studies investigating surgical results to disease-specific survival or RFS, particularly in the elderly.

After selecting surgical candidates for gastrectomy, what would surgeons do for patients with impaired pulmonary function? Previous studies suggest several interventions including smoking cessation,[42] control of respiratory infection, preoperative lung expansion interventions (incentive spirometry,[43] deep breathing exercises,[44] and continuous positive airway pressure[45]), preoperative total enteral or parenteral nutrition[46] including immunonutrition,[47] improvement of anemia,[48] reducing the duration of surgery,[49] epidural analgesia,[50] use of nasogastric tubes for gastric decompression after surgery,[51] and laparoscopic operations that can reduce postoperative pain and pulmonary compromise.[52] In addition, preoperative rehabilitation (pre-rehabilitation) before upper abdominal surgery may help improve respiratory muscle strength.[53–55] We identified a poor OS in patients who underwent total gastrectomy, which is consistent with previous studies.[56–58]

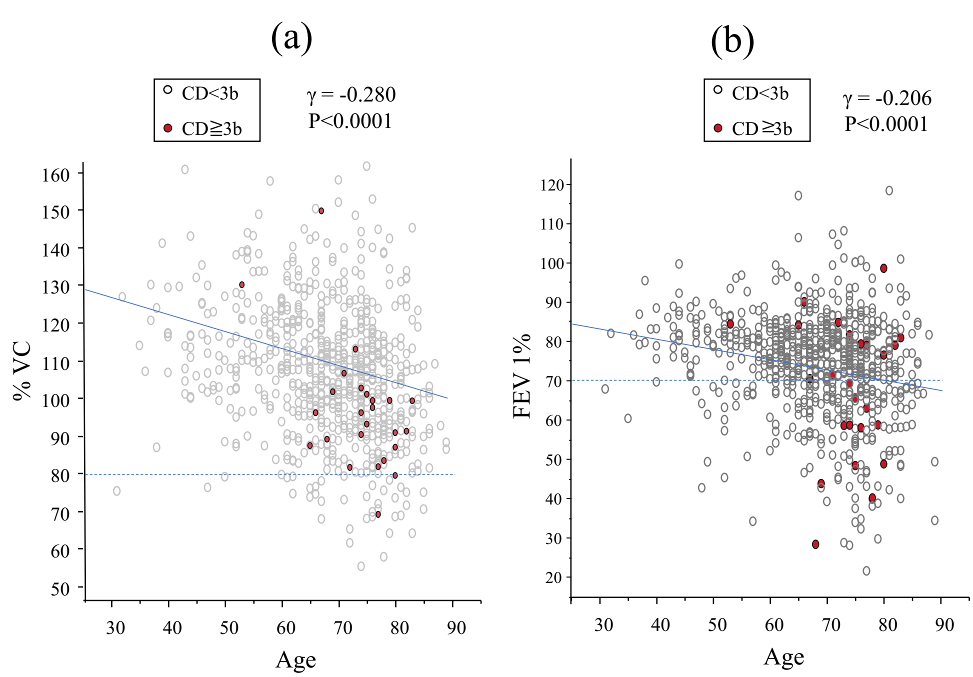

Fig. 2 **a** Correlation between age and %VC in terms of severe postoperative complication. The correlation was weak and significant. Severe postoperative complications were frequent in patients with age ≥ 75 years and %VC of 80–100%. **b** Correlation between age and FEV1% in terms of severe postoperative complications. The correlation was weak and significant. Severe postoperative complications were frequent in age ≥ 70 years and FEV1% < 85%

Table 5 Univariate and multivariate analyses of clinical factors for the prediction of overall survival

		Univariate analysis			Multivariate analysis		
		n	5-year survival	*p*	HR	95%CI	*p*
Age	< 75 years	514	79.3%	**< 0.0001**	1		
	≧ 75	236	62.9%		1.55	1.10–2.17	**0.0131**
Sex	Male	494	73.3%	0.2619			
	Female	256	78.0%				
Body mass index (BMI)	< 18.5	90	67.5%	0.6086			
	18.5–25	501	74.9%				
	> 25	159	78.9%				
Preoperative comorbidity	Absent	285	83.1%	**< 0.0001**	1		
	Present	465	69.5%		1.5	1.08–2.11	**0.0149**
%VC	< 80 (%)	41	60.0%	**0.0214**	1.95	1.06–3.33	**0.0332**
	≧ 80	709	75.7%		1		
FEV1%	< 70 (%)	223	70.4%	0.2354	1.04	0.74–1.43	0.8359
	≧ 70	527	76.3%		1		
Preoperative blood data							
Albumin	< 3.5 (g/dL)	141	52.7%	**< 0.0001**	1.27	0.83–1.92	0.2637
	≧ 3.5	608	79.6%		1		
Hemoglobin	< 10 (g/dL)	103	55.8%	**< 0.0001**	1.11	0.71–1.70	0.6433
	≧ 10	646	77.7%		1		
Platelets count	< 15 ($\times 10^4$/μL)	79	59.9%	**0.0016**	1.38	0.88–2.11	0.1571
	≧ 15	670	76.4%		1		
Lymphocyte	< 1000 (/μL)	81	68.6%	0.1124			
	≧ 1000	653	75.3%				
Mean corpuscular volume (MCV)	< 100 (fl)	670	75.1%	0.5708			
	≧ 100	80	73.4%				
Neutrophil-to-lymphocyte ratio (NLR)	< 4	621	76.9%	**0.0040**	1		
	≧ 4	124	63.0%		1.07	7.20–1.56	0.7356
Surgical approach	Laparotomy	597	70.1%	**< 0.0001**	1		
	Laparoscopy	153	93.1%		0.53	0.25–1.03	0.0632
Surgical procedure	Distal gastrectomy	509	81.9%	**< 0.0001**	1		
	Total gastrectomy	241	60.5%		1.77	1.31–2.41	**0.0003**
Stage	I	413	88.7%	**< 0.0001**	1		
	II	141	67.7%		2.81	1.76–4.49	**< 0.0001**
	III	196	49.8%		7.44	4.72–11.77	**< 0.0001**
Clavien–Dindo classification	< 3b	725	76.3%	**< 0.0001**	1		
	≧ 3b	25	31.6%		3.19	1.78–5.33	**0.0003**
Postoperative adjuvant chemotherapy	done	220	66.0%	**< 0.0001**	0.53	0.36–0.78	**0.0014**
	not done	530	78.9%		1		

Bold values indicate significant difference ($p < 0.05$)

Total gastrectomy leads to a limited postoperative diet, dysphagia, dry mouth, and reflux symptoms, which affect the patient's quality of life; therefore, total gastrectomy should be avoided if the proximal margin is negative.[59] Considering that it is technically possible, "function-preserving" gastrectomy including proximal gastrectomy and subtotal gastrectomy may be considered.[60] Less invasive palliative resection may be beneficial, especially for vulnerable patients.

This study has some limitations. First, the results might have been biased because of the retrospective and single-center design; therefore, the results could not be extrapolated to other institutions. The usefulness of spirometry should be determined in a well-designed randomized controlled trial. Second, we did not analyze the lung diffusing capacity, cardiopulmonary function tolerance, or blood gas, which might have helped precisely evaluate pulmonary function. However, %VC and FEV1% are widely used and

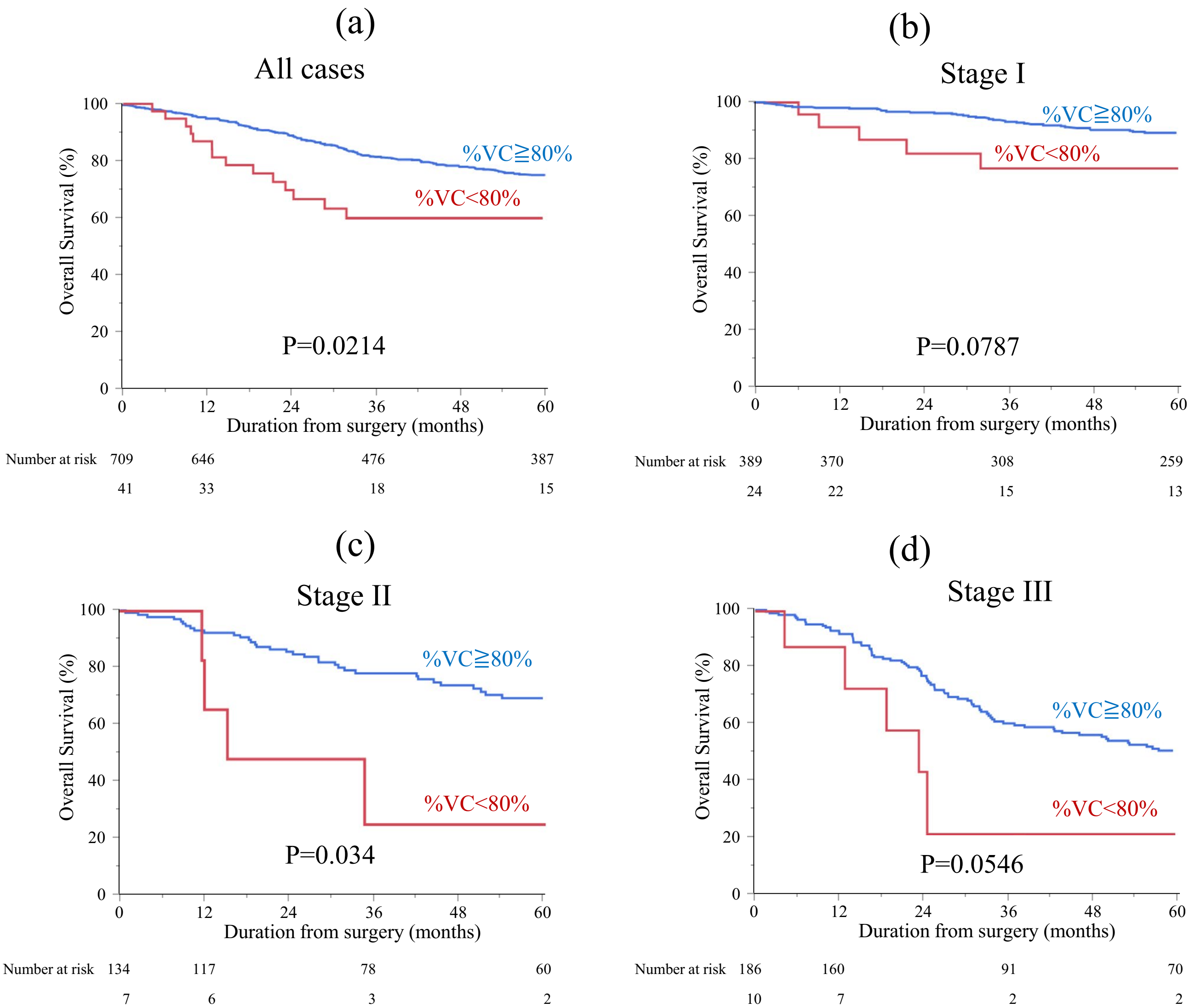

Fig. 3 The OS curves of all patients (**a**) and patients in stages I (**b**), II (**c**), and III (**d**) according to the %VC. OS was consistently lower in patients with %VC < 80% than in those with %VC ≥ 80% in stages I–III

are easily understandable respiratory parameters. Third, relatively few patients underwent laparoscopic gastrectomy ($n = 153$; 20.4%). The clinical significance of preoperative pulmonary function varies in the era of laparoscopic and robotic surgery. Further investigations are required in patients undergoing laparoscopic or robotic gastrectomy. Fourth, the multivariate analysis of clinical factors related to severe postoperative complications revealed no statistically significant independent factors because of the small number of patients with CD ≥ 3b. The outcome criteria for postoperative complications in previous studies include any complication, CD ≥ 2, CD ≥ 3a, infectious complications, and anastomotic leakage.[61,62] We selected CD ≥ 3b (serious complications requiring interventions with general anesthesia) as an outcome criterion because it affects the preoperative treatment decisions. Additional analysis for factors related to postoperative complications (CD ≥ 3a) indicated significant associations with FEV1% < 70%, serum albumin < 3.5 g/dl, and total gastrectomy (Supplementary Table 3). Fifth, frailty (unintentional weight loss, exhaustion, low physical activity, slowness, and weakness), a widely recognized impaired physical response to stress and prevalence with increasing age, was not investigated as factors affecting short- and long-term patient outcomes.[63,64] The definitions of frailty vary across studies, with no consensus in terms of preoperative physical function and short- and long-term postoperative outcomes.[6,8,9,65] However, our results suggest that multiple comorbidities, %VC < 80% and FEV1% < 70%, are potential

Table 6 Relation between the cause of death and %VC

	All cases ($n = 750$)		%VC < 80% ($n = 41$)		%VC ≧ 80% ($n = 709$)		p
Death from malignancy	151	(20.1%)	6	(14.6%)	145	(20.5%)	0.4821
Gastric cancer	129	(17.2%)	6	(14.6%)	123	(17.3%)	0.8142
Other cancers	22	(2.9%)	0	(0.0%)	22	(3.1%)	0.6262
Death from non-malignant disease	38	(5.1%)	7	(17.1%)	31	(4.4%)	**0.0012**
Pneumonia	12	(1.6%)	4	(9.8%)	8	(1.1%)	**0.0028**
Cardiovascular disease	4	(0.5%)	0	(0.0%)	4	(0.6%)	> 0.9999
Gastrointestinal perforation	4	(0.5%)	0	(0.0%)	4	(0.6%)	> 0.9999
Sepsis	3	(0.4%)	0	(0.0%)	3	(0.4%)	> 0.9999
Renal failure	3	(0.4%)	0	(0.0%)	3	(0.4%)	> 0.9999
Cerebrovascular disease	3	(0.4%)	1	(2.4%)	2	(0.3%)	0.1554
Senility	1	(0.1%)	0	(0.0%)	1	(0.1%)	> 0.9999
Surgery related	1	(0.1%)	0	(0.0%)	1	(0.1%)	> 0.9999
Others	7	(0.9%)	2	(4.9%)	5	(0.7%)	0.0514
Unknown	3	(0.4%)	1	(2.4%)	2	(0.3%)	0.1554

Bold values indicate significant difference ($p < 0.05$)

predictors of frailty. Further research based on a common definition of frailty in a larger cohort is required.

In conclusion, FEV1% < 70% is associated with severe postoperative complications (CD ≥ 3b), whereas %VC < 80% is associated with poor OS independent of the cancer stage because of death from non-malignant disease and pneumonia. Spirometry can provide important information and help surgeons discuss the risks and benefits of surgery with patients, perform perioperative management, and select a surgical procedure for patients undergoing gastrectomy for GC, particularly in patients aged ≥ 75 years and those with multiple comorbidities.

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Author Contribution AS wrote the manuscript, analyzed the data, and received funding. HM, HN, and YY prepared the materials and collected the data. NY contributed to the study conception and design and analyzed the data. The first draft of the manuscript was written by AS, and all authors commented on the previous versions of the manuscript. All authors have read and approved the final manuscript.

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Data Availability The data that support the findings of this study are available from the corresponding author (NY) upon reasonablerequest.

Declarations

Ethics Approval All procedures followed were in accordance with the ethical standards of human experimentation and the Helsinki Declaration. This study was approved by our institutional ethics committee.

Informed Consent Informed consent was waived owing to the retrospective nature of this study (2022–004).

Conflict of Interest The authors declare no competing interests.

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