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Preoperative Frailty Assessed Comprehensively by a Questionnaire Predicts a Poor Survival Following Curative Resection of Gastric Cancer

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Abstract. *Background/Aim: The concept of frailty has been attracting attention as a comprehensive indicator of the various effects of aging, but no conclusion has been reached on how to evaluate it. The present study investigated the adverse effect of preoperative frailty on short- and long-term outcomes in patients with gastric cancer using a questionnaire about frailty. Patients and Methods: One hundred and twenty-five patients with pathological stage (p Stage) I/II/III who underwent radical gastrectomy for gastric cancer at the Department of Gastroenterological Surgery, Osaka, Japan from April 2015 to December 2016 were enrolled in this study. The frailty index (FI) was calculated by dividing the total score of 50 questions consisting of 1 point per question by 50. The study used multiple logistic regression analysis with 5-year overall survival (OS) as the endpoint to create a receiver operating characteristic (ROC) curve to determine the cut-off point for the FI. The short- and long-term outcomes of the frail and non-frail groups were then compared, and prognostic factors for OS were examined. Results: Regarding the short-term outcomes, the postoperative complication rates did not differ significantly between the two groups. Regarding the 5-year OS rates of the patients with p Stages II/III, the outcomes in the frail group were significantly poorer than those in the non-frail group. In the multivariate analysis of OS, frailty was independently associated with unfavorable outcomes in patients with p Stages II/III gastric cancer. Conclusion: Frailty evaluation in this study may be useful in predicting long-term prognosis in patients undergoing surgical treatment for advanced gastric cancer.*

With the aging of society, opportunities for physicians to treat elderly patients are increasing. Population aging means that the population of elderly individuals with gastric cancer has also been increasing (1). Elderly people generally have lower physiological reserves than younger ones and are, therefore, considered to have inferior treatment outcomes.

However, it is a well-known fact that age and physiological reserve are not the only causes of deterioration of treatment outcomes. In recent years, the concept of frailty has been advocated, and social interest is increasing. Buchner and Wagner defined frailty as a condition of reduced physiological reserve and susceptibility to disability (2). Since then, attention has been focused on the physical aspects of frailty, and many studies have been conducted. Recently, however, it has been recognized that frailty has three domains: physical (physical frailty), psychological/cognitive (psychological frailty), and social (social frailty), each of which is thought to influence each other and have a negative impact on health. Rookwood *et al*. considered that frailty syndrome is caused by

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the accumulation of various diseases and decreased activities of daily living and proposed the need for a comprehensive evaluation based on the concept of comprehensive geriatric assessment (CGA) (3). From an overall perspective, it is also possible that a certain number of non-elderly patients may also qualify as frail. However, the definition of frailty is not fixed at present, and there are various evaluation methods.

The evaluation of frailty using a questionnaire can reflect not only physical problems but also psychological and social ones. However, few studies have assessed the impact of frailty on treatment outcomes of gastrectomy in patients with gastric cancer using a questionnaire. The present study therefore investigated the adverse effects of preoperative frailty on short- and long-term outcomes in patients with gastric cancer, including young people, using a questionnaire about frailty.

Patients and Methods

Patients. A total of 149 consecutive patients underwent curative gastrectomy for pathological stage (p Stage) I/II/III gastric cancer at the Department of Gastroenterological Surgery, Osaka Metropolitan University, between April 2015 and December 2016. Twenty-four patients who could not answer the questionnaire on frailty before surgery were excluded from the analysis. Ultimately, 125 patients were enrolled in this study. Clinicopathologic variables and postoperative complications were extracted from medical records, operative records, and pathology reports. Tumors were histologically diagnosed based on the Japanese Classification of Gastric Carcinoma, 15th edition (4).

Frailty assessment. The questionnaire, consisting of 50 variables, was developed with slight modifications to the questionnaire on frailty reported by Searle *et al*. (5) (Table I, Table II). The questionnaire consists of five categories: 1) background and history, 2) quality of life (QOL), 3) self-perception, 4) life functioning, and 5) nutrition, with 1, 2, and 5 corresponding to the assessment of physical frailty, 3 to psychological frailty, and 4 to social frailty. The score for each question was either 0 or 1. The total score for the 50 questions divided by 50 was then used as the FI.

Receiver operating characteristic (ROC) curves for FI were generated for a multiple logistic regression analysis in the present study with the 5-year overall survival (OS) as the endpoint. This determined the optimal cutoff point for FI. Patients were classified into either the frail or non-frail group according to the cut-off point.

Treatment strategy. All patients were managed routinely according to the Japanese Gastric Cancer Treatment Guidelines 2014 (ver. 4) (6). Laparoscopic gastrectomy was performed in patients who met the two following criteria: ≤cT2 and ≤cN1. Other patients underwent gastrectomy by laparotomy.

Evaluation of the outcome. We evaluated the postoperative complications that developed within 30 days after gastrectomy. In this study, postoperative complications were evaluated according to the Clavien-Dindo (CD) classification (7). We defined postoperative complications as those with a CD grade of ≥3a. The definition of whether or not adjuvant chemotherapy was performance for three months or longer. We also compared the five-year OS between the frail and non-frail groups stratified by all patients and disease stages and examined the prognostic factors for the OS at p Stage II/III.

Statistical analyses. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University), which is based on R (The R Foundation for Statistical Computing, Vienna, Austria) and R commander (8). Fisher's exact test and the chi-squared test were used to compare categorical variables, and the Mann-Whitney *U*-test was used to compare continuous variables. The OS was defined as the time from surgery until death. Survival curves were generated using the Kaplan-Meier method, analyzing differences by log-rank test. Univariate and multivariate hazard ratios were calculated using the Cox proportional hazard model, and all variables with $p<0.1$ in the univariate analysis were entered into the multivariate analysis. All reported *p*-values were two-sided, setting statistical significance at $p<0.05$.

Results

Patient characteristics. Of the 149 cases, 125 cases (83 males and 42 females) were included in the final analysis. The median age was 70 years. The 5-year OS rate was 81% for the entire cohort. The FI ranged from 0 to 1, and the median (range) was 0.13 (0.01-0.512). The area under the ROC curve in the multiple logistic regression analysis was 0.553. At an FI of 0.176, the projected 5-year OS was optimal. The FI cut-off point was therefore set at 0.176, and subjects were subsequently classified as either frail (FI ≥0.176) or non-frail (FI <0.176). The frail group included 35 patients, and the non-frail group included 90 patients.

The patient characteristics and preoperative factors were compared between the two groups and shown in part of Table III. The frail group was significantly older than the non-frail group (75 *vs*. 68.5 years; $p=0.002$). Furthermore, significant differences between the groups were observed in terms of the Hb (11.6 *vs*. 13 g/dl; $p<0.001$), serum albumin (3.69 *vs*. 4.06 g/dl; $p<0.001$), and ASA-PS (1/2/3) score (0%/71.4%/28.6% *vs*. 15.6%/75.6%/8.9%; $p=0.001$). In all five categories related to frailty (background and history, QOL, self-consciousness, life functioning, and nutrition), the frail group had worse values than the non-frail group ($p<0.001$, respectively). In contrast, the clinical depth of the tumor, lymph node metastasis, and stage did not differ significantly between the two groups.

Short-term outcomes. A comparison of perioperative and pathologic factors for patients in both groups is shown in the lower part of Table III. No significant differences were observed between the two groups in terms of the type of surgery, surgical approach, operative time, or intraoperative blood loss. Furthermore, the postoperative complication rate did not differ significantly between the frail and non-frail groups (17.1% *vs*. 10%; $p=0.357$). In contrast, no significant differences were observed between the groups in terms of pathological advanced stage, although histologically undifferentiated cases were significantly less frequent in the frail group than in the non-frail

Table I. *Variables included in the frailty.*

Background and history	1. Over 80 years old	Yes=1, No=0
	2. Smoking	10 years=1, <10 years=0.5, No=0
	3. High blood pressure	Yes=1, No=0
	4. Stroke	Yes=1, No=0
	5. Hyperlipidemia	Yes=1, No=0
	6. Cirrhosis	Yes=1, No=0
	7. Chronic lung disease	Yes=1, No=0
	8. History of cancer	Yes=1, No=0
	9. Taking anticoagulants/antiplatelet drugs	Yes=1, No=0
	10. Taking immunosuppressive drugs	Yes=1, No=0
	11. Taking 4 or more medicines	Yes=1, No=0
	12. Diabetes	Insulin=1, Hypoglycemic drug=0.5, No=0
	13. Ischemic heart disease	Myocardial infarction=1, CABG=0.75, Catheter treatment=0.5, Taking medicine=0.25, No=0
	14. Dementia	Severe=1, Moderate=0.5, Mild=0.25, No=0
	15. Chronic kidney disease	Dialysis=1, eGFR<40=0.75, eGFR:41-60=0.5, eGFR:61-80=0.25, eGFR>81=0
Quality of life	16. Help with grooming	Yes=1, No=0
	17. Help with dressing	Yes=1, No=0
	18. Help getting in/out of chair	Yes=1, No=0
	19. Help with bathing	Yes=1, No=0
	20. Help with walking around house	Yes=1, No=0
	21. Help with meal preparations	Yes=1, No=0
	22. Help with finances	Yes=1, No=0
	23. Help with driving a car	Yes=1, No=0
	24. Help with shopping	Yes=1, No=0
	25. Help up/down stairs	Yes=1, No=0
	26. Help with housework	Yes=1, No=0
	27. Help with using Toilet	Yes=1, No=0
	28. Help with walking	Wheelchair=1, Walker=0.75, Wand=0.5, No=0
	29. Insomnia	Most of time=1, sometimes=0.5, Rarely=0
	30. Anorexia	Yes=1, No=0
Self-perception	31. Feel useless	Most of time=1, sometimes=0.5, Rarely=0
	32. Feel sad	Most of time=1, sometimes=0.5, Rarely=0
	33. Feel tired	Most of time=1, sometimes=0.5, Rarely=0
	34. Lethargy	Within 1 year=1, Within 1 month, No=0
	35. Feel depressed	Most of time=1, sometimes=0.5, Rarely=0
	36. Self rating of health	Poor=1, Normal=0.5, Good=0
	37. Feel lonely	Most of time=1, sometimes=0.5, Rarely=0
	38. Anxiety	Most of time=1, sometimes=0.5, Rarely=0
	39. Forgetfulness	Most of time=1, sometimes=0.5, Rarely=0
Living function	40. Turtle back	Yes=1, No=0
	41. How health has changed in last year	Yes=1, No=0
	42. No regular exercise	Yes=1, No=0
	43. Deafness	Yes=1, No=0
	44. No family and friends	Yes=1, No=0
	45. Living alone	Yes=1, No=0
	46. Grip strength (kg)	See Table II
Nutrition	47. Weight loss of 5% or more in half a year	Yes=1, No=0
	48. Hb<11	Yes=1, No=0
	49. Body mass index (kg/m^2)	<18 or 30<=1, 25-30=0.5, 18-25=0
	50. Serum albumin (g/dl)	<3.5=1, ≥3.5=0

group (p=0.041). Regarding discharge, patients who could not be discharged home and were transferred to another hospital for medical treatment were significantly more frequent in the frail group than in the non-frail group (14.3% *vs*. 2.2%; p=0.018).

Long-term outcomes. The median duration of follow-up in this study was 60 (range=1-76) months. Regarding the OS among all patients, no significant difference was found between the frail group and the non-frail group (5-years OS

Table II. *Classification of grip strength.*

	Male	Female
Age	Grip strength	Grip strength
≤64	≥30	≥18
65-69	≥27	≥18
70-74	≥26	≥15
75-79	≥24	≥14
≥80	≥22	≥13

Applicable=1, not applicable=0.

rates: 73.5% *vs*. 83.9%, p=0.183) (Figure 1A). In the frail group versus the non-frail group, the 5-year OS rates by pathological disease stage were as follows: p Stage I, 90.9% *vs*. 91.7%; p Stage II, 57.1% *vs*. 93.3%; p Stage III, 20% *vs*. 61.4%; p Stage II/III, 42% *vs*. 74%. In p Stage I, outcomes were not significantly different between the groups (p=0.841); however, in p Stage II/III, the outcome was significantly poorer in the frail group than in the non-frail group (p=0.015) (Figure 1B, C).

To determine the reason for this result, we examined the rate of postoperative adjuvant chemotherapy in patients with p Stage II/III (Figure 2A). The proportion of patients who received postoperative adjuvant chemotherapy was 38.5% in the frail group and 68.3% in the non-frail group, showing a lower treatment rate in the frail group, although the difference was not significant (p=0.1). Furthermore, the number of p Stage III patients treated with S-1 and docetaxel or oxaliplatin was significantly fewer in the frail group than in the non-frail group (0% *vs*. 58.3%; p=0.019, Figure 2B).

Univariate and multivariate analyses. We investigated risk factors for the OS in p Stage II/III patients. Univariate and multivariate analyses of the OS data are shown in Table IV. A univariate analysis indicated that frailty was predictor of the OS (p=0.021). In the multivariate analysis of the OS, frailty and p Stage III were independently associated with unfavorable outcomes in patients with p Stage II/III gastric cancer (p=0.008, p=0.043, respectively). The hazard ratio for frailty was 3.642 [95% confidence interval (CI)=1.395-9.508].

Discussion

The short-term results of this study showed no notable association between frailty and postoperative complications. However, several studies on sarcopenia and frailty that did not include social and psychological factors have shown a significant association with postoperative complications (9). We also previously reported that, in gastric cancer patients, a low preoperative muscle mass increases the risk of postoperative complications, especially infectious complications (10). Lutz *et al*. showed that, as skeletal muscle mass decreases and adipose tissue mass increases, the production of anti-inflammatory cytokines and adiponectin decreases, and levels of inflammatory molecules, such as leptin, chemelin, resistin, TNF-α, IL-1, and IL-6, increase (11). These mechanisms suggest that sarcopenia patients are in a pro-inflammatory state, leading to decreased immunity and reduced postoperative wound healing, which may affect the risk of postoperative complications (12).

A comprehensive index of frailty that includes psychological and social aspects is the clinical frailty scale (CFS), a simple 9-point global scale (13). Tanaka *et al*. reported that preoperative frailty in gastric cancer assessed using the CFS was an independent prognostic factor but not an independent risk factor for postoperative complications, and there are few reports of frailty assessed using indices that include psychological and social aspects as risk factors for postoperative complications (14). This suggests that a decrease in physical reserve, including sarcopenia, is particularly likely to influence postoperative complications.

While the present study did not find a significant association between frailty and complication rates, many frail patients cannot be discharged home and must be transferred to other hospitals. This suggests that not only physical factors but also psychological and social factors, such as the patient home environment, may have a significant impact on being discharged home.

Regarding prognosis, there was no clear difference in the prognosis between the frail and non-frail groups for gastric cancer of p Stage I, but the frail group had a worse prognosis than the non-frail group for gastric cancer of p Stage II/III. Furthermore, frailty was an independent prognostic factor for the OS in p Stage II/III gastric cancer. Tanaka *et al*. reported that, in frailty assessed by the CFS in patients over 80 years old who underwent laparoscopic gastrectomy, similar to our results, there was no marked difference in the OS in p Stage I, but for p Stage II/III, the OS was significantly worse in frail patients than in non-frail patients (14). The main reason for this result may be that many patients in the frail group could not be discharged home after surgery and had to be transferred to other hospitals for rehabilitation and recuperation, and as a result, few patients were able to receive chemotherapy even if they were eligible for postoperative adjuvant chemotherapy as shown in Figure 2A. In addition, as shown in Figure 2B, the fact that frail patients in p Stage III did not receive double postoperative adjuvant chemotherapy may have been influenced by a comprehensive assessment of frailty that included not only physiological reserve but also psychological and social background. However, the lack of a marked difference in the prognosis for gastric cancer of p Stage I may have been attenuated by that comprehensive assessment.

Various indices have been reported for the assessment of frailty; Fried *et al*. defined patients who had three or more of the five items of Shrinking, Weakness, Exhaustion,

Table III. *Summary of patient characteristics and short-term outcomes (n=125).*

Variables		Frail (n=30)	Non-frail (n=95)	*p*-Value
Patient characteristics				
Age, years	Median (range)	73.5 (51-88)	69 (27-83)	0.023
Sex, n (%)	Male	22 (73.3)	61 (64.2)	0.386
	Female	8 (26.7)	34 (35.8)	
Body mass index, kg/m^2	Average±SD	21.6±3.2	22.3±3.3	0.307
Hb, g/dl	Average±SD	11.7 ±1.9	12.9±1.7	0.001
Serum albumin, g/dl	Average±SD	3.66±0.51	4.05±0.38	<0.001
CRP, mg/dL	Median (range)	0.1 (0.01-2.87)	0.07 (0.01-2.17)	0.038
ASA-PS, n (%)	1	0 (0)	14 (14.7)	0.003
	2	21 (70)	72 (75.8)	
	3	9 (30)	9 (9.5)	
Frail index (FI)	Median (range)	0.228 (0.195-0.512)	0.105 (0.01-0.19)	<0.001
Background and history	Median (range)	0.275 (0.117-0.473)	0.1 (0-0.333)	<0.001
Quality of life	Median (range)	0.067 (0-0.9)	0 (0-0.1)	<0.001
Self-consciousness	Median (range)	0.389 (0.056-0.833)	0.111 (0-0.5)	<0.001
Living function	Median (range)	0.429 (0-0.857)	0.143 (0-0.571)	<0.001
Nutrition	Median (range)	0.25 (0-1)	0.125 (0-0.75)	0.015
Clinical depth of tumor, n (%)	cT1a	1 (3.3)	6 (6.3)	0.148
	cT1b	12 (40)	48 (50.5)	
	cT2	7 (23.3)	11 (11.6)	
	cT3	9 (30)	17 (17.9)	
	cT4a	1 (3.3)	13 (13.7)	
Clinical lymph node metastasis, n (%)	cN0	22 (77.1)	72 (75.8)	0.811
	cN (+)	8 (73.3)	23 (24.2)	
Clinical stage, n (%)	cStage I	18 (60)	61 (64.2)	0.832
	cStage II (IIA and IIB)	6 (20)	15 (15.8)	
	cStage III	6 (20)	19 (20)	
Short-term outcomes				
Type of surgery, n (%)	TG	5 (16.7)	26 (27.4)	0.428
	DG	24 (80)	67 (70.5)	
	PG	1 (3.3)	2 (2.1)	
Surgical approach, n (%)	Laparotomy	15 (50)	39 (41.1)	0.406
	Laparoscopy	15 (50)	56 (58.9)	
Operative times, min	Median (range)	253 (154-357)	255 (148-426)	0.552
Intraoperative blood loss, ml	Median (range)	110 (5-875)	100 (5-1,250)	0.735
Postoperative complications, n (%)	Grade 3 or more	5 (16.7)	10 (10.5)	0.352
Discharge, n (%)	Home	26 (86.7)	92 (96.8)	0.056
	Another hospital	4 (13.3)	3 (3.2)	
Hospital stay after operation, days	Median (range)	12 (9-68)	11 (8-57)	0.251
Pathological depth of tumor, n (%)	pT1 (a/b)	16 (53.3)	47 (49.5)	0.987
	pT2	3 (10)	10 (10.5)	
	pT3	8 (26.7)	25 (26.3)	
	pT4 (a/b)	3 (10)	13 (13.7)	
Pathological lymph node metastasis, n (%)	pN0	19 (63.3)	61 (64.2)	0.772
	pN1	4 (13.3)	11 (11.6)	
	pN2	5 (16.7)	11 (11.6)	
	pN3 (a/b)	2 (6.7)	12 (12.6)	
Pathological stage, n (%)	pStage I (A/B)	18 (60)	53 (55.8)	0.845
	pStage II (A/B)	6 (20)	18 (18.9)	
	pStage III (A/B/C)	6 (20)	24 (25.3)	
Histology, n (%)	Differentiated	23 (76.7)	55 (57.9)	0.084
	Undifferentiated	7 (23.3)	40 (42.1)	

ASA-PS: The American Society of Anesthesiologists physical status; SD: standard deviation; TG: total gastrectomy; DG: distal gastrectomy; PG: proximal gastrectomy.

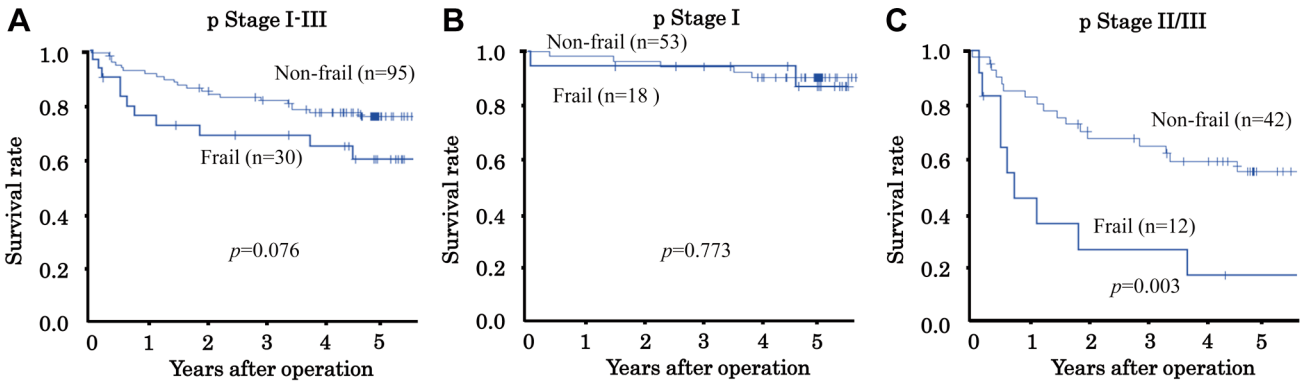

Figure 1. *The overall survival (Kaplan–Meier) in the frail and non-frail groups by disease stage. (A) p Stage I-III (p=0.183), (B) p Stage I (p=0.841), (C) p Stage II/III (p=0.015).*

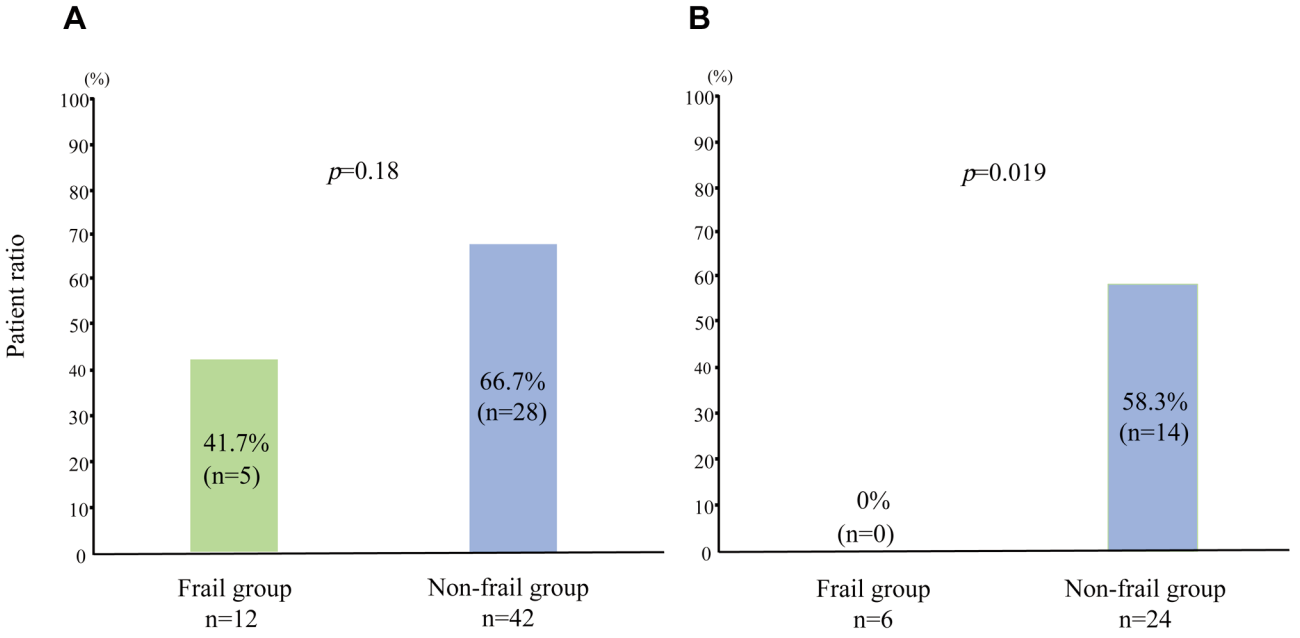

Figure 2. *(A) Patient ratios of undergoing adjuvant chemotherapy for at least 3 months for p Stage II/III gastric cancer (frail group: 38.5% vs. non-frail group: 68.3%; p=0.1). (B) Patient ratio of performing doublet adjuvant chemotherapy (S-1+ DTX or L-OHP) over 3 month or more for p Stage III gastric cancer (frail group: 0% vs. non-frail group: 58.3%; p=0.019).*

Slowness, and Low activity as being frail, and those who corresponded to one or two items had pre-frailty (15). Kristine *et al*. showed an association with frailty as assessed by the Study of Osteoporotic Fractures (SOF) index, which consists of three simple items: weight loss, inability to rise from a chair, and loss of energy (16, 17). However, all of these studies assessed frailty based on physical factors alone.

In gastric cancer, preoperative sarcopenia, malnutrition, and frailty assessed by the SOF index have been reported to adversely affect long-term prognosis, but all of them assessed frailty based on physical factors and nutritional status (18-20). Reports on frailty in gastric cancer patients assessed by a comprehensive index and treatment outcome are rare, except for a study using the CFS by Tanaka *et al*. (14). In the present study, we used a questionnaire consisting of 5 categories and 50 items, as shown in Table I and Table II, which we believe can more accurately assess frailty than other indicators of frailty. The frail group had significantly

Table IV. *The risk factors for relapse-free survival of 54 patients after surgery for p Stage II/III gastric cancer.*

		Univariate analysis		Multivariate analysis	
Variables	Comparison	Hazard ratio (95.0%CI)	*p*-Value	Hazard ratio (95.0%CI)	*p*-Value
Age	≥75 *vs*. <75 Years	1.074 (0.467-2.471)	0.867		
Sex	Male *vs*. female	1.051 (0.457-2.42)	0.906		
ASA-PS	3 *vs*. 1, 2	3.336 (1.293-8.608)	0.013	2.498 (0.922-6.766)	0.072
Serum albumin	<3.5 *vs*. ≥3.5 g/dl	1.018 (0.35-2.97)	0.974		
CRP	≥0.5 *vs*. <0.5 mg/dl	1.49 (0.201-11.06)	0.696		
Frail	Present *vs*. absent	3.183 (1.403-7.221)	0.006	2.651 (1.12-6.275)	0.027
Surgical procedure	TG *vs*. DG, PG	0.869 (0.402-1.881)	0.722		
Surgical approach	Laparotomy *vs*. laparoscopy	1.0849 (0.435-2.701)	0.863		
Operative time	>237.5 *vs*. ≤237.5 min*	1.415 (0.647-3.095)	0.385		
Intraoperative blood loss	>200 *vs*. ≤200 ml*	0.946 (0.438-2.043)	0.887		
Postoperative complications	≥Grade 3a *vs*. Grade 1, 2	2.019 (0.876-4.656)	0.099		
pStage	III *vs*. II	1.392 (0.63-3.078)	0.414		
Histology	Undifferentiated *vs*. differentiated	1.629 (0.753-3.527)	0.215		

*Cutoff values are median.

higher frail scores in all five categories than the non-frail group, confirming that the questionnaire used in this study is an accurate indicator of frailty.

There are few reports of improved long-term outcomes with nutrition and rehabilitation interventions for frail patients, although there have been reports of decreased complications and shorter hospital stays after surgery with these interventions (21). However, these interventions will never improve postoperative outcomes for all frail patients. Therefore, it is important for patients assessed as being frail to be offered preoperative nutrition and rehabilitation interventions as well as preoperative home care coordination and application for long-term-care services to support their discharge home. This will help maintain these patients' QOL, which in turn will increase the proportion of patients receiving adjuvant chemotherapy and improve the prognosis.

Several limitations associated with the present study warrant mentioning. First, this study was conducted at a single institution, and the number of patients evaluated was small. A larger multicenter study is needed to validate the results of this study. Second, these results are based on a questionnaire that was created by making original modifications to an existing questionnaire. Its validity as a questionnaire to assess frailty is thus debatable and needs to be validated against Fried's criteria and other measures of frailty. Third, since frailty is a concept originally intended for the elderly, it should also be considered for elderly patients. Fourth, the cut-off values for the FI used in this study were calculated from an ROC analysis, and further validation studies with larger sample sizes should be conducted to determine more qualified cut-off values. In addition, prospective studies should be conducted to analyze the impact of interventions, such as early home care application, nutrition, and rehabilitation.

Conclusion

The five-category frailty questionnaire used in this study is a comprehensive index that covers psychological and social factors of patients. The frailty assessed by this questionnaire is a useful indicator, in accordance with the recent concept of frailty, and may be useful in predicting the long-term prognosis of patients undergoing surgical treatment for advanced gastric cancer.

Conflicts of Interest

There are not any financial or other interests with regard to the submitted manuscript that might be construed as a conflict of interest.

Authors' Contributions

TTa and KS contributed significantly to the study design, data analysis, and drafted the manuscript. KR, TM, HM, SN, SD, MN, YM, MY, TTo, NK, HT, and SL participated data collection and assisted with data interpretation. KS and MO critically reviewed and revised the manuscript. KM is a chairperson of our department and supervised the entire process. All Authors read and approved the final manuscript.

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