Original Article

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Impact of sarcopenia on S1 adjuvant chemotherapy and prognosis in pancreatic cancer patients

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SUMMARY Although the importance of adjuvant chemotherapy (AC) has been recognized in pancreatic cancer (PC) patients, there are few studies to address the underlying mechanisms of failure to complete AC. This study aims to investigate the relationship between nutritional state represented by sarcopenia and failure to complete AC in patients after curative-intent surgery for PC. This study included 110 patients who underwent pancreaticoduodenectomy for potentially resectable pancreatic cancers with intention of adjuvant S-1. Sarcopenia was defined using the psoas muscle mass index with cutoff values of 6.36 cm^2/m^2 for men and 3.92 cm^2/m^2 for women, which were calculated with a 3-D volumetric software. The relation between sarcopenia and successful AC and long-term survival were investigated. Twenty-nine (26%) patients were diagnosed as having sarcopenia (Sarcopenia group). Sarcopenia group comprised significantly older patients than Non-sarcopenia group (72 *vs*. 67 years old, $p = 0.0087$). AC was successfully completed in 14 patients (48%) in Sarcopenia group compared to 72 patients (89%) in Non-sarcopenia group ($p < 0.0001$). Multivariate analysis identified age ≥ 70 years and sarcopenia as significant risk factors for failure of AC. Among patients ≥ 70 years old, rate of successful AC was significantly higher in sarcopenia groups than non-sarcopenia group (17% *vs*. 78%, $p < 0.001$). In conclusions, age and sarcopenia were critical risk factors for the failure of 6 months of adjuvant chemotherapy. Among elderly patients, sarcopenia can predict the poor success rate of AC.

Keywords pancreatic cancer, sarcopenia, adjuvant therapy, nutrition, prognosis

1. Introduction

Despite recent improvements in diagnostic and therapeutic modalities, pancreatic cancer (PC) still has an extremely poor prognosis (*1*). Although only surgery may lead to a complete cure, most patients develop recurrence even after curative-intent surgery (*2,3*) . At present, adjuvant chemotherapy (AC) is one of the mainstays for the treatment of resectable PC (*4-6*) . A recent large-scale clinical study has shown that the completion of planned AC rather than early initiation was a critical prognostic factor for patients with PC (*7*) . For PC patients, pancreaticoduodenectomy has been established as a standard procedure. Although the importance of the completion of AC has been recognized, there are few studies to address the underlying mechanisms of failure to complete AC in PC patients.

In 2013, the Japan Adjuvant Study Group of Pancreatic Cancer (JASPAC-01) phase III trial demonstrated that S-1 was significantly more effective than gemcitabine as an AC for Japanese patients who underwent curative surgery for PC (*5*) . Therefore, AC with S-1 after curative surgery is considered the standard therapy for these patients in Japan.

We hypothesized that nutritional factors would have a significant relation to the capacity of each patient to complete the planned adjuvant therapy after pancreaticoduodenectomy for PC patients. Here we investigated the clinicopathological, sarcopenia, and nutrition state factors associated with failure to complete AC in patients after curative-intent surgery for PC.

2. Patients and Methods

2.1. Patients

This single-center retrospective study was approved by the institutional review board of the Cancer Institute

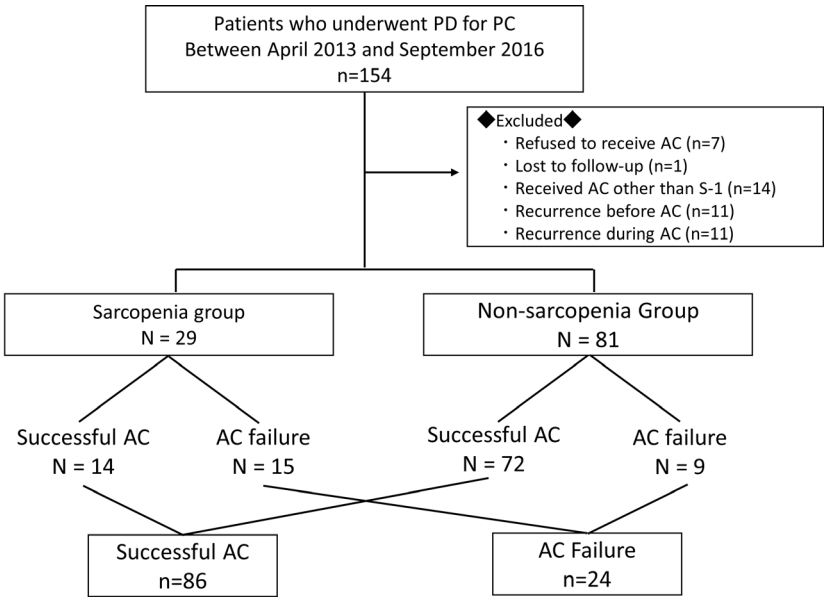

Figure 1. Patient flow of this study.

Hospital with waived informed consent (ID number: 2017-GA-1019-0040). From April 2012 to March 2015, 154 patients with potentially resectable PC underwent pancreaticoduodenectomy with curative intent at Cancer Institute Hospital, Tokyo, Japan. We excluded; (1) 14 patients who received AC other than S-1; (2) 7 patients who refused to receive AC; (3) 11 patients who had early recurrence before AC introduction; (4) 11 patients who had recurrence during AC; (5) 1 patient who we lost to follow-up (1 patients). Finally, 110 patients were the subject of analysis in the present study. A flow diagram of the patient selection is shown in Figure 1.

2.2. Perioperative nutritional management

All patients underwent pancreaticoduodenectomy with regional lymph nodes (LNs) nodal dissection with or without nerve plexus dissection. In principle, hemi-circumferential dissection of nerve plexus around the superior mesenteric artery (SMA) was conducted in patients with suspicious or apparent perineural invasion toward the SMA (*8,9*). After admission, patients were treated in accordance with our clinical pass for pancreaticoduodenectomy. In brief, patients ate ordinal meals until night two days before the surgery, took liquid nutrition on the day before surgery, and drank one liter of oral rehydration solution until 3 h before surgery. After surgery, the nasogastric tube was removed just after airway extubation. Oral intake was initiated on postoperative day (POD) 1, beginning with pure water. Patients began to eat liquid food on POD 4, starting with rice gruel and soft food on POD 6 and advancing in steps to regular food intake. If the patient had a finding of clinically relevant postoperative pancreatic fistula, conservative treatment with prolonged drain placement was chosen (*10,11*) . Postoperative pancreatic fistula (POPF) and delayed gastric emptying (DGE) were defined based on international guidelines (*12,13*) . Other postoperative complications were defined according to the Clavien-Dindo classification (*14*) .

2.3. Adjuvant Chemotherapy

AC was administered after confirming sufficient patient recovery for chemotherapy based on oral intake, performance status, and absence of intractable diarrhea. The patients received S-1 chemotherapy and were followed on an outpatient basis. The patients received 40 mg of S-1 per square meter of body surface area twice a day for 4 weeks, followed by 2 weeks of rest as one course (6-week schedule), and this was continued for 6 months after surgery. The patients with a body surface area < 1.25 m^2 received 80 mg daily, those with a body surface area of 1.25 m^2 or more, but < 1.5 m^2, received 100 mg daily, and those with a body surface area of 1.5 m^2 or more received 120 mg daily.

The need for a reduction of the starting dose, a delay in treatment, or a dose reduction in the patients who received S-1 in clinical practice was determined following the criteria of the JASPAC-01 trial (*5*) . Briefly, the treatment was delayed when patients had hematological adverse events of grade 3 or more, or non-hematologic adverse events of grade 2 or more, until all adverse events recovered to grade 0 or 1, and then was started at a reduced dose of 100, 80 or 50 mg, based on the body surface area described above. The patients who started with the 6-week schedule of S-1 and experienced the adverse events described above at a reduced dose were switched from the 6-week schedule to a 3-week schedule (2 weeks of treatment followed by 1 week of rest).

2.4. Follow-up during S-1 treatment

In principle, patients underwent hematologic tests and assessments of clinical symptoms every 2 weeks during adjuvant therapy. The presence of relapse was determined using imaging studies, including ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI), appropriately. Patients underwent at least one of these imaging examinations at 3-month intervals during S-1 treatment. We defined achievement of more than 6 months of S1 adjuvant therapy as "successful adjuvant therapy" based on a previous report (*9*) .

2.5. Evaluation of clinical parameters and sarcopenia

The toxicities during adjuvant chemotherapy were graded according to the CTCAE ver. 4.0 criteria. Renal impairment was measured in terms of the creatinine clearance (CCr), calculated by the formula proposed by Cockroft and Gault (*15*). For the evaluation of the volume of skeletal muscle, we measured the psoas muscle mass index (PMI, cm^2/m^2) (*16*). Cross-sectional areas of the left and right psoas muscles at the level of the third lumbar vertebra (L3) were estimated in our study population. This was accomplished by first identifying individual vertebral levels on each patient's CT scan. We then selected the individual imaging slice at the superior aspect of L3 and outlined the borders of the left and right psoas muscles. The area of the resulting enclosed regions was then computed to generate the cross-sectional area of the psoas muscles. These steps were completed in a semi-automated fashion using algorithms programmed in VINCENT. We defined sarcopenia using sex-specific cutoff values of PMI, which were 6.36 cm2/m^2 for men and 3.92 cm^2/m^2 for women according to the previous report (*16*). As a barometer of nutritional assessment, Onodera's prognostic nutritional index (PNI) was used. The preoperative PNI was calculated as 10 × albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3) (*17*).

2.6. Statistical analyses

Patients were categorized into two groups regarding the presence of sarcopenia on preoperative CT findings (sarcopenia group, 29 patients; non-sarcopenia group, 81 patients). The clinicopathological parameters between groups were compared using the Mann-Whitney *U* test and the Fisher's exact test as appropriate. Continuous variables were expressed as median values with range. A multiple logistic regression analysis was used to identify the factors independently associated with failure to more than 6 months of AC.

Statistical analyses were performed using JMP statistical discovery software (JMP version 11.0; SAS Institute, Cary, NC). p value less than 0.05 was considered statistically significant.

3. Results

3.1. Background and short-term outcomes

Table 1 shows the patient's demographics and surgical outcomes. Sixty-three patients (57%) were male. Sixteen patients (15%) received neoadjuvant chemotherapy. Twenty-nine patients (26%) needed preoperative drainage of the biliary tract. The median value of PMI was 7.11 cm^2/m^2 in male patients and 4.71 cm^2/m^2 in female patients. Twenty-nine (26%) patients were diagnosed as having sarcopenia (Sarcopenia group). Sarcopenia group comprised significantly older patients than Non-sarcopenia group (72 *vs*. 67 years old, p = 0.0087). Preoperative CEA, CA19-9, and tumor size were not significantly different between groups (CEA, 3.2 *vs*. 2.4 ng/mL, p = 0.08: CA19-9, 68.4 *vs* 86.7 IU/L, p = 0.78; size, 3.4 *vs*. 3.0 cm, p = 0.76). Operation duration, estimated intraoperative blood loss, and incidence of blood transfusion were similar among groups. Hemi-circumferential dissection of nerve plexus around the SMA was likely performed more frequently in non-sarcopenia group than sarcopenia group, but not statistically significant (68% *vs*. 52%, p = 0.13). Postoperative pancreatic fistula, delayed gastric emptying, surgical site infections, and diarrhea were similarly observed among groups. Complications equal to or greater than Clavien-Dindo grade IIIa were more frequent in sarcopenia groups than non-sarcopenia group (17% *vs*. 2%, p = 0.0133). Postoperative hospital stay and mortality rate were not significantly different among groups. R0 resection rate (100% *vs*. 96%, p = 0.2933) and incidence of pathological positive lymph node (72% *vs*. 73%, P = 0.29) were similar among the groups.

3.2. Adjuvant Chemotherapy

Table 2 shows the details of AC in the whole cohort including reasons for failure of AC in 24 patients of the failure group. AC was completed in 14 patients (48%) in Sarcopenia group compared to 72 patients (89%) in Non-sarcopenia group ($p < 0.0001$). Among 24 patients with unsuccessful AC, it was abandoned in 10 patients mainly due to poor performance status or insufficient oral intake. The reasons for discontinuation in 14 patients included fatigue in 4 patients, anorexia in 2 patients and other symptoms.

Univariate analysis revealed that age ≥ 70 years ($p < 0.0001$), sarcopenia ($p < 0.0001$), serum CEA ≥ 2.7 ng/dL (p = 0.0103), tumor size ≥ 3.2 cm (p = 0.0146) and CCr < 60 mL/min (p = 0.0004) were significant risk factors for failure to achieve 6 months of AC. Multivariate analysis identified age ≥ 70 years (odds ratio [OR], 21.9; 95% confidence interval [CI], 4.01 to 120.29; p = 0.0004) and sarcopenia (OR, 6.98; 95% CI, 1.83 to 26.50; p = 0.0044) as significant risk factors for failure of successful AC (Table 3).

Table 1. Patients characteristics, surgical outcomes, and postoperative complications

Variables	Total $n = 110$	Sarcopenia $n = 29$	Non-sarcopenia $n = 81$	p-value
Age, years	68 (46-86)	72 (54-86)	67 (46-80)	0.009
Male: Female	63: 47	18: 11	45: 36	0.66
Body mass index, kg/m^2	21.5 (15.8-28.3)	20.0 (15.8-26.6)	22.0 (17.1-28.3)	0.0008
Prognostic nutritional index	40.5 (22.0-51.0)	40.0 (29.0-45.0)	41.0 (22.0-51.0)	0.35
Diabetes, *n* (%)	43 (39%)	15 (52%)	28 (34%)	0.13
Neoadjuvant chemotherapy, *n* (%)	16 (15%)	6 (20%)	10 (12%)	0.36
Preoperative drainage of bile duct, *n* (%)	39 (36%)	11 (38%)	28 (35%)	0.14
CEA, ng/mL	2.7 (0.5-19.8)	3.2 (0.9-19.8)	2.4 (0.5-16.7)	0.076
CA19-9, IU/L	80.6 (2-50,000)	68.4 (2-2,859.5)	86.7 (2-50,000)	0.78
UICC stage (IA/IB/IIA/IIB/III)	8/18/4/46/33	3/5/0/10/11	5/13/4/36/22	0.51
Tumor size, cm	3.2 (0.5-9.6)	3.4 (0.5-7.1)	3.0 (1.4-9.6)	0.76
Operative time (min)	501 (363-920)	517 (384-920)	500 (363-777)	0.62
Estimated blood loss (mL)	540 (85-2,700)	540 (180-1,830)	540 (85-2,700)	0.98
Intraoperative blood transfusion, *n* (%)	0 (0-1,360)	5 (17%)	6 (7%)	0.15
Nerve plexus dissection of the SMA	70 (64%)	15 (52%)	55 (68%)	0.22
R0 resection rate (0/1)	107/3	29/0	78/3	0.29
incidence of pathologically positive lymph node	80 (72%)	21 (72%)	59 (72%)	0.96
Pancreatic fistula ≥ grade B, *n* (%)	20 (18%)	4 (14%)	16 (20%)	0.58
Delayed gastric emptying ≥ grade B, *n* (%)	16 (14%)	5 (17%)	11 (14%)	0.76
Organ/space SSI, *n* (%)	34 (30%)	9 (32%)	25 (31%)	1.00
Diarrhea, *n* (%)	37 (33%)	10 (34%)	27 (33%)	0.98
Clavien-Dindo Classification ≥ IIIa, *n* (%)	7 (6%)	5 (17%)	2 (2%)	0.013
Pleural effusion	1	0	1	
Ascites	2	2	0	
Intraabdominal bleeding	2	1	1	
Sepsis	1	1	0	
Postoperative hospital stay (days)	26 (12-106)	28 (16-106)	25 (12-63)	0.20
Mortality	1 (1%)	1 (3%)	0 (0%)	0.26

Continuous data are expressed as median with range. SSI, surgical site infection; SMA, Superior mesenteric artery.

Table 2. The details of failure of adjuvant therapy

Type		Grade 1/2/3/4/5
Abandoned	10	
Poor performance status	4	-
Insufficient oral intake	4	-
Neutropenia	1	-
Postoperative complication	1	-
Withdrawn after initiation of chemotherapy	14	
Fatigue	4	0/4/0/0/0
Anorexia	2	0/2/0/0/0
Pigmentation	1	0/1/0/0/0
Arrhythmia	1	1/0/0/0/0
Hyperglycemia	1	0/0/1/0/0
Eye tearing	1	1/0/0/0/0
Neutropenia	1	0/1/0/0/0
Dehydration	1	0/0/1/0/0
Liver dysfunction	1	1/0/0/0/0
Sepsis	1	-

When we examined patients who were 70 years or over, rate of successful AC was significantly lower in sarcopenia groups than non-sarcopenia group (3 patients (17%) *vs*. 23 patients (78%), $p < 0.0001$, Table 4).

3.3. Long-term Survival

Overall survival was compared between 29 sarcopenia patients and 81 non-sarcopenia patients, with a follow-up period of at least 15 months. In comparison with sarcopenia, a significantly higher OS was observed in non-sarcopenia (Figure 2A, $p = 0.017$, Median survival time (MST); 44 *vs*. 25 months). Overall survival was compared between the patients with failed AC and those with successful AC. Thirteen of 24 patients with failed AC, and 26 of 86 patients with successful AC, with a follow-up period of at least 15 months. A significantly higher OS was observed in the patients with successful AC than those with failed AC (Figure 2B, $p = 0.001$. MST; 44 *vs*. 24 months).

4. Discussion

In this study, we investigated the profile of AC after pancreaticoduodenectomy for PC and analyzed the relationship between AC failure and preoperative sarcopenia, which was defined based on cross-sectional areas of the left and right psoas muscles at the third lumbar spine. Our results indicated that sarcopenia was the significant risk factor for failure to complete the planned AC. To the best of our knowledge, this is the first report to reveal the strong correlation between sarcopenia and AC in patients with PC. In this series, we used sarcopenia using sex-specific cutoff values for PMI were 6.26 cm^2/m^2 for men and 4.64 cm^2/m^2 for women, and we used the sarcopenia using sex-specific cutoff values for PMI were 6.36 cm^2/m^2 for men and 3.92 cm^2/m^2 for women according to the previous report. But

Table 3. Univariate and Multivariate analysis or risk factors associated with failure to more than 6 months of planned adjuvant chemotherapy

Variables		Univariate analysis		Multivariate analysis	
	n	Odds ratio (95%CI)	*p*-value	Odds ratio (95%CI)	*p*-value
Age (years)		25.38 (5.55-115.9)	< 0.0001	21.97 (4.01-120.29)	0.0004
≥ 70	48				
< 70	62				
Gender		1.45 (0.58-3.61)	0.42		
Female	47				
Male	63				
Diabetes		1.42 (0.57-3.56)	0.45		
Present	43				
Absent	67				
Neoadjuvant chemotherapy		0.80 (0.20-3.08)	0.75		
Present	16				
Absent	94				
CEA (ng/ml)		3.79 (1.37-10.47)	0.01	1.89 (0.49-7.23)	0.35
≥ 2.7	56				
< 2.7	54				
CA19-9 (U/ml)		2.41 (0.93-6.22)	0.07		
≥ 80.6	55				
< 80.6	55				
Body mass index (kg/m^2)		1.02 (0.41-2.54)	0.95		
< 22	59				
≥ 22	51				
Sarcopenia		8.57 (3.13-23.42)	< 0.0001	6.98 (1.83-26.50)	0.004
Present	29				
Absent	81				
Creatinine clearance		6.43 (2.27-18.17)	0.0004	1.93 (0.48-7.77)	0.35
< 60	21				
≥ 60	89				
Prognostic nutritional index		1.60 (0.64-3.99)	0.31		
< 37	45				
≥ 37	65				
UICC stage		0.87 (0.34-2.18)	0.77		
≥ II B	67				
< II B	43				
Size (cm)		3.78 (1.37-10.47)	0.01	3.64 (0.94-14.07)	0.06
≥ 3.2	56				
< 3.2	54				
Estimated blood loss (ml)		0.60 (0.24-1.51)	0.28		
≥ 540	56				
< 540	54				
Operation duration (min)		0.47 (0.18-1.20)	0.12		
≥ 500	57				
< 500	53				
Intraoperative blood transfusion		3.50 (0.96-12.72)	0.06		
Present	11				
Absent	99				
Pancreatic fistula		0.57 (0.15-2.17)	0.42		
≥ grade B	20				
< grade B	90				
Delayed gastric emptying		1.23 (0.35-4.23)	0.74		
≥ grade B	16				
< grade B	94				
Organ/space SSI		1.46 (0.56-3.77)	0.43		
Present	34				
Absent	76				
Diarrhea		0.76 (0.28-2.05)	0.60		
Present	37				
Absent	73				

CI, confidence interval; UICC, Union for International Cancer Control; SSI, surgical site infection.

there were comparable results.

In the current series, sarcopenia was a predictor of survival following pancreaticoduodenectomy as well, with sarcopenic patients having a significantly increased risk of death. Sarcopenia has been reported to be an objective measure of patient frailty that was strongly associated with long-term outcomes independent of tumor-specific factors. Peng *et al*. have recently reported that total psoas area (TPA) was measured on preoperative cross-sectional imaging in 557 patients undergoing resection of pancreatic adenocarcinoma between 1996 and 2010 (*18*). Sarcopenia was defined as the presence of a TPA in the lowest sex-specific quartile. The impact of sarcopenia on 90-day, 1-year, and 3-year mortality was assessed relative to other clinicopathological factors. Sarcopenia was associated

Table 4. Surgical outcomes and postoperative complications among elderly patients

Variables	Sarcopenia, *n* = 18	Non-sarcopenia, *n* = 30	*p*-value
UICC stage (IA/IB/IIA/IIB)	0/1/8/9	0/2/9/19	0.60
Tumor size, cm	3.6 (1.8-7.1)	3.0 (1.4-4.5)	0.14
Estimated blood loss, mL	505 (205-1,830)	540 (150-2,700)	1.0
Operative time, min	479 (384-920)	490 (363-777)	0.73
Intraoperative blood transfusion, mL	0 (0-1360)	0 (0-560)	0.27
Nerve plexus dissection of the SMA	8 (44%)	22 (73%)	0.02
Pancreatic fistula ≥ grade B, *n* (%)	3 (17%)	5 (17%)	1.0
Delayed gastric emptying ≥ grade B, *n* (%)	4 (22%)	4 (13%)	0.75
Diarrhea, *n* (%)	5 (28%)	15 (50%)	0.20
Clavien-Dindo Classification ≥ III, *n* (%)	4 (22%)	3 (10%)	0.25
Postoperative hospital stay (days)	33 (16-106)	28 (16-63)	0.32
Mortality, *n* (%)	1 (5%)	0 (0%)	0.19
Successful adjuvant chemotherapy, *n* (%)	3 (17%)	23 (78%)	< 0.0001

Continuous data are expressed as median with range. SSI, surgical site infection; SMA, Superior mesenteric artery

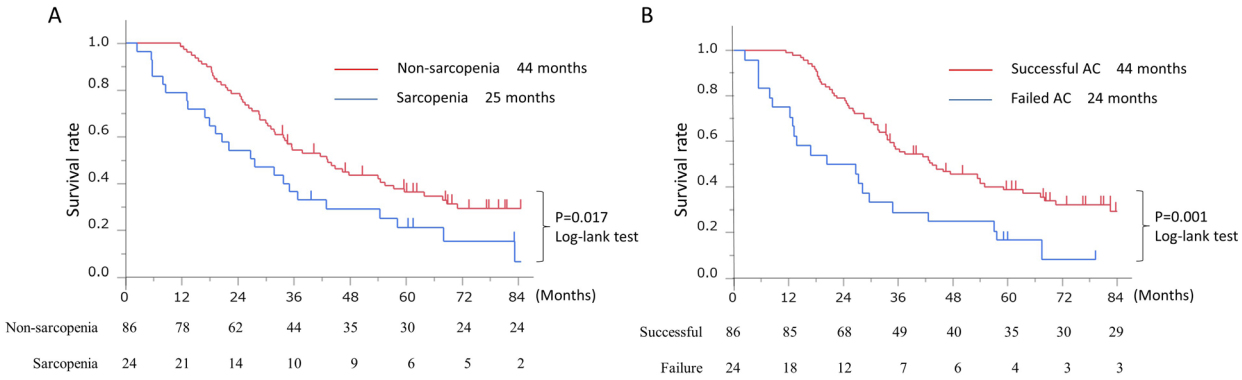

Figure 2. Kaplan-Meier analysis of overall survival according to sarcopenia or successful adjuvant chemotherapy. A: Significantly higher overall survival was observed in patients with non-sarcopenia than those with sarcopenia (p = 0.017, Median survival time (MST); 44 *vs*. 25 months). **B:** Significantly higher overall survival was observed in patients with successful adjuvant chemotherapy than those with failure of adjuvant chemotherapy (p = 0.017, MST; 44 *vs*. 24 months).

with an increased risk of 3-year mortality (HR = 1.68; $p < 0.001$).

For surgical treatment of pancreatic cancers, successful and suitable AC has become a key factor to achieve better overall survival, and this fact has been proved by reliable randomized prospective trials (*4,5*). However, these recent trials included patients with a good postoperative course, which allowed patients to match the eligibility criteria to undergo the planned regimen of AC set for trials. To date, however, the factors for the failure to complete or introduce the AC have not been fully elucidated. Aoyama *et al*. have recently reported that a creatinine clearance (CCr) < 60 mL/min was a significant risk factor for the discontinuation of S-1 AC, even though the renal function was judged to be normal based on the serum creatinine level (*19*). Otherwise, lower preoperative prognostic nutritional index (PNI) level, intraoperative blood transfusion, and organ and/or space SSI were critical risk factors for the failure to complete AC. Based on these backgrounds, we analyzed the various preoperative factors to predict the failure to complete AC. As a result, age, sarcopenia, preoperative CEA, creatinine clearance and tumor size were found to be potential risk factors for the failure to complete AC. Furthermore, multivariate analysis indicated that age ≥ 70 years and sarcopenia were significantly independent factors. Therefore, relatively poor preoperative patient condition may be importantly associated with the tolerability of chemotherapy after pancreatic resection. In addition, preoperative CEA and tumor size seems to be important critical risk factors for the failure to complete AC. One possible estimation of this result indicates that more advanced tumor status causes the more deteriorated patient status and poorer nutrition deprived by the tumor-associated burden, which leads to poor tolerance of AC.

As for relation between achievement of adjuvant therapy and age, our series included only 2 patients who failed to complete AC when stratified under 70 years old, and rate of sarcopenia in patients of 70 years old or younger was significantly lower than that in patients over 70 years old (15% *vs*. 38%, $p < 0.001$). Therefore, sarcopenia seems to have insignificant impact on AC in patients under 70 years old. On the other hand, sarcopenia had significantly negative impact on successful AC in patients over 70 years old. We expect

that evaluation of sarcopenia would be useful to predict the risk of failure in AC after PD for PC patients over 70 years old.

As shown in the Results, each laboratory datum of patient's background could not predict the failure risk of AC. Sarcopenia may reflects systemic tolerance ability for burden of surgery or chemotherapy and could be used as a good surrogate to predict the tolerability for multidisciplinary treatment for PDAC. Other possible speculation is that BSA of patients with sarcopenia may be overestimated. Since the dose intensity of AC is usually determined based on BSA, patients with sarcopenia might have undergone rather overdosed chemotherapy, which might have negative impact on continuance of AC. Due to limited number of patients of the current series, we didn't demonstrate significant difference of adverse events of AC between two groups, which should be investigated in future larger series.

As for long-term survival, sarcopenia showed significant impact on overall survival. However, survival after resection of PDAC is affected by not only patient's factors but also by tumor state. In our result, tumor size and CEA tended to be greater in sarcopenia group than those in non-sarcopenia group, although statistical significance was not proved. Further accumulation of patient number is needed to clarify the confounding of these factors.

It is critically important to examine if the suitable nutritional or immunologic support can improve patient condition and enhance the completion rate of planned AC. According to recent guidelines (*20*), it is recommended to evaluate the patient nutritional status since the beginning of treatment and to carefully control it throughout the treatment. Although many studies addressed the nutritional assessment or intervention on cancer patients, there are few studies about the perioperative nutritional support for the PC patients receiving curative-intent treatments. Since this issue becomes more important especially in the era of the multidisciplinary treatment, further prospective studies are clearly required.

This study has some limitations. Firstly, due to limited number of patients in single-center retrospective analysis, our results would be influenced by bias. Secondly, our retrospective data lacks preoperative trends of body weight or oral intake status, which would hamper to distinguish the reason of sarcopenia, for example, dietary habits or deterioration by malignant disease. Thirds, our study population mainly includes patients who underwent upfront resection. Therefore, results of our study should not be simply generalized in the modern era of neoadjuvant therapy for PC.

In conclusion, age and sarcopenia were significant risk factors for the failure to more than 6 months of adjuvant chemotherapy. Especially in elderly patients, sarcopenia has critical impact on AC, and preoperative physical and nutritional intervention to resolve sarcopenia should be considered.

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