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Original article

Potential role of surgical resection for pancreatic cancer in the very elderly

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ABSTRACT

Background: There is increasing need to evaluate the surgical indication of pancreatic cancer in very elderly patients. However, the available clinical data are limited, and the optimal treatment is still controversial. The aim of this study was to evaluate the benefit of pancreatic resection in pancreatic cancer patients over the age of 80.

Methods: Between 2005 and 2012, 26 octogenarian patients who received pancreatic resection and 20 who received chemotherapy for pancreatic cancer were retrospectively reviewed. Clinicopathological factors, chemotherapy administration status, and survival were compared. Univariate and multivariate analysis of prognostic factors for survival was performed.

Results: Postoperative major complication rate was 8%, with no mortality. The one-year survival rate and median survival time of the surgery and chemotherapy groups were 50% and 45%, and 12.4 months and 11.7 months, respectively ($P = 0.263$). Of the 26 resected cases, 6 completed the planned adjuvant chemotherapy treatment course. The median survival time of those 6 completed cases was significantly longer than that of the 20 not completed cases (23.4 versus 10.0 months, $P = 0.034$). Furthermore, a multivariate analysis of the 26 resected cases showed that distant metastasis (HR 3.206, 95%CI 1.005−10.22, $P = 0.049$) and completion of the planned adjuvant therapy (HR 4.078, 95%CI 1.162−14.30, $P = 0.028$) were independent prognostic factors of surgical resection.

Conclusions: Surgical resection was safe, but not superior to chemotherapy for pancreatic cancer in octogenarians. In the very elderly, only selected patients may benefit from pancreatic resection.

Introduction

Pancreatic cancer is the fourth leading cause of cancer death in Europe and the United States [1,2], and the number of newly diagnosed cases is increasing over the years. The growing population of elderly patients has contributed to this increase. In Japan, patients aged over 75 years accounted for 49.7% of pancreatic cancer incidence in 2010, and the proportion is estimated to increase to 64.6% by 2030. Furthermore, patients over 80 years of age were a notable rate of 32.1% [3,4]. Since the elderly population is underrepresented in large clinical studies [5–7], clinical standards and treatment indication that are widely accepted today may need to be revised to suit this population, since highly invasive pancreatic surgical procedures and cytotoxic agents may not be tolerable in the frail and comorbid elderly.

With the advance of surgical technique, the mortality and morbidity after pancreatic resection has decreased, so as in high-volume surgical centers, it has become a feasible procedure even for elderly patients [8–14]. Furthermore, previous studies have shown that pancreatic resection can be safely performed even in the patients aged 80 years and over [8,11,12]. However, these studies were based on a population mostly of diseases other than

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pancreatic cancer, such as benign and low-grade malignancies, and included only a relatively small number of pancreatic cancer [8,13,15–17]. Since pancreatic cancer resection requires higher technique, and inflicts greater surgical invasiveness to the patient, it may not be concluded from these studies whether pancreatic surgery can be safely performed for pancreatic cancer patients aged over 80. Furthermore, more importantly, the survival benefit of surgical resection for pancreatic cancer patients aged over 80 is also uncertain, especially under the current circumstances.

In addition, the efficacy of chemotherapy in elderly pancreatic cancer patients is also unclear, since only a few studies have addressed this issue [18–20]. Sehgal et al. reported, from the results of multivariate analysis in a large retrospective study, that elderly patients over 70 years of age who were able to receive chemotherapy had benefit on prognosis, with comparable results to younger patients [18]. In regard to standard clinical evidence based on large prospective clinical trials, the elderly are either excluded from the eligibility criteria, or represent only a small proportion of the total population in the study [5–7]. Therefore, the toxicity profiles and survival benefit of chemotherapy are largely unknown, especially in pancreatic cancer patients aged over 80.

Taken together, it remains unclear whether surgical resection or chemotherapy is the optimal treatment for pancreatic cancer in the very elderly. The purpose of this retrospective observational study is to evaluate the effect of cancer treatment on pancreatic cancer patients aged over 80, particularly with the aim to assess the validity of pancreatic resection. As a collaborative study of two high-volume centers for pancreatic cancer treatment, we compared octogenarian pancreatic cancer patients who received pancreatic resection with those who received chemotherapy without surgery. Prognostic factors were extensively investigated.

Patients and methods

Patients and treatment

A total of 46 patients over 80-years old who underwent pancreatic resection (surgery group) or chemotherapy (chemotherapy group) as the initial treatment for pancreatic cancer between March 2005 to December 2012 at the Nara Medical University Hospital and Kansai Medical University Hospital were enrolled in this collaborative study (KANAPS-05 project study). The clinicopathological factors were retrospectively analyzed. Patients provided written informed consent before treatment according to the rules and regulations of each institution.

In the surgery group, 26 octogenarian patients (7.6%) out of 340 patients with resectable tumors who underwent pancreatectomy were included. Surgical procedure, including lymphadenectomy and vascular resection was applied according to institutional policy and cancer board recommendation. Para-aortic lymph node sampling was performed by harvesting the lymphocellular aortocaval tissue in the area between the celiac trunk and the inferior mesenteric artery, for the purpose of stage definition. Exclusion criteria included no consent to treatment, dementia, and non-independent living. Some patients received adjuvant therapy of gemcitabine, S-1 or liver perfusion chemotherapy [21,22]. Pancreatic fistula was defined according to the guidelines of the International Study Group on Pancreatic Fistula (ISGPF) [23]. Postpancreatectomy hemorrhage (PPH) and delayed gastric emptying (DGE) were defined according to the guidelines of the International Study Group of Pancreatic Surgery (ISGPS) [24,25]. The Clavien–Dindo classification was used to evaluate postoperative complications [26]. Negative resection margin was defined as no tumor invasion beyond the surgical resection plane, i.e., 0 mm distance at resection plane. Resected tumors were classified according to the TNM staging system of the International Union Against Cancer (UICC) [27]. Anorexia and diarrhea status were evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

In the chemotherapy group, 20 octogenarian patients (5.7%) out of 353 patients were included. Fifteen patients had unresectable tumors, including 6 metastatic and 9 locally advanced cancers. Among these patients, one was initially planned for radical surgery, but was found unresectable at laparotomy due to liver metastasis. One patient received bypass surgery preceding chemotherapy. These patients were included in this group. Five patients with resectable tumors refused surgery and received chemotherapy. Either monotherapy or combination therapy of gemcitabine, S-1 or erlotinib was administered according to the attending physician's choice with the informed consent of patients.

Performance status was determined according to the Eastern Cooperative Oncology Group (ECOG) scale. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). As a barometer of nutritional assessment, Onodera's prognostic nutrition index (PNI) was used [28,29]. The preoperative PNI was calculated as 10 x albumin (g/dL) + 0.0051 $\times$ total lymphocyte count (per mm^3). The Charlson comorbidity index was used for assessment of pretreatment comorbidity [30].

Statistical analysis

Chi-square and Fisher's exact test was used for categorical variables, as appropriate. Student's t-test was used for continuous variables. Survival curves were estimated using the Kaplan–Meier method. The log-rank test was used to detect differences between curves. Survival time was calculated from the date of surgery in the surgery group, and the date of treatment start in the chemotherapy group. Patients alive at the time of follow-up point were censored. Date of last follow-up was December 2013. Univariate and multivariate analysis of prognostic factors were calculated with the cox proportional hazards model. Prognostic factors in the univariate analysis with a $p < 0.1$ were included in the multivariate analysis. Differences were considered significant when $p < 0.05$. All statistical analyses were conducted with the SPSS Statistics 22 (SPSS, Chicago, IL, USA).

Results

Study population

Twenty-six patients who had received surgical resection were classified as the surgery group, while 20 patients who had received chemotherapy without surgery were classified as the chemotherapy group (Table 1). Two patients in the chemotherapy group received concurrent radiotherapy. The median age was 82 in both groups. The proportion of female patients was higher in the surgery group than that in the chemotherapy group. The performance status was comparably worse in the chemotherapy group. There were no patients with dementia in both groups. Furthermore, there were no significant differences between two groups in BMI, several pretreatment laboratory values, PNI and the Charlson comorbidity index. Clinically diagnosed metastatic disease determined by pretreatment imaging studies was found in 30% of the chemotherapy group.

Surgical outcome

Peri-operative outcome and pathological diagnosis are shown in Table 2. Ten cases (39%) had combined resection of the portal vein. Major post-operative morbidity with a Clavien–Dindo grade over

Table 1
Patient characteristics.

	Surgery (n = 26)	Chemotherapy (n = 20)	*P*
Median age (years), range	82 (80–87)	82 (80–88)	0.36
Sex			
Male	9 (35%)	12 (60%)	0.04
Female	17 (65%)	8 (40%)	
ECOG performance status			
0	23 (88%)	14 (70%)	0.058
1	3 (12%)	5 (25%)	
2	0	1 (5%)	
BMI (kg/m^2)	20.9 ± 3.9	20.4 ± 3.4	0.33
Dementia	0	0	–
Albumin (g/dL)	3.7 ± 0.52	3.7 ± 0.48	0.34
Hemoglobin (g/dL)	11.5 ± 1.8	11.6 ± 1.7	0.42
Creatinine (mg/dL)	0.73 ± 0.31	0.79 ± 0.25	0.24
Prognostic nutrition index	43.9 ± 5.9	44.9 ± 5.5	0.27
Charlson comorbidity index			
0–1	18 (69%)	13 (77%)	0.43
2–4	8 (31%)	7 (23%)	
Clinically diagnosed distant metastasis	0	6 (30%)	0.004

BMI body mass index, *ECOG* Eastern Cooperative Oncology Group.

Table 2
Perioperative characteristics and postoperative outcomes of resected cases.

	N or mean (% or ±SD)
Operation procedure	
Pancreatoduodenectomy/total pancreatectomy	16/1 (65)
Distal pancreatectomy	9 (35)
Vessel resection	10 (39)
Blood loss (ml)	
Pancreatoduodenectomy/total pancreatectomy	891 ± 803
Distal pancreatectomy	557 ± 342
Vessel resection	
Yes	1318 ± 958
No	534 ± 351
Operative time (min)	
Pancreatoduodenectomy/total pancreatectomy	349 ± 80
Distal pancreatectomy	227 ± 90
Complications	
All Morbidities (Clavien–Dindo)	
0–I	13 (50)
II	11 (42)
IIIa	2 (8)
Post operative pancreatic fistula (ISGPF)	
A	3 (12)
B	2 (8)
C	0
Delayed gastric emptying (ISGPS)	
A	1 (4)
B	2 (8)
C	0
Postpancreatectomy hemorrhage (ISGPS)	
A	1 (4)
B	0
C	0
Intra abdominal abscess	1 (4)
Length of hospital stay (days)	25.8 ± 16.5
Readmission within 30days	2 (8)
Mortality	0
UICC Stage	
IA	1 (4)
IB	1 (4)
IIA	8 (31)
IIB	12 (46)
III	0
IV	4 (15)
Lymph node metastasis	16 (62)
Resection margin	
R0	19 (73)

ISGPF International Study Group of Pancreatic Fistula, *ISGPS* Internation Study Group of Pancreatic Surgery, *UICC* the Union for International Cancer Control.

III was seen in 2 distal pancreatectomy cases (8%) that had pancreatic fistula. Readmission within 30 days was seen in 2 cases (8%). There was no mortality. Lymph node metastasis was pathologically identified in 16 patients (62%). As a result of para-aortic lymph node sampling, 4 cases showed positive nodes, which were undetected in preoperative imaging. These cases were defined as UICC Stage IV as final diagnosis, and were included in the surgery group for survival analysis. The complete resection, i.e. R0, was achieved in 19 patients (73%).

Adjuvant chemotherapy

Thirteen of the 26 cases (50%) in the surgery group received adjuvant chemotherapy. Eight had gemcitabine monotherapy, 2 had S-1 monotherapy, and 3 had liver perfusion chemotherapy. Six patients out of 13 (46%) completed the planned adjuvant chemotherapy. Of the 7 cases that discontinued adjuvant therapy, the reasons for discontinuation were poor general condition in 3 cases, chemotherapy-related adverse events in 2, and postoperative recurrence in 2 cases. Of the 13 cases that could not administer adjuvant therapy, the reasons for non-administration were poor general condition in 6 cases, no consent to treatment in 5 cases, and postoperative early recurrence in 2 cases.

Chemotherapy regimen in patients who received chemotherapy but no surgery

In the chemotherapy group, 10 cases had gemcitabine monotherapy, 3 had S-1 monotherapy, 6 had gemcitabine/S-1 combination therapy, and 1 had gemcitabine/erlotinib therapy. Six of the gemcitabine treated cases received second-line therapy by S-1, and 2 of the gemcitabine/S-1 treated cases received second-line therapy by gemcitabine.

Prognostic analysis in all patients aged over 80

Only one case with cancer-unrelated death occurred in the entire study population. We evaluated the survival of the surgery and chemotherapy groups. There was no significant difference in prognosis of patients aged over 80 between the surgery and chemotherapy groups (Fig. 1). The one-year survival rate and

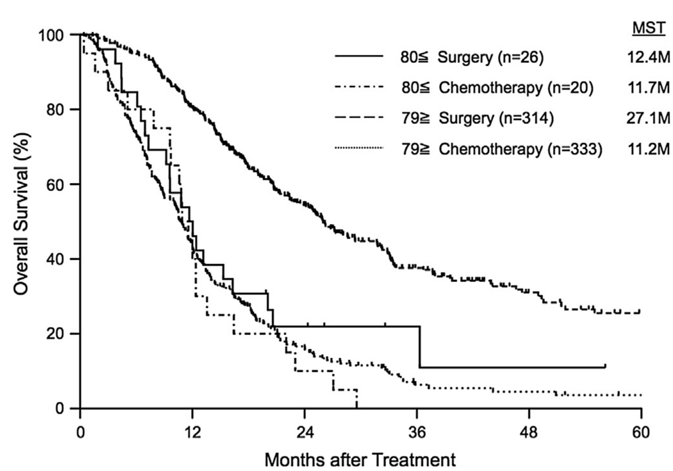

Fig. 1. Overall survival curves of the surgery and chemotherapy groups. There was no significant difference in overall survival between the surgery and chemotherapy groups in patients aged over 80. In comparison with patients under 79 years of age, the prognosis of the elderly patients with surgery was significantly worse than that in the younger patients (P < 0.001).

median survival time (MST) of the surgery and chemotherapy groups were 50% and 45%, and 12.4 months and 11.7 months, respectively (P = 0.263). In comparison with patients under 79 years of age, the prognosis of the elderly patients with surgery was significantly worse than that in the younger patients (P < 0.001, Fig. 1).

Furthermore, there was no significant difference between the two groups after excluding the 6 distant metastasis cases in the chemotherapy group from analysis. Likewise, there was no significant difference between the groups after excluding patients with either or both positive para-aortic lymph nodes and R1 margins from the surgery group. Prognostic analysis of all 46 treated cases showed that surgical resection was not associated with survival (HR 1.491, 95%CI 0.793–2.804, P = 0.215) (Table 3). On the other hand, there were significant differences in BMI, PS status and metastatic status. Furthermore, BMI and metastatic status were defined to be independent predictors for prognosis.

Prognostic analysis of patients treated with pancreatic surgery

Next, we analyzed the prognostic factors for long-term survival in the surgery group. Although the 17 patients with Charlson comorbidity index 0 to1 had a longer MST than the 9 patients with 2–4, there was no significant difference between these groups (12.9 months versus 9.9 months). There was no significant difference in survival according to adjuvant chemotherapy regimen. Multivariate analysis indicated that distant metastasis (HR 3.206, 95%CI 1.005–10.22, P = 0.049) and the completion of the planned adjuvant therapy (HR 4.078, 95%CI 1.162–14.30, P = 0.028) were independent prognostic factors of surgical resection (Table 4). The MST of the 6 cases that completed the planned adjuvant therapy was significantly longer than that of the 20 not completed cases (23.4 months versus 10.0 months, P = 0.034) (Fig. 2).

Table 3
Univariate and multivariate analysis of risk factors for survival of all patients in a Cox proportional hazards model.

	n	Univariate analysis			Multivariate analysis		
		HR	95% CI	*P*	HR	95% CI	*P*
Age (years)							
<82	18						
≥82	28	0.826	0.440–1.552	0.5534			
Sex							
Female	25						
Male	21	1.306	0.698–2.443	0.4040			
BMI (k/m^2)							
≥20.7	22						
<20.7	24	2.237	1.120–4.469	0.0226	2.538	1.244–5.176	0.0104
PS							
0	37						
1–2	9	2.797	1.251–6.252	0.0122	2.088	0.895–4.874	0.0886
CCI							
0–1	30						
2–4	16	1.219	0.634–2.343	0.5533			
PNI							
≥43.5	25						
<43.5	21	1.626	0.867–3.048	0.1299			
Hb (g/dL)							
≥11.1	24						
<11.1	22	0.966	0.515–1.812	0.9143			
M status							
M0	36						
M1	10	3.081	1.385–6.854	0.0058	3.331	1.414–7.843	0.0059
Surgical resection							
Yes	26						
No	20	1.491	0.793–2.804	0.2145			

BMI body mass index, *CCI* Charlson comorbidity index, *Hb* hemoglobin, *PNI* prognostic nutrition index, *PS* performance status.

Table 4
Univariate and multivariate analysis of risk factors for survival of resected patients in a Cox proportional hazards model.

	n	Univariate analysis			Multivariate analysis		
		HR	95% CI	*p*	HR	95% CI	*p*
Age (years)							
<82	9						
≥82	17	0.562	0.235–1.346	0.1960			
Sex							
Female	17						
Male	9	1.217	0.499–2.966	0.6655			
BMI (kg/m^2)							
≥20.9	13						
<20.9	13	2.062	0.830–5.126	0.1192			
PS							
0	23						
1	3	1.901	0.539–6.698	0.3176			
PNI							
≥43.5	13						
<43.5	13	2.01	0.831–4.862	0.1214			
Hb (g/dL)							
≥11.5	7						
<11.5	19	0.923	0.370–2.303	0.8634			
Charlson index							
0–1	17						
2–4	9	1.68	0.687–4.108	0.2555			
Blood loss (ml)							
<556	13						
≥556	13	1.966	0.807–4.792	0.1370			
C/D							
≤Grade II	24						
≥Grade III	2	2.657	0.592–11.93	0.2021			
N status							
N0	10						
N1	16	1.575	0.632–3.922	0.3292			
M status							
M0	22						
M1	4	3.017	0.955–9.534	0.0599	3.206	1.005–10.22	0.0491
Resection margin							
R0	19						
R1	7	1.454	0.554–3.817	0.4473			
Adjuvant therapy initiation							
Initiated	13						
Not initiated	13	1.459	0.603–3.530	0.4025			
Adjuvant therapy completion							
Completed	6						
Not completed	20	3.536	1.020–12.25	0.0464	4.078	1.162–14.30	0.0282

BMI body mass index, *C/D* Clavien Dindo, *Hb* hemoglobin, *PNI* prognostic nutrition index, *PS* performance status.

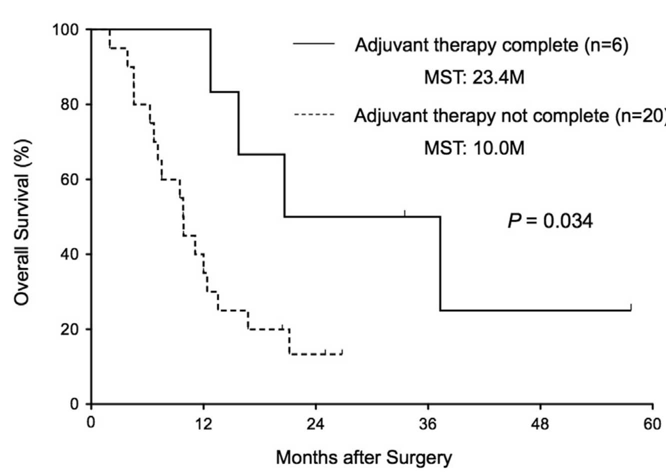

Fig. 2. Overall survival curves of adjuvant chemotherapy completed group and not completed group. The adjuvant chemotherapy completed group had significantly longer survival rate (23.4 months versus 10.0 months, P = 0.034).

Potential factors that may affect adjuvant therapy completion

Finally, we analyzed the factors for completion of adjuvant therapy in the surgery group. There was no statistically significant difference in all pre-operative demographics and surgical outcome, including ECOG performance status, Charlson comorbidity index, and UICC stage, between patients with and without the completion of planned adjuvant chemotherapy (Table 5). However, some factors that trended to differ between the groups were noteworthy. In the completed group, the larger proportion of male patients, higher BMI, higher PNI, lower Clavien–Dindo grade, and shorter length of hospital stay were observed compared to the non-completed group. Furthermore, the period from the date of surgery to the initiation of adjuvant therapy tended to be shorter in the completed group than the non-completed group (34 ± 4.5 days versus 47 ± 19.5 days).

In addition, to evaluate the impact of late complications on the completion of adjuvant therapy, we compared body weight, anorexia, and diarrhea status at 6 and 12 months after surgery (Table 5). As a result, the adjuvant completed group tended to have higher body weight at 6 months after surgery, although the difference did not reach statistical significance. However, there was no significant difference in the body weight loss rate at 6 months between groups (6.3 ± 9.3% in the completed group versus 7.5 ± 9.4% in the non-completed group). Therefore, the preoperative physical strength and constitution of the elderly patients may be a critical factor to complete the adjuvant therapy.

Table 5
Patient characteristics according to adjuvant chemotherapy completion status.

	Completed (n = 6)	Not completed (n = 20)	*p*
Median age (years), range	82 (80–83)	82 (80–87)	0.15
Sex			
Male	4 (67%)	5 (25%)	0.13
Female	2 (33%)	15 (75%)	
ECOG Performance status			
0	5 (83%)	18 (90%)	1.00
1	1 (17%)	2 (10%)	
BMI (kg/m^2)	22.7 ± 2.6	20.4 ± 4.1	0.15
Hemoglobin (g/dL)	12.2 ± 2.6	11.2 ± 1.5	0.42
eGFR (mL/min/1.73 m^2)	62.7 ± 13.6	72.4 ± 21.1	0.26
Prognostic nutrition index	46.6 ± 6.6	43.1 ± 5.6	0.14
Charlson comorbidity index			
0–1	4 (67%)	12 (60%)	1.00
2–4	2 (33%)	8 (40%)	
Operation procedure			
Pancreatoduodenectomy/Total Pancreatectomy	3/0 (50%)	13/1 (70%)	0.62
Distal pancreatectomy	3 (35%)	6 (30%)	
Blood loss (ml)			
Pancreatoduodenectomy/Total Pancreatectomy	659 ± 397	941 ± 869	0.94
Distal pancreatectomy	622 ± 368	525 ± 360	0.90
Operative time (min)			
Pancreatoduodenectomy/Total Pancreatectomy	337 ± 44	352 ± 87	0.40
Distal pancreatectomy	218 ± 83	232 ± 101	0.90
Complications			
All Morbidities (Clavien–Dindo)			
0–I	4 (67%)	9 (45%)	0.64
II–IIIa	2 (33%)	11 (55%)	
Length of hospital stay (days)	20.8 ± 13.6	27.3 ± 17.3	0.41
UICC Stage			
IA–IIA	2 (33%)	8 (40%)	1.00
IIB–IV	4 (67%)	12 (60%)	
Resection margin			
R0	4 (67%)	15 (75%)	0.64
Body weight (kg)			
at 6 months after surgery	50.1 ± 7.3	40.9 ± 8.8	0.05
at 12 months after surgery	48.3 ± 10.2	38.6 ± 5.6	0.22
Diarrhea			
at 6 months after surgery			
grade 0	6 (100%)	15 (100%)	–
grade 1–2	0	0	
at 12 months after surgery			
grade 0	6 (100%)	5 (100%)	–
grade 1–2	0	0	
Anorexia			
at 6 months after surgery			
grade 0	4 (67%)	7 (50%)	0.34
grade 1	2 (33%)	3 (21%)	
grade 2	0	4 (29%)	
at 12 months after surgery			
grade 0	4 (67%)	4 (80%)	0.63
grade 1	1 (17%)	1 (20%)	
grade 2	1 (17%)	0	

BMI body mass index, *ECOG* Eastern Cooperative Oncology Group, *eGFR* estimated glomerular filtration rate, *UICC* the Union for International Cancer Control.

Discussion

Our data suggest that pancreatectomy was feasible for pancreatic cancer patients over 80 years of age. We had a rather aggressive approach towards surgery and tended to resect even locoregionally advanced disease. Reflecting this aggressive approach, the vessel resection rate in this study was remarkably higher than what was reported in previous studies [11–13,15,16]. Nonetheless, major complication rate was as low as 8%. More importantly, there was no mortality in this study, while previous studies reported the mortality to be 2–6% in pancreatic cancer patients aged over 80 [9,11–14]. Accumulating data from previous studies have suggested that the morbidity and mortality after pancreatectomy are acceptable in elderly patients. Our data further support the safety of pancreatic resection even in pancreatic cancer patients aged over 80.

In contrast to our expectations, pancreatic resection was not associated with improved prognosis compared to the chemotherapy group under the current circumstances. Both surgery and chemotherapy group patients were found to be fit at primary assessment, and were referred to our institutes with the intent of treatment. Physiological functions, comorbidity and nutrition status were comparable between the two groups. The performance status had a tendency to be better in the surgery group. Furthermore, 30% of patients in the chemotherapy group had clinically diagnosed distant metastases. Nevertheless, the prognosis was not significantly better in the surgery group. Several previous studies reported that the median postoperative survival time of pancreatic cancer patients aged over 80 years was between 11 and 17 months [9,11,16,17]. These data are consistent with our results. In contrast, Turrini et al. reported the MST to be 30 months in octogenarians, and stated that very elderly patients could benefit from pancreatic resection [12]. However, they have also shown very few 3-year actual survivors, and the 5-year-survival rate was 0%. Therefore, further evaluation may still be needed to determine the indication of surgical resection for pancreatic cancer in the very elderly.

One major factor that may have contributed to the low prognostic benefit of surgery was the adjuvant therapy administration status [12]. This study showed that the completion of the planned adjuvant treatment schedule has a significant impact to post-surgical survival. However, the administration of adjuvant chemotherapy was not a prognostic factor. This was probably due to the high rate of early treatment discontinuation observed in most of the cases that did not complete the planned therapy. The significance of completion and continuation of adjuvant therapy in pancreatic cancer was shown in the follow-up report of the ESPAC-3 study [31]. Although therapeutic benefit of chemotherapy, especially post-operative adjuvant therapy in the very elderly, is still widely unknown, a few retrospective studies suggest similar benefits of chemotherapy in physically fit elderly patients compared to younger patients [18,19].

There are few reports to address the efficacy of adjuvant therapy in elderly pancreatic cancer patients [20,32]. The elderly are susceptible to many distinct geriatric factors related to chemotherapy discontinuation. It has been reported that cognitive function and dependence are associated to treatment toxicity and dose reduction of chemotherapy [33]. Moreover, worse performance status was reported to be associated with higher chemotherapy-related toxicity [34]. In our study, the majority of adjuvant therapy discontinuation or non-administration was due to deterioration of performance status. We conceived that the surgical invasiveness of pancreatic resection had a prolonged influence and caused delay in physical recovery from surgery [35]. Therefore, only physiologically fit, independent, perceptive patients who will be able to tolerate not only surgery, but as well as post-operate therapy, may be candidates for pancreatic resection for pancreatic cancer in the very elderly.

There are many limitations in this study. First, this is a retrospective observational study. Since this is not a case matched study, or an intent-to-treatment manner analysis, the background demographics, especially the tumor status, may be biased. Therefore, the other statistical methods such as propensity score analysis should be considered in the future. In addition, histologically confirmed tumor staging could not be achieved in all unresectable cases, therefore, stage migration in the chemotherapy group may be inevitable. However, at least 30% of the chemotherapy group had clinically diagnosed metastatic disease, though only 15% in the surgery group. It is noteworthy, that survival was not significantly different between both groups even though the chemotherapy group had a possible higher distant metastasis rate. Second, the study population is biased, so the results do not reflect the general octogenarian population. All subjects were a selected subset of comparatively fit patients, and were referred to our institutions with the intent of treatment. However, even when considered capable of tolerating cancer treatment upon conventional clinical interview, many cases in either treatment group had poor prognosis. It is conceivable that hazardous effect will exceed benefit in cancer treatment, whatever the modality, in the frail subset of octogenarian patients.

In conclusion, although pancreatic resection can be safely performed in pancreatic cancer patients over 80 years of age, significant superiority in the prognostic benefit compared to chemotherapy alone was difficult to be achieved. Even in technically resectable disease, only a certain physiologically fit subgroup, that can tolerate not only surgical resection, but as well as post-operative treatment, may benefit from surgery.

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