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Survival benefit of surgery for very elderly patients with pancreatic cancer: what extent of pancreatectomy is acceptable?

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ABSTRACT

The purpose of this study is to clarify the survival benefit and acceptable extent of surgery for very elderly patients with pancreatic cancer. Patients (n=55) ≥80 years with resectable pancreatic cancer were studied. 29 underwent pancreatectomy, 16 underwent chemotherapy, and 10 received best supportive care. Uni and multivariate analysis were performed to explore predictive factors for overall survival (OS) with surgery and chemotherapy (n=45). Postoperative survival of PD (pancreatoduodenectomy) and DP (distal pancreatectomy) and of PD-PVR (PD with portal vein resection) and PD were compared. OS was equivalent with surgery and chemotherapy (median survival time [MST]; 685 vs. 626 days, respectively; p=0.057); 6 patients surivived ≥3 years after surgery. Pancreatectomy was not a prognostic factor. Survival was significantly worse with PD-PVR than with PD, but equivalent with PD and DP. Within 2 years after PD-PVR, 8 patients have died. Surgery was not a positive prognostic factor for very elderly patients with pancreatic cancer, but was the sole chance for survival ≥3 years. Indication for PD-PVR for very elderly patients should be determined more cautiously compared with that for non-elderly patients.

Keywords: pancreatic cancer, very elderly patients, pancreatoduodenectomy, portal verin resection

Abbreviations:
OS: overall survival
RFS : recurrence free survival
PD : pancreatoduodenectomy
DP : distal pancreatectomy
PD-PVR : PD with portal vein resection
MST: median survival time
BSC : best supportive care
mGPS : modified Glasgow Prognostic Score
CA19-9 : carbohydrate antigen 19-9

INTRODUCTION

The number of patients with pancreatic cancer aged ≥80 years is increasing. There were 12,726 cases involving elderly patients, which accounted for 33.9% of the total number of cases of pancreatic cancer occurring in 2015.[1] Nevertheless, the target age of most previous clinical studies relating to pancreatic cancer was ≤80 years. Thus, whether recent clinical standard therapies for pancreatic cancer are appropriate for the very elderly population remains unknown.

Given the prevalence of pancreatic cancer in the very elderly patients and the lack of reliable evidence for a treatment strategy for very elderly patients, we had two research questions.

First, 'Does surgery really have a survival benefit for very elderly patients with pancreatic cancer?' To the best of our knowledge, few studies to date have directly compared the long-term outcomes of very elderly patients with resectable pancreatic cancer treated with either pancreatectomy or chemotherapy.[2,3]

Second, 'What extent of pancreatectomy is acceptable or justified for very elderly patients?' Generally speaking, the surgical indication for very elderly patients with pancreatic cancer should be determined based on the balance of surgical invasiveness and expected prognosis for each procedure. With the advances in surgical techniques and perioperative management, many studies have shown that aggressive pancreatic resection can be safely performed, even in very elderly patients[4-10]; however, no study has directly compared the outcomes of several types of pancreatectomy with their various degrees of invasiveness including, such procedures as pancreatoduodenectomy (PD) versus distal pancreatectomy (DP), and PD with portal vein resection (PD=PVR) vursus PD without PVR.

The aim of this study was to clarify the survival benefit and the acceptable extent of surgery for very elderly patients with pancreatic cancer.

METHODS

Patients

We retrospectively reviewed the records of consecutive patients ≥80 years of age who underwent any treatment for pancreatic cancer (clinical stage 1, 2A, or 2B) as based on the General Rules for the Study of Pancreatic Cancer, 7th edition, Japanese Pancreas Society[11] at Aichi Cancer Center between 1996 and 2017. For purposes of comparison, consecutive patients < 80 years of age who underwent surgery for pathological stages 1, 2A, or 2B pancreatic cancer during the same study period were also reviewed. Patients who underwent pancreatectomy were classified either as PD (pancreatoduodenectomy) or DP (distal pancreatectomy) patients according to the surgical procedure. PD patients were also subdivided into PD-PVR (pancreatoduodenectomy-portal vein resection) patients and PD only patients. This study was approved by the Ethics Review Committee of our center (2018-1-376).

Surgical indications

The indication of surgery for individual patients was decided at a multidisciplinary conference of pancreatic surgeons, medical oncologists, and radiologists. In principle, pancreatectomy was permitted only for patients who met the following criteria: written consent to surgery, no dementia, independent living without nursing, independent walking without assistance, and no severe systemic disease.

Assessment of outcomes

The following 3 issues were assessed.

1. The clinical characteristics of patients and overall survival (OS), as determined from the date of treatment initiation, were compared between very elderly patients (≥80 years of age) who underwent surgery, chemotherapy, or best supportive care (BSC). The date of treatment initiation was defined as the date of surgery for patients who underwent surgery, or as the date when the histopathological diagnosis of pancreatic cancer was made for those who received chemotherapy or BSC. The Cox proportional hazard model was used to explore the possible prognostic factors in the patients who underwent surgery or chemotherapy.

2. The clinical characteristics, surgical outcome, and postoperative survival were compared between the PD and DP very elderly patients, and between the PD only and PD-PVR very elderly patients.

3. Surgical outcome and postoperative survival were compared between very elderly patients (≥80 years of age) and non-very elderly patients (<80 years of age). Postoperative survival was also compared between very elderly and non-very elderly patients stratified by type of surgical procedure (PD only, PD-PVR, and DP).

Performance status (PS) was defined according to the Eastern Cooperative Oncology Group (ECOG).[12] The modified Glasgow Prognostic Score (mGPS) was determined based on the pre-treatment serum levels of C-reactive protein (CRP) and albumin. The patients were scored as follows: CRP (≤1.0 g/dL), mGPS=0; CRP (≥1.0 g/dL) and albumin (≥3.5 g/dL), mGPS=1; CRP (≥1.0 g/dL) and albumin (<3.5 g/dL), mGPS=2.[13] The Charlson Comorbidity Index (CCI) was used to quantify the each patints' burden of disease.[14] Tumor size, portal vein invasion, and lymph node metastasis were diagnosed on pre-treatment contrast-enhanced computed tomography (CT) axial images. Portal vein invasion was defined as tumor contact with the portal vein or superior mesenteric vein (SMV). Lymph node metastasis was defined as the presence of a regional lymph node larger than10mm. The Clavien-Dindo (C-D) classification was applied to postoperative complications.[15] Postoperative pancreatic fistula (POPF) was assessed according to the definition of the International Study Group of Pancreatic Surgery (ISGPS).[16]

Statistics

Continuous variables were expressed as median and range. The Chi-squared test or Fisher's exact probability test was performed for categorical variables. The Mann-Whitney U test was applied for comparison of continuous variables. Survival time was defined as the duration between the time of any treatment initiation and the time of death or latest follow up. OS was calculated using the Kaplan-Meier method and differences were evaluated using the logrank test. A p value <0.05 was considered statistically significant.

Statistical analysis was carried out with SPSS version 21.0 software (IBM, Armonk, New York, USA) or Stata version 14.2 (Stata Corp., College Station, TX, USA).

RESULTS

The study enrolled 55 consecutive patients (≥80 years of age) with clinical stage 1, 2A, or 2B pancreatic cancer. Of these, 29 (52.7%) underwent surgery, 16 (29.1%) underwent chemothrapy, and the remaining 10 (18.2%) received BSC. Among 29 patients who underwent surgery, PD only was performed in 10, PD-PVR in 10, and DP in 9 patients. During the enrollment period of the study, a total of 379 consecutive non-very elderly (< 80 years of age) patients with pathological stage 1, 2A, or 2B pancreatic cancer who underwent surgery were identified. Among them, PD

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only, PD-PVR, and DP were performed in 176, 86, and 117 patients, respectively.

Prognostic impact of pancreatectomy for very elderly patients

When comparing pre-treatment characteristics among patients who underwent surgery (Surg), those who underwent chemotherapy (Chemo), and those who received best supportive care (BSC) (Table 1), we found that the serum CA19-9 level and tumor size were significantly higher in Chemo patients than in Surg patients. Moreover, the percentage of patients with poor performance status and portal vein invasion tended to be higher in the Chemo patients than in the Surg patients.

When comparing survival rates after treatment initiation (Figure 1), we found that there was no statistically significant difference between Surg and Chemo or between Chemo and BSC, while the survival rate was significantly better for Surg than for BSC (median survival time [MST] : Surg, 685 days, Chemo, 626 days, BSC, 284 days). Six Surg patients survived over 3 years, while Chemo and BSC patients did not survive over 3 years. Thus, the 3-year survival rate was 30.8% for Surg patients, while it was 0% for Chemo and for BSC patients. On the other hand, 15 Surg patients (51.7%) have died within 2 years after surgery.

Table 1 Comparison of clinical characteristics of very elderly patients with pancreatic cancer

	Surg (S) (n=29)	Chemo (C) (n=16)	BSC (B) (n=10)	p (S/C)	p (C/B)
Age, years*	82 (80–88)	82 (80–85)	84 (81–88)	0.310	0.004
Male gender	14 (48.3)	13 (81.3)	5 (50.0)	0.055	0.189
PS≥1	3 (10.3)	6 (37.5)	6 (60.0)	0.050	0.422
mGPS≥1	4 (13.8)	3 (18.8)	3 (30.0)	0.686	0.644
Alb, g/dl*	3.9 (3.2–4.7)	3.9 (3.0–4.5)	3.9 (2.8–4.8)	0.385	0.452
CCI*	1 (0–5)	2 (0–4)	1 (0–4)	0.237	0.551
Ph cancer	20 (69.0)	13 (81.3)	5 (50.0)	0.491	0.189
CEA, ng/ml*	3.6 (1.8–18.4)	5.2 (1.5–49.6)	4.4 (1.6–14.1)	0.115	0.586
CA19-9, U/ml*	83.0 (0.1–1879.0)	346.9 (1.6–10020.0)	98.4 (1.5–987.0)	0.021	0.109
Tumor size, mm*	22 (9–42)	27 (17–40)	27 (14–40)	0.016	0.660
cPV1	11 (37.9)	11 (68.8)	5 (50.0)	0.065	0.425
≥cN1	4 (13.8)	4 (25.0)	1 (10.0)	0.427	0.617

Values in parentheses are percentages unless indicated otherwise; *values are median (range).
Surg: surgery
Chemo: chemotherapy
BSC: best supportive care
PS: performance status
mGPS: modified Glasgow prognostic score
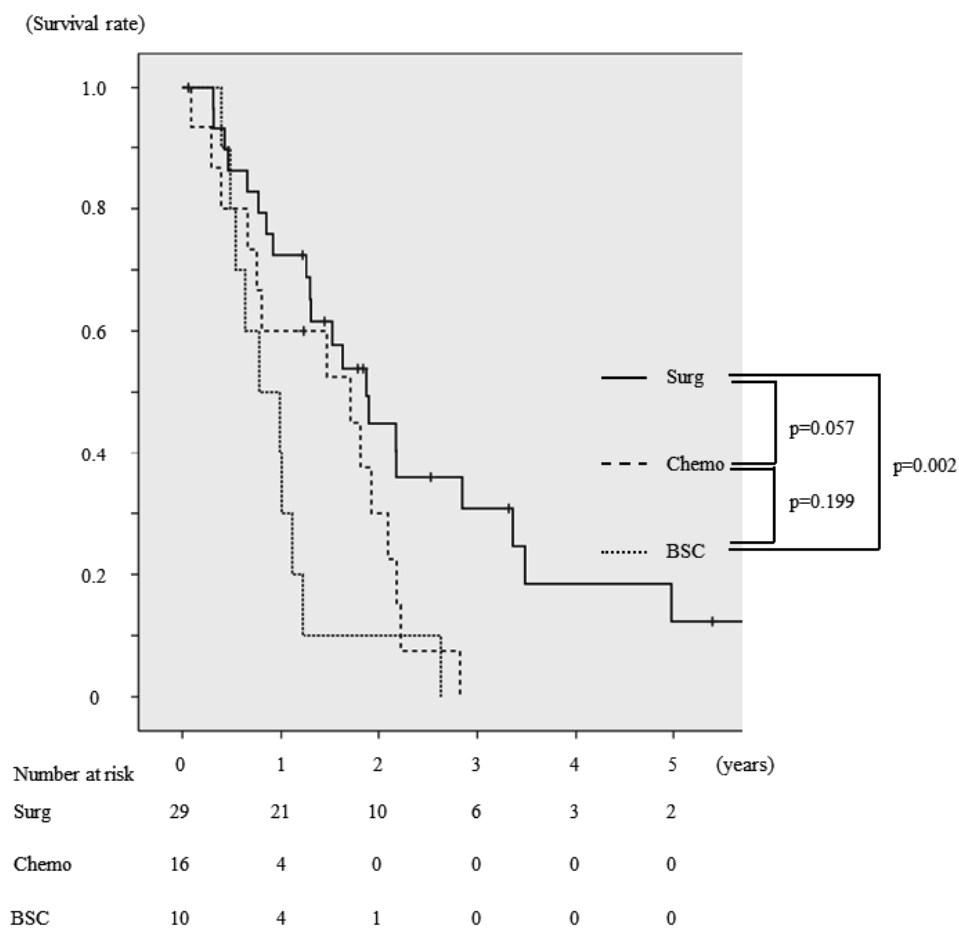Alb: albumin
CCI: Charlson comorbidity index
Ph: pancreatic head
CEA: carcinoembryonic antigen
CA19-9: carbohydrate antigen 19-9
cPV1: clinical portal vein invasion
cN1: clinical node positive

(Survival rate)

Fig. 1 The overall survival after treatment initiation

There was no statistically significant difference between patients who underwent surgery (Surg) and those who underwent chemotherapy (Chemo).

Solid line: Surg, thick dotted line: Chemo, thin dotted line: best supportive care (BSC).

On uni and multivariate analyses (Table 2), execution of pancreatectomy did not corelate with OS. On the other hand, portal vein invasion was identified as independent prognostic factor for very elderly patients with pancreatic cancer.

Table 2 Prognostic factors of very elderly patients with pancreatic cancer

	Univariate analysis			Multivariate analysis		
	HR	95% CI	p	HR	95% CI	p
Pancreatectomy	0.507	0.249–1.034	0.062	0.887	0.303–2.594	0.887
Male gender	1.015	0.510–2.020	0.966	1.243	0.485–3.181	0.650
Age	0.885	0.739–1.060	0.183	0.862	0.707–1.051	0.141
PS≥1	1.827	0.728–4.586	0.199	1.633	0.493–5.411	0.422
mGPS≥1	0.560	0.210–1.492	0.246	0.604	0.200–1.819	0.370

CCI	1.142	0.829–1.572	0.417	1.253	0.848–1.852	0.258
Tumor size	1.038	0.999–1.079	0.056	0.978	0.915–1.045	0.504
≥cN1	2.335	0.990–5.509	0.053	2.614	0.667–10.242	0.168
cPV1	3.262	1.597–6.661	0.001	3.818	1.321–11.035	0.013
CEA	1.037	0.996–1.080	0.076	1.035	0.982–1.090	0.202
CA19-9	1.000	1.000–1.000	0.503	1.000	1.000–1.000	0.585

HR: hazard ratio
CI: confidence interval
PS: performance status
mGPS: modified Glasgow prognostic score
CCI: Charlson comorbidity index
cN1: clinical node positive
cPV1: clinical portal vein invasion
CEA: carcinoembryonic antigen
CA19-9: carbohydrate antigen 19-9

Comparisons between PD vs DP, and between PD only vs PD-PVR for very elderly patients

When comparing pre-operative characteristics according to surgical procedures (Table 3), we found that there was no statistically significant difference between PD and DP except for tumor size. Similarly, there was no statistically significant difference between PD-PVR and PD only. Surgical outcomes are compared in Table 4. When comparing PD and DP, we found that operative time was significantly longer for PD than for DP and significantly longer for PD-PVR than for PD only. Volume of total blood loss was also significantly larger for PD than for DP and significantly larger for PD-PVR than for PD only. As for complication rate, there were no significant differences between PD and DP or between PD-PVR and PD only. There was no mortality in any of the groups. Although there was no statistically significant difference in duration of drain placement between PD and DP, the hospitalization period was significantly longer for PD than for DP. There were no significant differences in the rates of initiating and completing adjuvant chemotherapy.

Table 3 Comparison of clinical characteristics between patients who underwent PD-PVR, PD only, and DP

	PD (n=20)			DP (n=9)	p (PD vs. DP)	p (A vs. B)
		A: PD-PVR (n=10)	B: PD only (n=10)			
Age, years*	82 (80–88)	82 (80–89)	82 (80–87)	82 (80–88)	0.799	0.853
Male gender	9 (45.0)	5 (50.0)	4 (40.0)	5 (55.6)	0.700	>0.999
PS≥1	2 (10.0)	1 (10.0)	1 (10.0)	1 (11.1)	>0.999	>0.999
mGPS≥1	3 (15.0)	0 (0)	3 (30.0)	1 (11.1)	>0.999	0.211
Albumin, g/dl	3.8 (3.2–4.7)	3.9 (3.2–4.5)	3.8 (3.2–4.7)	4.2 (3.6–4.6)	0.183	0.912
Lung capacity, ml	2330 (979–3543)	2434 (1890–3543)	1976 (979–3240)	2650 (1960–3616)	0.153	0.247
CCI*	1 (0–5)	1.5 (0–5)	1 (0–3)	0 (0–3)	0.069	0.353
CEA, ng/ml*	3.7 (1.8–18.4)	3.4 (2.0–10.3)	3.9 (1.8–18.4)	3.4 (2.1–8.0)	0.627	0.739

CA19-9, U/ml*	137.0	105.2	194.1	56.6	0.085	0.739
	(4.0–1879.0)	(10.1–636.0)	(4.0–1879.0)	(0.1–303.9)		
Tumor size, mm*	25 (13–42)	25 (13–42)	26 (15–38)	15 (9–26)	0.005	0.796
Pathological node positive	14 (70.0)	8 (80.0)	6 (60.0)	4 (44.4)	0.237	0.628

Values in parentheses are percentages unless indicated otherwise; *values are median (range).
PD: pancreatoduodenectomy
DP: distal pancreatectomy
PVR: portal vein resection
PS: performance status
mGPS: modified Glasgow prognostic score
CCI: Charlson comorbidity index

Table 4 Comparison of surgical outcomes between patients who underwent PD-PVR, PD only, and DP

	PD (n=20)			DP (n=9)	p (PD vs. DP)	p (A vs. B)
		A: PD-PVR (n=10)	B: PD only (n=10)			
Operative time, min*	364	446	319	218	<0.001	0.004
	(225–552)	(317–552)	(225–496)	(114–291)		
Total blood loss, ml*	555	770	458	230	0.007	0.043
	(140–2200)	(350–2200)	(140–1000)	(70–2420)		
Complications	13 (65.0)	7 (70.0)	6 (60.0)	6 (66.7)	>0.999	>0.999
Complications,						
CD grade 2/3/4	10 (50.0)	6 (60.0)	4 (40.0)	4 (44.4)	>0.999	0.656
POPF, grade B or C	1 (5.0)	0 (0)	1 (10.0)	2 (22.2)	0.220	>0.999
Abscess formation	1 (5.0)	1 (10.0)	0 (0)	1 (11.1)	0.532	>0.999
DGE	6 (30.0)	3 (30.0)	3 (30.0)	1 (11.1)	0.382	>0.999
Surgical site infection	1 (5.0)	1 (10.0)	0 (0)	0 (0)	>0.999	>0.999
Pneumonia	3 (15.0)	3 (30.0)	0 (0)	1 (11.1)	>0.999	0.211
Small bowel obstruction	2 (10.0)	1 (10.0)	1 (10.0)	0 (0)	>0.999	>0.999
Delirium	4 (20.0)	2 (20.0)	2 (20.0)	1 (11.1)	>0.999	>0.999
Mortality	0 (0)	0 (0)	0 (0)	0 (0)	>0.999	>0.999
Drain placement, days*	6 (4–22)	6 (4–7)	7 (5–22)	7 (5–42)	0.253	0.315
Hospitalization, days*	24 (14–120)	26 (14–120)	23 (14–41)	16 (11–43)	0.044	0.353
Initiation of AC	7 (35.0)	3 (30.0)	4 (40.0)	6 (66.7)	0.226	>0.999
Completion of AC	3/7 (42.9)	2/3 (66.7)	1/4 (25.0)	3/6 (50.0)	>0.999	0.486

Values in parentheses are percentages unless indicated otherwise; *values are median (range).
PD: pancreatoduodenectomy
DP: distal pancreatectomy
PVR: portal vein resection
CD: Clavien-Dindo classification
POPF: postoperative pancreatic fistula
DGE: delayed gastric emptying
AC: adjuvant chemotherapy

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There was no statistically significant difference in postoperative survival between PD and DP patients (MST: PD, 694 days vs. DP, 480 days; 3 year survival: PD, 24.7% vs. DP, 44.4%, p=0.771). On the other hand, postoperative survival was significantly worse for PD-PVR than for PD only (MST: PD-PVR, 559 days vs. PD only, 1040 days; 3 year survival: PD-PVR, 13.3% vs. PD only, 35.6%, p=0.039) (Figure 2). Among PD-PVR patients, 4 patients died within 1 year, and 8 patients died within 2 years after surgery.

There were 21 patients who have died after surgery (PD-PVR, n=9; PD only, n=6; DP, n=6). Among them, 6 patients (PD-PVR, n=4; PD only, n=2) died from causes unrelated to pancreatic cancer, which accounted for 28.6% of all death events. Detailed causes of death unrelated to pancreatic cancer were pneumonia (n=2), aortic dissection (n=1), acute myocardial infarction (n=1), infirmity (n=1), and drowning (n=1).

There were 19 patients in whom recurrence developed (PD-PVR, n=7; PD only, n=6; DP, n=6). Among them, systemic chemotherapy was performed for 11 (PD-PVR, n=2; PD only, n=5; DP, n=4), while BSC was selected for the remaining 8 patients (PD-PVR, n=5; PD only, n=1; DP, n=2).
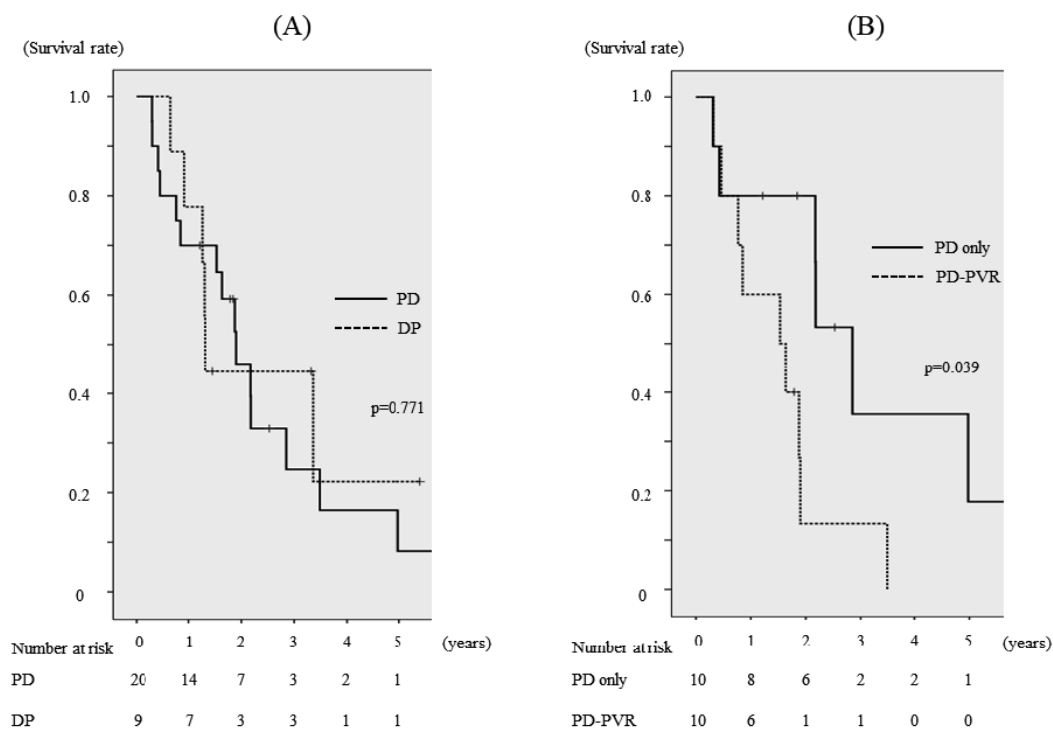
Fig. 2 Comparison of postoperative survival
Fig. 2A: There was no statistically significant difference in postoperative survival between PD and DP patients. Solid line: PD, dotted line: DP
Fig. 2B: Postoperative survival was significantly worse for PD-PVR than for PD only. Solid line: PD only, dotted line: PD-PVR

Comparison between very elderly and non-elderly patients

Surgical outcomes were compared between the very elderly and non-very elderly patients in Table 5. The differences between the outcome measures in the 2 groups were not significant,

except for the duration of drainage. The postoperative survival of very elderly patients was significantly worse than that of non-very elderly patients (MST, 685 days vs 1020 days, respectively; p=0.039) (Figure 3A). The differences between postoperative survival in the PD-only very elderly and non-very elderly patients and DP very elderly and non-very elderly patients were not significant. Among the patients who underwent PD-PVR, postoperative survival was significantly worse in very elderly patients than in non-very elderly patients (MST, 559 days vs 847 days, respectively; p=0.020) (Figure 3B, 3C, 3D).

Table 5 Comparison of surgical outcomes between very elderly and non-very elderly patients

	Very elderly (n=29)	Non-elderly (n=379)	p
Operative time, min*	317 (114–552)	352 (107–923)	0.276
Total blood loss, ml*	460 (70–2420)	455 (20–8040)	0.863
Complications, CD grade 3/4	6 (47.4)	101 (26.6)	0.662
POPF, grade B or C	3 (10.3)	87 (23.0)	0.162
Drain placement, days*	6 (4–42)	8 (4–101)	0.009
Hospitalization, days*	22 (11–120)	24 (3–171)	0.799
Mortality	0 (0)	1 (0.26)	>0.999

Values in parentheses are percentages unless indicated otherwise; *values are median (range).
CD: Clavien-Dindo classification
POPF: postoperative pancreatic fistula
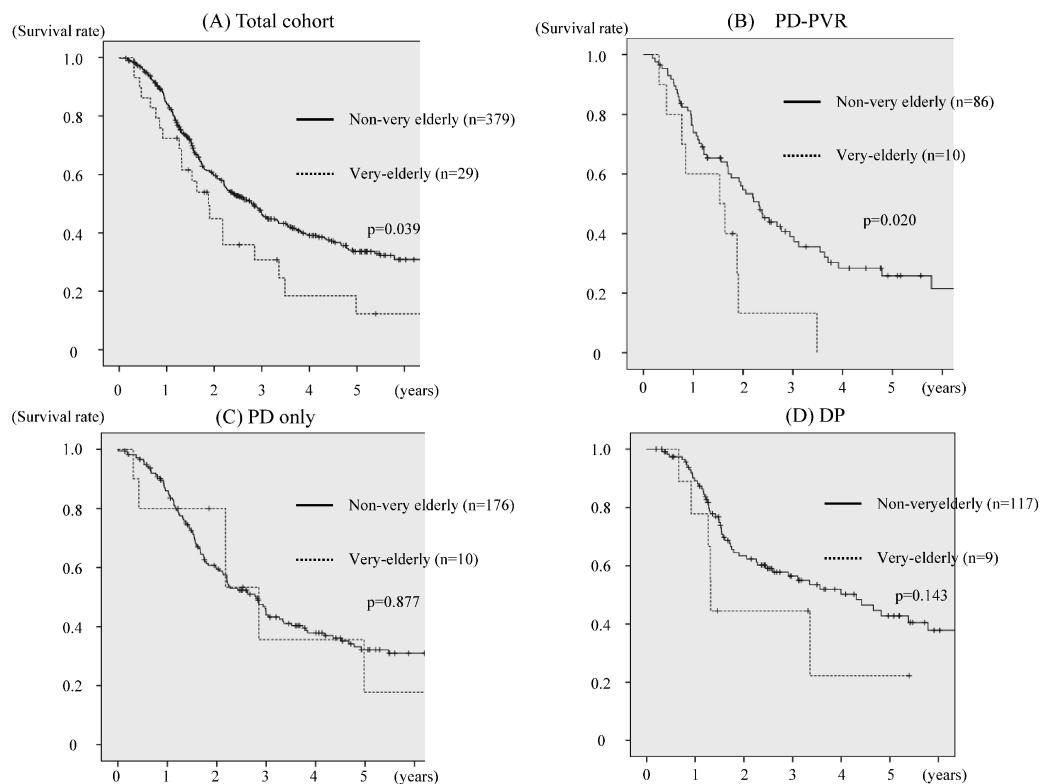
Fig. 3 Comparison of postoperative survival between very elderly and non-very elderly patients
Fig. 3A: Total cohort.
Fig. 3B: Patients who underwent PD-PVR.
Fig. 3C: Patients who underwent PD only.
Fig. 3D: Patients who underwent DP.
          Solid line: non-very elderly patients, dotted line: very elderly patients.

DISCUSSION

To the best of our knowledge, few studies have directly compared the long-term outcomes of elderly patients with pancreatic cancer between those who underwent surgery and those who received chemotherapy. Marmor et al compared survival outcomes of elderly patients with resectable pancreatic adenocarcinoma between those who underwent pancreatectomy and those who received chemotherapy using the Surveillance, Epidemiology, and End Results (SEER) Medicare database from the United States[2]. Their study was valuable in terms of analyzing a large cohort of elderly patients with pancreatic cancer (n=2629). Unfortunately, however, their study defined 'elderly patients' as patients aged ≥65 years. Therefore, a comparison between pancreatectomy and chemotherapy in very elderly patients (≥80 years) which we really wanted to see was performed only in a subgroup analysis. Moreover, possibly because their study used a large-scale national clinical database, it lacked the detailed information of oncological and physical pre-treatment characteristics including tumor marker values or a nutritional index, and detailed causes of death. In Japan, Kinoshita et al compared the outcomes of 26 octogenarian patients who underwent pancreatic resection and 20 octogenarians who received chemotherapy for pancreatic cancer.[3] However, their study included as many as 10 patients (surgery group, n=4, chemotherapy group, n=6) with distant metastasis. Thus, their study could not compare the outcomes of octogenarians with 'same staged' or 'resectable' pancreatic cancer.

In our study, patients who underwent surgery had more favorable oncologic and physical pre-treatment characteristics than those who received chemotherapy in terms of tumor markers, tumor size, the rate of clinical portal vein invasion, and the rate of poor performance status. Nevertheless, surgery could not demonstrate significant survival superiority over chemotherapy. On multivariate analysis, execution of pancreatectomy did not show a positive prognostic impact on OS. These results in themselves were not surprising, because they were consistent with the results of the two previously mentioned reports. Marmor et al demonstrated that the survival benefit of surgery was attenuated as the cohort became older in a subgroup analysis. Kinoshita et al also concluded that surgical resection was not superior to chemotherapy for pancreatic cancer in octogenarians. However, we do not think that being very elderly is a contraindication for pancreatic surgery, since each treatment option has specific disadvantages. Mainly because of postoperative complications, surgery could be problematic if it led to the reduced physical fitness and/or worsening quality of life of the patient. Chemotherapy has adverse effects and requires frequent outpatient clinic visits which could be burdensome not only for patients but also their family. Moreover, surgery benefited some selected patients to a certain degree, because 6 patients who underwent pancreatectomy survived over 3 years, while no patient who did not undergo surgery survived over 3 years in our study. On the other hand, we should not overlook the fact that as many as 15 patients who underwent surgery (51.7%) died within 2 years after surgery. It is possible that they were not potential candidates for surgery. Stricter patient selection for surgery is needed for very elderly patients with pancreatic cancer.

In non-very elderly patients with pancreatic cancer invading the portal or superior mesenteric vein, PD with PVR is a widely accepted procedure in terms of both safety and prognostic power.[17,18] Murakami et al[18] investigated 937 patients who underwent PD (PD-PVR, n=435; PD only, n=502) in their multicenter observational study. They demonstrated that there were no differences in the frequency of postoperative complications, 30-day mortality, and 90-day mortality between the two groups. They also showed a favorable MST of 43.7 months in patients with resectable pancreatic cancer who underwent PD-PVR and received adjuvant chemotherapy. Even for elderly patients, several papers have reported the safety of PD-PVR associated with progress in surgical technique and perioperative management.[3,19] In our study, the morbidity rate (CD grade

2, 3, or 4 ; 60.0 %), mortality rate (0%), and postoperative hospitalization period (median of 26 days) of patients who underwent PD-PVR seemed to be acceptable, although the operative time and total blood loss volume were significantly greater than in those who underwent PD only. Therefore, similar to the results of previous studies, we also consider that PD-PVR for very elderly patients with pancreatic cancer is feasible in terms of short-term outcomes. However, it is still uncertain whether this procedure is really effective for prolonging survival time for very elderly patients. Fang et al[19] compared the postoperative survival between elderly patients who underwent PD-PVR and PD only. They foud no statistically significant difference between groups although their study defined 'elderly patients' as 65 years of age or older. On the other hand, we demonstrated that postoperative survival was significantly worse in patients who underwent PD-PVR than in those who underwent PD only, while such a difference was not observed between PD and DP. Indeed, among 10 patients who underwent PD-PVR, 4 patients died within 1 year, and as many as 8 patients died within 2 years after surgery. Needless to say, the validity of surgical procedures should be determined based on the balance between surgical invasiveness and life expectancy. From the standpoint of this principle, PD-PVR might be an ill-advised procedure for very elderly patients, while it is a widely accepted one for non-elderly patients. One of the possible causes for the poor prognosis of very elderly patients who underwent PD-PVR was high frequency of death due to causes unrelated to pancreatic cancer. In our study, 6 patients (PD-PVR, n=4; PD only, n=2) died from causes unrelated to pancreatic cancer, which accounted for 28.6% of the 21 deaths occurring after surgery. Of course, it is possible that unfavorable pre-operative oncological characteristics accounted for the miserable prognosis of patients with PD-PVR. Regardless, it is certain that the surgical indication for PD-PVR for very elderly patients should be determined more cautiously compared with that for non-very elderly patients.

We also compared the surgical outcomes of very elderly vs non-very elderly patients and did not find a statistically significant difference between the outcomes of the 2 patient groups. That was consistent with the findings of previous studies reporting on the safety of pancreatectomy for very elderly patients.[3-10,19] On the otherhand, in our study, the postoperative survival was significantly worse in the very elderly patients than in the non-very elderly patients. Subgroup analyses of each procedure showed that the difference tended to be more remarkable in patients who underwent PD-PVR than in the patients undergoing the other procedures. This result might be accounted for the high rate of death unrelated to cancer in the very elderly patients who underwent PD-PVR. However, since our study sample was too small to provide definitive findings regarding the reasons for the increased mortality of the PD-PVR patients, a large-scale multi-institutional study should be conducted.

The current study has limitations. Because it was a retrospective observational study in a single center, the number of very elderly patients was relatively small and the pre-treatment status might be biased, especially when comparing patients who underwent surgery with those who did not undergo surgery. It is possible that we could not show significant differences between the survival of patients who underwent chemotherapy vs those undergoing BSC, or of those patients who underwent surgery vs those undergoing chemotherapy only, because the size of our sample was too low. Moreover, since staging laparotomy or laparoscopic investigation was not performed in patients who did not undergo surgery, it is possible that a certain number of patients had metastatic disease in the chemotherapy or BSC group. Thus, stage migration in the non-surgery groups might have been inevitable.

In conclusion, surgery did not have a positive prognostic impact for very elderly patients with pancreatic cancer, although it was the sole chance for survival≥3 years. Although the short-term outcomes of pancreatectomies were acceptable, the surgical indication for PD-PVR for very elderly patients should be determined more cautiously compared with that for non-elderly patients.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no commercial interests.

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