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Original Article

Second pancreatectomy for recurrent pancreatic ductal adenocarcinoma in the remnant pancreas: A pooled analysis

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ABSTRACT

Objectives: The aim of this study was to examine the outcomes of second pancreatectomy for the treatment of recurrent pancreatic ductal adenocarcinoma (PDAC) in the remnant pancreas.
Method: Search of the PubMed database was undertaken to identify relevant English language studies. Pooled individually data were examined for clinical outcomes after second pancreatectomy for recurrent PDAC.
Results: A total of 19 articles involving 55 patients were eligible for inclusion. The median disease-free interval after initial resection was 33 (range 7–143) months. Of the 55 patients reported, 52 (94.5%) patients underwent completion total pancreatectomy in the second operation for recurrences, including 15 patients who developed recurrences more than 5 years after the initial operation. There was no perioperative death. The 1-, 3- and 5-year overall survival rate after the second pancreatectomy was 82.2%, 49.2% and 40.6% respectively.
Conclusion: Second pancreatectomy for recurrent PDAC can be performed safely with long-term survival in selected patients.

1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies, ranking the fourth leading cause of cancer-related death in the United States [1]. Even among patients who have received surgical resection, the 5-year survival rate is only about 20% mainly due to the high incidence of recurrence [2]. Local recurrence and liver metastasis are the major patterns of recurrence, often resulting in a dismal prognosis because both situations are oftentimes ineligible for surgical intervention and limited to palliative chemotherapy or best supportive care. The median disease-free survival is usually 7 months for local recurrence and 3 months for liver metastasis [3]. On the other hand, patients with a recurrent disease only in the remnant pancreas are candidates for surgical treatment. However, only few reports have presented their experience and practice with second operation for recurrent PDAC, and therefore the value of such aggressive surgery remains debatable [4–10]. Thus, we undertook a systematic review of the literature and pooled data from all individually documented patients to evaluate the long-term oncological outcomes of second pancreatectomy for recurrent PDAC after initial pancreatectomy with a relatively large number of patients.

2. Methods

This study was performed in accordance with the guidelines of preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2009 [11].

2.1. Literature review

A systematic search of the electronic PubMed database between 2000 and June 2016 was performed to identify relevant articles by using the following terms: remnant pancreatic cancer, remnant pancreas, repeat pancreatectomy, and second pancreatectomy. The reference lists of selected articles were checked manually for additional studies.

2.2. Inclusion criteria

(1) Papers presenting data on second pancreatectomy for recurrent PDAC in the remnant pancreas after initial pancreatectomy;

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(2) original data published; and
(3) availability of long-term outcomes.

2.3. Exclusion criteria

(1) Non-English language studies;
(2) reviews without original data and animal studies;
(3) the absence of individual patient data;
(4) duplications; and
(5) the absence of long-term data. To avoid study population heterogeneity, other types of pancreatic cancer such as adenosquamous carcinoma or mucinous carcinoma were also excluded.

Two investigators (JY and YZ) independently reviewed all the retrieved studies that met the inclusion and exclusion criteria. Discrepancies between the two reviewers were resolved by discussion and consensus. The following data were collected for each patient: sex, age, surgical procedures, disease-free interval (DFI) between the initial pancreatectomy and appearance of remnant PDAC, pathological features of operative specimens, adjuvant chemotherapy, 30-day mortality, recurrence and overall survival (OS) after second resection. Local recurrence was defined as cancer recurrence in local lymph nodes, recurrence in local connective soft tissue and remnant pancreas. Extra-pancreatic recurrence was defined as recurrence in the liver, peritoneum, retroperitoneum, lungs or any other site. Based on pathology, all resected tumors were reclassified in keeping with the seventh edition of the American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC) Tumor, Node, Metastasis (TNM) staging system [12].

2.4. Statistical analyses

Descriptive statistics are presented as percentages or mean values when applicable. Overall survival was estimated by Kaplan-Meier methods. Predictors of survival at univariate analysis ($P < 0.10$) were tested with multivariable Cox regression models. Hazard ratios (HR) were reported with 95% confidence intervals (CI). All statistical analyses were performed using SPSS statistical software (version 17.0; SPSS, Illinois, USA).

The study was approved by the Ethics Committee of our hospitals.

3. Results

3.1. Characteristics of the study population

Nineteen articles including a total of 55 patients were eligible for inclusion [4–10,13–24]. The results of study selection are shown in Fig. 1. No randomized trials were available. Characteristics of the published studies are outlined in Table 1. The initial pancreatectomies included pancreaticoduodenectomy in 33 patients, distal pancreatectomy in 21 patients, and duodenum preserving pancreas head resection in one patient. The median DFI between the initial pancreatectomy and appearance of remnant PDAC was 33 (range 7–143) months. Fifteen patients (27.2%) developed remnant PDAC beyond 5 years after the initial pancreatectomy. Fifty-two (94.5%) patients underwent completion total pancreatectomy in the second operation. Of the 55 patients, 17 patients received adjuvant chemotherapy (gemcitabine in 6, S-1 in 10, and gemcitabine + S-1 in one), 18 received no adjuvant chemotherapy, and no detailed information was available for the remaining 20 patients (see Table 2).

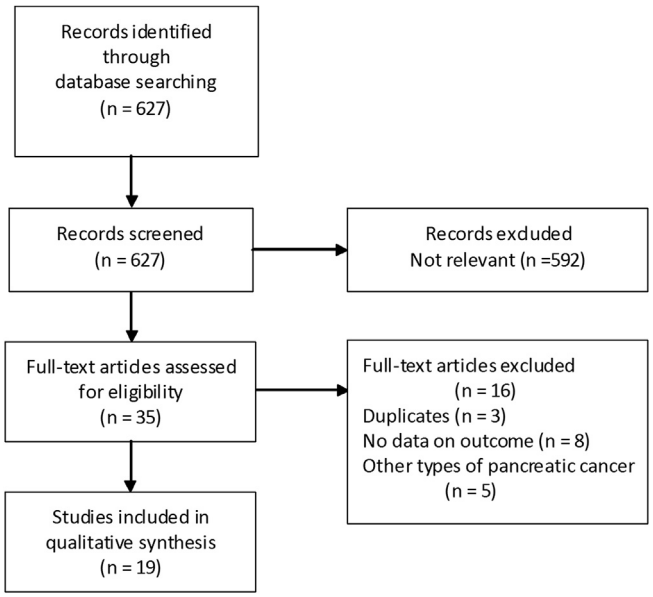

Fig. 1. Flow chart for the study selection.

Table 1
Characteristics of patients undergoing second pancreatectomy for recurrent pancreatic ductal adenocarcinoma.

Characteristics	First operation		Second operation	
	N*	Mean or %	N*	Mean or %
Sex				
Male	25	45.4	25	45.4
Female	30	54.6	30	54.6
Age, years	55	62.1 ± 11.1	–	–
Type of resection				
Pancreaticoduodenectomy	33	60.0	0	0
Distal pancreatectomy	21	38.2	2	1.7
DPPHR	1	0.8	1	0.8
Completion total pancreatectomy	0	0	52	94.5
Differentiation				
Well	16	31.4	17	33.3
Moderate	30	54.5	26	47.2
Poor	5	9.1	8	14.5
Tumor stage				
T1-T2	14	29.2	16	33.3
T3-T4	34	70.8	32	66.7
Nodal status				
N0	34	61.8	32	61.5
N1	21	38.2	20	38.5
Tumor size,mm				
≤20	13	39.4	6	31.6
>20	20 60.6	13 68.4		
UICC stage				
IA-IB	13	25	14	26.4
≥IIA	39	75	39	73.4
Resection margin				
R0	51	92.7	36	83.7
R1	4	7.3	7	26.3
Adjuvant therapy				
Yes	31	59.6	17	48.6
No	21	41.4	18	51.4

*No. of patients with available information.
DPPHR, duodenum preserving pancreas head resection.

3.2. Surgical outcomes after second pancreatectomy

There was no perioperative death in the second pancreatectomy. At the time of analysis, 23 patients died during the follow-up periods, and the other 32 patients were still alive. Recurrent disease

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