Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Efficacy of completion pancreatectomy for recurrence of adenocarcinoma in the remnant pancreas

Yusuke Nakayama, MD, PhD, Motokazu Sugimoto, MD, PhD, Naoto Gotohda, MD, PhD, Masaru Konishi, MD, and Shinichiro Takahashi, MD, PhD*

Department of Hepatobiliary and Pancreatic Surgery, National Cancer Center Hospital East, Kashiwa, Chiba, Japan

ARTICLE INFO

Article history:
Received 7 February 2017
Received in revised form
16 June 2017
Accepted 14 July 2017

Keywords:
Pancreatic ductal adenocarcinoma
Remnant pancreas
Completion pancreatectomy

ABSTRACT

Background: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer, with a high rate of recurrence even after complete surgical resection. The aim of this study was to investigate the impact of completion pancreatectomy (CP) on the clinical course of patients with recurrent PDAC in the remnant pancreas.

Materials and methods: Between January 2008 and December 2014, 194 patients underwent curative-intent surgical resection (initial pancreatectomy [IP]) for PDAC at our institution. The treatment and survival outcomes were evaluated according to the patterns of recurrence.

Results: Among 194 patients with IP, 127 patients (65.5%) developed recurrence. Of them, 11 patients (8.7%) developed recurrence in the remnant pancreas and were treated by CP. They showed a significantly longer median survival after the recurrence than the 28 patients who developed unresectable local recurrence and were treated by systemic chemotherapy (44 mo *versus* 11 mo, $P = 0.014$) or the 66 patients who developed distant metastasis and were treated by systemic chemotherapy (44 mo *versus* 13 mo, $P = 0.024$). Moreover, the median survival after CP was longer in the patients who received adjuvant chemotherapy after CP than in those who did not receive adjuvant chemotherapy (44 mo *versus* 14 mo, $P = 0.002$).

Conclusions: This study demonstrated that PDAC patients with resectable local recurrence in the remnant pancreas, who were treated by CP, had better survival outcomes than those with other patterns of recurrence. CP combined with adjuvant chemotherapy appeared to yield greater survival benefit.

Introduction

Although only surgical resection provides an opportunity for cure and prolonged survival in patients with pancreatic ductal adenocarcinoma (PDAC), the prognosis after surgery is still poor, with a reported 5-y survival rate of 12%-19%.[1-3] This poor prognosis is attributable to the high frequency of recurrence (80%) of PDAC even after complete surgical resection.[4-7] The reported median survival after surgical resection from previous studies is 23-24 mo.[8,9]

* *Corresponding author*. Department of Hepatobiliary and Pancreatic Surgery, National Cancer Center Hospital East, 6-5-1, Kashiwa-no-ha, Kashiwa, Chiba 277-8577, Japan. Tel.: +81-471-33-1111; fax: +81-471-31-9960.
E-mail address: msugimot@east.ncc.go.jp (M. Sugimoto).
0022-4804/$ – see front matter © 2017 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2017.07.016

Recent advances in diagnostic modalities, such as computed tomography (CT), magnetic resonance imaging, and endoscopic ultrasonography, have increased the number of patients diagnosed as having recurrent PDAC in the remnant pancreas during follow-up after initial pancreatectomy (IP).[6] Previous studies have demonstrated a survival benefit of completion pancreatectomy (CP) for patients with recurrence in the remnant pancreas.[4-7,10-13] However, there have been no previous reports offering detailed descriptions of the entire clinical course of patients with recurrent PDAC in the remnant pancreas, including the perioperative treatments of IP and CP. The aims of this study were to investigate (1) the predictive findings in PDAC patients who developed recurrence in the remnant pancreas and (2) the long-term outcomes after IP and CP in relation to the use of postoperative systemic chemotherapy.

Methods

Patients

The medical records of 223 PDAC patients who underwent surgical resection as IP at a single institution between January 2008 and December 2014 were reviewed. Of these patients, 15 diagnosed as having PDAC associated with intraductal papillary mucinous neoplasm were excluded. Of the remaining 208 patients, an additional 14 patients were excluded because they were lost to follow-up (six patients), died within 30 d after the surgery (two patients), or underwent total pancreatectomy as IP (six patients). The clinical courses of the remaining 194 patients who had undergone IP for PDAC were investigated. Of these, 127 developed recurrence after IP. The clinicopathological findings and survival outcomes of these patients with recurrence were investigated. Five surgeons performed the pancreatectomies during this study period. This study protocol was approved by the Institutional Review Board of the National Cancer Center, Japan, and the requirement for obtaining informed consent was waived.

Initial pancreatectomy

The extent of the PDAC at the initial diagnosis was classified as potentially resectable, borderline resectable, or locally advanced, according to the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology.[14] Patients with borderline resectable or locally advanced disease received chemotherapy or chemoradiotherapy as the primary treatment. The diagnosis and treatment strategies for individual patients were discussed and decided through multidisciplinary conferences involving surgeons, oncologists, and radiologists.

The IP consisted of either pancreaticoduodenectomy (PD) or distal pancreatectomy (DP). The standardized procedural details of PD and DP are described in our previous papers.[15,16] In both operations, the pancreatic resection margin was evaluated pathologically by intraoperative frozen section examinations. If adenocarcinoma was identified at the margin, additional pancreatic resection was carried out to pursue clearance of the tumor cells.

Follow-up after IP

After IP, all the patients were followed up at the outpatient clinic and monitored for recurrence by 3-monthly CT examinations of the chest, abdomen, and pelvis and blood tests, including measurement of the serum levels of carcinoembryonic antigen and carbohydrate antigen 19-9. Positron emission tomography-CT, pancreas-protocol CT, magnetic resonance imaging, and/or endoscopic ultrasonography were performed as needed to further evaluate any suspected recurrence. Patients with a preserved performance status were given adjuvant chemotherapy; this therapy was generally started 3 mo after IP and continued for 6 mo. None of the patients received adjuvant radiotherapy or chemoradiotherapy after IP.

The patterns of recurrence were categorized as local recurrence or distant metastasis. Local recurrence included recurrence in the remnant pancreas, peripancreatic soft tissue, or locoregional lymph nodes, as defined in previous papers.[6,17] Distant metastasis included metastasis to a distant organ, distant lymph nodes, and/or the peritoneal space.[18]

Completion pancreatectomy

Patients with local recurrence in the remnant pancreas that was determined by imaging examinations as being potentially resectable underwent CP. Local recurrences that were found to be borderline resectable or locally advanced were categorized as unresectable disease. After CP, patients with a preserved performance status received adjuvant chemotherapy in the same way as that after IP. The diagnosis and treatment strategies for recurrence in individual patients were discussed and decided through multidisciplinary conferences.

Pathological evaluation

Diagnosis of PDAC without a background of intraductal papillary mucinous neoplasm was confirmed by histopathology in all the patients. Pathological staging was performed according to the International Union Against Cancer TNM classification (seventh edition).[19] In addition, the histopathological findings of the primary lesion were also evaluated. On the basis of the gross and histological findings, the residual tumor status was classified as follows: no residual tumor (R0), microscopic residual tumor (R1), or macroscopic residual tumor (R2). R0 was defined as the absence of tumor at the resection margin (0 mm).[19]

Statistical analysis

The clinicopathological findings of the patients who developed recurrence after IP were compared according to the patterns of recurrence: resectable local recurrence, unresectable local recurrence, or distant metastasis. Continuous variables were compared by the Mann–Whitney test or the Kruskal–Wallis test and expressed as median values (with the ranges). Categorical variables were compared by Pearson's chi-square test or Fisher's exact test.

Overall survival (OS) was defined as the interval from the date of IP to the date of death or the date censored at the last