

REVIEW ARTICLE

Surgical treatment of liver metastases from pancreatic cancer

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Abstract

Pancreatic cancer is a disease with a poor prognosis. Most patients are diagnosed at an advanced and unresectable stage. Even if the primary cancer is radically removed, postoperative recurrence frequently occurs. Generally, metastatic liver tumors from pancreatic cancer are not indicated for surgical treatment. Here we evaluate the results of performing hepatectomy for liver metastases of pancreatic cancer. In our institute, six patients with liver metastases from pancreatic cancer were treated by partial hepatectomy. Overall 1-, 3- and 5-year survival rates of six patients after hepatectomy were 66.7%, 33.3% and 16.7%, respectively, and one patient was alive for 65.4 months. Performing a hepatectomy for liver metastases of pancreatic cancer, when combined with a pancreas resection, was recently considered to be a safe operation, and one that might offer prolonged survival for highly selected patients with curative resection of liver metastases. In the future, it will be necessary to develop new multi-modality therapies to improve the prognosis of pancreatic cancer.

Key Words: *Liver metastases, pancreatic cancer, hepatectomy*

Introduction

Pancreatic cancer has one of the worst prognoses of all gastrointestinal malignancies. When this cancer is detected using several examinations, many cases are already in well-advanced stages of metastases and dissemination with peripheral invasion of the retroperitoneum, vascular system, or nerves. The rate of resection is <10% and the 5-year survival rate is 7–25% in the curative resected cases [1–6]. Frequently, the types of recurrences from pancreatic cancer are liver metastases and peritoneum dissemination. These recurrent diseases are usually treated with palliative operations, chemotherapy or radiotherapy, rather than radical operations. Hepatectomy is a safe and potentially curative treatment for liver metastases from colorectal cancer and some kinds of malignancies [7,8]. There are some reports discussing hepatectomy for liver metastases from pancreatic cancer [9–25]. Here we review our experience with hepatectomy for treating metastatic nonneuroendocrine pancreatic cancer.

Patients and methods

From 1991 to 1995, 33 patients underwent hepatectomy for metastases from noncolorectal and nonneuroendocrine tumors in Hokkaido University Hospital and affiliated hospitals. Six patients (18.2%) underwent curative hepatectomy for liver metastases from pancreatic cancer. Prerequisites for a hepatectomy were: (1) the feasibility of a complete excision of all intrahepatic disease, (2) reliable control of the primary disease by means of extirpation, and (3) no extrahepatic diseases at the time of detection of resectable liver metastases. When liver metastases were combined with extrahepatic recurrences, hepatic resection was not indicated and systemic chemotherapy or radiotherapy was used to treat these recurrent diseases.

Results

The patients included one female and five males ranging between 48 and 77 years of age (average

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60.8). The histopathological types of primary pancreatic cancer were ductal adenocarcinoma in four patients, adenosquamous carcinoma in one, and cystadenocarcinoma in one. None were neuroendocrine cell tumors. Lymph node status of origin was positive in three patients and negative in three. The timing of liver metastases was almost synchronous in five and metachronous in one. The diameter of liver tumors ranged from 1 to 7 cm (average 2.6 cm). Small nodules <2 cm were shown in four patients. The operative method of hepatectomy was partial resection for all patients. Curative hepatectomy with no microscopic residual tumor on the edge of the liver was performed in five patients, but only one case was a macroscopic non-curative operation. There were no operative mortalities, but there were two complications (bleeding of duodenal ulcer and leakage from pancreatojejunal anastomosis). Recurrence after hepatectomy occurred in four patients, thereby excluding one noncurative patient. The recurrent lesions included remnant liver, peritoneum, and bone. One patient has survived with no evidence of recurrence for 5 years. Five patients died of cancer recurrence from 4.6 to 52 months after their hepatectomy. Overall 1-, 3- and 5-year survival rates of six patients after hepatectomy were 66.7%, 33.3%, and 16.7%, respectively (Figure 1).

Discussion

Since hepatectomy for liver metastases from pancreatic cancer were first reported in 1982, some groups performed hepatectomy aggressively [8–25] (Table I). Previous studies showed that morbidity ranged from 19% to 35% and mortality from 0% to 20% for hepatectomy [14,18,19,21,23]. In our study, the two cases with complications did not need further

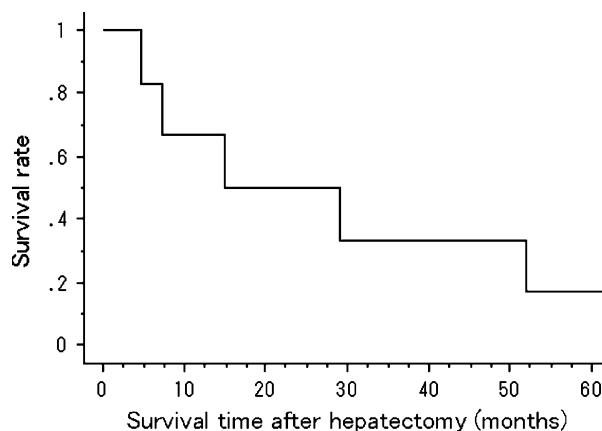


Figure 1. Overall survival curves after hepatectomy of liver metastases from pancreatic cancer.

operative treatment, and the mortality rate was 0%. As a result of recent advances in surgery, synchronous resection of the pancreas and liver has been made safe.

Then, these results showed that the survival time after hepatectomy was <1 year. There were just two long-term survivors noted in past literature [8,18]. One case was alive with no evidence of relapse for 65.4 months and the other case, with a cystadenocarcinoma of the pancreas, was alive for 70 months after a hepatectomy. In our report, one patient with the same type of cancer survived for 52.0 months after a hepatectomy. The biological behavior of this type may be different from pancreatic ductal adenocarcinoma.

Prognostic factors of noncolorectal and nonneuroendocrine liver metastases were reported to be the site of primary tumor, disease-free interval between resection of primary tumor and hepatectomy, and curative surgical margin. Most liver metastases from pancreatic cancer tend to be detected synchronously,

Table I. Published reports on hepatectomy of liver metastases from pancreatic cancer.

Ref. no.	Year	Authors	Number of patients	Prognosis
9	1982	Morrow et al.	1	–
10	1983	Thompson et al.	2	–
11	1986	Ekberg et al.	1	–
12	1987	Sesto et al.	1	–
13	1995	Schildberg et al.	5	3 years 0%, median 7 months
14	1997	Harrison et al.	2	–
15	1997	Howard	10	5–30 months (median 11)
16	1997	Takada et al.	11	Mean 6 months
17	1998	Lindell et al.	2	0.8 and 5 months
18	1998	Berney et al.	2	1 long-term survivor (70 months)
19	1998	Elias et al.	1	–
20	2000	Hemming et al.	2	–
21	2000	Benevento et al.	1	–
22	2001	Laurent et al.	2	–
23	2001	Takada et al.	2	7 and 22 months
8	2001	Yamada et al.	6	3 years 33%, 5 years 16%
24	2003	Pawlik et al.	4	–
25	2005	Weitz et al.	5	–

yielding a poor prognostic factor. However, it is not clear which characteristic factors are associated with good survival prognoses. In our experience, there was one 5-year survivor and three patients who survived for over 2 years. Most tumors were single and small in size. We believe that the resection of liver metastases from pancreatic cancer might be an effective treatment for highly selected patients, and further study is needed to clarify the role of hepatectomy because of the small number of patients in our series.

Thus, surgical treatment alone for liver metastases from pancreatic cancer cannot offer long-term survival for many patients with this disease. Yet, other treatments such as chemotherapy and radiotherapy also do not show positive outcome data. Studies of 5-fluorouracil (5-FU)-based postoperative chemoradiotherapy were reported by some groups [26–28], but their results failed to show that postoperative chemoradiotherapy had positive survival benefits for patients with pancreatic cancer. Since 1997 gemcitabine has been used as a systemic chemotherapy combined with radiotherapy. Many trials, using other anti-cancer drugs such as taxan, or new regimens such as preoperative chemoradiotherapy, have been performed. When standard strategies for pancreatic cancer with or without liver metastases are established, surgical treatment combining these chemotherapies with, perhaps, radiotherapy, may lead to improved prognoses for pancreatic cancer.

In conclusion, performing hepatectomy for metastases from pancreatic cancer might offer prolonged survival for highly selected patients with curative resection of liver metastases, and we should develop new multi-modality therapies for advanced pancreatic cancer in the future.

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