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Distal pancreatectomy with en bloc celiac axis resection for pancreatic body-tail cancer: Is it justified?

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to evaluate the safety and efficacy of distal pancreatectomy with en bloc celiac axis resection (DP-CAR) for pancreatic body-tail cancer.





Material/Methods: The medical records of 12 patients who underwent DP-CAR for pancreatic body-tail cancer were retrospectively studied, together with a literature review of studies including at least 3 cases of DP-CAR.

Results: There were no deaths among our 12 cases. Postoperative morbidity developed in 9 cases and was successfully managed by non-surgical treatment. No patients developed ischemic complications. Median overall survival was 10 months. A total of 19 studies involving 203 patients who underwent DP-CAR were included in the literature review. The overall morbidity and mortality rates were 50.2% and 3.0%, respectively. The overall median survival after surgery ranged from 9.3 to 26 months.

Conclusions: DP-CAR is a safe and effective treatment for patients with locally advanced pancreatic body-tail cancer.

Key words: **cancer of the pancreas • distal pancreatectomy • celiac axis resection • Appleby operation**

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Background

Pancreatic cancer carries one of the most dismal prognoses among gastrointestinal cancers and has a 5-year survival rate of 5% regardless of stage [1]. The mainstay of treatment has been surgical resection. Unfortunately, most patients with cancer of body and tail are considered unresectable at the time of diagnosis, mainly due to lesions invading the major vessels such as the celiac axis (CA) or the common hepatic artery (CHA) [2].

Distal pancreatectomy with en bloc CA resection (DP-CAR) combined total gastrectomy was first performed by Appleby in 1953 for advanced gastric cancer [3]. In 1976, Nimura applied the original Appleby operation for patients with advanced pancreatic body-tail cancer [4]. In 1987, Hishinuma modified this procedure with preservation of the whole stomach, which maintains a more normal gastrointestinal hormonal milieu, which in turn results in better nutritional status [5]. To date, data regarding DP-CAR for the surgical treatment of pancreatic body-tail cancer is limited due to the small number of patients.

In this study, based on literature review and retrospective results from our institution, we assessed the safety and efficacy of DP-CAR for pancreatic body-tail cancer.

Material and Methods

Patients

The medical records of patients who underwent DP-CAR for pancreatic body-tail cancer between January 2006 and June 2013 were retrospectively reviewed. Informed consent was obtained from all patients. Clinical variables including gender, age, symptoms, pathologic diagnosis, lesion size, operative records, post-operative morbidity, mortality, and follow-up records were evaluated. DP-CAR is indicated when preoperative dynamic thin-slice computed tomography (CT) shows a tumor of the body-tail of the pancreas involving or close to the CA, the CHA, and/or the origin of the splenic artery (SA); but not involving the proper hepatic artery (PHA), superior mesenteric artery (SMA), or gastroduodenal artery (GDA). In the surgical procedures, CA was divided at the origin from the aorta, whereas CHA was divided at the midway point, with care to protect GDA origin. Before division, CHA was transiently clamped and the blood flow of the PHA in the hepatoduodenal ligament was confirmed using pulsation of the PHA through GDA. After division of the CA, the artery and the surrounding nerve plexus was resected en bloc with the DP.

Literature review

Relevant studies were identified by searching the PubMed database from the date of the earliest report of DP-CAR in 1976

to June 2013, using the following search terms “distal pancreatectomy,” “Appleby operation,” and “celiac artery”. Only studies with at least 3 cases of DP-CAR published in the English language were included. In the case of multiple publications of a given cohort of patients, only the most recent one was used.

Statistical analysis

Descriptive analyses were used for all studies that involved DP-CAR.

Results

The authors' experience

During the study period, a total of 12 patients underwent a DP-CAR for pancreatic body and tail cancer. There were 8 males and 4 females, with a median age of 52 years (range 44–63). Ten patients had epigastric and/or back pain. The median operative time of the 12 patients was 330 (range 280–440) min, and the median intraoperative blood loss was 1200 (range 800–2400) mL. Eight patients (66.6%) required blood transfusion. To resect the tumor, combined organs resection included gastric wedge resection (n=7), partial transverse colon resection (n=5), and left kidney resection (n=3). There were no operative deaths. Nine (75%) patients had a total of 15 postoperative complications: International Study Group on Pancreatic Fistula (ISGPF) grade B pancreatic fistula (n=4); pneumonia (n=3); pleural effusion (n=3), intra-abdominal abscess (n=2); wound infection (n=2); and delirium (n=1). All of these complications were successfully managed by non-surgical treatment. No patients developed hepatic, gastric, or cholecystic ischemic complications. The median length of hospital stay was 21 (range 16–43) days.

The intractable preoperative abdominal and/or back pain was completely relieved immediately after surgery in all 10 patients. Seven patients died of tumor recurrence and 1 patient died of gastric bleeding. The median overall survival was 10 months after the operation (range 4–17 months).

Literature review

Nineteen studies involving 203 patients (including the present series) met the inclusion criteria and were included for review [2,5–20]. An overview of these studies is shown in Table 1. All these studies were observational. The sample size studies varied from 3 to 42 patients.

There were 6 operative deaths, yielding a mortality rate of 3.0%. Causes of death were: uncontrolled infection [13], respiratory failure secondary to severe methicillin-resistant *Staphylococcus*

Table 1. Literature review of DP-CAR for pancreatic body-tail cancer.

Reference	Year	Country	No. of patients	M/F	Age (years)	Operative time (min)	Blood loss (ml)	Morbidity (%)	Mortality (%)	Median survival (months)
Mayumi et al. [2]	1997	Japan	6	4/2	61.2	321	1777	2 (33.3)	0	9.5
Konishi et al. [6]	2000	Japan	4	0/4	57.2	419.5	4537	1 (25)	0	12
Miyakawa et al. [7]	2002	Japan	8	6/2	64	–	–	3 (37.5)	0	9.5
Sasson et al. [8]	2002	USA	4	–	–	–	–	–	0	17.5
Yamaguchi et al. [9]	2003	Japan	3	2/1	58.6	–	–	1 (33.3)	0	9.5
Gagandeep et al. [10]	2006	USA	3	3/0	57.6	585	1533	1 (33.3)	0	14
Shimada et al. [11]	2006	Japan	12	–	–	–	–	–	0	17
Hishinuma et al. [5]	2007	Japan	7	4/3	63.8	–	–	2 (28.5)	0	19
Sperti et al. [12]	2010	Italy	5	3/2	62.8	233	–	4 (80)	0	10
Wu et al. [13]	2010	China	11	5/6	56.9	316	936	4 (36.3)	1 (9)	14
Denecke et al. [14]	2011	Germany	6	4/2	62.1	286	–	3 (50)	0	12.7
Takahashi et al. [15]	2011	Japan	16	8/8	65	237	702	9 (56)	1 (6)	9.7
Baumgartner et al. [16]	2012	USA	11	5/6	61	494	700	5 (45)	2 (18)	26
Tanaka et al. [17]	2012	Japan	42	–	–	478	1030	18 (43)	2 (4.8)	24
Yamamoto et al. [18]	2012	Japan	13	10/3	64	620	1300	12 (92.3)	0	20.8
Jing et al. [19]	2013	China	24	18/6	54.5	200	1779	13 (54)	0	9.3
Okada et al. [20]	2013	Japan	16	11/5	63	298	1165	7 (43.5)	0	25
Present series	2013	China	12	8/4	52	330	1200	9 (75)	0	10

aureus [15], infected hematoma, bowel obstruction [16], and cardiac infarction and multiple organ failure [17]. Postoperative morbidity was recorded in 89 (50.2%) of 187 patients. The most common complication was pancreatic fistula, described in 28.9% of patients. Regarding ischemia-related events, ischemic gastropathy, stomach perforation, duodenal perforation, gallbladder perforation, liver abscess, and hepatic infarction were observed in 11 (6.1%), 1 (0.5%), 1 (0.5%), 1 (0.5%), 1 (0.5%), and 1 (0.5%) of patients, respectively. The overall median survival after surgery ranged from 8 to 26 months.

Discussion

Patients with locally advanced pancreatic body-tail cancer who did not undergo resection had a median survival of 5.8 months [21]. In contrast, surgical resection affords a median survival of 13–26 months [22,23]. The major merit of DP-CAR is it can increase tumor resectability and improve the survival of patients with pancreatic body-tail cancer involving or touching the CHA, the root of the SA, and/or the CA. Yamamoto et al. reported that the DP-CAR group had a significantly better prognosis

than the unresectable group (median survival time, 20.8 vs. 9.8 months; $P=0.01$) [18]. Wu et al. also found the DP-CAR group had significantly longer median survival time compared with those who received nonsurgical treatment C (14 vs. 5 months, $P=0.013$) [13]. Moreover, several studies have demonstrated that DP-CAR results in a similar overall survival to standard DP [2,13,18,20]. Although Takahashi et al. showed that median survival following DP-CAR was significantly worse than for those who underwent DP (9.7 vs. 30.9 months, $P=0.033$), these results could be biased by the patient selection. The R1 resection rates of their series were 44% in DP-CAR and 22% in DP [15]. There is evidence that R1 resection was associated with poor long-term survival [24].

The other potential benefit of DP-CAR is it dramatically improves quality of life. Pancreatic cancer frequently involves the celiac plexus or celiac ganglions and results in intractable abdominal pain. Medical treatment with pharmacological agents is often ineffective. It is difficult to achieve complete pain relief with neurolytic block of the celiac plexus, thoracoscopic splanchnicectomy, and intrathecal morphine delivered via subcutaneous pump [25]. By complete removal of celiac

plexus and celiac ganglions, as well as the retroperitoneal tissues, DP-CAR affords effective pain control. In addition, unlike pancreatoduodenectomy, DP-CAR preserved continuity of the alimentary tract in its entirety and therefore reduced the incidence of uncontrollable diarrhea caused by clearance of autonomic nerve tissue. Taken together, these results mean that DP-CAR is an effective therapy for patients with pancreatic body-tail cancer.

The mortality rate after DP-CAR was only 3.0%, emphasizing the current safety of this surgical procedure. Although the morbidity rate was high (50.2%), the most common complication was pancreatic fistula, which also frequently occurs in other types of pancreatic resection. The most critical complication of the DP-CAR is hepatobiliary and gastric ischemia, but these are rare, as demonstrated in the present study. This is most likely because of maintenance of the arterial blood supply for the hepatobiliary system and stomach via the SMA, pancreatoduodenal arcades, and gastroduodenal artery in DP-CAR. Therefore, it is necessary to confirm hepatic arterial inflow using pulsation or Doppler ultrasonography during the operation. If hepatic inflow is weak, reconstruction of the hepatic artery may be required [26]. Kondo et al. suggested that preoperative coil embolization of the CHA may prevent postoperative ischemic events by stimulating the development of collateral pathways from the SAM [25].

Owing to advanced stage of the disease, the majority of patients had less favorable long-term outcome after DP-CAR. In a study by Yamamoto et al., 4 patients in the DP-CAR group and 12 patients in the DP group received adjuvant chemotherapy

with gemcitabine in 9 patients and 5-fluorouracil + cisplatin in 7 patients. Given the relatively small number of patients enrolled, no significant difference was found in survival between those who did and those who did not undergo adjuvant chemotherapy (median survival time, 17.2 months vs. 22.2 months; $P=0.94$) [18]. Recently, a study from Japan determined the effect of adjuvant gemcitabine + S-1 therapy for patients with adenocarcinoma of the body or tail of the pancreas who had undergone surgical resection. Two-year survival rates of patients who did or did not receive postoperative adjuvant chemotherapy were 80% and 13%, respectively ($P<0.001$) [27].

In a study by Baumgartner et al., in 11 patients undergoing DP-CAR following a neoadjuvant chemotherapy course of gemcitabine, median overall survival was 26 months [16]. Given that there was no control group in this study, it is hard to determine the role of such a neoadjuvant approach. Further studies are needed to address this issue.

Conclusions

In conclusion, DP-CAR is a safe and effective treatment for patients with locally advanced pancreatic body-tail cancer. In patients with advanced stage of the disease, adjuvant therapy should be required.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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