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

Yan-Ming Zhou*  
Xiao-Feng Zhang*  
Xiu-Dong Li  
Xiao-Bin Liu  
Lu-Peng Wu  
Bin Li

* Yan-Ming Zhou and Xiao-Feng Zhang contributed equally to this work

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

Full-text PDF: http://www.medscimonit.com/download/index/idArt/889847
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, postoperative 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 epigastria 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) |
|-----------|------|---------|----------------|-----|-------------|---------------------|----------------|--------------|-------------|-------------------------|
| Okada et al. [6] | 2000 | Japan | 4 | 0/4 | 56.7 | 141.5 | 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 | 2/0 | 57.6 | 585 | 1537 | 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 |
| Sperli 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 |

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, \( P=0.033 \)) [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 ganglia, as well as the retroperitoneal tissues, DP-CAR affords effective pain control. In addition, unlike pancreateoduodenectomy, 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-fluourouracil + 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.

References:

1. Jemal A, Siegel R, Ward E et al: Cancer statistics. CA Cancer J Clin, 2009; 59(6): 225–49
2. Mayumi T, Nimura Y, Kamiya J et al: Distal pancreatectomy with en bloc resection of the celiac artery for carcinoma of the body and tail of the pancreas.Int J Pancreatol, 1997; 22: 15–21
3. Appleby LH: The coeliac axis in the expansion of the operation for gastric carcinoma. Cancer, 1953: 6: 704–7
4. Nimura Y, Hattoi T, Miura K et al: A case of advanced carcinoma of the body and tail of the pancreas resected by the Appleby operation (in Japanese). Operation, 1976; 30: 885–89
5. Hishinuma S, Ogata Y, Tomikawa M et al: Stomach-preserving distal pancreatectomy with combined resection of the celiac artery: radical procedure for locally advanced cancer of the pancreatic body. J Gastrointest Surg, 2007; 11: 743–49
6. Konishi M, Kinoshita T, Nakagori T et al: Distal pancreatectomy with resection of the celiac axis and reconstruction of the hepatic artery for carcinoma of the body and tail of the pancreas. J Hepatobiliary Pancreat Surg, 2007; 10: 183–87
7. Miyakawa S, Horiguchi A, Hanai T et al: Monitoring hepatic venous hemoglobin oxygen saturation during Appleby operation for pancreatic cancer. Hepatogastroenterology, 2002; 49: 817–21
8. Sasson AR, Hoffman JP, Ross EA et al: En bloc resection for locally advanced cancer of the pancreas: Is it worthwhile? J Gastrointest Surg, 2002; 6: 147–57
9. Yamaguchi K, Nakano K, Kobayashi K et al: Appleby operation for pancreatic body-tail carcinoma: report of three cases. Surg Today, 2003; 33: 873–78
10. Gagandeep S, Artinyan A, Jabbour N et al: Extended pancreatectomy with resection of the celiac axis: the modified Appleby operation. Am J Surg, 2006; 192: 330–35
11. Shimada K, Sakamoto Y, Sano T et al: Prognostic factors after distal pancreatectomy with extended lymphadenectomy for invasive pancreatic adenocarcinoma of the body and tail. Surgery, 2006; 139: 288–95
12. Sperli C, Berselli M, Pedrazzoli S: Distal pancreatectomy for body-tail pancreatic cancer: Is there a role for celiac axis resection? Pancreatology, 2010; 10: 491–98
13. Wu X, Tao R, Lei R et al: Distal pancreatectomy combined with celiac axis resection in treatment of carcinoma of the body/tail of the pancreas: a single-center experience. Ann Surg Oncol, 2010; 17: 1359–66
14. Denecke T, Andreou A, Podrabsky P et al: Distal pancreatectomy with en bloc resection of the celiac trunk for extended pancreatic tumor disease: an interdisciplinary approach. Cardiovasc Intervent Radiol, 2011; 34: 1058–64
15. Takahashi Y, Kaneoka Y, Maeda A et al: Distal pancreatectomy with celiac axis resection for carcinoma of the body and tail of the pancreas. World J Surg, 2011; 35: 2535–42
16. Baumgartner JM, Kraisinskas A, Dauudz A et al: Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic adenocarcinoma following neoadjuvant therapy. J Gastrointest Surg, 2012; 16: 1152–59
17. Tanaka E, Hirano S, Tsuchioka T et al: Important technical remarks on distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer (with video). J Hepatobiliary Pancreat Sci, 2012; 19: 141–47
18. Yamamoto Y, Sakamoto Y, Ban D et al: Is celiac axis resection justified for T4 pancreatic body cancer? Surgery, 2012; 151: 61–69
19. Jing W, Zhu G, Hu X et al: Distal pancreatectomy with en bloc celiac axis resection for the treatment of locally advanced pancreatic body and tail cancer. Hepatogastroenterology, 2013; 60: 187–90
20. Okada K, Kawai M, Tani M et al: Surgical strategy for patients with pancreatic body/tail carcinoma: who should undergo distal pancreatectomy with en-bloc celiac axis resection? Surgery, 2013; 153: 365–72
21. Shoup M, Conlon KC, Klimstra D et al: Is extended resection for adenocarcinoma of the body or tail of the pancreas justified? J Gastrointest Surg, 2003; 7: 946–52
22. Johnson CD, Schwall G, Flechtenmacher J et al: Resection for adenocarcinoma of the body and tail of the pancreas. Br J Surg, 1993; 80: 1177–79
23. Mitchem JB, Hamilton N, Gao F et al: Long-term results of resection of adenocarcinoma of the body and tail of the pancreas using radical antegrade modular pancreatectosplenectomy procedure. J Am Coll Surg, 2012; 214: 46–52
24. Nakao A, Harada A, Nonami T et al: Lymph node metastasis in carcinoma of the body and tail of the pancreas. Br J Surg, 1997; 84: 1090–92
25. Kondo S, Katoh H, Omi M et al: Radical distal pancreatectomy with en bloc resection of the celiac artery, plexus, and ganglions for advanced cancer of the pancreatic body: a preliminary report on perfect pain relief. JOP, 2001; 2: 93–97
26. Machado MA, Surjan RC, Nishinari K et al: Iliac-hepatic arterial bypass for compromised collateral flow during modified Appleby operation for advanced pancreatic cancer. Eur J Surg Oncol, 2009; 35: 1124–27
27. Murakami Y, Uemura K, Sudo T et al: Impact of adjuvant gemcitabine plus S-1 chemotherapy after surgical resection for adenocarcinoma of the body or tail of the pancreas. J Gastrointest Surg, 2009; 13: 85–92