

Selective Radical Resection for Unresectable Pancreatic Cancer

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ABSTRACT

Background and Objective: For inefficiency of chemotherapy and radiation against pancreatic cancer, resection rate for primary unresectable pancreatic cancer remains very low. This study was carried out to evaluate the safety and value of radical resection for unresectable pancreatic cancer (UPC).

Methods: Clinical data were analyzed retrospectively. In unresectable group, 360° resection of the involved artery sheath, resection and reconstruction of the involved artery, resection and reconstruction of the involved vein as well as resection and reconstruction of combined organs were performed. Operation time, intraoperative blood loss, ICU transitional treatment, pancreatic fistula, bleeding, reoperation and survival time were analyzed for two groups.

Results: Operation time and intraoperative blood loss were greatly increased in the unresectable group. The incidence of intractable diarrhea and abdominal hemorrhage in the unresectable group were higher. However, the rate of ICU transitional therapy, delayed gastric emptying and reoperation were lower. Grade-C pancreatic fistula occurred in neither group.

Conclusion: Surgical treatment through stringent selection for patients with unresectable pancreatic cancer is a safer technique and median post-operative survival time is similar to patients with resectable pancreatic cancer.

KEYWORDS: Pancreatic cancer; Radical resection; Complications; Survival time; Prognosis.

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INTRODUCTION

Patients with pancreatic cancer generally have poor prognoses.^{1,2} Because pancreas is closely related to the blood vessel and pancreatic cancer grows infiltratively, it is prone to invade portal vein, superior mesenteric vein (SMV) and superior mesenteric artery (SMA) that makes its surgical resection more difficult. In domestic and foreign guidelines for diagnosis and treatment of pancreatic cancer based on the relationship between tumor and blood vessel, pancreatic cancer is divided into three types: resectable, borderline resectable and unresectable. For pancreatic head carcinoma, if (1) superior mesenteric artery is encapsulated by the tumor more than 180° and the tumor is close to celiac artery trunk; or if (2) superior mesenteric vein or portal vein is involved

to make resection or reconstruction impossible; for pancreatic carcinoma of body and tail, if (1) superior mesenteric artery or celiac artery trunk is encapsulated more than 180°; or if (2) superior mesenteric vein and portal vein is involved to make resection or reconstruction impossible, the tumor is considered to be unresectable.^{3,4} However, in addition to preoperative imaging evaluation, the resectability of pancreatic cancer is closely related to the experience and ability of surgeons.^{5,6} There is no identical standard for clinical application in unresectable pancreatic cancer.^{7,8} We selectively carried out radical surgery upon some patients with unresectable pancreatic cancer and explored its safety and significance compared with the surgery for resectable pancreatic cancer.

METHODS

Patients with pancreatic cancer who underwent radical resection from August 2010 to January 2018 in Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine and had complete follow-up data were selected after taking approval from the Institutional Ethics Committee. Inclusion criteria were the patients being diagnosed as pancreatic cancer before operation through enhanced CT and/or enhanced MRI, together with tumor markers; no distant metastasis; with resectable tumor according to preoperative imaging and intraoperative judgment, vascular invasion and possible arterial sheath resection or vascular segmental resection and reconstruction. There were 77 patients with pancreatic cancer who underwent radical surgery during the above period, including 43 males and 34 females, aged 47-79 years, with a median age of 63.5 years. There was no significant difference in gender and age between the two groups ($P > 0.05$), which was comparable. According to the guidelines,³ 69 cases were declared resectable (to form a resectable group) and 8 cases were unresectable (to form an unresectable group) for more than 180° of arterial encapsulation or vein invasion was observed. There were 56 cases and 6 cases of pancreatic head carcinoma respectively in the resectable group and in the unresectable group, and 13 cases and 2 cases of pancreatic carcinoma of body and tail in the two groups respectively. There were seven cases of tumor invading artery and one case of tumor

invading vein causing neither resection nor reconstruction was included in the unresectable group (Table-1).

Treatment and Surgical Procedures

Radical resection with no preoperative chemotherapy was performed on the patients in the resectable group. While pancreaticoduodenectomy (PD) with standard or extended lymphatic dissection was performed upon the patients with pancreatic head carcinoma while pancreatic splenectomy with standard or extended lymphatic dissection was performed on the patients with pancreatic carcinoma of body and tail. Chemotherapy was performed for three cases in the unresectable group before operation, of which, two cases were treated with gemcitabine and one case was treated with modified Folfirinox. The other five cases refused preoperative chemotherapy, so they were not treated with it. PD was performed on the patients with pancreatic head carcinoma in the unresectable group. According to the preoperative imaging and intraoperative vascular exploration, 360° arterial sheath resection or resection and reconstruction of the involved artery and the involved vein was performed. Pancreatic splenectomy was performed on the patients with pancreatic carcinoma of body and tail in the unresectable group. According to preoperative imaging examination, intraoperative vascular exploration and adjacent organ involvement, 360° arterial sheath resection or resection and reconstruction of the involved artery and combined organs were performed. The 360° arterial sheath resection was performed (Fig:1) when SMA or celiac trunk artery sheath was encapsulated more than 180° but arterial sheath was not infiltrated. Arterial resection and reconstruction were performed on the patients with arterial adventitia and intimal infiltration (Fig:2). Respective anastomosis of Y-type iliac artery allografts with portal vein and venae jejunaes et ilei was performed on the patients whose SMV was all involved, with portal vein involvement at the top and jejunal ileal vein below (Fig:3). Extended lymphatic dissection was performed on the patients in the unresectable group.

Intraoperative and Postoperative Observation Indicators

Operation time, intraoperative blood loss, postoperative ICU transitional treatment, postoperative pancreatic fistula, bleeding, reoperation and survival time were recorded.

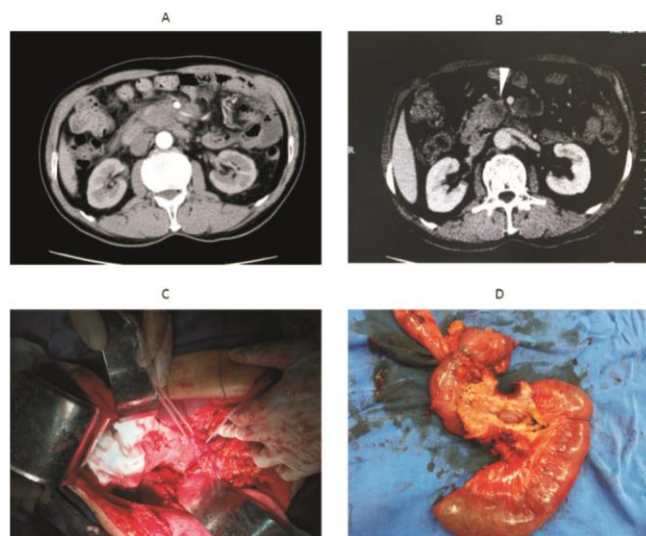
STATISTICAL ANALYSIS

SPSS-22 software was used for statistical analysis. Its measurement data were expressed by $\bar{x} \pm s$ and one-way ANOVA was adopted on the comparison between groups, while counting data were expressed by rate and Pearson X^2 was adopted on the comparison between groups. Survival analysis was performed by Log rank test. The difference with $P < 0.05$ was considered to be statistically significant.

RESULTS

In this research, no deaths occurred during perioperative period in any group. Compared with the resectable group, operation time and intraoperative blood loss in the unresectable group were greatly increased ($P < 0.01$). For postoperative complications, the frequency of intractable diarrhea and abdominal hemorrhage in the unresectable group were obviously higher than those in the resectable group ($P < 0.01$). The rate of ICU transitional therapy, delayed gastric emptying and reoperation in the unresectable group were significantly lower than the resectable group ($P < 0.01$). The patients in the unresectable group had a higher reports of pancreatic fistula than the patients in the resectable group ($P < 0.01$), but Grade C pancreatic fistula occurred in neither group. There were three cases (4.4%) in the resectable group with reported postoperative abdominal hemorrhage, of which, two cases received interventional embolization to stop bleeding and one case received reoperation to stop bleeding. In the unresectable group, one case (12.5%) of abdominal hemorrhage received interventional embolization to stop bleeding and no reoperation occurred. In the unresectable group, reoperation rate was significantly lower than that in the resectable group. Postoperative survival time of 69 patients with resectable pancreatic cancer was 8.2 –

72.4 months and median survival time was 15.8 months. In the unresectable group, postoperative survival of 8 patients was 8.1 – 26.3 months and median survival time was 14.3 months. With the same median survival time of the two groups ($P > 0.01$), there were three cases (4.4%) in the resectable group with survival time of longer than five years, but in the unresectable group, survival time of all the cases was less than three years. Long-term survivors in the resectable group were significantly more than the unresectable group ($P > 0.01$) (Table-2).



- Pancreatic CT showed that superior mesenteric artery was encapsulated more than 270°.
- CT showed that the tumor completely invaded superior mesenteric vein and occluded it to about 1.5 cm long. The arrow points to the occluded superior mesenteric vein.
- SMA sheath has been removed by 360°.
- In the isolated specimen, superior mesenteric artery and vein appeared to be encapsulated by the tumor more than 270°.

Figure 1: Case 6 in the unresectable group.

Left gastric artery and superior mesenteric artery were anastomosed and reconstructed. Left gastric artery was obliquely cut off to enlarge its lumen diameter. Distal left gastric artery was ligated and proximal left gastric artery was pulled down from splenic artery to anastomose with superior mesenteric artery. Triangular arrow points to left gastric artery and the arrow points to superior mesenteric artery.

Table 1: Clinical characteristics of patients enrolled in the unresectable group.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Age (years)	68	54	63	64	61	64	64	55
Gender	male	Male	male	female	male	male	male	female
Position	head of pancreas	head of pancreas	pancreatic body and tail	pancreatic body and tail	head of pancreas	head of pancreas	head of pancreas	head of pancreas
Tumor vascular invasion	more than 180° of SMA encapsulation	SMV was all involved with jejunal vein, ileum vein and portal vein	more than 180° of celiac trunk encapsulation	more than 180° of celiac trunk, hepatic artery and splenic artery encapsulation	more than 180° of SMA encapsulation and splenic vein involvement	more than 180° of SMA encapsulation and SMV invasion	more than 180° of SMA encapsulation	more than 180° of SMA encapsulation
Preoperative chemotherapy	No	No	Yes	Yes	No	Yes	No	No
Operation	PD+360° SMA sheath resection	PD + resection of affected segment vein + reconstruction of Y-type iliac artery and jejunal ileojejunal anastomosis	360° celiac trunk artery sheath resection + splenectomy	resection of celiac trunk and common hepatic artery with end-to-end anastomosis + pancreas body tail splenectomy	PD+SMA root resection, left gastric artery anastomosis with SMA end-to-end reconstruction, splenic vein resection in the invaded segment and other splenic vein exclusion	PD+360° SMA sheath resection + affected SMV resection and end-to-end anastomosis reconstruction	PD+360° SMA sheath resection	PD+360° SMA sheath resection
Operation time (min)	340	450	300	360	630	600	330	350
Intraoperative blood loss (ml)	700	800	900	700	900	1000	500	600
ICU transitional treatment	No	No	No	No	No	No	No	No
Pancreatic fistula	No	No	No	Grade B	No	No	No	Grade A
Diarrhea	Yes	No	No	No	Yes	Yes	No	Yes
Delayed gastric emptying	No	No	No	No	No	No	No	No
Postoperative bleeding	No	No	No	Yes	No	No	No	No
Reoperation	No	No	No	No	No	No	No	No
Postoperative chemotherapy	No	Yes	No	Yes	Yes	No	No	Yes
Survival time (months)	8.1	12.5	26.3	13.1	13.2	10.3	16.6	15.4

Table 2: Intraoperative and postoperative comparison between the two groups [cases (%)].

Group	Cases	In the operation				After the operation				Death during Perioperative Period	Median Survival Time (月/Months)
		Operation Time (min, $\bar{x}\pm s$)	Intraoperative Blood Loss (ml $\bar{x}\pm s$)	ICU Transitional Treatment	Pancreatic Fistula	Intractable Diarrhea	Delayed Gastric Emptying	Intraoperative Hemorrhage	Reoperation		
Resectable	69	329.4 ± 45.0	478.3 ± 190.0	3/69 (4.4)	9/69 (13.0)	1/69 1.4	5/69 7.2	3/69 4.4	1/69 1.4	0	15.8
Unresectable	8	432.5 ± 124.0 ^a	762.5 ± 168.5 ^a	0/8 (0) ^a	2/8 (25.0) ^a	4/8 (50.0) ^a	0/8 (0) ^a	1/8 (12.5) ^a	0/8 (0) ^a	0	14.3

Note: ^aP < 0.01

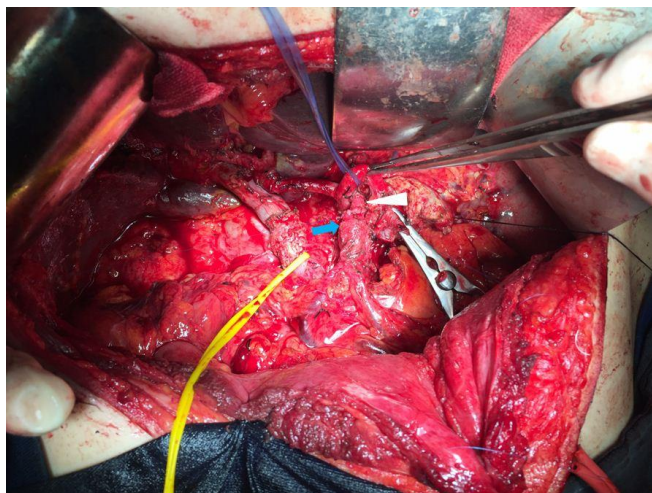


Figure 2: Case 5 in the unresectable group.

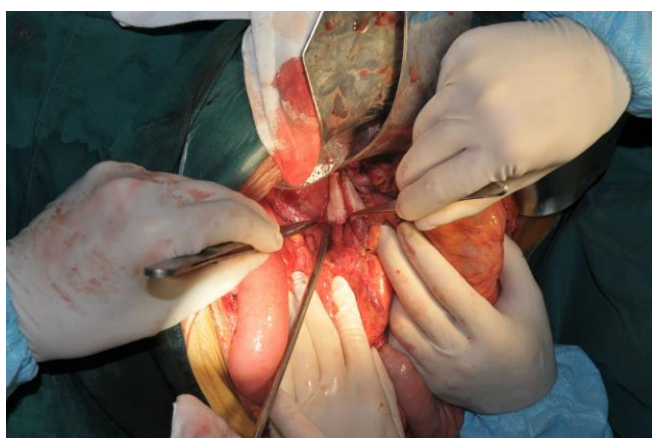


Figure 3: Case 2 in the unresectable group.

SMV was all involved, with portal vein involvement at the top and jejunal ileal vein below, respective anastomosis of Y-type iliac artery with portal vein and jejunal ileum vein.

DISCUSSION

Surgical treatment is considered as the most difficult decision for the surgeons treating patients with unresectable pancreatic cancer, but some scholars performed radical surgery on the patients with unresectable pancreatic cancer after strict selection.^{8,9} and achieved a similar survival time with the patients with resectable pancreatic cancer.^{7,10} Literature shows that even if radical R0 resection is not achieved, the prognosis of locally advanced pancreatic cancer could be improved.^{11,12}

In this study, after rigorous and systematic selection, 360° arterial sheath resection was performed on the patients with pancreatic cancer while arterial sheath was encapsulated more than 180° without arterial adventitia involved. Arterial resection and reconstruction with radical operations were performed on the patients with arterial adventitia & intimal infiltration. Reconstruction of Y-type iliac artery allografts in order to make portal vein and jejunal ileovenous anastomosis was performed on the patients whose SMV was completely involved, with portal vein involvement at the top and jejunal ileal vein below. These radical operations have been reported with a good outcome. In this study, death occurred during perioperative period in neither group. Although operation time and intraoperative blood loss in the unresectable group were significantly greater than those in the resectable group, the rate of postoperative ICU transitional therapy, delayed gastric emptying and reoperation were significantly lower than the resectable group ($P < 0.01$), and there was no Grade C pancreatic fistula. This indicates that it is safe to undergo surgical treatment for the patients with unresectable pancreatic cancer by stringent selection. In this research, median survival time was 15.8 months in the resectable group and 14.3 months in the unresectable group. There was no significant difference in median survival time between the two groups ($P > 0.01$). The patients in the unresectable group had the same median survival time of 11 – 18 months reported in previous literature^{1,2} for the patients with resectable pancreatic cancer. This proves that surgical resection for unresectable pancreatic cancer patients who are strictly selected is effective. However, long-term survival rate in the resectable group was significantly higher than that in the unresectable group ($P > 0.01$). Three cases (4.4%) in the resectable group had a survival time of more than five years and no patients (0%) in the unresectable group had a survival time of more than three years. Even there were two patients in the unresectable group with all negative lymph nodes (case 4, 0/16 and case 5, 0/27), their survival time was only 13 months. One died of Budd-Chiari syndrome with liver metastasis and the other died of consumption and malnutrition caused by refractory diarrhea. This indicated that even if arteriovenous invasion of pancreatic cancer

was caused only by a specific site of the tumor, it was also prone to early local recurrence and metastasis that resulted in poor long-term prognosis. Neoadjuvant chemotherapy is still the first choice for unresectable pancreatic cancer. Operation should be performed after conversion therapy. Intractable diarrhea is the most common complication after extended radical resection of pancreatic cancer, especially SMA sheath resection and SMA reconstruction. Nearly 50% of cases in the unresectable group presented with intractable diarrhea and one of them died of intractable diarrhea. Retaining artery sheath at the root of SMA as far as possible may reduce its frequency and severity.

Currently, resectability assessment of pancreatic cancer is based on preoperative imaging, so there is the possibility of over-diagnosis and under-diagnosis.⁶ Many guidelines consider greater than 180° of main artery encapsulation as a criterion of unresectable pancreatic cancer, but for many of these patients, the tumor has been proven technically resectable in surgery and biological benefits have been achieved.⁶

CONCLUSION

Radical resection for some patients with unresectable pancreatic cancer is technically feasible. Therefore, the author believes that it could be regarded as an option to give active surgical treatment to unresectable pancreatic cancer cases with rejection of neoadjuvant chemotherapy, unsatisfactory response or intolerance to chemotherapy, good general condition and no distant metastasis, which can alleviate the symptoms and provide a good basis for follow-up combined treatment. Of course, both arterial resection and reconstruction and 360° arterial sheath resection are technically difficult, which require sophisticated surgical planning, elaborate surgical operation and experienced surgical and anesthetic teams as a surety for better outcome.

LIMITATIONS OF THE STUDY

This study presents the experience of a single centre where involvement of multiple centres and surgeons and wide variety of patients could have given a more precise and reproducible data

regarding the feasibility and safety of this technique.

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CONFLICT OF INTEREST

None to declare.

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None to disclose.

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Author's Contribution

ALL AUTHORS: Conception, design, data acquisition and analysis, drafting of manuscript, approval of the final version of the manuscript to be published.