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Original article

Improvement of surgical and survival outcomes of patients with pancreatic cancer who underwent pancreaticoduodenectomy : A Chinese experience

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ABSTRACT

Objective: To analyze our experience and the surgical and survival outcomes of patients with pancreatic carcinoma who underwent pancreaticoduodenectomy (PD) by analysis of a retrospective cohort of 205 patients over a 10 years period.
Methods: The patients were categorized into two 5-year periods: period 1, from 2000 January 1 to 2004 December 31(group 1, $n = 48$) and period 2, from 2005 January 1 to 2009 December 31(group 2, $n = 157$). We analysis the data using statistical software and find the improvement of surgical and survival outcomes of PD for pancreatic cancer in the past 10 years.
Results: The two groups have similar age, sex distribution, comorbidity, preoperative serum tumor markers, patients number of preoperative biliary drainage and postoperative chemotherapy. More patients in group 2 underwent lymph nodes dissection ($P = 0.031$). And patients of group 2 had a better surgical outcomes and longer 5-year overall survival (8% vs. 19%, $P = 0.036$). The blood loss volume, transfusion volume, and the number of patients need blood transfusion were significantly fewer ($P < 0.001$) for the patients in group 2, however, the operation time was obviously lengthened ($P = 0.002$). Patients in Group 1 suffered more postoperative complications than those of the patients in group 2 ($P = 0.021$). A significant difference was reached for survival between the two group ($P = 0.036$).
Conclusions: A significant improvement of surgical and survival outcomes after PD for pancreatic cancer patients was achieved in the past 10 years. PD remains the only treatment option that potentially provides a cure for pancreatic head cancer, and postoperative chemotherapy may produce survival benefit.

1. Introduction

Pancreatic cancer is the eighth leading cause of cancer death [1] and leads to an estimated 227000 deaths per year worldwide. Pancreatic cancer is more common in elderly persons than in younger persons, and less than 20% of patients present with localized, potentially curable tumors. The overall 5-year survival rate among patients with pancreatic cancer is about 6% [2,3]. The majority of tumors (70–80%) develops in the head of the pancreas and cause obstructive jaundice. For patients with resectable disease, surgery remains the treatment of choice [4,5]. The operative procedures involve pancreatoduodenectomy, distal pancreatectomy, or total pancreatectomy depending on the location of the tumor. And we will research surgical and survival outcomes for pancreatic cancer after PD in order to identify if there is improvement in the recent years.

2. Patients and methods

Between 2000 and 2009, 205 consecutive patients who were diagnosed pancreatic cancer underwent pancreatoduodenectomy at the Department of Hepatobiliary Surgery, Tianjin Medical University Cancer Hospital, Tianjin, China. The patients were managed and operated according to the discussion opinion of all the surgeons. All data were collected prospectively by the first author of this article. The patients were categorized into two 5-year periods: period 1, from 2000 January 1 to 2004 December 31(group 1, $n = 48$) and period 2, from 2005 January 1 to 2009 December 31(group 2, $n = 157$).

All patients were followed up until their death or now and 5 patients defaulted the follow-up. Every patient was recommended receive Blood Tumor Marker (at least including CA 19-9 and CEA), B-Ultrasound and systematic chemotherapy (at least 6 cycles) monthly,

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CT or MR every 3–4 months. And the chemotherapy regimen in Group 1 consisted of fluorouracil and Calcium Folinate, FOLFOX, gemcitabine with or without CF, while patients in Group 2 mainly used gemcitabine with cisplatin or oxaliplatin. The diagnosis of recurrence was based on typical imaging findings on CT or MRI, and combining with tumor markers usually. Patients with recurrences were treated with multidisciplinary methods, for instance, radiotherapy, chemotherapy, symptomatic and supportive treatments.

Continuous data are expressed as mean ± Standard deviation. Categorical variables were analyzed by Chi-square test or Fisher's exact test, and continuous variables by Student's *t*-test. The Kaplan–Meier method and the life tables were applied for survival analyses. Length of survival was estimated as median number of months (95% confidence interval). Time-defined survival was analyzed in 1-, 3-, and 5-year interval and presented in percentage ± standard error. The survival analysis was performed using the time of PD to the date of death or last follow-up. $P < 0.05$ was considered significant. All statistical analyses were performed in the statistical software (SPSS 18.0 for Windows, SPSS Inc, Chicago, IL).

3. Results

Between January 2000 and December 2009, 205 patients with pancreatic cancer underwent pancreaticoduodenectomy, including 109 men (53.2%) and 96 women (46.8%). There were 48 patients in group 1 and 157 patients in group 2 which made our institute a high-volume center [6]. And the median age at diagnosis of pancreatic cancer was 55.5 years (range, 18–78 years). We can see from Table 1 that there were no significant different between the two groups with respect to the age, sex distribution, comorbidity, preoperative serum tumor markers, and patients number of preoperative biliary drainage except total and direct bilirubin which represents the severity of jaundice. The comparative data of the two groups was summarized in the Table 1.

The blood loss volume, transfusion volume, and the number of patients need blood transfusion were significantly fewer ($P < 0.001$) for the patients in group 2, however, the operation time was obviously lengthened ($P = 0.002$). Number of patients received PD, PPPD, PD with body and tail pancreatectomy was 42, 2, 4 in group 1, respectively, and those of the patients in group 2 were 148, 6, 3, respectively ($P > 0.05$). There was similar number of patients received PD with partial portal vein resection or SMV replacement or SMA reconstruction in the two periods ($P > 0.05$), however, more patients received lymph nodes dissection in Group 2($P = 0.031$). As time went by, our surgeons tend to deploy internal pancreatic duct stent rather than T tube and external pancreatic drainage ($P < 0.001$), while the pancreatic fistula rate didn't increase ($P = 1.00$) (Table 3). The mean diameter of the tumors for each patient was 3.8 cm (range, 1.5–7 cm), and it didn't exist difference between the two group, also with respect to pathology type ($P > 0.05$). However, the lymph nodes involvement was less ($P = 0.022$) and the tumor-node-metastasis (TNM) staging was worse ($P < 0.001$) in group 2 than that in group 1 (Table 2).

Patients in Group 1 suffered more postoperative complications than those of the patients in group 2 ($P = 0.021$). There was no obvious improvement in terms of pancreatic fistula, hemorrhage, DGE, although infection was significant reduced ($P = 0.004$) in period 2. It shows the similar hospital mortality between the two periods ($P = 1.00$), however, the hospital stay and postoperative blood transfusion were considerable fewer in group 2. There was more patients received postoperative chemotherapy in period 2, though there was no significant difference (Table 3).

There was no correlation between PF and external or internal pancreatic stent (Chi-square value = 0.056, $P = 0.810$). Meanwhile, DGE was associated with PPPD (Chi-square value = 22.364, $P = 0.001$).

The median overall survival for the entire cohort was 26.6 months, with 1-, 3-, 5-year overall survival rate of 59%, 26%, 14%, respectively. The median overall survival time of group 1 was 20.2 months, with 1-, 3-, 5-year survival of 45%, 17%, and 8%,

Table 1
Comparison of preoperative data.

	Group 1 ($n = 48$)	Group 2 ($n = 157$)	*P* value
Age	54.2 ± 13.2	55.9 ± 11.9	0.375
Male: Female	28:20	81:76	0.509
Comorbidity	18(37.5%)	74(47.1%)	0.251
Total bilirubin (μmol/L)	229.7 ± 202.4	144.3 ± 159.9	0.003
Direct bilirubin (μmol/L)	171.6 ± 152.0	111.7 ± 134.5	0.010
Serum CA19-9 (U/ml)	217.8 ± 171.2	1005.6 ± 4149.7	0.501
Serum CEA (μg/L)	3.4 ± 1.0	6.2 ± 12.7	0.500
Preoperative biliary drainage	2(4.2%)	16(10.2%)	0.254

Table 2
Comparison of operative and pathological data.

	Group 1 ($n = 48$)	Group 2 ($n = 157$)	*P* value
Blood loss (ml)	562.5 ± 331.7	351.3 ± 220.9	0.000
Blood transfusion (ml)	391.7 ± 342.6	121.3 ± 230.7	0.000
No. patients with blood transfusion	32(67%)	39(25%)	0.000
Operation time (min)	288.1 ± 95.0	342.9 ± 110.6	0.002
No. patients with PD	42(88%)	148(94%)	0.115
PPPD	2(4%)	6(4%)	0.914
PD with body and tail pancreatectomy	4(8%)	3(2%)	0.032
Patients with partial PV resection or SMV replacement	4(8%)	12(8%)	0.876
Patients with SMA reconstruction	0	4(3%)	0.264
Patients underwent lymph nodes dissection	4(8%)	35(22%)	0.031
Involvement of PV or SMV or SMA	4(8%)	16(10%)	1.000
Lymph Node Involvement	9(19%)	11(7%)	0.022
T tube	48(100%)	44(28%)	0.000
External pancreatic drainage	38(79%)	84(54%)	0.001
Internal pancreatic duct stent	2(4%)	71(45%)	0.000
Tumor size (cm)	3.7 ± 1.0	3.8 ± 1.3	0.355
Pathology type			0.805
Ductal Adenocarcinoma	43	136	
Other[a]	5	21	
TNM Stage			0.000
IA	2(4%)	2(1%)	
IB	20(42%)	38(24%)	
IIA	16(33%)	103(66%)	
IIB	8(17%)	10(6%)	
III	0	4(3%)	
IV	2(4%)	0	

PV: portal vein; SMV: superior mesenteric vein; SMA: superior mesenteric artery.
[a] Include (a) mucious adenocarcinoma, (b) adenosquamous carcinoma.

Table 3
Comparison of postperative data.

	Group 1 ($n = 48$)	Group 2 ($n = 157$)	*P* value
Complication	18(38%)	32(20%)	0.021
Pancreatic fistula	8(17%)	11(7%)	0.083
Infection	10(21%)	9(6%)	0.004
Postoperative hemorrhage	2(4%)	3(2%)	0.333
Delayed gastric emptying (DGE)	4(8%)	11(7%)	0.755
Hospital mortality	0	2(1%)	1.00
Hospital stay (days)	38.5 ± 15.5	27.2 ± 14.0	0.000
No. patients with postoperative transfusion	44(92%)	70(45%)	0.000
Postoperative blood transfusion	1020.8 ± 1019.0	314.0 ± 473.3	0.000
Postoperative chemotherapy	23(48%)	94(60%)	0.240