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The Choice of Palliative Treatment for Biliary and Duodenal Obstruction in Patients With Unresectable Pancreatic Cancer: Is Surgery Bypass Better?

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This study aimed to investigate the clinical significance of palliative operation for carcinoma of pancreas between bypass surgery and interventional therapy. Most patients with locally advanced pancreatic cancer cannot undergo resection and show obstructive jaundice at presentation. Methods of palliation in these patients comprise biliary stent or surgical bypass. We retrospectively analyzed the clinical data of 53 patients who underwent palliative treatment with incurable locally advanced pancreatic ductal adenocarcinoma. This retrospective study compared morbidity, mortality, hospital stay, readmission rate, and survival in these patients. A total of 31 patients underwent biliary bypass surgery, and 22 had interventional therapy. There was no significant difference in the patients' basic condition before operation and in the 30-day mortality between surgical palliation and intervention. However, there were some differences in the early complications, survival time, successful biliary drainage, and recurrent jaundice. Through analysis of these clinical data and the published studies, we conclude that surgical bypass is a better effective palliative method for patients than biliary and duodenum stent with locally advanced pancreatic cancer. Patients need to be carefully selected in consideration of operative risk and perceived overall survival.

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Pancreatic cancer is the fourth leading cause of cancer-related mortality in the world.[1] About 80% of patients who have received a diagnosis of pancreatic cancer already have other organ metastasis, as well as local tumor in the late stage.[2] Therefore, appropriate palliation for the main symptoms, such as obstructive jaundice, duodenal obstruction, and pain, is most important.

However, there is controversy on how to provide better palliative treatment for these patients. Several therapeutic methods can be options. Some surgeons hold the view favoring resection surgery in the palliative way, arguing that it could offer a survival advantage or better palliation and has equivalent morbidity and mortality rates to surgical bypass,[3] but some surgeons do not agree with this view. Comparing to palliative resection, biliary bypass (choledochojejunostomy and cholecystojejunostomy) and biliary stent are also the choices of palliative treatment. The advantage of biliary stents is that the procedure is mini-invasive, which is well tolerated by patients. However, this method is limited by the recurrence of jaundice secondary to stent migration or accretion. Tumor progression and duodenal invasion may cause therapy to fail. Some surgeons also thought that surgical bypass was the best palliative treatment for carcinoma of the pancreas[4] because stenting of the biliary system requires periodic changes of the endoprosthesis and causes associated hospitalization.[5] Therefore, there is controversy on how to provide effective palliative treatment for those patients who have locally advanced pancreatic cancer. The goal of therapy for these patients is to obtain the most complete and prolonged remission of symptoms possible, with the least intervention-related morbidity and mortality.[6] The aim of this research was to compare morbidity and mortality rates and the effectiveness of palliative methods between patients matched for tumor size and clinical stage who underwent surgical bypass or biliary and duodenal stent for locally advanced pancreatic cancer.

Patients and Methods

Patients and data collection

We carried out a retrospective analysis of patients who underwent palliative treatment with primary cancer of the head of the pancreas, requiring palliation of their malignant obstructive jaundice in our hospital from January 2008 to December 2011. Excluded from this research were any patients who underwent palliative resection, had no obstructive jaundice at the time of diagnosis, or had other periampullary cancer (distal bile duct, ampulla of Vater, and duodenum). All patients with metastatic disease proven by radiologic or surgical assessment were excluded. Patients with histologic diagnoses other than adenocarcinoma were also excluded.

The tumors of these patients were unresectable because of local vascular invasion to the superior mesenteric vein, portal vein, superior mesenteric artery, hepatic artery, or celiac artery. The tumor size was 5.46 ± 2.24 cm in the surgical bypass group, and 5.54 ± 1.10 in the stent group. The tumors of these patients were all in stage 3 according to the NCCN guideline of pancreatic adenocarcinoma. The definition of hospital stay was the time of being in the hospital after the patient's surgical or interventional procedure. Information and data on short- and long-term morbidity in terms of postoperative complications and hospital readmissions and mortality were collected. Long-term disease-specific survival data were collected by telephoning the number of patients from hospital records.

All patients undergoing interventional therapy underwent biliary stenting following percutaneous transhepatic cholangial drainage (PTCD) and duodenal stent if clinical symptoms of gastric outlet obstruction were present. All patients undergoing palliative surgery underwent a double bypass comprising a hepatojejunostomy-en-Y and gastrojejunostomy.

This study complied with the standards of the Helsinki Declaration and current ethics guideline and was approved by the Institutional Ethics Board.

Statistical analysis

Survival time is defined as counting from the day of surgery until death. According to the medical records, survival or death information can be obtained by telephone contact with patients' relatives. Description of continuous data were expressed as mean and standard deviation (SD). Statistical analysis of continuous data used the Student *t*-test or Mann-Whitney *U* test for parametric and nonparametric data, respectively. Statistical

Table 1 Basic condition of patients before surgical bypass or interventional palliation

	Surgical double bypass	Interventional therapy	*P* value
No. of patients	31	22	
Male, n	19	8	
Female, n	12	14	
Mean age, y	61.0 ± 9.4	64.7 ± 9.3	>0.05
Total bilirubin, mmol/L	237.56 ± 106.11	263.31 ± 115.82	>0.05
Direct bilirubin, mmol/L	133.78 ± 58.98	144.20 ± 52.43	>0.05
Alanine aminotransferase, mmol/L	316.19 ± 194.40	336.32 ± 216.96	>0.05
ALP, mmol/L	668.17 ± 538.80	702.37 ± 683.99	>0.05
Albumin, g/L	36.40 ± 4.00	36.07 ± 3.79	>0.05
Tumor size, cm	5.46 ± 2.24	5.54 ± 1.10	>0.05

ALP, alkaline phosphatase.

analysis of proportions used a χ^2 test or Fisher exact test. Kaplan-Meier survival curve was used to calculate the incidence of cumulative event, and was tested by the use of log rank. In all analyses, a *P* value <0.05 was considered statistically significant. The clinical results were analyzed using a statistical analysis program package (SPSS 19.0, SPSS Inc, Chicago, Illinois).

Results

In this research, a total of 53 patients were included. Of these, 31 underwent palliative surgery and 22 underwent interventional therapy. Basic demographic and hematologic data are displayed in Table 1. The tumor size and stage are displayed in Table 1. No other values differed statistically between the groups.

There were no significant differences in mortality rates between the patients who underwent palliative surgery and those who underwent palliative biliary and duodenal stent (Table 2). In the surgical group, no one was dead within 30 days. In the stent group, causes of death were cholangitis. Treatment of surgical palliation was successful in 29 of the 31 patients. Treatment of palliative stenting was successful in 21 of the 22 patients. The success was determined by normalization of the serum bilirubin levels and symptom improvement (Table 2). In the surgical group, the mean maximal preoperative bilirubin level was 237.56 ± 106.11 mmol/L, and the mean minimal postoperative level was 55.8 ± 30.54 mmol/L. In the stent group, the mean maximal preoperative bilirubin level was 263.31 ± 115.82 mmol/L, and the mean minimal postoperative level was 102.95 ± 55.43 mmol/L. There were 7 patients who had experienced complications within 30 days in surgical palliation group. Of these 7 patients, 4 had wound infections, 1 patient had upper gastrointestinal bleeding, and 2 had postoperative prolonged ileus. There was 1 patient who had experienced complications within 30 days in the palliative stenting group, and the main problem for this patient was stent blockage. In the first admission period, the postoperative stay of the palliative

Table 2 Basic condition of patients after surgical bypass or interventional palliation

	Surgical double bypass	Interventional therapy	*P* value
Total bilirubin, mmol/L	55.8 ± 30.54	102.95 ± 55.43	<0.001
Direct bilirubin, mmol/L	23.24 ± 15.44	64.47 ± 18.86	<0.001
Alanine aminotransferase, mmol/L	79.20 ± 60.09	83.33 ± 4.98	>0.05
ALP, mmol/L	257.40 ± 145.97	284.83 ± 112.76	>0.05
Mean postoperative hospital stay during the first admission period, days	22.86 ± 4.36	15.90 ± 2.69	<0.05
Mean survival, mo	14.29 ± 7.45	5.73 ± 2.53	<0.001
Early complications in 30 days, No.	7	1	NS
30-day mortality, n	0	1	NS
Readmission reason, n			
Cholangitis	2	3	NS
Gastrointestinal obstruction	0	5	NS
Recurrent jaundice	2	6	NS

ALP, alkaline phosphatase; NS, not significant.

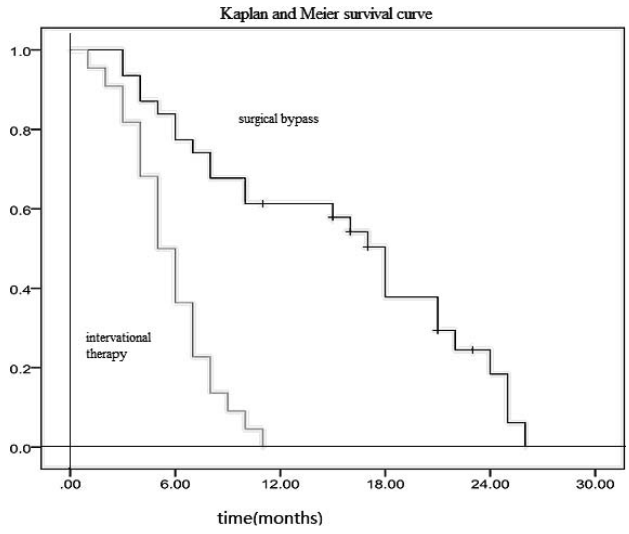

Fig. 1 Actuarial Kaplan-Meier survival analysis of patients who underwent surgical double bypass compared with patients who received interventional therapy.

surgery group was longer than that of the palliative stenting group. Although the patients who underwent a surgical bypass had a longer postoperative hospital stay during the first hospitalization, they had a longer overall survival than patients who underwent interventional treatment (Fig. 1).

The main reasons for readmission were gastrointestinal obstruction and recurrent jaundice in both groups. There were 14 patients in the palliative stenting group who had complications for readmission because of acute cholangitis, recurrent jaundice, and gastric outlet obstruction. Of these 14 palliative stenting patients, 5 developed intractable vomiting, which had radiologic evidence of gastric outlet obstruction. Recurrent jaundice occurred in 6 patients in the palliative stenting group. In the palliative surgery group there were 4 patients who had complications for readmissions because of acute cholangitis or recurrent jaundice. In the palliative surgery group, 2 patients had acute cholangitis and 2 patients had recurrent jaundice.

Discussion

In this single-center retrospective trial of comparison between bypass surgery and interventional therapy, we found that surgical bypass can be performed with mortality rates equivalent to those of biliary stenting in selected patients. Our findings agree with those of two previous retrospective studies of incurable, locally advanced pancreatic ductal adenocarcinoma that compared morbidity, mortality, hospital stay, readmission rate, and survival. In a study of 56 patients, Scott *et al*[7] reported that surgical bypass can be performed with morbidity and mortality rates equivalent to those of biliary stenting in selected patients, but with a significantly lower risk of readmission. In a similar study involving 69 patients, Kim *et al*[8] reported that the patients who underwent surgical palliation had a longer hospital-free survival rate, although they had a longer postoperative hospital stay during the first admission period. From our study and these 2 studies, we can find that surgical bypass can be performed with mortality and morbidity rates similar to those for interventional therapy, but with a longer hospital stay during the first admission period. Rates of late complications and readmissions were higher for patients who underwent palliative biliary stenting than for those who underwent surgical bypass.

Obstructive jaundice is present in approximately 90% of patients with pancreatic cancer at the time of diagnosis.[9] Relief of obstructive jaundice should always be a major therapeutic goal, because jaundice is harmful for the liver and other organs. Therefore, the best palliative treatment for obstructive jaundice should be simple, have less trauma, have a low mortality and recurrence rate, produce a better quality of life for patients, and offer a shorter time in the perioperative period of overall survival time. Percutaneous or endoscopic palliation of obstructive jaundice can resolve biliary compression with lower early morbidity compared with open biliary bypass surgery. A study implied that for surgical bypass, the mortality rate is 1% to 5%, and the operative morbidity rate is 20% to 30%.[10] Stent occlusion and the growth of tumor may be the main reason for recurrent jaundice. Patients have to be in the hospital for treatment again and again in their limited survival time. Past study by Castaño *et al*[11] shows that interventional therapy may be associated with fewer early complications and surgical bypass with fewer late complications. Past study by Kim *et al*[8] shows that, compared with biliary stent, surgical biliary bypass has higher success rates in relieving obstructive jaundice, and patients have lower rates of recurrent jaundice as well as longer survival time and longer median hospital-free survival. Above all, because of its morbidity and mortality rates similar to those of biliary stent, and its lower rates of late complications and readmissions, surgical bypass can be a better choice for obstructive jaundice.

At the time of diagnosis, only about 19% of pancreatic cancer patients present with symptoms of gastric and duodenal obstruction, such as nausea and vomiting. About 30% to 50% of all patients will eventually develop malignant gastric outlet obstruction during the course of their disease.[12] Gastrojejunostomy and duodenal stenting are the only choices for these patients. At present, the success rate for placement of duodenal stents is 92% to 100%. The recovery of digestive system is rapid, usually within24 hours in 75% to 93% of cases.[13] Some new studies have shown similar success rate for these two techniques, but with fewer complications, more rapid resumption of alimentation, and shorter hospitalization for endoscopic treatment.[14] However, there are some problems for endoscopic treatment, such as a greater risk of stent migration, and a duodenal stent may impair function of the biliary stent in approximately 20% of cases.[15] Therefore, the patients who undergo endoscopic palliation of a biliary obstruction with gastric outlet obstruction cannot benefit. In our hospital, it is our policy to perform a gastrojejunostomy at the time of biliary bypass. The use of a routine gastrojejunostomy in some studies showed that gastrojejunostomies can be performed with no increase in morbidity and mortality.[16] They also hold the view that a gastrojejunostomy and biliary bypass be undertaken as a single procedure. In the present study, 5 patients in the endoscopic stent group developed gastric outlet obstruction. This also supports the use of prophylactic gastrojejunostomy in patients who underwent operative intervention. Gastrointestinal obstruction also could be treated by large-diameter metal stents by interventional therapy.[17] They are more expensive than conventional stents; metallic stents are purported to have longer patency, but this treatment also has its limitations. Metallic and large-diameter stents may still become occluded by tumor ingrowth or overgrowth.

The survival of patients who underwent bypass was longer than that of those who underwent stenting. This may also be influenced by our policy of selecting the patients, and the fact that patients with distant pancreatic metastases were excluded from the study. It is accepted that through avoiding recurrent admissions for jaundice and concurrent cholangitis, surgical bypass may contribute to the increased survival in this group, in spite of these considerations.

A potential limitation of this study is that it is a retrospective, single-center study. Therefore, a large-scale prospective validation study is needed to confirm the results. In conclusion, we hold the view that the surgical double bypass is an effective method of palliating patients with locally advanced pancreatic adenocarcinoma. Although stent therapy offers a shorter hospital stay and a lower rate of early complications, it involves a higher rate of late complications and a higher rate of readmission than surgical bypass. Meanwhile, we have shown that surgical bypass can be performed with mortality rates and therapy success equivalent to those of endoscopic stenting, and that it results in a lower rate of late complications. Surgical bypass in this study was associated with prolonged survival compared with palliative stenting. Although the precise reasons for this remain unclear, it should be an important consideration when considering palliation for patients with pancreatic cancer.

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