ORIGINAL ARTICLE

Surgical bypass vs. endoscopic stenting for pancreatic ductal adenocarcinoma

Edwina N. Scott, Giuseppe Garcea, Helena Doucas, Will P. Steward, Ashley R. Dennison & David P. Berry

Department of Hepatobiliary and Pancreatic Surgery, Leicester General Hospital, Leicester, UK

Abstract

Background: The majority of patients with pancreatic cancer are non-resectable and jaundiced at presentation. Methods of palliation in such patients with locally advanced disease comprise endoscopic placement of a biliary endoprosthesis or surgical bypass.

Methods: This retrospective study compared morbidity, mortality, hospital stay, readmission rate and survival in consecutive patients with incurable locally advanced pancreatic ductal adenocarcinoma.

Results: We identified a total of 56 patients, of whom 33 underwent endoscopic stenting and 23 underwent a surgical bypass consisting of a hepaticojejunostomy-en-Y and a gastrojejunostomy. There were no significant differences in complication or mortality rates between patients undergoing palliative stenting and those undergoing palliative surgery. However, after excluding admissions for chemotherapy-related problems, the number of readmissions expressed as a percentage of the group population size was greater in stented patients compared with biliary bypass patients (39.4% vs. 13.0%, respectively; $P < 0.05$). Overall survival amongst patients undergoing palliative bypass was significantly greater than in stented patients (382 days vs. 135 days, respectively; $P < 0.05$).

Conclusions: On analysis of these data and the published literature, we conclude that surgical bypass represents an effective method of palliation for patients with locally advanced pancreatic cancer. Patients need to be carefully selected with regard to both operative risk and perceived overall survival.

Correspondence

Giuseppe Garcea, Department of Hepatobiliary and Pancreatic Surgery, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW, UK. Tel: + 44 116 4508. Fax: + 44 116 4736. E-mail: gg43@le.ac.uk

Introduction

Up to 80% of ductal adenocarcinomas of the head of the pancreas are not resectable at presentation.[1,2] As 70–90% of patients with carcinomas of the head of the pancreas and ampullary region have jaundice at presentation,[3–5] palliation that ensures biliary drainage represents a large proportion of the hepatobiliary surgeon's workload.

Various therapeutic options have been described. Some centres advocate resection surgery even in the palliative setting, arguing that it may offer a survival advantage or better palliation and has equivalent morbidity and mortality rates to bypass surgery,[6–8] but these results are disputed by other groups.[9] Other options include surgical biliary bypass incorporating either an hepatojejunostomy (choledochojejunostomy),[10–12] cholecystojejunostomy[12,13] or cho-ledochoduodenostomy[10,12] with or without a concomitant gas-trojejunostomy.[14] More recently, these procedures have been undertaken laparoscopically, with reportedly low morbidity and mortality.[15,16]

In addition, biliary endoprostheses can be employed to relieve biliary stasis. Internal drainage of the biliary tree via the transhepatic route was first described in 1978.[17,18] The introduction of endoscopically placed stents enabled the use of larger-calibre endoprostheses.[19,20] The advantage of biliary stents is that their positioning is a minimally invasive procedure which is well tolerated by patients. However, their palliative potential is limited by the recurrence of jaundice secondary to stent migration or accretion. Tumour progression and duodenal invasion may render repeated stenting impossible.

The aim of this study was to compare morbidity and mortality rates and effectiveness of palliation between patients matched for tumour size and clinical stage who underwent surgical by-pass or endoscopic stenting for locally advanced pancreatic adenocarcinoma.

Materials and methods

Study methodology

Case notes were analysed retrospectively for all patients who presented consecutively to the University Hospitals of Leicester from January 2003 to April 2004 with primary cancer of the head of the pancreas, requiring palliation of their malignant obstructive jaundice. Data were divided into two treatment groups consisting of, respectively, patients who underwent stenting +/− chemotherapy and patients who underwent palliative surgery +/− chemotherapy. All patients with metastatic disease proven by radiological or surgical assessment were excluded from the final analyses. Patients with histological diagnoses other than adenocarcinoma were also excluded.

Date of diagnosis was the first computed tomography (CT) scan date. Tumour size was defined by surgical or radiological staging. In patients for whom no histology was available, the diagnosis of pancreatic cancer was based on information from the clinical history, radiology reports and tumour marker levels. CA19.9 was considered significant if it was above the upper normal limit of our local laboratories (>37 kU/l). Patients with normal CA19.9 values were excluded from the final analyses.

Initial hospital stay duration was defined as the time spent in hospital after the patient's surgical or endoscopic procedure. Data on short- and longterm morbidity in terms of postoperative complications and hospital readmissions were collected. Perioperative complications were defined as occurring within 30 days after stent insertion or surgery. Thirty-day mortality for each type of treatment was calculated. Longterm disease-specific survival data were collected by telephoning the appropriate general practice surgery or from hospital records. The selection of patients for palliative surgery over endoscopic palliation was based on patient preference and judged fitness for operative intervention.

Data were analysed using SPSS Version 11.5 (SPSS Inc., Chicago, IL, USA). Median survival was analysed by the log rank test and represented by Kaplan–Meier graphs. Other continuous data of normal distribution were analysed by descriptive analysis with means compared by independent t-test. Categorical variables were analysed using Fisher's exact test. A P-value of <0.05 was considered statistically significant.

Endoscopic technique

Patients undergoing therapeutic stenting received a plastic endoprosthesis using a side-viewing endoscope under fluoroscopic guidance. The stent position was confirmed by its anatomic location, visualization of bile drainage and injection of contrast into the stent following placement to ensure its position above the bile duct stricture.

Surgical technique

All patients undergoing palliative surgery underwent a double bypass comprising a hepatojejunostomy-en-Y and gastrojejunostomy (Fig. 1).

Results

Within the study period, a total of 56 eligible patients were identified. Of these, 33 underwent endoscopic stenting and 23 underwent palliative surgery. Follow-up ranged from 1 to 86 weeks. Baseline demographic and haematological values are displayed in Table 1. Patients undergoing palliative surgery had significantly lower CA19.9, despite having equivalent tumour sizes. No other values differed statistically between the groups.

There were no significant differences in immediate complication or mortality rates between patients who underwent palliative stenting and those who underwent palliative surgery (Table 2). In the surgical group, the one death was attributed to respiratory infection complicated by multiple organ failure. In the stent group, causes of death were cholangitis ($n = 1$), acute renal failure ($n = 2$), upper gastrointestinal haemorrhage ($n = 1$) and respiratory complications ($n = 2$). After excluding admissions for chemotherapy-related problems (diarrhoea, skin rashes, anaemia or vomiting occurring within 48 hours of treatment) the number of readmissions expressed as a percentage of the group population size was greater in stented patients compared with biliary bypass surgery patients (39.4% vs. 13.0%, respectively) (Fig. 2). The total length of stay in hospital per patient was also lower in the surgical bypass group, even including their postoperative stay (34.1 days vs. 10.2 days). The main reasons for readmission were jaundice
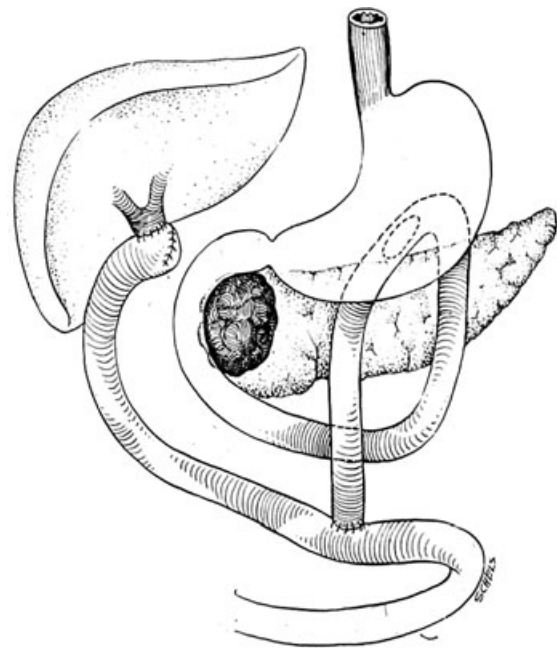

Figure 1 Surgical bypass procedure, final reconstruction

**Table 1** Demographic variables among patients undergoing endoscopic stenting and palliative surgery

Variable	Palliative surgery group (n = 23)	Endoscopic stent group (n = 33)	Significance
Gender			
Male	57%	49%	NS
Female	43%	51%	
Median age, years	65.2	69.0	NS
Median CA19.9, kU/l	1153.00	3878.50	<0.05
Median bilirubin, kU/l	189	290	NS
Median white cell count, ×10^9/l	8.00	8.00	NS
Median C-reactive protein, mg/l	19.00	31.50	NS
Median tumour size, mm	30.00	32.50	NS

NS, not significant

Table 2 Hospital stay, complications and mortality within 30 days after palliative surgery or endoscopic stenting

Variable		Palliative surgery group (n = 23)	Endoscopic stent group (n = 33)	*P*-value
Complications	Sepsis	10	7	NS
		43.5%	21.2%	
	Bleeding	8	5	NS
		34.9%	15.1%	
	Stent blockage	NA	2	NA
			6.1%	
30-day mortality		1	6	NS
		4.3%	18.1%	

NS, not significant; NA, not applicable
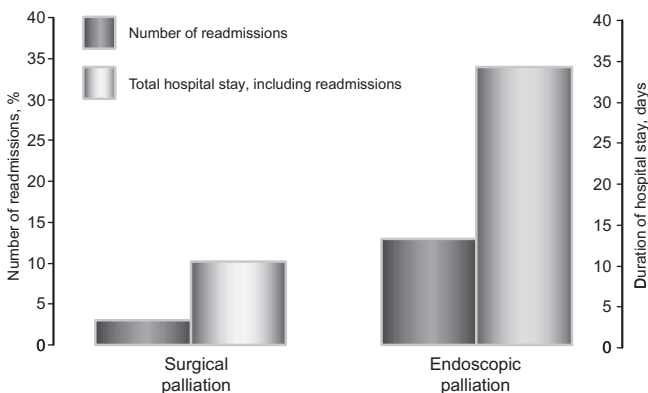
Figure 2 Number of readmissions and total length of hospital stay following palliative surgery and endoscopic stenting, respectively (*P* < 0.05)

and sepsis, which accounted for 76.9% of all readmissions. Two patients in the endoscopic stent group developed intractable vomiting, which persisted despite discontinuing their chemotherapy, and had radiological evidence of gastric outlet obstruction. Neither individual proceeded to intervention as they quickly succumbed from advanced disease.

Overall survival amongst patients undergoing palliative bypass was significantly greater than in stented patients at 382 days vs. 135 days, respectively (Fig. 3). Preoperative CA19.9 also appeared to influence survival: in both groups, patients with CA19.9 values <1000 survived significantly longer than those with CA19.9 >1000 (Fig. 4).

Discussion

Overall, these results suggest that surgical bypass can be performed with equivalent morbidity and mortality rates to biliary stenting in selected patients, but with a significantly lower risk of readmission. Hence, better palliation can be achieved in patients who are able to tolerate biliary bypass surgery. However, quality of life data are needed to add further strength to this observation. The increased survival observed in the surgical bypass cohort is probably the result of a better overall state of fitness, reflected in the lower median age of patients undergoing surgery. In addition, patients who underwent bypass surgery had significantly lower CA19.9 levels than those who underwent endoscopic stenting (Table 1). In this study, we found CA19.9 levels >1000 to be associated with significantly lower survival than levels <1000 (Fig. 4). Hence, despite our attempts to match patients using radiological imaging, it is possible that patients who underwent endoscopic
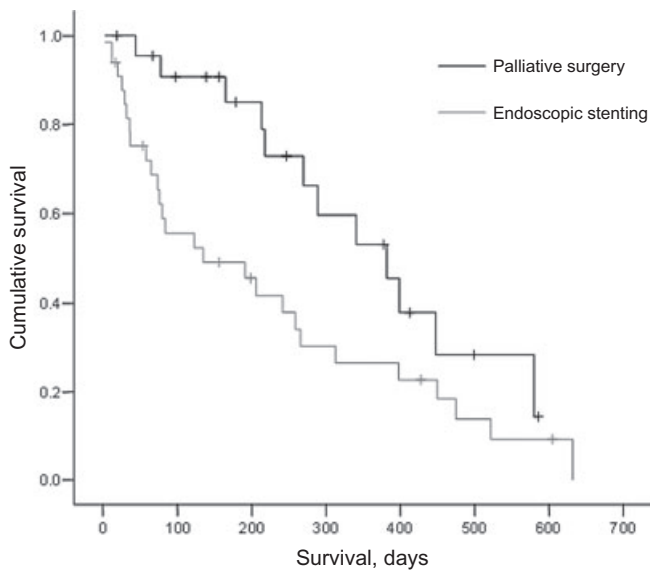
Figure 3 Survival following palliative surgery and endoscopic stenting, respectively ($P < 0.05$)
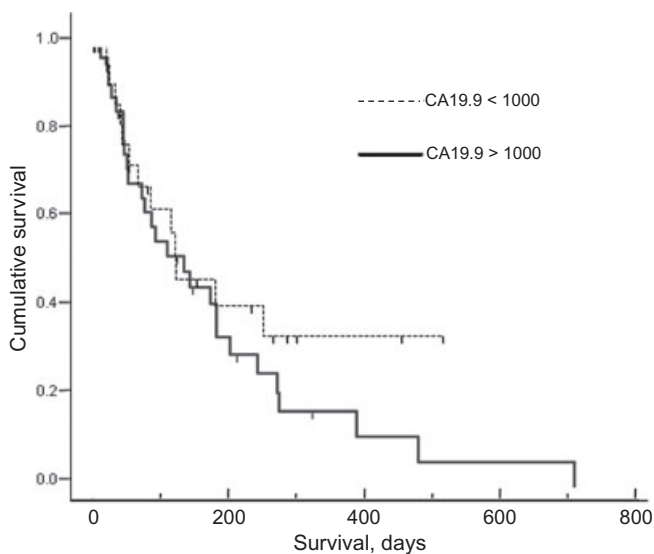

Figure 4 Survival and preoperative CA19.9 values ($P < 0.05$)

stenting had a higher occult tumour burden than those who underwent bypass surgery, which would doubtless have negatively impacted on their longterm survival.

The survival of patients who underwent bypass may also be influenced by our unit's relatively conservative policy regarding the selection of patients for pancreatic adenocarcinoma resection[21] and the fact that no patients with distant pancreatic metastases were included in the study. Despite these considerations, it is conceivable that by avoiding recurrent admissions for jaundice and concurrent sepsis, surgical bypass may contribute to the increased survival in this group.

There are relatively few data examining the relative merits of surgical bypass vs. endoscopic stenting in the literature: we found only three randomized trials and a number of largely retrospective studies, which are summarized in Table 3.[22–33] In a review of the randomized trials, Schwarz *et al.* concluded that an endoprosthesis should be placed if there was evidence of hepatic, peritoneal or pulmonary metastases or if the patient had significant co-morbidity precluding surgery.[34] However, it is worth noting that a later meta-analysis noted that the evidence did not allow for a definitive conclusion on which treatment was preferable.[35] Despite this, the overall pattern would appear to indicate that, for the most part, surgical bypass can be performed with similar morbidity and mortality rates to endoprosthesis, but with a longer initial hospital stay. Rates of late complications and readmissions are greater in patients who undergo biliary stenting than in those who undergo biliary bypass.

These published data would suggest that biliary endoprosthesis should be reserved for those with a shorter expected survival and that surgical palliation should be offered to those patients who are expected to live longer and who are able to tolerate surgical intervention. The cut-off in survival determining these two treatment modalities has often been quoted at 6 months.[22,23,25,29,34,36] Outwith anaesthetic considerations, tumour-related determinants of poor survival in the palliation of pancreatic cancer include C-reactive protein levels,[37] leucocytosis,[37] duodenal invasion,[38] liver metastases,[38] peritoneal dissemination,[38] high bilirubin,[39] low haemoglobin,[39] low albumin,[39] presence of ascites[40] and the Karnofsky index of performance status.[41] These considerations are useful when selecting cases appropriate for bypass procedures vs. endoscopic stenting.

During surgery, it is our policy to perform a gastrojejunostomy at the time of a biliary bypass. It is probably worth noting that one patient who underwent endoscopic palliation of a biliary obstruction re-presented with gastric outlet obstruction. The use of a routine gastrojejunostomy is in keeping with current literature showing that gastrojejunostomies can be performed with no increase in morbidity and mortality and recommending that a gastrojejunostomy and biliary bypass be undertaken as a single procedure.[14,36,42–46] The fact that two patients in the endoscopic stent group in the present study developed gastric outlet obstruction also supports the use of prophylactic gastrojejunostomy in patients undergoing operative intervention. It has been reported that patients with liver metastases and carcinomatosis do not survive long enough to develop gastric outlet obstruction;[10] however, these patients would make poor surgical candidates and are best treated using endoscopic means.

It remains to be seen what impact metallic stents will have on surgical bypass procedures. Although they are more expensive than conventional stents, metallic stents are purported to have longer patency, but may still become occluded by tumour ingrowth or overgrowth.[47] Only one study, to date, has compared surgical bypass with metallic stents; it concluded that metallic stents were cost-effective when compared with surgical bypass but

Table 3 Summary of available literature comparing endoscopic biliary endoprosthesis with surgical palliation

Study, author(s), year	Study type	Number of patients	Findings	Study conclusions
Sunpawervong et al., 2005[22]	Retrospective	116	No difference in survival time, morbidity or cost-effectiveness; surgical palliation resulted in significantly less common late complications (jaundice)	In favour of surgical palliation
Nuzzo et al., 2004[23]	Retrospective	84	Higher incidence of complications in stented group, with frequent hospital admissions and lower quality of life	In favour of surgical palliation
Santagati et al., 2003[24]	Retrospective	107	Higher complication rate, mortality rate and hospital stay in surgically palliated patients	In favour of endoscopic palliation
Maosheng et al., 2001[25]	Retrospective	(Metallic stents)	Higher rate of late complications in metallic stent group, but shorter hospital stay and lower cost	In favour of surgical palliation in patients expected to live >6 months
Wagner et al., 2000[26]	Retrospective	348	–	In favour of surgical palliation
Raikar et al., 1996[27]	Retrospective	66	Endoscopic treatment resulted in shorter hospital stays at reduced cost, with equivalent survival	In favour of endoscopic palliation
Smith et al., 1994[28]	Randomized	204	Lower mortality and complication rates with stenting, but higher rate of late complications	Both effective palliative treatments
van den Bosch et al., 1994[29]	Retrospective	148	Higher early morbidity and mortality in surgical bypass, higher late complications with stenting	Surgical palliation if life expectancy >6 months
Anderson et al., 1989[30]	Randomized	50	No differences in survival or palliation	In favour of endoscopic palliation
Shepard et al., 1988[31]	Randomized	52	No difference in overall survival, more readmissions in the stented group, but total time in hospital still shorter than in those undergoing surgical bypass	Endoscopic palliation is a good alternative to surgery
Sonnenfeld et al., 1986[32]	Retrospective	41	Major complications more common in surgical bypass group with longer hospital stays; no difference in mortality or survival	–
Bornman et al., 1986[33]	Randomized	53	Shorter hospital admission in the stented group, but higher rate of readmissions longterm; no difference in survival	–

had a higher rate of late complications.[25] The use of self-expanding metal stents to treat malignant gastroduodenal outlet obstruction raises the possibility of using endoscopic stents solely to palliate advanced pancreatic cancer without the need for bypass,[48,49] although it would appear that even these gastrointestinal stents are susceptible to tumour ingrowth.[50] More data are needed to evaluate this further.

Major limitations of this study refer to its retrospective nature and small sample size. In conclusion, we tentatively suggest that, based on evidence from our own data and the published literature, the surgical double bypass is an efficacious means of palliating patients with locally advanced pancreatic adenocarcinoma. The published literature suggests that surgical bypass offers a lower rate of late complications, but involves a higher rate of initial complications and a longer hospital stay than stenting. By contrast, we have shown that surgical bypass can be performed with equivalent morbidity and mortality rates and length of initial hospital stay as endoscopic stenting, and that it results in a lower rate of late complications. Surgical bypass in this series is 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.

Conflicts of interest

None declared.

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