Published in final edited form as:

J Gastrointest Surg. 2011 November ; 15(11): 1917–1927. doi:10.1007/s11605-011-1665-9.

Palliative Surgical Management of Patients with Unresectable Pancreatic Adenocarcinoma: Trends and Lessons Learned from a Large, Single Institution Experience

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This study was presented at the 52nd Annual Society for Surgery of the Alimentary Tract Meeting, May 6–10, 2011, Chicago, IL, USA

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Abstract

Introduction—Routine palliative bypass has been advocated for palliation of patients with pancreatic adenocarcinoma who have inoperable disease discovered at the time of surgery. We examined trends in the relative use of palliative bypass over time with an emphasis on identifying changes in surgical indications, type of bypass performed, as well as perioperative outcomes associated with surgical palliation.

Methods—Between 1996 and 2010, 1,913 patients with pancreatic adenocarcinoma in the head of the pancreas were surgically explored. Data regarding preoperative symptoms, intraoperative findings, type of surgical procedure performed, as well as perioperative and long-term outcomes were collected and analyzed.

Results—Of the 1,913 patients, 583 (30.5%) underwent a palliative procedure. Most patients presented with jaundice (72.2%). The majority of patients were evaluated by CT scan (97.4%), which revealed a median tumor size of 3.2 cm. Most patients who underwent surgical palliation (64.5%) had a double bypass, while a minority had either gastrojejunostomy (28.2%) or hepaticojejunostomy (7.2%) alone. While the number of pancreaticoduodenectomies remained relatively stable over time, there was a temporal decrease in the utilization of palliative bypass ($P < 0.001$). Unanticipated locally advanced disease vs. liver/peritoneal metastasis as the indication for palliative surgery also changed over time (1996–2001: 47.8% vs. 52.2%; 2002–2007: 49.2% vs. 50.8%; 2008–2010: 17.2% vs. 82.7%) ($P = 0.005$). Palliative failure rates were 2.3% after hepaticojejunostomy and 3.1% after gastrojejunostomy. Patients with unsuspected metastatic disease had a worse survival compared with patients who had locally unresectable disease (median survival: 5 vs. 8 months, respectively; HR = 1.43, $P = 0.001$).

Conclusion—Palliative bypass procedures were less frequently performed over time, probably due to a significant decrease in the rate of unanticipated advanced locoregional disease at the time of exploration. While palliative bypass was effective, survival in the setting of metastatic disease was extremely short.

Keywords

Pancreatic cancer; Palliation; Outcomes; Survival; Double bypass; Biliary bypass; Gastric bypass

Introduction

Pancreatic cancer is the fourth leading cause of cancer-related death in Western society, with an estimated 43,000 new cases diagnosed in the United States in 2010.¹ Resection, in conjunction with adjuvant chemoradiation therapy, is associated with a 5-year survival of 20%.^{2,3} The majority of patients, however, present with advanced disease, making curative intent surgery not a therapeutic option. In fact, up to 80% of patients with pancreatic cancer are inoperable at the time of presentation either due to locally advanced or metastatic disease. The care of patients with advanced pancreatic cancer is challenging. While systemic chemotherapy aims to prolong survival, one of the main goals in caring for these patients is palliation, to ensure adequate and effective management of symptoms. Patients with pancreatic cancer located in the head of the gland can present with debilitating symptoms including gastric outlet obstruction, biliary tract obstruction, pruritis and pain.^{4–6} Palliation is, therefore, a key component of the therapeutic management of patients with pancreatic cancer.

While chemoradiation may be a reasonable palliative approach to some patients with advanced pancreatic cancer,⁷ surgery has traditionally been an important modality to palliate many of these patients. Specifically, routine palliative bypass has been advocated for palliation of patients with adenocarcinoma in the head of the pancreas who were explored with curative intent but have inoperable disease discovered at the time of surgery. Surgical palliative procedures may include bypasses such as hepaticojejunostomy or gastrojejunostomy, as well as chemical celiac splanchnectomy. Over the last several decades, with the development and refinement of endoscopically placed biliary and enteric stents, there have been significant advances in nonoperative palliation.⁸ In addition, better preoperative cross-sectional imaging has decreased the likelihood of finding locally unresectable disease at the time of surgery. As such, the role, indication, and relative utilization of palliative surgical procedures for advanced pancreatic cancer are ill-defined. While some surgeons favor the traditional “double bypass” procedure that combines hepatico- and gastrojejunostomy at the time of laparotomy, other surgeons are more selective and perform bypass procedures based on individual patient’s preoperative laboratory values (e.g. bilirubin) or symptoms. In addition, some surgeons question the benefit of surgical palliation itself, given the limited life expectancy of patients with advanced pancreatic cancer. The objective of the current study was to examine the trends over time in the relative use of palliative bypass among patients with adenocarcinoma of the head of the pancreas in a large single institution series. In particular, we sought to identify any changes in surgical indications, type of bypass performed, as well as perioperative outcomes associated with surgical palliation.

Methods

Patients and Data Collection

Between January 1, 1996 and July 1, 2010, 1,913 patients who underwent surgery for pancreatic adenocarcinoma were identified from the Johns Hopkins Hospital pancreas database. Patients undergoing palliative surgical procedures, including biliary and enteric bypass, as well as celiac plexus block were identified through a retrospective chart review, as well as a query of hospital billing records using the appropriate Current Procedural Terminology (CPT) codes [43820, 47760, 47765, 47780, 47785, 64530, 64680]. The study was approved by the Johns Hopkins Institutional Review Board.

Data were collected regarding patient demographics, preoperative symptoms, intraoperative findings, type of surgical procedure performed, as well as perioperative and long-term outcomes. Specifically, standard demographic and clinicopathologic data were collected including sex, age, and American Society of Anesthesia (ASA) classification. Data on preoperative symptoms, laboratory values (i.e. total bilirubin, carbohydrate antigen 19–91 [CA-19-9], etc.), findings on preoperative imaging, as well as history of endoscopic/percutaneous procedures were recorded. Data were also collected on the primary tumor and the presence of any metastatic disease. Operative reports were reviewed to determine initial operative intent, type of procedure performed, as well as the indication for palliation. Postoperative complications were assessed and graded according to the Clavien-Dindo classification system.⁹ Length of hospital stay and readmissions were recorded. Postoperative mortality was defined as death in the hospital or within 30 days of operation. Long-term complications including late biliary and enteric obstruction were recorded. Survival status was determined using both hospital records as well as the Social Security Death Index.

Statistical Analysis

Mean and median values were used to describe continuous data, with discrete variables displayed as totals and frequencies. Univariate comparisons were assessed using the chi-square test for dichotomous and categorical variables and ANOVA for continuous variables. When assessing temporal trends, the data were separated into terciles (1996–2001, 2002–2007, and 2008–2010) based upon the year of operation. Trends in ordinal data were evaluated using the linear-by-linear association test and variables among the three terciles were compared using ANOVA for continuous variables and Pearson's chi-square tests were used to compare categorical variables as appropriate.

Cumulative event rates were calculated using the method of Kaplan and Meier and survival curves were compared using the log-rank test. Overall survival time was calculated from the date of the operation to the date of last follow-up or death. Univariate and multivariate modeling of survival were performed using Cox proportional hazards models. Covariates were included in the multivariate Cox model based on statistical significance in the univariate models ($P < 0.05$). Relative risks were expressed as hazard ratios (HR) with a 95% confidence interval (CI). All reported P -values are two-tailed, and for all tests, $P < 0.05$ was considered statistically significant. All statistical analyses were performed using the SPSS version 19.0 for Microsoft Windows (LEAD Technologies, Inc., Chicago, IL) statistical software package.

Results

Patient and Surgical Details

Of the 1,913 patients who underwent surgery for pancreatic adenocarcinoma in the head of the pancreas, 1,330 patients (69.5%) underwent a pancreaticoduodenectomy; 583 patients (30.5%) underwent surgical palliation and are the focus of the current study. Table 1 outlines the demographic and clinical characteristics of the 583 patients managed with surgical palliation; in general, these data were not substantially different than the summary data previously published on patients undergoing curative intent pancreaticoduodenectomy from our institution.¹⁰ Median patient age was 66 years (range, 36–98 years) and there was a slight male predominance ($n = 320$, 54.9%) in the cohort. While most patients did not have many medical comorbidities as reflected in their low 1–2 ASA classification ($n = 393$; 67.4%), one-third of patients had an ASA classification of 3–4 ($n = 190$; 32.6%). At the time of presentation, most patients had jaundice ($n = 421$, 72.2%) with a median peak bilirubin level of 3.0 mg/dl (range, 0.2–42.4 mg/dl). Gastric outlet obstruction ($n = 66$, 11.3%) and emesis ($n = 105$, 18.0%) were less common on presentation. The diagnostic imaging modality of choice was a computed tomographic (CT) scan in the overwhelming majority of patients ($n = 568$, 97.4%); fewer patients underwent magnetic resonance imaging (MRI) ($n = 31$, 5.3%). Median tumor size on cross-sectional imaging was 3.2 cm (range 1.0–15.0 cm). On imaging, 61 patients (10.5%) had disease that was preoperatively deemed to be either locoregionally unresectable ($n = 33$, 5.7%) or metastatic in nature ($n = 28$, 4.8%). Prior to surgery, two-thirds of patients ($n = 370$; 63.5%) had undergone biliary drainage either via an endoscopic ($n = 274$, 47.0%) or percutaneous ($n = 96$, 16.5%) approach. Seven patients (1.2%) had an endoscopic enteric stent placed prior to surgery. Among the 583 patients who underwent surgical palliation, few received neoadjuvant therapy ($n = 38$, 6.5%; chemoradiation therapy, $n = 25$ vs. chemotherapy only, $n = 13$).

At the time of surgery, 522 patients (89.5%) who were explored with curative intent were discovered to have unanticipated locally advanced disease ($n = 237$, 40.6%) or distant metastases ($n = 285$, 48.9%) that precluded pancreaticoduodenectomy. Of those patients with distant metastases, most patients had incidental liver metastases ($n = 218$, 37.4%)

discovered at surgery while fewer patients had peritoneal carcinomatosis or other distant metastases ($n = 67$, 11.5%). In addition to the 522 patients with unanticipated advanced disease, 61 patients (10.5%) had known advanced disease and underwent planned surgical palliation for failed nonsurgical management of obstructive symptoms.

Surgical palliation consisted of a bypass procedure in the majority of patients ($n = 553$, 94.9%) while 30 patients (5.1%) underwent exploratory laparotomy, biopsy, and chemical celiac block only. The type of palliative surgical bypass consisted of a classic double bypass (i.e., hepaticojejunostomy combined with gastrojejunostomy) in the majority of patients ($n = 357$, 64.6%); 40 patients (7.2%) underwent hepaticojejunostomy only and 156 patients (28.2%) underwent gastrojejunostomy only.

Palliative Surgery for Pancreatic Cancer: Trends Over Time

Certain patient characteristics varied over time (Table 2). Patients undergoing palliative bypass for pancreatic cancer had fewer preoperative comorbidities as reflected by improving ASA scores (ASA score 1–2: 1996–2001, 60.2% vs. 2002–2007, 77.5% vs. 2008–2010, 83.9%; $P = 0.001$). There was an increase in the number of patients who presented with jaundice (1996–2001, 69.6% vs. 2002–2007, 82.6% vs. 2008–2010, 80.6%; $P = 0.002$) with a corresponding increase in the use of preoperative biliary stents (1996–2001, 59.5% vs. 2002–2007, 71.8% vs. 2008–2010, 70.9%; $P = 0.01$). Among those patients undergoing palliative bypass, the median tumor size based on cross-sectional imaging decreased over time (1996–2001, 3.9 cm vs. 2002–2007, 3.3 vs. 2008–2010, 3.2 cm; $P = 0.006$). In addition, the proportion of patients who ultimately underwent palliative bypass, but who were initially treated with neoadjuvant therapy increased over the time periods examined (1996–2001, 3.2% vs. 2002–2007, 5.2% vs. 2008–2010, 29.0%; $P = 0.001$).

The overall utilization of surgical palliation dramatically decreased over the time periods examined ($P < 0.001$) (Fig. 1). Of note, the temporal change in the relative utilization of surgical palliation was most pronounced over the last 5 years examined. Specifically, while the total number of annual pancreaticoduodenectomies remained relatively stable over time, the case volumes of palliative bypass procedures for pancreatic adenocarcinoma substantially decreased (average annual volume: 1996–2001, 39.2% vs. 2002–2007, 26.5% vs. 2008–2010, 10.7%; $P = 0.001$). The specific palliative operative intervention utilized at the time of surgery also changed over time. Intraoperative celiac plexus block was employed with decreasing frequency (1996–2001, 94.5% vs. 2002–2007, 87.3% vs. 2008–2010, 77.4%; $P = 0.003$). While the use of hepaticojejunostomy alone (1996–2001, 10.0% vs. 2002–2007, 3.8% vs. 2008–2010, 3.2%; $P = 0.02$) gradually decreased over time, the use of the classic double bypass (1996–2001, 57.9% vs. 2002–2007, 75.1% vs. 2008–2010, 58.1%; $P = 0.001$) and gastrojejunostomy alone (1996–2001, 32.0% vs. 2002–2007, 21.1% vs. 2008–2010, 38.7%; $P = 0.01$) varied over time (Table 2). There was also a trend toward fewer patients undergoing planned palliative surgery over time (1996–2001, 12.6% vs. 2002–2007, 8.5% vs. 2008–2010, 6.5%; $P = 0.22$). In addition to the general decline in palliative surgical operations for pancreatic cancer, the indications for palliative surgery also changed. Specially, over time fewer patients were found to be unresectable due to unanticipated locally advanced disease at the time of surgery (1996–2001: 47.8% vs. 2002–2007: 49.2% 2008–2010: 17.3%; $P = 0.005$). In contrast, among patients who were explored with curative intent but ultimately underwent palliative surgery, distant metastases as the indication for palliation became more prevalent (1996–2001: 52.2% vs. 2002–2007: 50.8% vs. 2008–2010: 82.7%; $P = 0.005$) (Fig. 2).

Short- and Long-term Outcome

Following palliative bypass, the mean length of stay was 10 days (median, 8 days; range, 1–85 days) (Table 3). The mean length of stay following palliative bypass decreased over time (1996–2001: 11 days vs. 2002–2007: 9 days vs. 2008–2010: 10 days; $P = 0.007$). Morbidity occurred in 203 patients (36.7%) (major complication: $n = 78$, 14.1%) with most complications being infectious in nature ($n = 74$, 13.4%), including wound infections ($n = 24$, 4.3%), cholangitis ($n = 11$, 2.0%) and intraabdominal abscess ($n = 5$, 0.9%). Overall morbidity rates decreased over time (1996–2001: 41.4% vs. 2002–2007: 41.3% vs. 2008–2010: 29.0%; $P = 0.03$) (Table 2). There were only nine perioperative deaths during the entire study period for an overall mortality of 1.6%. Postoperatively, 99 patients (17.9%) were readmitted after a median of 30 days (range, 4–353 days). Post-palliative surgery readmissions were related to recurrent late biliary ($n = 29$, 5%) and gastric outlet obstruction ($n = 22$, 4%), with a subset of these patients representing palliative surgical “failures.” Specifically, among patients who underwent hepaticojejunostomy ($n = 397$), 9 patients (2.3%) had a recurrent biliary obstruction; among patients who underwent gastrojejunostomy ($n = 513$), 16 patients (3.1%) had recurrent gastric outlet obstruction.

Median survival following palliative bypass for pancreatic adenocarcinoma was 6 months (Fig. 3). On univariate analysis, several factors were associated with a worse outcome including ASA score 3–4, elevated preoperative CA 19–9 level ≥ 350 U/ml, tumor size ≥ 3.5 cm, and presence of unanticipated metastatic disease (Table 4). Patients who were explored with curative intent and were found unresectable due to locally advanced disease had a median survival of 8 months compared with only 5 months for patients who had unanticipated liver metastasis and 4 months for patients with metastatic peritoneal disease ($P = 0.001$) (Fig. 4).

The median survival of the 30 patients who underwent exploratory laparotomy, biopsy, and chemical celiac block only was 3 months. On multivariate analysis, after controlling for competing risk factors, CA 19–9 (HR 1.64, 95% CI 1.19–1.28; $P = 0.003$), tumor size (HR 1.47, 95% CI 1.07–2.04; $P = 0.02$), and the presence of unanticipated metastatic disease (HR 1.52, 95% CI 1.08–2.14; $P = 0.02$) remained independently associated with a worse survival.

Discussion

In caring for patients with pancreatic cancer, while the ultimate aim of surgery is cure, palliation is also an important goal. The palliation of pain, obstruction, and other symptoms from advanced malignancies has always been an intrinsic element of the surgical management of cancer. This is particularly important among patients with pancreatic adenocarcinoma, as only 10% to 20% of patients present with resectable disease while the majority of patients are simply candidates for medical palliation.^{11,12} The role of surgical palliation has evolved over the past several decades concurrent with advances in nonoperative percutaneous and endoscopic palliative approaches.⁶ The relative role of operative vs. nonoperative palliative approaches remains somewhat ill-defined with randomized data showing advantages to surgical palliative bypass vs. endoscopic stenting with less reobstruction following surgery.^{13–16} However, patients with distant metastasis are generally considered worse candidates for surgical palliation compared with patients who have locally advanced disease.^{12,17} As such, the role of surgical palliation in the current era of nonoperative palliative techniques is controversial, with little data to suggest which patients may benefit the most from surgical palliation. The current study is important because it reports, to our knowledge, the largest single institution experience with palliative surgical management of pancreatic cancer. We were able to examine trends in indication, utilization, and outcomes after palliative bypass over a 15-year period. We noted that the relative use of palliative pancreatic operations dramatically decreased over time, with a

decrease in the proportion of palliative bypass procedures in relation to potentially curative pancreaticoduodenectomy from over 40% in the 1990s to less than 10% by 2009. The relative decrease in the use of palliative bypass was probably related to our finding that over time fewer patients were found to be unresectable due to unanticipated locally advanced disease at the time of surgery (1996–2001: 47.8% vs. 2002–2007: 49.2% 2008–2010: 17.3%; $P = 0.005$).

Data from the current study show that surgical palliation can be accomplished with low morbidity and near zero mortality. Previous studies have reported morbidity and mortality of 30% and 2%, respectively.^{4,18} We report an overall morbidity of 36.7%, but importantly also found that morbidity had decreased over the time periods examined (Table 2). In addition, most complications were minor in nature with only nine patient deaths in the perioperative period for an overall mortality of 1.6%. These data compare favorably with short-term outcome data from series of patients treated with endoscopic palliative treatments. For example, in a series of 221 patients with pancreatic carcinoma who were palliated with an endoscopic approach, Huibregtse et al. reported a procedure-related mortality of 2%.¹⁹ Not only is surgical palliation of pancreatic cancer safe, it also was found to be efficacious. Specifically, the readmission rate following surgical palliation was only 17.9% with readmissions being related to recurrent late biliary ($n = 29$, 5%) or gastric outlet obstruction ($n = 22$, 4%). In fact, when we examined those patients who underwent hepaticojejunostomy ($n = 397$) or gastrojejunostomy ($n = 513$), only nine patients (2.3%) and 16 patients (3.1%), respectively, re-presented with biliary or gastric obstruction. Taken together, our data strongly suggest that palliative bypass for pancreatic adenocarcinoma is both safe and efficacious in relieving symptoms.

Data on the trends in the use of palliative surgical bypass are lacking, providing little insight into how often surgical palliation is currently still being used at major pancreatic surgical centers. In the current study, we report an overall utilization of palliative surgery of 30.5% among patients explored for pancreatic cancer in the head of the gland. In what is probably the second largest reported series ($n = 136$), Muller et al. reported an overall 22% utilization of palliative bypass procedures among 627 patients diagnosed with pancreatic adenocarcinoma between 2001 and 2005 at the University of Heidelberg.²⁰ Unlike the previous study by Muller et al., we were able to characterize the relative annual volume of palliative pancreatic surgery over time and noted a dramatic incremental decrease. In fact, only 10% of surgical procedures for pancreatic head cancers were palliative in nature by 2009 (Fig. 1). The reason for the decrease in the use of palliative surgery for inoperable pancreatic cancer is undoubtedly multifactorial. Among the reasons for the decrease may be the greater use of nonoperative palliative approaches among those patients identified preoperatively to have inoperable disease. In addition to the general decline in palliative surgical operations for pancreatic cancer, another interesting finding of the current study was that the indications for palliative surgery also changed. Specially, among patients who were explored with curative intent but ultimately underwent palliative surgery, the main indication changed over time from unanticipated locally advanced disease to distant metastasis (Fig. 2). As such, the decrease in palliative surgery performed at our institution was probably related, in part, to the dramatic decrease in the number of patients found to be unresectable due to unanticipated locally advanced disease at the time of surgery. Part of this change may reflect an increase utilization of concomitant portal vein resection by our group and others to extirpate locally advanced disease at the time of surgery.²¹ Another reason for this change probably reflects an evolution in cross-sectional imaging. Specifically, with the introduction of multidetector CT imaging that can be reconstructed in a 3-D format, the relation of the pancreatic tumor to adjacent critical vascular structures such as the superior mesenteric artery and superior mesenteric vein can be very accurately characterized.²² In contrast, small hepatic metastases (<1 cm) often still cannot be reliably identified on

preoperative CT imaging.²³ In fact, the sensitivity of CT to detect metastasis ranges from only 38% to 73%.^{22,24,25} For this reason, some surgeons advocate routine diagnostic laparoscopy to avoid unnecessary laparotomy.²⁶ Diagnostic laparoscopy appears to have the highest yield in the setting of elevated CA-19-9 levels (>130 U/ml).²⁷ Using a more selective approach based on preoperative suspicion of metastatic disease, we noted a temporal increase in the utilization of diagnostic laparoscopy at our institution (Table 2). As metastatic disease has become the main reason for inoperability, it is increasingly important to determine the benefit of palliative surgical bypass in this cohort of patients.

When trying to assess the benefit of any surgical procedure, the life expectancy of the patient obviously factors heavily into the decision making process. This is particularly true among patients with noncurative pancreatic cancer. In the current study, similar to previous reports,^{12,17,28} we noted that patients who were explored with curative intent and were found unresectable due to locally advanced disease had a longer median survival compared with patients who had unsuspected liver metastasis (8 months vs. 5 months, respectively; $P = 0.001$). In addition, even after controlling for metastatic disease site on multivariate analysis, we noted that several other factors were independently associated with a significantly worse survival. These factors included ASA score 3–4, elevated preoperative CA 19–9 level, and tumor size. Interestingly, Muller et al.²⁰ had also identified both ASA score and CA 19–9 as being independent indicators of poor survival. In the current study, the median survival of the 30 patients who underwent exploratory laparotomy, biopsy, and chemical celiac block only was 3 months. While this survival was less than the survival of patients with local advanced disease (8 months), it was comparable to the survival of patients with liver metastases (5 months) or peritoneal/other metastases (4 months). In aggregate, these data suggest that survival among patients with metastatic disease is particularly poor (<6 months) and the use of surgical bypass should be considered carefully in this subset of patients—especially if the patient also has a high ASA score and CA 19–9 level. Since these patients have a life expectancy of less than 6 months, if the patient is asymptomatic from a gastrointestinal standpoint and is already palliated with a biliary stent, surgical palliation may not be warranted.

The current study had several limitations. Although the data reflect a single institutional experience, there have been changes in the surgical staff over time that may have introduced a “provider” effect on the relative use of palliative surgery over time. While our data established a clear decrease over time in the relative utilization and indication for palliative surgical procedures for pancreatic cancer, we were not able to fully define the reasons for these trends. Attempts at correlating the temporal shifts with changes in cross-sectional imaging at our institution proved not to be feasible due to the staggered nature of how new equipment was introduced and the variability related to which equipment was used on any given day. In addition, we did not correlate the relative use of surgical procedures with nonoperative palliative approaches for patients with pancreatic cancer at our institution over the same time period. Because data were derived from a surgical database, accurate acquisition of nonoperative palliative procedures was not feasible. The use of nonoperative palliative procedures for pancreatic cancer was, however, not the focus of the current study. Rather, we sought to examine the role of surgical palliation for pancreatic cancer with regards to its safety, efficacy, and relative use over time.

In conclusion, we demonstrate that surgery remains an effective palliative method of pancreatic cancer. While a “general” clinical decision making algorithm would not be appropriate—as each clinical situation needs to be individualized—data from our study should help to inform the practice of surgeons operating on this complex group of patients. Specifically, we have shown that overall morbidity after palliative bypass has decreased over time and perioperative mortality is minimal. Palliative bypass procedures were less

frequently performed over time, probably due to a significant decrease in the rate of unanticipated advanced locoregional disease at time of exploration. In contrast, intraoperative discovery of distant metastasis at the time of surgery was found to be the most common indication for surgical bypass in the current era. Survival in the setting of metastatic disease following palliative bypass was, however, extremely short. Although we identified several factors (ASA score 3–4, elevated preoperative CA 19–9 level, tumor size 3.5 cm) that may aid in selection, future molecular markers such as DPC4²⁹ will hopefully better identify that subset of patients with a nonmetastatic phenotype who may benefit the most from surgical palliation.

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Fig. 1.
Annual case volumes of pancreaticoduodenectomy vs. palliative bypass for pancreatic adenocarcinoma between January 1996 and July 2010 at the Johns Hopkins Hospital

Fig. 2.
Trends in the relative indications for palliative bypass surgery over the time periods examined

Fig. 3.
Overall survival of all patients undergoing palliative bypass for pancreatic adenocarcinoma
($n = 553$)

Fig. 4. Survival after palliative bypass for patients explored with curative intent ($n = 494$), stratified by indication for palliative bypass. Median survival: locally advanced disease, 8 months vs. liver metastases, 5 months vs. peritoneal/other metastases, 4 months ($P = 0.001$)

Table 1

Demographics, preoperative presentation and operative details of patients undergoing surgical palliation ($n = 583$)

Variable	N (%) / median (range)
Demographics	
Median age (years)	66 (36–98)
Gender	
Female	263 (45.1%)
Male	320 (54.9%)
ASA	
1–2	393 (67.4%)
3–4	190 (32.6%)
Preoperative presentation	
Symptoms	
Vomiting	105 (18.0%)
Jaundice	421 (72.2%)
Gastric outlet obstruction	66 (11.3%)
Enteric stent	7 (1.2%)
Biliary stent	370 (63.5%)
Endoscopic	274 (47.0%)
Percutaneous	96 (16.5%)
Laboratory values	
Peak bilirubin (mg/dl)	3.0 (0.2–42.4)
Last preoperative bilirubin (mg/dl)	1.4 (0.2–35.4)
CA 19–9 (U/ml)	351.3 (1.0–50119.0)
CEA (ng/ml)	5.4 (0.6–176.8)
Imaging	
CT	568 (97.4%)
MRI	31 (5.3%)
PET	5 (0.9%)
Radiographic tumor size (cm)	3.2 (1.0–15.0)
Preoperative chemotherapy	38 (6.5%)
Preoperative radiation	25 (4.3%)
Operative details	
Reason for palliation	
Locally advanced disease	237 (40.6%)
Presence of liver metastases	218 (37.4%)
Presence of peritoneal/other metastases	67 (11.5%)
Known inoperable with obstructive symptoms	61 (10.5%)
Extent of palliative surgery	
Bypass	553 (94.9%)

Variable	<i>N</i> (%) / median (range)
Exploration and biopsy	30 (5.1%)
Celiac block	523 (89.7%)
Type of bypass (<i>n</i> = 553)	
Hepaticojejunostomy only	40 (7.2%)
Gastrojejunostomy only	156 (28.2%)
Double bypass	357 (64.6%)
Type of gastrojejunostomy (<i>n</i> = 513)	
Antecolic	29 (5.7%)
Retrocolic	484 (94.3%)

Table 2

Trends in indication and outcomes after palliative bypass between 1996 and 2010 (N, %)

Variable	1996–2001 (n = 309)	2002–2007 (n = 213)	2008–2010 (n = 31)	p-value
Age (years), mean ± SD	65±10.9	66±11.1	67±11.3	0.37
Male gender	169 (54.7%)	110 (51.6%)	21 (67.7%)	0.24
ASA score				0.001
1–2	186 (60.2%)	165 (77.5%)	26 (83.9%)	
3–4	123 (39.8%)	48 (22.5%)	5 (16.1%)	
Jaundice	215 (69.6%)	176 (82.6%)	25 (80.6%)	0.002
Preoperative gastric outlet obstruction	42 (13.6%)	19 (8.9%)	4 (12.9%)	0.26
Preoperative biliary stent	184 (60%)	153 (71.8%)	22 (70.9%)	0.01
Preoperative enteric stent	3 (1.0%)	3 (1.4%)	0 (0%)	0.75
Radiographic tumor size (cm), mean ± SD	3.9±1.9	3.3±1.3	3.2±0.9	0.006
Neoadjuvant therapy	10 (3.2%)	11 (5.2%)	9 (29.0%)	0.001
Planned operative intent				
Curative	270 (87.4%)	195 (91.5%)	29 (93.5%)	0.22
Palliative	39 (12.6%)	18 (8.5%)	2 (6.5%)	
Reason for unresectability ^a				0.005
Locally advanced disease	129 (47.8%)	96 (49.2%)	5 (17.2%)	
Unanticipated metastases	141 (52.2%)	99 (50.8%)	24 (82.7%)	
Diagnostic laparoscopy	7 (2.2%)	4 (1.9%)	3 (9.6%)	0.03
Type of bypass				0.001
Hepaticojejunostomy only	31 (10.0%)	8 (3.8%)	1 (3.2%)	
Gastrojejunostomy only	99 (32.0%)	45 (21.1%)	12 (38.7%)	
Double bypass	179 (57.9%)	160 (75.1%)	18 (58.1%)	
Type of gastrojejunostomy				0.28
Antecolic	12 (4.3%)	14 (6.8%)	3 (10.0%)	
Retrocolic	266 (95.7%)	191 (93.2%)	27 (90.0%)	
Celiac block	292 (94.5%)	186 (87.3%)	24 (77.4%)	0.003
Length of hospitalization (days), mean ± SD	11±8.0	9±7.1	10±12.0	0.007
Any complication	128 (41.4%)	88 (41.3%)	9 (29.0%)	0.03
Major complication	51 (16.5%)	26 (12.2%)	1 (3.2%)	0.08
Mortality	5 (1.6%)	4 (1.9%)	0 (0%)	0.74
Readmissions	59 (19.1%)	35 (16.4%)	5 (16.1%)	0.71
Late enteric obstruction	13 (4.2%)	9 (4.2%)	0 (0%)	0.51
Late biliary obstruction	16 (5.2%)	13 (6.1%)	0 (0%)	0.36

P-values of <0.05 are highlighted in bold

^aPatients explored with curative intent

Table 3

Perioperative and long-term outcomes after palliative bypass for pancreatic ductal adenocarcinoma in the head of the pancreas ($n = 553$)

Variable	N (%)
In hospital morbidity and mortality	
Complications	203 (36.7%)
Minor complications (I–II)	125 (22.6%)
Major complications (III–V)	78 (14.1%)
Mortality (V)	9 (1.6%)
Specific complications	
Liver abscess	5 (0.9%)
Cholangitis	11 (2.0%)
Pleural effusion	14 (2.5%)
Biliary fistula	8 (1.4%)
Sepsis	11 (2.0%)
Hemorrhage	6 (1.1%)
Wound infection	24 (4.3%)
Intraabdominal abscess	11 (2.0%)
Other	107 (19.3%)
Median length of stay (days)	8 (1–85)
Late morbidity and mortality	
Readmission	99 (17.9%)
Median time to readmission (days)	30 (4–853)
Reason for readmission	
Liver abscess	3 (0.5%)
Cholangitis	11 (2.0%)
Pleural effusion	2 (0.4%)
Biliary fistula	2 (0.4%)
Sepsis	2 (0.4%)
Hemorrhage	2 (0.4%)
Wound infection	7 (17.5%)
Intraabdominal abscess	6 (1.1%)
PV thrombosis	2 (0.4%)
Biliary obstruction	29 (5.2%)
Enteric obstruction	9 (1.6%)
Gastric outlet obstruction	13 (2.3%)
Other	28 (5.1%)
Postoperative stenting	
Biliary stent	29 (5.2%)
Enteric stent	11 (1.9%)
Overall late obstruction	
Biliary	25 (4.5%)

Variable	N (%)
Enteric	18 (3.2%)
Both	4 (0.7%)
Median time to obstruction (months)	1 (0–28)

Table 4

Univariate and multivariate analyses of survival after palliative bypass for pancreatic ductal adenocarcinoma in the head of the pancreas

Variable	Univariate analysis		Multivariate analysis	
	Crude hazard ratio [95% CI]	p-Value	Adjusted hazard ratio [95% CI]	p-Value
Age 65 years	1.22 [1.02–1.46]	0.03	1.17 [0.85–1.62]	0.34
Male gender	0.96 [0.80–1.14]	0.64		
Ethnicity				
White	Reference group			
Black	1.22 [0.89–1.66]	0.22		
Other	0.63 [0.35–1.15]	0.13		
ASA score 3–4	1.22 [1.02–1.47]	0.04	1.08 [0.76–1.52]	0.69
Peak bilirubin 3 mg/dl	1.03 [0.85–1.25]	0.74		
Last preop bilirubin 2 mg/dl	1.18 [0.98–1.18]	0.08		
Preop CA 19-9 350 U/ml	1.58 [1.25–1.99]	0.001	1.64 [1.19–2.28]	0.003
Preop CEA 5 ng/ml	1.00 [0.99–1.01]	0.47		
Tumor size 3.5 cm	1.30 [1.01–1.66]	0.04	1.47 [1.07–2.04]	0.02
Preoperative biliary stent	1.38 [0.57–3.33]	0.46		
Preoperative enteric stent	0.97 [0.85–1.11]	0.65		
Preoperative chemo/XRT	0.96 [0.64–1.44]	0.85		
Diagnostic laparoscopy	0.94 [0.53–1.68]	0.84		
Type of bypass				
Hepaticojejunostomy only	Reference group			
Gastrojejunostomy only	1.28 [0.89–1.83]	0.19		
Double bypass	0.94 [0.67–1.33]	0.73		
Laparoscopically completed bypass	2.07 [0.66–6.45]	0.21		
Reason for bypass				
Locally advanced disease	Reference group		Reference group	
Unanticipated metastatic disease	1.43 [1.18–1.72]	0.001	1.52 [1.08–2.14]	0.02
Palliation for obstructive symptoms (known unresectable)	1.62 [1.20–2.20]	0.002	0.93 [0.54–1.61]	0.54
Celiac block	0.95 [0.69–1.31]	0.76		

P-values of <0.05 are highlighted in bold