Dual stenting for both CBD and duodenum versus surgical bypass in the management of advanced head of pancreas cancer

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Background
As 70–90% of patients with carcinomas of the head of the pancreas and ampullary region have jaundice at presentation and going to have gastric outlet obstruction, palliation that ensures biliary and gastric drainage represents a large proportion of the hepatobiliary surgeon's workload. As barely 20% of patients with pancreatic cancer are suitable for curative resection, good palliative therapy is extremely important.

Aim of the work
To compare the effectiveness of palliation between patients with advanced head of pancreas cancer who underwent surgical bypass and those who underwent dual stenting and morbidity and mortality rates of both procedures.

Patients and methods
This prospective study was conducted between April 2015 and April 2017. Only 38 patients were eligible for this study. Follow-up was at 1, 3, and 6 months after each procedure. Evaluation of patients regarding efficacy and feasibility, morbidity, mortality, hospital stay, ICU admission, readmission rate, and survival was done.

Results
We identified 38 patients, of whom 19 underwent endoscopic stenting and 19 underwent a surgical bypass either by choledechojejunostomy or cholecystojejunostomy-en-Y with gastrojejunostomy. There were no significant differences in complications or mortality rates; however, all results were in favor of dual stenting, owing to short procedure time, hospital stay, ICU admission, and survival rates being better than surgical bypass, although without significance.

Conclusion
Dual stenting was found to be more feasible and efficient in palliation of advanced head of pancreas cancer with short procedure time and short hospital stay and less morbidity and mortality and ICU admission with higher cost in comparison with surgical bypass. Surgical bypass is mandatory in patient with gastric outlet obstruction or failed Endoscopic Retrograde Cholangiopancreatography (ERCP) trial due to huge mass obstructing the duodenum.

Keywords:
advanced head of pancreas cancer, dual stenting, palliative management of head of pancreas cancer, surgical bypass

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Introduction

Locally advanced pancreatic cancer is defined as a tumor that involves vascular structures such as the superior mesenteric artery, celiac axis, or superior mesenteric–portal vein confluence. The median survival time for patients with unresectable, locally advanced, nonmetastatic disease is ~6–11 months, and those with metastatic disease show a median survival time of 2–6 months. In addition to a short survival time, patients with unresectable locally advanced pancreatic cancer have a poor quality of life. Pain, jaundice, and malnutrition are the most common complications. Any method to ameliorate these complications or to increase survival time would be a positive step [1].

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

Surgical palliation has been advocated as the treatment of choice for younger patients (<60 years of age),

patients with expected survival more than 6 months, and patients with impending duodenal obstruction. Published prospective, randomized studies comparing the effectiveness of biliary endoprosthesis versus surgical bypass have suggested the superiority of endoscopic stenting in palliation. Biliary endoprostheses have been used with shorter hospitalization and similar morbidity to that of surgical bypass. The major drawback to endobiliary stenting has been the occurrence of recurrent jaundice owing to late stent occlusion [3].

Only 5–20% of pancreatic head carcinomas are resectable at the time of presentation. For patients with obvious nonresectable disease, endoscopic techniques have been developed as alternatives to traditional surgical management. Biliary stenting and duodenal self-expandable endoprostheses have been promoted as the treatment of choice because of their low morbidity. Assessing unresectability still remains difficult in some cases in spite of improvement in imaging procedures, and purely nonsurgical palliation may, in these cases, overlook resectable tumors [4].

Patients and methods

A prospective single-blinded randomized controlled clinical trial was conducted. We follow the ethical research values according to our IRB commitee and after we explain the procedures we got a written concent from the patients.

Patients

During the period between April 2015 and April 2017, 45 patients of advanced unresectable head of pancreas cancer with obstructive jaundice (according to National Comprehensive Cancer Network clinical staging of pancreatic cancer) had been allocated into either of two groups: group A (n=19) patients underwent dual stenting for both Common Bile Duct (CBD) and duodenum, and group B (n=19) patients underwent surgical exploration and palliative surgical bypass in Zagazig University Hospitals. Two patients who did not meet the criteria of the study (cancer head of pancreas without jaundice or being resectable) were excluded, and five patients were lost to follow-up, so only 38 patients were available for this study. Follow-up was done at 1, 3, and 6 months after each method. Follow up of the patients was done by laboratory examination and imaging of biliary tract after stent placement. Informed written consent regarding the procedure was taken from every patient after explanation of both techniques in details.

This study was conducted to assess both procedures, dual stenting for both CBD and duodenum or palliative surgical bypass in the management of advanced cancer head pancreas in zagazig university hospitals.

Preoperative data evaluation

Age and sex distribution

The age of the patients and baseline demographic data to be evaluated were analyzed and compared between both groups.

Clinical history

Clinical picture at time of the presentation showed that all cases presented with progressive jaundice, as it is one of inclusion criteria, along with epigastric pain, discomfort, cachexia, and vomiting, to be assessed and compared. Comorbidities that may affect the outcome of the procedure in the form of diabetes mellitus, hypertension, HCV +ve marker cases, history of other cancers, cardiac troubles, renal impairment, and chest complications were recorded. Situs inversus totalis is not considered as a comorbidity but is challenging in ERCP procedure, as in right-sided ERCP (mirror image technique).

Radiological reports

Abdominal ultrasound, computed tomography scan, MRI, or Magnetic Reasonsnce Cholangiopancreatography (MRCP) finding of pancreatic malignancy were done. All patients were subjected to at least two radiological modalities, which was sufficient in diagnosis of head of pancreas cancer to be confirmed by laboratory test by either tumor markers or histopathology.

Laboratory reports

Total and direct bilirubin level, gamma-glutamyltransferase, alkaline phosphatase, aspartate amino transferase (AST), white cell count, hemoglobin level, albumin level, International Normalised Ratio (INR), Carcinoembrionic Antigen (CEA), and Carbohydrate Antigen 19-9 (CA 19-9) were recorded.

Pathological reports

Pancreatic biopsy through Fine Needle Aspiration Cytology (FNAC) or Tru-cut biopsy, was done whenever possible under guidance of imaging (not for all cases but for doubtful ones with normal CA 19-9). The patients were diagnosed by the use of abdominal computed tomography-guided biopsy or raised level of CA 19-9.

All the patients were for palliation; the inoperability was determined by the presence of metastatic

pancreatic cancer by the documentation of liver metastasis on imaging studies, or local vascular invasion. Suitability for general anesthesia was determined, and detection of gastric outlet obstruction was taken in consideration by clinical evidence or barium study or upper endoscopy.

Patients were randomly assigned to endoscopic group or surgical group; the selection of patients for palliative over endoscopic palliation was based on patient preference and judged fitness for operative intervention.

Methods

Preoperative management

After being fully assessed, and fulfilling the anesthetic requirement, cardiac consultation for each patient above 40 years old or who had a history of cardiac trouble; preparation of the patients with fully hydration and vitamin K supplementation; correction of any bleeding tendency with fresh frozen plasma, dicynone and kapron; correction of anemia by packed RBCs or full blood transfusion; and correction of hypoalbuminemia by plasma or humane albumin transfusion were done. Fully written consent was taken from each patient for the procedure that would be done. The patients had to fast for at least 8 h preoperatively, take medications for hypertension, and control diabetes by insulin short-acting type for both oral hypoglycemic or insulin dependent according to the reading of serum blood sugar. Preoperative antibiotic was taken 1 g cefotax 1 h preoperatively.

For patients of endoscopy (19 patients), we prepared the endoscope and checked the equipment: sphincterotomes, catheters, guide wires, and the availability of suitable sized self-expandable covered metallic stent. The procedure was done under general anesthesia with oral endotracheal intubation, with the patient in left lateral position (except for one case with situs inversus totalis, where we used right lateral position with mirror image technique), using a therapeutic side viewing duodenoscope PENTAX EPK-I version with 4.2-mm operating channel. For intraoperative medication, we gave buscopan to help relax the smooth muscles of gastrointestinal tract, thus decreasing motility, or we can give Glucagon. Atropine intravenously or antifoam solution (i.e. simethicone) was used to improve visualization.

Description: the Niti-S biliary covered stent consists of the implantable metallic stent and introducer system; the stent is made of nitinol wire. It is a flexible, fine mesh tubular prosthesis, and it has eight radiopaque markers: three on each end and two in the center.

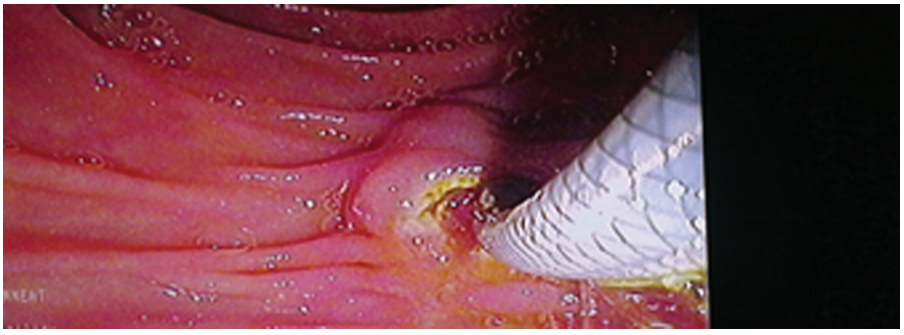
The procedure was follows: ERCP should be performed before placement of the Niti-S stent to characterize the biliary tract morphology and extent of the malignant disease (180 cm introducer usable length). Examination of the stricture was done endoscopically and fluoroscopically.

Stent deployment procedure

Under endoscopic guidance, the introducer system is positioned to the center of the target stricture exactly.

Once the introducer system is in the correct position for deployment, the proximal valve of the Y-connector is unlocked by turning the valve more than twice in an anticlockwise direction. To begin stent deployment, immobilization of the hub is done in one hand and grasping the Y-connector with the other hand. The Y-connector is gently glided back along the pusher toward the hub. When the radiography marker reaches proper place exceeding center of target stricture, the Y-connector is pulled back continually until the stent is fully deployed (Fig. 1).

Figure 1

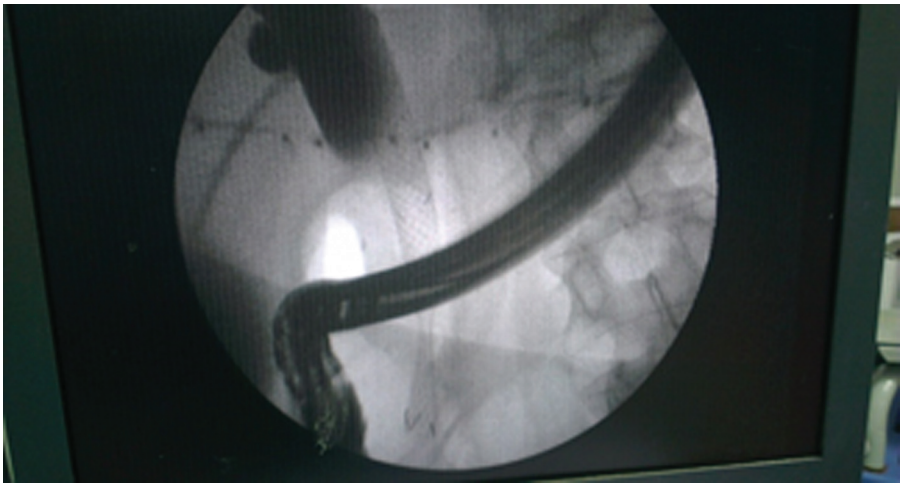


Stent deployment.

Figure 2

Endoscopic view showing the stent inside CBD.

Figure 3



C-arm fluoroscopic view after CBD stent deployment in its place.

After stent deployment

The stent is fluoroscopically and endoscopically examined to confirm expansion (Figs 2 and 3).

The introducer system, guide wire, and endoscope are carefully removed from the patient. If excessive resistance is felt during removal, wait 3–5 min to allow further stent expansion.

Balloon dilatation inside the stent can be performed on demand.

Regarding duodenal stenting

Description

The Niti-S and ComVi Pyloric/Duodenal Stent consists of the implantable metallic stent and introducer system.

The stent is made of nitinol wire. It is a flexible, fine mesh tubular prosthesis that has radiopaque markers on at each end and at the center (Fig. 4).

Principle of operation and the procedure

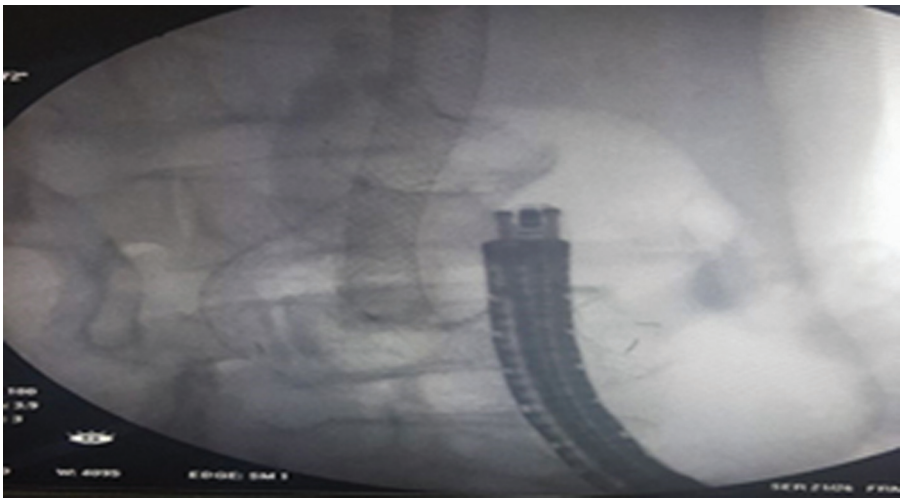
The same as CBD stent

For patients undergoing surgical bypass (19 patients), we prepared for surgical bypass. We had the blood ready if transfusion is needed and availability of an ICU place if needed. Patients of surgical group were subjected to bilo-enteric bypass: cholecystojejunostomy or choledochojejunostomy. In roux-en-Y-choledocho-jejunostomy, the first loop of jejunum was brought up to the fundus of the gall bladder, an incision was made in each one and side-to-side anastomosis was constructed.

Gastrojejunostomy was done routinely in our study to solve the problem of impending gastric outlet obstruction.

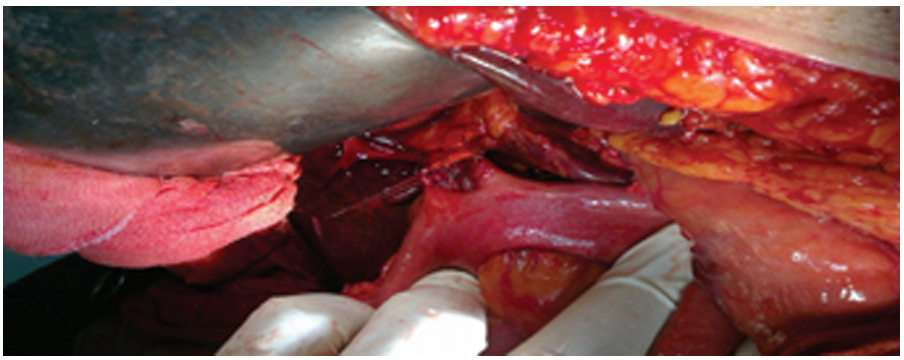
The procedure is done under general anesthesia with endotracheal intubation, with the patient in supine position. The incision was either midline incision or

Figure 4



C-arm fluoroscopic view showing duodenal stent after deployment.

Figure 5



Choledechojejunostomy.

Figure 6

Enteroenterostomy.

bilateral subcostal incision, re-evaluating the patient intraoperatively for liver metastasis, Lymph Node (LN) assessment, vascular invasion (encasement of Superior Mesentric Artery (SMA), Superior Mesentric Vein (SMV), and/or portal vein), and/or peritoneal nodules. Decision for bypass was taken for either choledechojejunostomy (Fig. 5) or cholecystojejunostomy and either Roux-en-Y or using simple loop with enteroenterostomy (Fig. 6) with gastrojejunostomy (Fig. 7). Absorbable 3-0 vicryl suture was used to establish the anastomosis. Intraoperative complications, difficulties, operative time, and need for blood transfusion were reported.

Figure 7

Gastrojejunostomy.

Data collection and analysis

The initial hospital stay duration was defined as the time spent in the hospital after the patient's surgical or endoscopic procedure. Data on short-term and long-term morbidity in terms of postoperative complications and hospital readmissions were collected. Perioperative complications were defined as occurring within 30 days after dual stent insertion or surgery. Thirty-day mortality for each group of treatment was calculated. The follow-up data were collected within 1 month, within 3 months, and within 6 months after each procedure (follow-up evaluation included clinical assessment, assessment of serum bilirubin and liver enzymes levels, and imaging of biliary tract immediately before and after stent placement or surgical intervention). Follow-up was done by arrangement of regular meeting for each patient by telephoning the patients or their relatives nearby. Cooperative behavior was variable, but most of them cooperated.

Readmission if happened due to complications of surgery or stenting excluding complications of chemotherapy.

Data were collected and compared between the two groups regarding the success and effectiveness of the procedure, mean procedure time, hospital stay, ICU stay, morbidity, and mortality.

The lifetime costs of endoscopic versus surgical palliation for malignant obstructive jaundice are difficult to assess. In our hospital as in other university hospitals in Egypt, the staff's fees and hospital admissions are sponsored by the government, so the collected costs in our study are limited to the accessories, drugs, and other requirements (such as suture materials and stents) that were used in the operating or endoscopic room. The cost extends to involve the postoperative care until hospital discharge.

Statistical analysis

All data were collected, tabulated, and statistically analyzed using SPSS 18.0 for Windows (SPSS Inc., Chicago, Illinois, USA) and MedCalc 13 for Windows (MedCalc Software bvba, Acacialaan, I stand, Belgium). Continuous data are expressed as the mean±SD and median (range), and the categorical data are expressed as a number (percentage). Continuous variables were checked for normality by using Shapiro–Wilk test. Independent Student's t test was used to compare two groups of normally distributed data. Mann–Whitney U test was used to compare two groups of non-normally distributed data. Friedman's test was used to compare between repeated measurements of non-normally distributed variable. Percentages of categorical variables were compared using the χ^2 test. All tests were two sided. P value less than 0.05 was considered statistically significant (S), P value less than 0.01 was considered highly statistically significant (HS), and P value more than or equal to 0.05 was considered not statistically significant (NS).

Results

Demographic data

In our study, 38 eligible patients were identified to have advanced head of pancreas cancer. Of these, 19 underwent endoscopic dual stenting and 19 underwent palliative surgical bypass. Follow-up within 1, 3, and 6 months was done. Baseline demographic data are shown in Table 1.

Table 1 Comparison between studied groups regarding the demographic data

Demographic data	Endoscopic group (*N*=19) [*n* (%)]	Bypass group (*N*=19) [*n* (%)]	Test	*P* value (significance)
Age (years)			*Z*	
Mean±SD	54.89±11.67	52.53±12.70	−1.127	0.260 (NS)
Median (range)	55 (30–77)	48 (32–75)		
Sex			χ^2	
Male	16 (84.2)	11 (57.9)	3.199	0.074 (NS)
Female	3 (15.9)	8 (42.1)		

Z, Mann–Whitney *U* test. χ^2, χ^2 test. *P* value less than 0.05 is significant.

Table 2 Comparison between studied groups regarding the perioperative data

Perioperative data	Endoscopic group (*N*=19) [*n* (%)]	Bypass group (*N*=19) [*n* (%)]	Test	*P* value (significance)
Duration of procedure (min)			MW	
Mean±SD	69.47±23.56	164.21±20.90	−5.331	<0.001 (HS)
Median (range)	60 (45–120)	180 (120–180)		
Intraoperative difficulties			χ^2	
No	8 (42.1)	9 (47.3)	0.000	1.000 (NS)
Yes	11 (57.9)	10 (52.7)		
ICU admission			χ^2	
No	13 (68.4)	8 (42.1)	2.661	0.103 (NS)
Yes	6 (31.6)	11 (57.9)		
Hospital stay (days)			MW	
Mean±SD	1.26±0.45	7.94±2.54	−5.486	<0.001 (HS)
Median (Range)	1 (1–2)	7 (6–14)		

MW, Mann–Whitney. χ^2, χ^2 test. HS, highly significant.

In endoscopic group, the mean age was 54.89±11.67 years in comparison with the bypass group, with mean age of 52.53±12.70 years, with no significant difference, and according to sex distribution, in the endoscopic group, males (84.2%) were more than females (15.9%), but there was no significant difference in comparison in bypass group between male (57.9%) and females (42.1%).

Clinical history and comorbidity

All cases in both groups have jaundice (as it is an inclusion criteria). Pain was found in 63.2% of endoscopic group and 78.9% in bypass group, with no significant difference. Vomiting was found in 21.1% of endoscopic group and in 63.2% in bypass group, with highly significant difference. Weight loss was found in 26.3% in endoscopic group and 31.6% in bypass group, with no significant difference (Table 2). Surgical bypass was better choice for those patient presented with vomiting as it represents gastric outlet obstruction, which necessitates bypass.

Regarding the comorbidity in endoscopic group, there were five (26.3%) cases with positive HCV markers, five (26.3%) cases with diabetes mellitus, three (15.8%) cases with hypertension, and two (10.5%) cases with other cancer (cancer breast), whereas in the bypass group, there were 10 (52.6%) cases of diabetes mellitus and two (10.5%) cases with hypertension, with no significant difference in comparison with the bypass group. However, for the HCV +ve markers, there was a significant difference between the studied groups, where 26.3% of endoscopic group had +ve markers versus 0% of bypass group (P=0.016).

Two (10.5%) cases of surgical bypass that had diabetes mellitus had wound infection but respond to conservative treatment: wound care and antibiotics. This may be attributed to the effect of diabetes mellitus on wound healing.

Combination of diabetes mellitus and hypertension increases the risk of atherosclerosis with subsequent increase of the risk of pulmonary embolism and death (additionally by prolonged procedure time). This occurred in three patients. The HCV +ve markers cases were significantly more common in endoscopic group, but with no effect on the result, except for the choice of anesthesia; we used isoflurane instead of fluothane, as the latter is hepatotoxic.

Preoperative laboratory findings

Preoperative total serum bilirubin in endoscopic group was significantly higher than in bypass group (mean, 18.45 vs. 10.99 mg/dl; P<0.001). Although the preoperative bilirubin level was higher in endoscopic group, the result in lowering bilirubin

was better, making it more efficient. Albumin level was significantly higher in bypass group than in endoscopic group (mean, 3.27 vs. 2.73 g/dl; P=0.049). Albumin level is important in wound healing and anastomosis. INR was significantly higher in endoscopic group than bypass group but without bleeding tendency (mean, 1.25 vs. 1.04; P<0.001). White blood cells were significantly higher in endoscopic group than bypass group (mean, 9.71 vs. $6.87\times10^3/mm^3$; P=0.007), in cases of active cholangitis or inflammation laboratory finding would be influenced (as elevated white blood cellsso we exclude these cases. There was no significant difference between both groups regarding liver enzymes, alkaline phosphatase, gamma glutamyl transferase, platelet count, and hemoglobin level.

Tumor markers

In our study, we found significant difference in the level of AFP as it was higher in endoscopic group than bypass group. This may be attributed to the more advancement of the disease (mean, 56.11 vs. 36.06; P=0.003). However, there was no significant difference between both groups regarding CEA and CA 19-9. CA 19-9 was high in most cases, except in three cases that needed to be proven by Tru-cut computed tomography-guided biopsy, which revealed adenocarcinoma.

Preoperative imaging findings

All cases in both groups had CBD dilatation and Intrahepatic Biliray Radical Dilatation (IHBRD). Not all criteria of advanced head of pancreas cancer were found in all cases, but each case had some of these criteria, but with no significant difference between both groups, except for SMA invasion, which was significantly higher in bypass group than endoscopic group (26.3 vs. 0%; P=0.016).

Perioperative data

Duration of procedure was significantly higher in bypass group in comparison with endoscopic group (mean, 164.21 vs. 69.47 min; P<0.001). Hospital stay was significantly higher in bypass group in comparison with endoscopic group (mean, 7.94 vs. 1.26 days; P<0.001) owing to wound care and waiting for starting oral feeding. However, there was no significant difference between both groups regarding ICU admission or intraoperative difficulties (Table 2).

Intraoperative difficulties

In endoscopic group, we faced some difficulties in the form of difficult cannulation of the papillae owing to distortion by the pancreatic head mass effect and improper size of the stent used; we faced a case of situs inversus totalis, which is a challenging case, as it need a special technique, mirror image technique; intraoperative bleeding obscuring the field; and anesthetic problem with hypotension. We failed in one case owing to huge mass obstructing the duodenum and failed cannulation.

In the bypass group, difficult manipulation was encountered in three (15.8%) cases, so we did cholecystojejunostomy. Intraoperative bleeding was seen as another problem we faced in five (26.3%) cases but was controlled.

Follow-up data between both groups

There was no significant difference between both groups regarding follow-up data of serum bilirubin, liver enzymes, and albumin level at 1-, 3-, and 6-month follow-up. However, according to morbidities we encountered in surgical bypass, there was a case of hematemesis, which was controlled by medical treatment and compensation, and also one case showing biliary fistula, which responded to conservative measures.

Follow-up data in endoscopic group

There was a highly significant improvement of total serum bilirubin level: decrease in bilirubin level (P<0.001) and direct bilirubin level (P<0.001). There was significant improvement of liver enzymes: alanine transaminase (ALT) (P=0.014) and AST (P=0.004).

Follow-up data in bypass group

There was high significant improvement of total serum bilirubin level: decrease in bilirubin level (P<0.001)

Table 3 Comparison between studied groups regarding the outcome and mortality

Outcome and mortality	Endoscopic group (N=19) [n (%)]	Bypass group (N=19) [n (%)]	Test	P value (significance)
Outcome			χ^2	
Failed	2 (10.5)	4 (21.1)	0.792	0.374 (NS)
Success	17 (89.5)	15 (78.9)		
1-month mortality			χ^2	
Survive	17 (89.5)	13 (68.4)	2.533	0.111 (NS)
Died	2 (10.5)	6 (31.6)		

χ^2, χ^2 test.

and direct bilirubin level ($P<0.001$). There was significant improvement of liver enzymes: ALT ($P<0.001$), AST ($P<0.001$).

Outcome and mortality

Both procedure was successful more in endoscopic group but with no significance (89.5 vs. 78.9%; $P=0.374$), 1 month mortality was higher in bypass group than endoscopic group but also with no significance (31.6 vs. 10.5%; $P=0.111$) (Table 3).

Death in surgical bypass occurred in six cases: two cases owing to severe attack of hematemesis, two cases died from fecal fistula and hypovolemic shock, one case owing to pulmonary embolism, and one case owing to bad general and chest condition postoperatively.

We found that with long procedure time in difficult cases of endoscopy, the prognosis was bad, and death occurred in two cases due to pulmonary embolism and shock.

Discussion

Unfortunately, only ~10–20% of patients are 'resectable' at the time of diagnosis. Even among those patients who undergo resection for pancreatic cancer and have tumor-free R0 margins, the 5-year survival rate after resection is only 10–25% with the median survival of 15–19 months. A locally advanced stage is identified in 25–35% of patients and is associated with a median survival of 6–10 months. The vast majority of these patients develop metastatic disease within the first year of therapy. At presentation, 45–55% of patients are in metastatic or 'advanced' stage (Fig. 8). The prognosis of patients with advanced disease remains extremely poor, with a median survival of 6 months [5].

As barely 20% of patients with pancreatic cancer are suitable for curative resection, good palliative therapy is extremely important.

Pancreatic cancer incidence and death rates increase with advancing age, with a steep increase after the age of 50 years. Around nine in 10 patients with pancreatic cancer are at least 55 years old, and the average age at the time of diagnosis is 71 years. Approximately half of all patients with pancreatic cancer had developed cancer after the age of 71 years, and pancreatic cancer rarely develops before the age of 45 years [6].

Pancreatic cancer is ~30% more common in men than in women. During 2005–2009, the age-adjusted incidence rate (per 100 000 persons) of pancreatic cancer was 13.6 for men and 10.5 for women, with age-adjusted death rate of 12.5 for men and 9.5 for women. This could partly be owing to increased use of tobacco in men. The lifetime

Figure 8

Endoscopic view of huge pancreatic mass protruding through duodenum.

risk of developing pancreatic cancer is ~1.5% for both men and women [7].

In the USA, pancreatic cancer contributed to 32 300 estimated deaths in 2006 of an estimated 33 730 new pancreatic cancer cases. Overall, 80% of pancreatic cancers manifest clinically in patients aged 60–80 years; only ~10% of patients are below the age of 50 years. Pancreatic cancer is found more commonly in men. Predisposing risk factors include cigarette smoking, chronic pancreatitis, exposure to radiation and chemicals, diabetes mellitus, and hereditary cancer syndromes [8].

Clinical history and comorbidity

All cases in both groups have jaundice (as it is an inclusion criteria). Pain was found in 63.2% of endoscopic group and 78.9% in bypass group, with no significant difference. Vomiting was found in 21.1% of endoscopic group and in 63.2% in bypass group, with highly significant difference, and weight loss was found in 26.3% in endoscopic group and 31.6% in bypass group, with no significance. Surgical bypass was better choice for those patient presented with vomiting as it represent gastric outlet obstruction which necessitates bypass.

In our study, as we did short-term prospective trial. We did gastrojejunostomy as the patients had large-sized tumor and suspected to have gastric outlet obstruction. In endoscopic group, we did dual stenting in advance to avoid gastric outlet obstruction. If the tumor is large in size causing gastric outlet obstruction it is Obligatory to do surgical bypass with prophylactic gastrojejunostomy.

In Maire and Sauvanetb study, duodenal stenosis occurred in 25% of patients. Several studies have shown that duodenal stenting is a safe and effective method to palliate gastric or duodenal obstruction. Technical and clinical success rates reported in the literature are 75–100 and 77–100%, respectively.

Surgical biliary bypass and gastrojejunostomy are the other classic options for palliative treatment in patients with unresectable pancreatic cancer. Endoscopic biliary stenting is equivalent to surgical bypass in terms of efficacy and overall survival but is associated with a lower complication rate and shorter hospital stay [9].

A single metallic biliary and/or duodenal stent was safe and sufficient in most patients with unresectable pancreatic cancer and biliary/duodenal stenosis and long survival. The combination of biliary and duodenal stenting was possible and effective when necessary. Results suggest that an 'exclusive endoscopic approach' for the treatment of biliary and duodenal stenoses is feasible, safe, and effective in short and long term in these patients. This should afford patients greater palliative comfort, permitting rapid use of antitumoral agents [10].

Perioperative data (duration of procedure, ICU admission, and hospital stay)

Duration of procedure was significantly higher in bypass group in comparison with endoscopic group (mean, 164.21 vs. 69.47 min; $P<0.001$). Hospital stay was significantly higher in bypass group in comparison with endoscopic group (mean, 7.94 vs. 1.26 days; $P<0.001$) owing to wound care and waiting for starting oral feeding. However, there was no significant difference between both groups regarding ICU admission or intraoperative difficulties.

In our study, ICU admission was more encountered in surgical bypass group than endoscopic group but with no significant difference. ICU admissions in endoscopic group was for observation and monitoring of cardiac and chest condition. We noticed that with prolonged and difficult endoscopic stenting, the prognosis was bad even if successful stenting was done at the end. On the contrary, ICU admissions in surgical bypass group were for bad general condition of these patients, intraoperative bleeding, attack of hematemesis encountered (two cases), and long procedure time.

There was a lower incidence of the need for ICU admission after endoscopic biliary stenting in a randomized trial of endoscopic stenting versus surgical bypass in malignant bile duct obstruction [11].

The endoscopic palliation was associated with a significant short ICU stay. The patients with bile leak and electrolyte imbalance or patients with cholangitis and septicemia were admitted to ICU. In addition, patients with abnormal blood gases or hepatorenal failure were admitted to ICU. Consequently, we had a long ICU stay in surgical group, which increased the cost of the operation. However, this high cost of long ICU stay was still less than the cost of the stent [12].

A prospective randomized study published in 2004 comparing the two techniques showed shorter operative time and shorter hospitalization with more rapid resumption of alimentation for endoscopic

treatment, but there was no difference in morbidity or mortality [13].

More recent retrospective studies have shown similar success rate for the two techniques, but with fewer complications, more rapid resumption of alimentation, and shorter hospitalization for endoscopic treatment [14].

Intraoperative difficulties and complications

We found in our study that complications as intraoperative bleeding, difficult manipulation, long procedure time, long exposure to anesthesia, long postoperative ICU admission, and long hospital stay were encountered in surgical bypass group more than endoscopic group, but with no statistical significance. Two (10.5%) cases of surgical bypass that had diabetes mellitus had wound infection but respond to conservative treatment: wound care and antibiotics. This may be attributed to the effect of diabetes mellitus on wound healing.

In the endoscopic group, we faced some difficulties in the form of difficult cannulation of the papillae owing to distortion by the pancreatic head mass effect; conversion to surgical bypass was done in one case owing to improper size of the stent used, so we needed to repeat the procedure later on; a case of situs inversus totalis, which was a challenging case, as it need a special technique, mirror image technique; intraoperative bleeding obscuring the field; and anesthetic problems with hypotension.

In patients with malignant distal biliary tree obstruction owing to advanced carcinoma, endoscopic stenting with metallic stents is associated with fewer complications and shorter total hospital stay, but with a higher risk of recurrent biliary obstruction than surgery [15].

The available evidence confirms that endoscopic metal stents appear to be the intervention of choice for maintaining luminal patency with minimal risks in malignant distal biliary obstruction. Their potential disadvantages, such as permanency and effect on surgical resection are not an issue in most cases. However their cost-effectiveness may be limited in patients with expected survival less than 4 months [16].

The preference of the managing team between surgical or nonsurgical derivation(s) should guide investigations. If a surgical derivation is favored, preoperative diagnosis of respectability is useful. Indeed, if during the operation the tumor is resectable, it is resected, and if not, a double derivation is performed and possibly celiac alcoholization with antalgic intent. If the operating team believes that bile duct and/or duodenal derivations can be performed with endoscopic or radiologic guidance, resectability should be evaluated to reserve this treatment for tumors that are clearly not resectable [17].

Fewer studies have been published comparing surgical bypass with metal prostheses, but the results consistently report improved quality of life at 30 days and decreased costs for endoscopic treatment [18]. Older studies have reported high morbidity and mortality (nearly 20%) for gastroenteric anastomosis.

Endoscopic palliation is associated with shorter hospitalization than the surgical palliation. There was a prolonged hospitalization (mean, 3±1 days) in the endoscopy group, which is explained by the fact that all the patients were admitted to the hospital for laboratory, and radiological evaluation before randomization to either endoscopy or surgery. An additional factor is the repeated attempts of endoscopic stenting (needed in three patients) [12].

Outcome and mortality: the feasibility and efficacy

We found better result with metallic stent than surgical bypass, and this makes endoscopic more feasible and efficient than surgical bypass. In our study, there was a highly significant improvement of total serum bilirubin level: decrease in bilirubin level and direct bilirubin level. There was significant improvement of liver enzymes, ALT and AST, in both groups, but with no significance difference between them.

Both procedures were successful, being more in endoscopic group, but with no significance (89.5 vs. 78.9%; P=0.374). One-month mortality was higher in bypass group than endoscopic group, but also with no significance.

The results of controlled trials of palliation of obstructive jaundice by stenting or surgical bypass do not favor one method for use in all cases. The advantages of operation include unequivocal assessment of resectability, better long-term bile-duct patency, a lower risk of cholangitis, and the ability to perform a gastric bypass to provide prophylaxis against future duodenal obstruction [19].

Inal and colleagues focused on the long-term outcomes of biliary and duodenal stents in a homogeneous and monocentric series of consecutive patients with

unresectable cancer of the head of the pancreas. Biliary stenosis occurred in 81% of patients and endoscopic biliary stent deployment was successful on an intent-to-treat basis in 88% of patients. However, with improvement in survival, as observed in the present study, the choice of palliative treatment options should carefully be taken into account [10].

Surgical palliation of obstructive jaundice can be achieved by endoscopic, percutaneous, and surgical means. Although both surgery and endoscopy are equally effective options, endoscopic drainage with the insertion of a stent into the bile duct has been shown to significantly reduce the length of hospitalization and is associated with lower procedure morbidity and mortality [20].

Survival rates in our study at 1 month revealed that mortality was higher in bypass group than endoscopic group, but also with no significance (31.6 vs. 10.5%; P=0.111). Mortality was due to attacks of hematemesis in two cases in surgical bypass group, but in endoscopic group, mortality was due to hypotension, bradycardia, and bad general condition. Combination of diabetes mellitus and hypertension increases the risk of atherosclerosis with subsequent increase of the risk of pulmonary embolism and death (super added by prolonged procedure time); this occurred in three patients.

Pancreatic cancer is one of the most lethal cancers, characterized by invasive growth and rapid dissemination, despite a relatively well-differentiated histomorphology [21].

A randomized controlled trial comparing endoscopic therapy versus surgical bypass in 50 patients with malignant biliary obstruction stated that survival rates were higher in the endoscopy group (22±3 vs. 16±2 weeks) (Kassis M, *et al.* [26]).

In our study, tumor marker CA 19-9 was high in most cases, except in three cases, which needed to be proven by Tru-cut biopsy, which revealed adenocarcinoma. CA19-9 was more in bypass group than endoscopic group, but with no significance (mean, 481.87 vs. 732.37; P=0.737), but these value had no effect on the results.

CA19.9 levels more than 1000 seem to be associated with significantly lower survival than levels less than 1000. Hence, despite our attempts to match patients using radiological imaging, it is possible that patients who underwent endoscopic stenting had a higher occult tumor burden than those who underwent bypass surgery, which would doubtless have negatively affected their long-term survival [22].

Correlation of different parameters with survival in univariate analysis was analyzed. Age, sex, weight loss, American Society of Anesthesiologist score, pain, jaundice, presence of diabetes mellitus, operation time, type of surgery, surgical morbidity, medical morbidity, presence of liver metastasis, presence of peritoneal metastasis, leukocytes, hemoglobin, albumin, C-reactive protein, CEA, and CA 19-9 were tested to evaluate whether they had an association with survival. The univariate analysis showed that an American Society of Anesthesiologist score of III, daily pain, operation time 240 min, presence of metastasis, elevated leukocytes (1.5 g/l), low albumin (30 g/l), elevated C-reactive protein (50 mg/l), CEA (10 U/l), and CA 19-9 (100 U/ml) were associated with significantly poorer survival (Müller MW *et al.* [27]).

Cost

The cost cannot be accurately evaluated as the salary of the doctors and medical stuff are on the government, and the main cost difference between both groups depends mainly on the cost of endoscopic (2500 EGP) and the metallic stent cost (8000 EGP) although less hospital stay and less ICU Admissions in stenting still the cost of the stent is the main obstacle face us.

Endoscopic stenting is the accepted initial treatment for the palliation of jaundiced patients, with a lower complication rate than surgery, although there is a risk of stent occlusion and the need for repeat procedures. Exceptions include patients undergoing laparotomy. The study by Hasssanen A, *et al.* [13] does not support the evidence of low cost of endoscopic palliation. The reduction in mean length of hospital and ICU stay was not translated to low cost of the procedure. This is attributed to the high cost of the metallic stent itself. Endoscopically treated patients demonstrated better quality of life compared with those who underwent surgical drainage procedure.

In palliative stenting, it is potentially not cost effective to use self-expanding metal stents in patients with shorter life expectancy given their expense relative to plastic stents. The presence or absence of distant metastases can help guide what type of stent should be used, but predictive mortality models may offer a way to further stratify patients in an accurate and cost-effective fashion. Double-layer stents may provide a less expensive option for some patients, while still maintaining superiority to regular plastic stents [23].

Endoprosthesis should be placed if there was evidence of hepatic, peritoneal, or pulmonary metastases or if the patient had significant comorbidity precluding surgery. 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. Despite this, the overall pattern would appear to indicate that, 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 [24, 25].

Conclusion

Endoscopic dual stenting was found to be more feasible and efficient in palliation of advanced head of pancreas cancer with short procedure time and short hospital stay and less morbidity and mortality and ICU admission but more cost in comparison with surgical bypass. We do not have to expose these patient to painful experience such as abdominal exploration except if we intend to do gastric bypass as well. In patient who experience gastric outlet obstruction or failed endoscopic trial (as huge mass obstructing the duodenum) or in younger patients, surgical bypass in these situations will be more reasonable.

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Conflicts of interest

There are no conflicts of interest.

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