

ORIGINAL ARTICLE

ENDOSCOPIC METALLIC STENTING VERSUS SURGICAL BYPASS IN CASES OF INOPERABLE PANCREATIC HEAD CARCINOMA

By

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Aim: To compare endoscopic metallic stenting with surgical bypass in palliation of patients with inoperable pancreatic head carcinoma.

Methods: This prospective study included consecutive patients with obstructive jaundice due to inoperable pancreatic head carcinoma that were admitted to The Department of General Surgery, Minia University Hospital between July 2007 and September 2008.

Results: Endoscopic stenting was successful in 14 of 15 patients (93.3%) of the endoscopy group. The mean bilirubin level decreased from 25.1 ± 11.3 mg before the procedure to 5 ± 2.1 mg/dL at the 4 weeks follow-up, and this difference was statistically significant (Paired "t" test, $P < 0.0001$). Surgical bypass was successful in 14 of 15 patients (93.3). The mean bilirubin level decreased from 26.1 ± 10.1 mg before the procedure to 4 ± 2.7 mg/dL at the 4 weeks follow-up, and this difference was statistically significant (Paired "t" test, $P = 0.0001$).

The mean procedural time was 45 ± 15 minutes in endoscopy group, and 90 ± 39 minutes in surgical group ("t" test, $P = 0.0003$).

The mean hospital stay was 3 ± 1 days in endoscopy group versus 7 ± 3 days in surgical group ("t" test, $P = 0.0001$).

The mean ICU stay was 2.1 ± 1.4 in endoscopy group versus 5.4 ± 2.9 days in surgical group ("t" test, $P = 0.0005$). The mean cost of endoscopic stenting was 4000 ± 300 LE in the endoscopy group versus 2600 ± 200 LE in the surgical group ("t" test, $P = 0.0001$).

The mean of morbidity rate was 3.2 ± 1.4 in endoscopy group versus 7.4 ± 3.2 in the surgical group ("t" test, $P = 0.0001$).

Conclusion: Both endoscopic metallic stenting and surgical therapies are equally effective in term of palliation of obstructive jaundice. Endoscopic drainage is characterized by low procedure time, short hospital stay and low morbidity. However, it is associated with high cost.

Keywords: Endotherapy, surgical palliation, malignant obstructive jaundice.

INTRODUCTION

Among cancers of the gastrointestinal tract, carcinoma of the head of the pancreas is the third most common malignancy and the fifth leading cause of cancer-related mortality.⁽¹⁾ It is difficult to diagnose in its early stages. About 60%-80% of patients with periampullary carcinoma are inoperable either due to distant metastasis or local vascular invasion.⁽²⁾

Despite advances in understanding the pathology and biology of the disease, as well as improved diagnostic imaging and staging studies, overall 5-year survival rate

is less than 5%. Even with the most effective standard therapies, the collective median survival time of all patients is 4-6 months, regardless the method of therapy used.⁽³⁾ This is due to biliary obstruction which aggravates the patient's already poor clinical condition by causing cholangitis, pruritus, nutritional deficiencies through malabsorption, weight loss and progressive hepatic failure.⁽⁴⁾ Because curative outcomes or long-term remissions are not likely to occur in a disease so biologically aggressive, most patients are in need for palliative measures; which are usually considered as more a hope than standard for most patients.⁽⁵⁾ Before the mid-1980s, palliation was provided primarily

through surgical bypass.⁽⁶⁾ As early as 1980, attempts were made to place stents in the biliary tree, first through the percutaneous transhepatic route and subsequently through endoscopic retrograde cholangiopancreatography (ERCP).⁽⁷⁻⁸⁾ The results of some studies showed that endoscopic drainage offers effective short-term relief of jaundice and low morbidity and mortality rates as compared to surgical drainage⁸⁻⁹. However, the results of other studies are in favor of surgical palliation.⁽²⁾

The purpose of this prospective study is to compare endoscopic stenting with surgical bypass in palliation of patients with inoperable pancreatic head carcinoma and to evaluate the primary outcome; the success and effectiveness, secondary outcome as; mean procedure time, hospital stay, intensive care unit (ICU) stay, cost, morbidity and mortality.

PATIENTS AND METHODS

This prospective study included consecutive patients with malignant obstructive jaundice due to inoperable pancreatic head carcinoma that were admitted to The Department of General Surgery, Minia University Hospital in period between July 2007 and September 2008. Written informed consent was given from all included patients.

Patients were subjected to complete clinical, laboratory, and radiological investigations. The patients were diagnosed by the use of abdominal CT guided biopsy, raised levels of CA 19-9. All the included 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 the possibility of gastric outlet obstruction in all the patients was excluded by endoscopy. Patients were randomly assigned to endoscopic group or surgical group. The random assignments were made using a list of sealed envelopes. Patients of endoscopy (15 patients) were subjected to ERCP under general anesthesia and nasal endotracheal intubation, with the patient lying in the left lateral position using a therapeutic side viewing duodenoscope (Olympus, model TJF-140) with an accessory channel diameter of at least 4.2 mm. A 9-Fr introducer system was used -under fluoroscopic guidance- upon which the stent was held, compressed and elongated by a cylindrical rolling membrane (the outer sheath). The delivery catheter had three markers: one at a first-proximal portion (the proximal marker), the second at the actual stent length position (the stent length marker), and the third at the distal position of the loaded stent (the distal marker). Stent deployment was accomplished by withdrawing the outer sheath while fixing the inner catheter, figure 1. The metallic stents which were used had an intrinsic expanding force "self expandable" uncovered endoprosthesis (Boston Scientific). Abdominal radiograph was taken at the end of the procedure to

detect the start of its expansion. Patients of surgical group (15 patients) were subjected to surgical bilio-enteric bypass; cholecystojejunostomy or choledochojejunostomy. Roux-en Y choledochojejunostomy was constructed. . Absorbable 3-0 Vicryl sutures were used to establish the anastomoses. In cholecystojejunostomy, the 1st loop of jejunum was brought up to the fundus of the gall bladder, and an incision was made in each one and side-to-side anastomosis was constructed.

Gastrojejunostomy was not routine in our study. It was indicated only if there was a preoperative diagnosis of gastric outlet obstruction (endoscopically and or radiologically) or if the surgeon was suspicious of the obstruction during the operation. The data were collected and compared between the two groups as regard the; the success and effectiveness of the procedure, mean procedure time, hospital stay, intensive care unit (ICU) stay, cost, morbidity and mortality.

Total lifetime costs of endoscopic versus surgical palliation for malignant obstructive jaundice are difficult to assess.⁽¹⁰⁾ In our hospital, as in other university hospitals in Egypt, the surgeon's fees and hospital admissions are sponsored from the government. So the collected costs in our study were limited to the accessories, drugs and other requirements (as suture material, stents) which were used in the operating or endoscopy room. The costs extended to involve the postoperative care until hospital discharge. The actual value of the hospital costs were obtained from the billing administrative office in the hospital. The diagnosis of acute cholangitis was based on a combination of upper abdominal pain, jaundice, chills and fever (temperature >37.5).⁽¹¹⁾ The diagnosis of acute pancreatitis was based on a combination of typical abdominal pain and rise of serum amylase levels three times or greater than the normal value.⁽¹²⁾ The diagnosis of acute cholecystitis was based on clinical (abdominal pain and fever), laboratory (leukocytosis), and ultrasonic examination (distended gallbladder or pericholecystic fluid).⁽¹³⁾ The diagnosis of stent occlusion was based on presentation with jaundice, cholangitis, or cholestasis which necessitates an intervention.⁽¹⁴⁾

Follow-up evaluation included clinical assessment, assessment of serum bilirubin and liver enzyme levels and imaging of the biliary tract immediately before and after stent placement or surgical intervention and at 1, 3, 6 months after each.

Statistical analysis: Data entry and analysis were all done with IBM compatible computer soft wear called SPSS for windows version 13 and microstate and instate programs. Quantitative data were presented by mean and standard deviation (mean + SD), while qualitative data were presented by frequency distribution. For comparison between quantitative data, two sample "t" test was used for two independent samples and paired "t" test for paired observations. For comparison between

qualitative data, test of proportions (z test) was used. Kaplan-Meier survival curves were compared between groups. P value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Thirty patients were included in the study, 20 males (66.6%) and 10 females (33.4%). The demographic data of patients undergoing endoscopic metallic stenting (endoscopic group) or surgical bypass (surgical group) were shown in Table 1. Endoscopic group included 15 patients, 10 males (67%) and 5 females (33%), with mean age of 60.2±11.9 years. Surgical group included 15 patients, 11 males (73%) and 4 females (27%), with mean age of 60.7±8.9 years.

Clinically, all patients of both groups were seen to present with malignant obstructive jaundice.

Pancreatic adenocarcinoma was diagnosed by CT guided biopsy in 9 patients (5 patients were in endoscopic group, and 4 patients were in surgical group). Elevated CA 19-9 and abdominal CT were diagnostic in 21 patients (10 patients were in endoscopic group, 11 patients were in surgical group).

Inoperability was due to local vascular invasion in 17 patients (56.6%) and liver metastases in 13 patients (43.4%). In endoscopic group, it was due to local vascular invasion in 9 patients (60%) and liver metastases in 6 patients (40%) while in surgical group it was due to local vascular invasion in 8 patients (53%) and liver metastases in 7 patients (47%).

Endoscopic stenting and deployment was successful in 14 of 15 patients (93.3%) of the endoscopy group, Table 2. This was confirmed by serial measurements of serum bilirubin, Table 3, and serial plain radiographic imaging of the abdomen. The mean bilirubin level decreased from 25.1±11.3mg before the procedure to 5±2.1mg/dL at the 4 weeks follow-up, and this difference was statistically significant (Paired "t" test, $P < 0.0001$). Failed procedure was encountered in one patient. It was due to very tight stricture with failure to be negotiated by the guide wire and was treated by percutaneous route.

Bilio-enteric bypass was done in 15 patients of surgical group. Cholecystojejunostomy was done in 10 patients (7 males and 3 females). Choledochojejunostomy was done in the remaining 5 patients (4 males and 1 female). Gastrojejunostomy was done in 4 patients.

The mean bilirubin level decreased from 26.1±10.1 mg before the procedure to 4±2.7 mg/dL at 4 weeks follow-up, and this difference was statistically significant (Paired "t" test, $P = 0.0001$). There is no significant difference as regard the success of relieve of jaundice

between the 2 groups, (test of proportion "z" test, $P = 0.5$), Table 3.

The mean procedural time was 45±15 minutes in endoscopic group, and 90±39 minutes in surgical group ("t" test, $P = 0.0003$).

The mean hospital stay was 3 ± 1 days in endoscopic group versus 7 ± 3 days in surgical group ("t" test, $P = 0.0001$).

The mean ICU stay was 2.1±1.4 in endoscopic group versus 5.4±2.9 days in surgical group ("t" test, $P = 0.0005$).

The mean cost of endoscopic stenting was 4000 ± 300 LE in the endoscopic group versus 2600 ± 200 LE in the surgical group ("t" test, $P = 0.0001$).

The mean of morbidity rate was 3.2±1.4 in endoscopic group versus 7.4±3.2 in the surgical group ("t" test, $P = 0.0001$). In the endoscopic group, pancreatitis was diagnosed in 2 patients, cholecystitis in 2 patients and stent occlusion in 2 patients that needed endoscopic re-intervention. The cause of occlusion was tumor ingrowth. The mean stent patency was 190±56 days. In the surgical group, wound infection was in 6 patients; abdominal wound dehiscence was in 1 patient, cholangitis in 3 patients, bile leak in 3 patients and biliary peritonitis in 1 patient with fatal outcome due to septicemia. The incidence of these complications was higher in subgroup of cholecystojejunostomy than choledochojejunostomy. All patients with cholangitis, bile leak, biliary peritonitis were seen in this subgroup.

There is no related mortality in the endoscopy group, while there were three operative related mortality in the surgical group. It was due to myocardial infarction in one patient and he died in the ICU two hours postoperatively. The second patient died three days postoperatively due to hepatorenal failure. The third patient died seven days postoperatively from sepsis and multiple organ failure.

The mean duration of the follow up was 6±3.1 months. Reintervention due to gastric outlet obstruction was required in 4 patients; 2 in the endoscopy group and 2 in the surgical group. None of patients who had undergone Roux-en-Y choledochojejunostomy and simultaneously gastrojejunostomy required intervention later during the follow up.

During the follow up, the survival rates were similar in patients of both groups. The mean survival time was 120±31 days in the endoscopy group versus 112±26 days in the surgical group, ("t" test, $P = 0.5$). Kaplan-Meier survival curve (Fig 2) showed similar survival in patients managed by surgery or endoscopic stenting.

Table 1. Characteristics of patients.

Variable	Endoscopy group	Surgical group	P value
Mean age \pm SD (years)	60.2 \pm 11.9	60.7 \pm 8.9	0.9
Female/male	5/10(50%)	4/11(36%)	0.3
Clinical presentation:			
Jaundice	15(100%)	15(100%)	0.1
Pain	11(73%)	12(80%)	0.3
Metastatic disease	6(40%)	7(46%)	0.3
Local vascular invasion	9(60%)	8(53%)	0.3 5

Table 2. Outcome measure.

Outcome	Endoscopy group	Surgical group	P value
Success rate (%)	93	93	0.5
Mean survival time \pm SD (days)	120 \pm 31	112 \pm 26	0.5
Mean hospital stay \pm SD (days)	3 \pm 1	7 \pm 3	0.0001
Mean ICU stay \pm SD (days)	2.1 \pm 1.4	5.4 \pm 2.9	0.0005
Mean procedure time \pm SD (min)	45 \pm 15	90 \pm 39	0.0003
Mean morbidity rate \pm SD	3.2 \pm 1.4	7.4 \pm 3.2	0.0001
Mortality related procedure (%)	0(0%)	3 (20%)	0.03
Mean cost \pm SD (LE)	4000 \pm 300	2600 \pm 200	0.0001

Table 3. Serial follow up of total bilirubin of the two groups.

Total Bil (mg %)	Endoscopic group	Surgical group	P value
Before procedure	25 \pm 11.3	26 \pm 10.1	0.8
After 1 week	19 \pm 6.7	19 \pm 5.2	0.9
After 2 weeks	12 \pm 4.3	11.1 \pm 3.6	0.5
After 4 weeks	5 \pm 2.1	4 \pm 2.7	0.3

Bil: bilirubin.



Fig 1. Metallic stent in the CBD (endoscopic view).

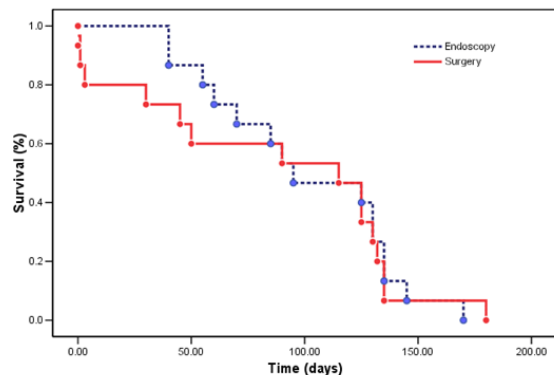


Fig 2. Kaplan-Meier survival curve in patients managed by surgery or endoscopic stenting.

DISCUSSION

Surgical palliation of obstructive jaundice can be achieved by endoscopic, percutaneous, and surgical means.⁽¹⁵⁾ 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.⁽¹⁶⁾ In the present study, we have a similar result and both methods are equally effective in relieving of the jaundice.

Most endoscopic drainage procedures with the insertion of a metal stent are done as a same day procedure.⁽¹⁷⁾ So, Endoscopic palliation is associated with shorter hospitalization than the surgical palliation. In our study, there was a prolonged hospitalization (mean of 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 3 patients).

Han et al⁽¹⁸⁾ showed 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. In our study, 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.

The surgical palliation of malignant obstructive jaundice due to advanced pancreatic cancer has a high morbidity and mortality rates.⁽¹⁹⁾ In the present study, we have similar results when compared with endoscopic palliation.

A randomized controlled trial comparing endoscopic therapy vs. surgical bypass in 50 patients with malignant biliary obstruction stated that survival rates were higher in the endoscopy group (22 ± 3 weeks vs. 16 ± 2 weeks) 17. In the present study, the survival rate is similar in both groups and this may be attributed to diagnosis of the disease in an advanced stage.

Martin et.al.⁽²⁰⁾ performed a study about cost comparison of surgery and endoscopy in this issue. Results revealed that the cost of endoscopic drainage procedure is significantly less than the surgical procedure with shorter hospitalization and lower total cost of care. Our results do not support this 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.⁽³⁾ Metal stent insertion is associated with a prolonged stent patency compared with plastic stents, and consequently better patient compliance and improved patient survival.⁽²¹⁾ The incidence of recurrent jaundice after biliary stenting has decreased with the use of expandable metallic stents compared with plastic stents, but still tumor ingrowths can cause late stent occlusion.⁽²²⁾ This was seen in two patients in our study.

Still there is controversy as regard the method of surgical biliary bypass. It can be done by cholecystojejunostomy, choledochoduodenostomy or hepaticojejunostomy. Operative morbidity and mortality are similar for both cholecystojejunostomy and hepaticojejunostomy, but the success rate in alleviating jaundice is higher for choledochojejunostomy or hepaticojejunostomy than for cholecystojejunostomy (97% vs. 87%).⁽²³⁾ Also, the incidence of recurrent jaundice and cholangitis is 8% for cholecystojejunostomy and 0% for hepaticojejunostomy because of late obstruction of the cystic duct with tumor.⁽²⁴⁻²⁵⁾ In the present study, 2 patients (13.3%) with cholecystojejunostomy developed recurrent jaundice as compared to none after hepaticojejunostomy. Another controversy over surgical bypass is whether gastric bypass should be done routinely or not. If gastrojejunostomy is not done at the time of biliary bypass, around 13%-21% of patients will require gastrojejunostomy and additional 20% of patients will die with some symptoms of duodenal obstruction.⁽²⁵⁾ A prospective randomized controlled trial also confirmed that prophylactic gastrojejunostomy should be done; otherwise 19% of patients require intervention for duodenal obstruction, when they are unfit for surgical procedure.²⁶ Many surgeons do not prefer prophylactic gastrojejunostomy 27 because of fear of higher morbidity but this was not found to be true in a prospective randomized controlled trial.⁽²⁴⁾ In the present study, prophylactic gastrojejunostomy was not done because of the fear of higher morbidity and mortality. However, combined biliary and gastric bypass is a practical option.⁽²⁶⁾

In our study, the incidence of gastric outlet obstruction is low and this is explained by short life span in those patients.

Overall, our data reflect that endoscopic metallic stent palliation of malignant obstructive jaundice due to advanced cancer pancreas is better than open surgical bypass regarding the shorter hospital stay, short procedure time, low morbidity and low mortality. Its main concern is the high cost.

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