

Palliative treatment for malignant jaundice: endoscopic vs surgical approach

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Abstract. – In this retrospective, comparative study a total of 107 patients, presenting with malignant inoperable strictures of common bile duct, due to a pancreatico-biliary malignancy, underwent palliative treatments. In a group, consisting of 82 patients (76.64%), endoscopic stenting procedures were performed; polyethylene stents or self-expanding metal stents were applied in 37 and 45 patients, respectively. The prerequisites for a successful endoscopic stenting were a) accuracy of diagnosis and b) exclusion of patients presenting with tumors potentially treatable by a curative resection. In the other group, consisting of 25 patients (23.36%), biliary-enteric bypass procedures were performed.

Endoscopic treatment was successful in 97.5% of the cases (80/82); complication rate was 7.3% (6 patients on 82), and mortality rate was 3.6% (3 patients on 82). Median hospital stay was 13.4 and 7.3 days in patients treated with plastic stents and metallic stents, respectively.

Bypass surgery was successful in 99% of the cases (24/25); complication rate was 24% (6 patients on 25), and mortality rate was 16% (4 patients on 25). Median hospital stay was 26 days.

For the patients in whom a curative resection could not be performed, both the above mentioned methods resulted in a high rate of immediate technical and therapeutic success. However, the surgical approach showed a significantly higher rate in procedure-related mortality and morbidity; in addition, the hospital stay lasted longer in surgically treated patients. The patients who are definitely unsuitable for curative resection are better managed by positioning a stent. The use of metal stents should be preferred in those less serious patients who may supposedly survive longer.

Key Words:

Endoscopic stenting, Endoscopic metal endoprosthesis, Bilioenteric bypass, Pancreaticobiliary malignancy.

Introduction

Biliary obstruction is a frequent presenting feature of pancreaticobiliary malignancy. Unfortunately, when a diagnosis of pancreaticobiliary malignancy is made the patient is usually in a terminal stage^{1,2}. However, a palliative treatment of biliary obstruction is advisable to mitigate the effects of jaundice, independently of whether a surgical resection for attempting a cure is feasible or not. Endoscopic stent drainage has been proposed as an alternative to biliary-enteric bypass surgery to palliate malignant biliary obstruction. In addition, alternative approaches to biliary stent placement have prompted a particular interest towards a comparative evaluation aimed at assessing optimal stent material and design, as well as stent placement strategies.

Pancreatic cancer incidence tripled from 1920 to 1970; during such a time period the age-adjusted mortality rate increased from 2.9/100,000 to 9/100,000³.

The incidence rates of pancreatic cancer for white men decreased after 1974; as a consequence the overall incidence showed levelled values, although rates of pancreatic cancer for women and black men have continued to rise⁴.

In the United States, the age-adjusted incidence is currently 10.1/100,000 person-years for men and 7.5/100,000 person-years for women. The risk of developing pancreatic cancer increases with age; most cases occur in patients aged > 50 yrs, with special reference to those aged 60-85 yrs. Cancer of pancreas is more common in men, with reported relative risk from 1.3 to 1.7; it shows similar rates of incidence in western industrialized countries (approximately 9/100,000 to 10/100,000)⁶. A similar pattern has been observed for colorectal cancer⁷.

Several risk factors for pancreatic cancer have been identified. Smoking is the most corroborated risk factor^{8,9}. The risk of smokers developing pancreatic cancer is from 1.6 to 3.1 times higher than that of non-smokers⁷. Alcohol consumption has been identified as a risk factor for pancreatic cancer in several studies. A Norwegian study suggested that the risk for heavy alcohol users was 5.4 times higher than that for the general population¹⁰.

The effect of coffee consumption on pancreatic cancer is interesting. McMahon et al. reported a strong dose-response relationship between coffee consumption and pancreatic cancer¹¹.

Certain fruits and vegetables have been shown to induce a protective effect against pancreatic cancer. High citrus fruit¹², vegetable¹³, fiber¹⁴ and vitamin¹⁵ diets have been linked to decreased risk for developing pancreatic cancer. A possible mechanism for the anticancer action of citrus fruits is the inhibition of the K-ras oncoprotein by limonene¹⁶.

Pancreatic cancer distribution is as follows: 95% of the cases arise from the exocrine pancreas, with about 70% of them located in the head of the pancreas; most of the remaining 5% of the cases are islet cell tumors¹⁷.

Common presenting signs and symptoms of pancreatic cancer include jaundice, weight loss and abdominal pain. Jaundice develops in 47% of patients with pancreatic cancer. Such a sign occurs less frequently in patients with tumors of the pancreatic body and tail. When pain is present, it is usually consequent to liver metastases or to lymph node involvement at the level of the porta hepatis leading to biliary obstruction. Weight loss occurs in about 60% of the cases. It has been described as rapid and progressive, and is due to both anorexia and pancreatic exocrine insufficiency.

Pain is the third common symptom associated with pancreatic cancer. Pain is present at some time in 80% of patients affected by such a malignancy. Pain from cancer of pancreas is the result of tumor infiltration of the neural plexus surrounding both the proximal superior mesenteric artery (SMA) and the celiac axis and terminating in the celiac ganglia. Palpable gallbladder (Courvoisier's sign), glucose intolerance, migratory thrombophlebitis, weakness, fatigue, GI tract hemorrhage and splenomegaly are less frequent signs and symptoms of pancreatic cancer¹⁸.

Biliary obstruction results in a variety of biochemical and physiologic disturbances, such as elevated serum bilirubin, altered liver function tests, as well as impaired hepatic and renal functions with associated coagulation problems.

In view of the fact that most patients with pancreatic cancer are diagnosed at an advanced and inoperable stage of the disease, the intent of treatment is palliation. Among these patients, some will survive only a few weeks, many of them will die within six months, but some others may survive in a fairly good health condition for longer time. Until recently, two kinds of therapeutic options were offered to such patients: (a) surgical bypass and (b) endoprosthesis. The percutaneous insertion of an endoprosthesis has been shown to provoke an excess morbidity¹⁹ due to a 12 French gauge access through the liver, and it should not be considered as the primary option for common bile duct obstruction, although it can be recommended for the palliative treatment of porta hepatis strictures.

Materials and Methods

The present investigation consisted of a retrospective study in which two methods of treatment for inoperable malignant strictures of common bile duct were compared: (a) endoscopic stenting (plastic or metallic) and (b) surgical bypass. All the patients enrolled in the study presented with jaundice due to a distal malignant common bile duct obstruction, and all were considered as inoperable. The resectability was determined by TNM classification (Table I)²⁰.

The following seven criteria were taken into consideration for inclusion in the study: age, sex, amount of weight loss, tumor size and histological type, presence or absence of distant metastases, and total serum bilirubin level on the day prior to treatment. Such criteria had been previously reported or studied in the literature as potentially related to survival of patients with pancreatobiliary cancer; such data are usually available in the common set of clinical, biological and morphological investigations.

Table I. Evaluating resectability of pancreatic cancer by TNM classification.

Stage	TNM	Clinical and Radiological Criteria
I Resectable	T1, N0, M0	Tumor limited to pancreas No evidence of lymph node metastasis Absence of distant disease
II Locally advanced	T1-2, N0-1, M0	Tumor extends directly to any of the following: duodenum, bile duct, retroperitoneal tissues, including connective tissue and nerve plexus. No evidence of lymph node metastasis or metastasis of group 1* lymph node alone Absence of distant disease
III Metastatic disease	T2-3, N0-N2, M0	Tumor extends directly to any of the following: stomach, colon, spleen, omentum, mesocolon, adjacent large vessels including portal vein, celiac artery and superior mesenteric artery and vein (excluding splenic vessels). No evidence of lymph node metastasis or metastasis to group 2# lymph nodes.
IV General carcinoma	T2-3, N3, M0-M1	Metastasis to group 3§ lymph nodes. Distant metastasis

*Group 1: head (PY, APD, PPD, CH), body-tail (CH, SB, IB, SP); #Group 2: head (HDL, MC, SM), body-tail (SMA, LG, CT, APD, PPD); §Group 3: head (PA, CT, LG), body-tail (PA, PY).

A total of 107 patients were included in the study. The endoscopic treatment was performed in a group of 82 patients and consisted in positioning an endoprosthesis according to the classic endoscopic technique. In 37 patients polyethylene stents were used, whereas the remaining 45 patients were treated with self-expanding metal stents. The patient characteristics are shown in Table II. In all patients tumor size was obtained by tomography or ultrasound scans.

The surgical bypass was performed in a group of 25 patients. Seven patients were treated with a choledochoduodenostomy, 14 patients with a choledochojejunostomy, and 4 patients with a cholecystenterostomy.

Results

The endoscopic treatment was successful in 80/82 cases (97.5%). Procedure-related complications and mortality were 7.3% (on 82 patients) and 3.6% (on 82 patients), respectively, with no difference between polyethylene and self-expanding metal stents. The following complications were observed: 4 cases of

biliary sepsis, 1 case of pancreatitis, 1 case of paralytic ileus. One patients died within 10 days of primary stent insertion from biliary sepsis and two patients from upper digestive tract haemorrhage, in which the causative role of endoscopic procedures, although suspected, remained unproven. In the endoscopic treatment group the relief of jaundice was

Table II. Patient characteristics.

Patients	107
Mean Age	71.6
Age range	37-96
Sex F/M	58/49
Percentage weight loss	
Mean	10.3
Range	0-31
Diagnosis	
Pancreatic cancer	78 (72.8%)
Cholangiocarcinoma	15 (14.2%)
Ampullary cancer	6 (5.6%)
Metastatic lymph nodes	8 (7.4%)
Tumor size in mm	
Median	30
Range	10-80
N° of patients with liver metastases	19 (17.7%)
Mean bilirubinaemia before management (µmol/l)	216.7

very similar, namely 99% for the self-expanding metal stent subgroup and 97% for the polyethylene stent subgroup. Median survival in the self-expanding metal stent subgroup was 6.8 months, whereas in the polyethylene stent subgroup was 6.1 months. Mean hospital stay for the self-expanding metal stent subgroup was 7.3 days; in the polyethylene stent subgroup the mean hospital stay was considered to be 13.4 days, that is, comprehensive of two or three additional admissions required for replacing the obstructed stent. Both types of stents offer similar relief of jaundice and there is no evidence of any difference in perioperative and postoperative events. Overall patient survival is not significantly different when stent occlusions are treated with stent replacement as needed. Total resource utilization including need for repeat Endoscopic Retrograde Cholangiopancreatography (ERCP), total hospital stay, and cost was reported to be lower with metal stents as compared with plastic stents.

A surgical bypass procedure was performed in a group of 25 patients. In these patients a choledochoduodenostomy was done in 7, a choledochojejunostomy in 14, and a cholecystenterostomy in 4 cases. The type of biliary bypass did not significantly influence the complication rate, outcome or long-term survival. During surgical treatment, biliary drainage was successful in 96% (24/25 patients). Procedure-related complications and mortality were 24% (6/25 patients) and 16% (4/25 patients), respectively. Two patients had bile leakage, peritonitis and abscess, 1 patient had gastric stasis, 2 patients developed severe acute renal failure and 1 patient had severe cholangitis. The latter patient was treated with drainage by a Percutaneous Transhepatic Cholangiography (PTC) modal-

ity. Two patients died from acute renal failure, 1 patient from pulmonary embolism and 1 patient from drainage failure. Median survival was 6.7 months. Median hospital stay was 26 days (range 8-85).

Discussion

This study was programmed in order to provide a basis for advising patients on the possibility of having their jaundice relieved either by an endoscopic stenting procedure or by a surgical bypass procedure.

The prerequisites for a successful endoscopic stenting are (a) accuracy of diagnosis and (b) exclusion of patients presenting with tumors potentially treatable by a curative resection. This evaluation is simple whenever metastases are evident or whenever serious medical disorders are coincidental, thus precluding resection, but it may be difficult when a solitary primary lesion is detected.

The present study shows that, for the patients in whom a curative resection could not be performed, either methods under study resulted in a high rate of immediate technical and therapeutical success. However, the surgical approach showed a significantly higher rate in procedure-related mortality and morbidity (Table III).

Endoscopic stenting significantly reduced the duration of hospital stay, despite the need for stent replacement in those patients who had an extended survival. The period of hospital stay may be reduced even further by the use of self-expanding metal stents. A comparative trial^{21,22} between metal and polyethylene stents showed that the former significantly reduced the incidence of cholangitis, stent fail-

Table III. Outcome measures.

	Metallic stent	Plastic stent	Surgery
Total patients	45	37	25
Relief of jaundice	100%	98%	99%
Complications*	7.3% [†]	7.3% [†]	24% [‡]
Mortality*	3.6% [†]	3.6% [†]	16% [‡]
Median hospital stay (days)	7.3	13.4	26
Median overall survival (months)	6.8	6.1	6.7

*Metallic and plastic stents combined; [†]On 82 patients; [‡]On 25 patients.



Figure 1. ERCP show a distal obstruction of common bile duct.

ure, hospital stay and cost of treatment, thus suggesting that an endoscopic metal endoprosthesis is the gold standard for the palliative treatment of malignant obstructive jaundice. As a consequence of this retrospective study, it may be postulated that patients, who are possibly suitable for curative surgical resection, could undergo an operation to assess

resectability without extensive investigations to assess operability. After the assessment has revealed an inoperable tumor, the patient requires both biliary and gastric bypasses. On the contrary, the patient who is definitely unsuitable for curative resection is better managed by an endoscopic stenting procedure, preferably a metal stent in those less serious



Figure 2. Self-expanding metal stent in common bile duct for pancreatic cancer.

patients who may supposedly survive longer; whenever a late duodenal obstruction develops, operative intervention becomes appropriate, unless intraluminal metal stents prove to be effective.

The decision is more difficult in patients with unresectable disease who may be poor operative risk. The results show that surgical and endoscopic approaches have both advantages and disadvantages. We did not address quality of life issues directly and did not attempt to assess the relative cost-effectiveness of the procedures under study. These items, as well as the level of specialistic expertise available, will influence the therapeutic decision, that should be taken by the attending physician in strict cooperation with the fully informed patient.

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