

Endoscopic palliative treatment of pancreatic cancer

D. Xinopoulos, D. Dimitroulopoulos

SUMMARY

Pancreatic cancer is a significant clinical challenge worldwide. Despite advances in surgical techniques and new chemotherapy drugs less than 5% of all patients survive past 5 years and at the time of diagnosis almost 85% of patients are unsuitable candidates for curative resection of the tumor. Thus, most of them will need palliative treatment. Endoscopic palliative treatment of pancreatic cancer is primarily directed at relief of obstructive jaundice and duodenal obstruction. Obstructive jaundice occurs in the vast majority of patients with unresectable pancreatic carcinoma and endoscopic palliation is considered now as the method of choice for all the cases that are not candidates for possible curative resection. On the other hand, endoscopic placement of an expandable metal enteral stent in cases with duodenal obstruction due to pancreatic cancer, is a relatively new technique that must be performed in selected patients with advanced disease.

Key words: pancreatic cancer, endoscopic palliation, obstructive jaundice, duodenal obstruction, stent, endoprosthesis

Pancreatic cancer remains a significant clinical challenge worldwide. An estimated 31,860 patients in the United States, 50,000 in Europe, and more than 210,000 worldwide are diagnosed with pancreatic cancer each year.^{1,2} Despite advances in surgical techniques and new chemotherapy drugs for gastrointestinal cancers, the mortality rate from pancreatic cancer remains high. Only 20% of patients survive past 1 year, and less than 5% of all patients survive past 5 years.³ Unfortunately, at the time of diagnosis, almost 85% of patients are deemed unsuitable candidates for curative resection, and most

of them will need palliative treatment.⁴⁻⁶

Palliative intervention is primarily directed at relief of obstructive jaundice, pain, and nausea and vomiting due to duodenal obstruction. Endoscopic therapy offers a noninvasive management option for all three symptoms. For obstructive jaundice, endoscopic therapy is the preferred mode of palliation.⁷

PALLIATION OF OBSTRUCTIVE JAUNDICE

Obstructive jaundice occurs in 70-80% of patients with unresectable pancreatic cancer at presentation.⁴⁻⁶ Prolonged biliary obstruction usually results in malabsorption and consequent progressive malnutrition, pruritus, recurrent attacks of cholangitis, and liver dysfunction. Therefore, relief of obstructive jaundice is essential to improve quality and length of life.⁸

Biliary decompression often has a dramatic effect and usually leads to relief of pruritus within a few days. Biliary decompression for patients with malignant jaundice can be achieved by surgery or by nonsurgical methods such as endoscopic or percutaneous endoprosthesis placement. The success rate for initial relief of biliary obstruction using surgical approaches varies between 75% and 100%.⁹ Nonoperative techniques may be used as a temporary measure to alleviate acute biliary obstruction or as a more permanent decompression measure in patients with advanced unresectable disease or concurrent medical conditions that are contraindications to anesthesia and major surgery. Thus, before considering either a surgical or endoscopic drainage procedure, it is important to establish that jaundice is caused by obstruction of the biliary ductal system rather than by extensive intrahepatic tumor deposit leading to functional liver failure. The presence of extensive intrahepatic metastasis along with absence of significant biliary dilation by noninvasive imaging studies should alert the clinician to this possibility.

Gastroenterology Unit, "Aghios Savvas" Cancer Hospital, Athens, Greece

Author for correspondence:

D.Dimitroulopoulos, Parnassou 35, GR 152 34 Halandri, Athens-Greece, Tel. 003010-6892460, E-mail: dimdim@otenet.gr

Table 1. Results of randomized controlled trials comparing endoscopic therapy vs surgical bypass in patients with malignant biliary obstruction.

| | Shepherd (10) | | Andersen (11) | | Dowsett (12) | | Smith (13) | |
|---------------------------------|---------------|---------|---------------|---------|--------------|---------|------------|---------|
| | Stent | Surgery | Stent | Surgery | Stent | Surgery | Stent | Surgery |
| Number of patients | 23 | 25 | 25 | 25 | 65 | 62 | 101 | 103 |
| Success | 82% | 92% | 96% | 88% | 94% | 94% | 92% | 92% |
| Complication | 30% | 56% | 36% | 20% | 23% | 50% | 11% | 29% |
| 30-day mortality | 9% | 20% | 20% | 24% | 6% | 15% | 8% | 15% |
| Length of hospital stay (days) | 5 | 13 | 26 | 27 | 11 | 15 | 19 | 26 |
| Recurrent jaundice/cholangiitis | 30% | 0% | 0% | 0% | 17% | 3% | 36% | 2% |
| Survival (weeks) | 22 | 18 | 12 | 14 | 22 | 16 | 21 | 26 |

Comparing endoscopic with surgical palliation of malignant obstructive jaundice due to unresectable pancreatic cancer, several randomized trials revealed that both methods appear to be effective palliative treatments, with the former having fewer early treatment-related complications and the latter having fewer late complications.¹⁰⁻¹³ Although, endoscopic stenting significantly reduced the length of hospital stay, this difference was eliminated when readmissions for recurrent biliary obstruction and duodenal obstruction were taken into account.

Recurrence of jaundice and cholangiitis due to stent occlusion requiring repeated hospital visits is a drawback of endoscopic palliation. However, with the availability of expandable metal stents, such episodes occur less frequently. Although metallic stents have a higher patency rate compared to plastic stents, their initial costs are also higher. Cost effective analyses have shown that initial endoscopic placement of metallic stents is cost effective in patients who survive longer than 6 months.¹⁴⁻¹⁷

Patients with locally advanced, nonmetastatic pancreatic cancer have a median survival of 10 to 14 months (with current chemotherapy and chemoradiation regimens).³ The decision to perform endoscopic biliary stent-

ing versus surgical bypass in this patient group remains controversial. The desire to avoid palliative surgery that provides no anticancer treatment is balanced by the need for durable biliary decompression without the risk of recurrent cholangiitis secondary to stent occlusion. Endoscopic metallic expandable stents become obstructed by tumor or tissue ingrowth through the interstices of the metal mesh or by overgrowth at either end of the stent.⁷ To overcome this, metallic stents covered with polyurethane have been developed. Results from small trials have shown that covered metallic stents prevent tumor ingrowth and may provide longer patency rates.¹⁸⁻²⁰

Before endoscopic placement of biliary endoprosthesis, endoscopic retrograde cholangiopancreatography must be performed, to evaluate the biliary tree and the pancreatic duct. Preceding the procedure, antibiotics should be administered prophylactically, and coagulopathy should be treated if present. The location and length of the biliary stricture must be determined accurately, and the proximal biliary tree also must be opacified to correctly assess the proximal extent of the stricture and to exclude the presence of additional proximal strictures. Deep cannulation of the biliary system must be per-

Table 2. Results of controlled trials comparing metal stents with plastic stents.

| | Knyrim (15) | | Davids (16) | | Carr-Locke (18) | |
|--------------------|-------------|-------|-------------|-------|-----------------|-------|
| | Plastic | Metal | Plastic | Metal | Plastic | Metal |
| Number of patients | 31 | 31 | 56 | 49 | 78 | 86 |
| Drainage | 100 | 100 | 95 | 96 | 95 | 98 |
| Occlusion | 22 | 43 | 54 | 33 | 13 | 13 |
| 30-day mortality | 9 | 13 | 4 | 14 | 5 | 5 |
| Patency (days) | 43 | 22 | 126 | 273 | 62 | 111 |

formed, and a guidewire should be manipulated across the stricture to maintain access. At this stage, an endoscopic transpapillary wire-guided brush cytologic specimen or forceps biopsy may be obtained from the area of the stricture, if indicated.

The main causes of failure to place a biliary stent endoscopically include obstruction of the duodenum and the inability to cannulate the common bile duct or pass a guidewire through the stricture. In these cases, a combined percutaneous endoscopic "rendez vous" technique is useful to access the biliary system and place a stent across the biliary stricture.

Complications of stent placement include short-term complications related to endoscopic retrograde cholangiopancreatography (e.g. pancreatitis, cholangiitis, perforation) and delayed complications related to stent placement (e.g. stent migration, stent fracture, stent occlusion), if it is plastic or uncovered.

American Gastroenterological Association (AGA) suggest in the AGA technical review on the epidemiology, diagnosis and treatment of pancreatic ductal adenocarcinoma that: "patients who require relief of bile duct obstruction and are not candidates for possible curative resection should undergo endoscopic stent placement. Patients who receive stents need ongoing surveillance and management by a multidisciplinary team for postprocedure complications such as stent-associated cholangiitis".²¹

PALLIATION OF DUODENAL OBSTRUCTION

At the time of diagnosis, 30-45% of patients with pancreatic cancer complain of nausea and vomiting and approximately 5% develop duodenal obstruction at some point before their death.²² As pancreatic tumors enlarge, there is an increased risk of duodenal invasion and obstruction. Tumors located in the pancreatic head and uncinate process tend to obstruct the second and third parts of the duodenum, while tumors in the pancreatic body and tail tend to obstruct the fourth portion of the duodenum.

Although surgical gastrojejunostomy remains the standard treatment modality for duodenal obstruction, it has a mortality rate up to 10% as well as associated morbidity, additional high cost, and prolonged hospitalization. The introduction of expandable metallic stents has provided an additional means of controlling gastroduodenal obstruction in some of these patients. Although there are no large randomized trials comparing endoscopic duodenal stenting to traditional surgical bypass, preliminary data from small case series suggest that self-

expandable enteral stents can effectively relieve duodenal obstruction in selected patients with advanced pancreatic cancer.²³ In these series gastroduodenal stenting was successful in 80-90% of cases and was provided adequate relief of obstruction in most patients.²⁴⁻²⁷

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