Endoscopic Retrograde Cholangiopancreatography and Endoscopic Endoprosthesis Insertion in Patients With Klatskin Tumors

Chi-leung Liu, MB, BS, FRCS(Edin); Chung-mau Lo, FRACS, FRCS(Edin); Edward C. S. Lai, MS, FRACS, FRCS(Edin); Sheung-tat Fan, MS, FRCS(Glasg)

Objective: To assess the value and the associated morbidity of endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic endoprosthesis insertion in the treatment of patients with Klatskin tumors.

Design: Retrospective study.

Setting: A tertiary referral center.

Patients: Fifty-five consecutive patients with Klatskin tumors diagnosed through typical cholangiographic and computed tomographic findings.

Intervention: Standard ERCP with endoscopic stenting technique was employed. Once the diagnosis of Klatskin tumor was confirmed on cholangiogram, endoscopic stenting was performed to bypass the stricture. Multiple stents were inserted if necessary to ensure adequate biliary drainage.

Main Outcome Measures: The success rate of ERCP and endoscopic endoprosthesis insertion, successful drainage rate, early complications of endoscopic procedure, procedure-related mortality, and long-term outcome of endoprosthesis.

Results: Of the 55 patients, cholangiography was performed in 53 (96%). In the 49 patients in whom endoscopic stenting was attempted, the procedure was successful in 28 patients (57%) at the first attempt and 8 patients (16%) at the second attempt, resulting in a cumulative success rate of 73%. Only 20 of these patients had satisfactory biliary drainage, resulting in an overall successful drainage rate of 41%. Early complications, including acute cholangitis, acute pancreatitis, and post-papillotomy bleeding occurred in 14 patients (25%). Three patients (5%) died of procedure-related complications. The median patency of the first endoprosthesis inserted was 1 week (range, 0-8 wk). The 30-day mortality rate was 18%.

Conclusions: In patients with Klatskin tumors, ERCP and endoscopic endoprosthesis insertion have a low successful drainage rate, are associated with high morbidity and procedure-related mortality, and have a limited effect on long-term palliation. Endoscopic retrograde cholangiopancreatography and endoscopic endoprosthesis insertion have a limited value in the management of patients with Klatskin tumors.

Arch Surg. 1998;133:293-296

ENDOSCOPIC retrograde cholangiopancreatography (ERCP) is frequently used in the management of patients with malignant hilar biliary obstruction that includes Klatskin tumor. As patients often present with obstructive jaundice, diagnostic ERCP is frequently performed as part of the initial investigation. In addition, endoscopic endoprostheses are often inserted either as preoperative drainage for those considered to have resectable disease, or as a palliative treatment for those considered unsuitable for curative resection. Endoscopic endoprosthesis insertion as a palliative treatment has been reported to have a highly successful drainage rate in patients with malignant hilar biliary obstruction. It is not clear, however, whether similar results can be reproduced in a group of patients with Klatskin tumor only. On the other hand, significant early morbidity and procedure-related mortality have been associated with endoscopic endoprosthesis insertion in patients with malignant hilar biliary obstruction, despite multiple stent insertion. In this retrospective study, we analyzed our experience of ERCP in patients with Klatskin tumors to assess the value and associated morbidity of endoscopic endoprosthesis insertion in their treatment.

RESULTS

Of the 55 patients with Klatskin tumors who underwent ERCP, a cholangiography was performed on 53 patients (96%).
PATIENTS AND METHODS

Between January 1989 and June 1996, ERCP with attempted endoscopic stenting was performed on 55 consecutive patients with Klatskin tumors. The diagnosis was made from typical findings on a cholangiogram and computed tomographic scan. Thirty-seven men and 18 women with a median age of 68 years took part in the study. Their main presenting symptom was jaundice with significant weight loss. The mean duration of jaundice before presentation was 24 days. Only 4 (7%) of the patients presented with acute cholangitis. The clinical parameters of the patients are summarized in Table 1. The type of biliary obstruction was categorized according to Bismuth classification on the basis of cholangiographic findings: type I, 10 patients (18%); type II, 18 patients (33%); type III, 22 patients (40%); and type IV, 5 patients (9%). Among these 55 patients, 37 were considered unsuitable for resection on the basis of significant medical illness or extensive tumor involvement as defined by cholangiography, computed tomography, or angiography. In the other 18 patients, ERCP and attempted endoscopic stenting were performed as preoperative initial investigation and biliary drainage.

All endoscopic examinations and stenting were performed by 4 experienced endoscopists at the Surgical Endoscopy Unit, Queen Mary Hospital, Hong Kong, People's Republic of China, a tertiary referral center with a busy endoscopic service and about 700 ERCPs performed each year. All patients underwent ERCP and endoscopic stenting and received intravenous sedation and local anesthesia. Intra-venous antibiotics were given prophylactically before and for at least 24 hours after the procedure. Once the diagnosis was confirmed on cholangiogram, endoscopic stenting using a polyethylene endoprosthesis was performed to bypass the stricture, and multiple stents were inserted if considered necessary to secure adequate biliary drainage. The endoprosthesis was inserted over the guidewire and coaxial catheter via the working channel of the endoscope using a standard technique. Insertion of the endoscopic endoprosthesis was considered unsuccessful after the failure of 2 attempted endoscopic procedures. We did not use a combined percutaneous-endoscopic technique with our patients.

Successful endoprosthesis placement with adequate drainage was defined as successful stent insertion across the stricture with good bile drainage together with clinical improvement of obstructive jaundice as evidenced by a 20% reduction in the serum bilirubin level within the first week. Early complications were defined as those occurring within 30 days after the endoscopic procedure. Cholangitis was diagnosed when there were clinical features of sepsis without other apparent cause together with derangement of liver function. Procedure-induced pancreatitis was diagnosed when serum amylase levels rose to more than twice the normal limit (<110 U/L) together with notable abdominal pain after the procedure. Postpapillotomy bleeding was considered significant when blood transfusion of more than 2 units was required or when therapeutic endoscopy or surgery was necessary for hemostasis. Thirty-day mortality was defined as death within 30 days of the first attempted insertion of the endoscopic endoprosthesis, whether the insertion was successful or not. Procedure-related mortality was defined as death directly related to a complication of ERCP, including papillotomy or endoprosthesis insertion. Follow-up of all patients was complete, and all patients were informed of the possible symptoms of stent blockage so that early stent replacement could be performed whenever required. Stent patency was regularly assessed with use of both clinical and biochemical parameters. Stent blockage was suspected whenever increase in jaundice or acute cholangitis occurred or deterioration of liver function was evident in the blood biochemistry test results. Stent blockage was then confirmed with endoscopic examination.

Two patients for whom cannulation of the bile duct had failed because of anatomical and technical reasons underwent percutaneous transhepatic cholangiography and drainage. Endoprosthesis insertion was not attempted in 4 patients after cholangiography. Two of these patients were considered unsuitable for endoscopic stenting because of diffuse segmental involvement of the tumor; in the other 2 patients, the operation proceeded without preoperative endoscopic stenting. In the remaining 49 patients, endoscopic endoprosthesis insertion was successful in 28 patients (57%) at the first attempt and in 8 patients (16%) at the second attempt, resulting in a cumulative success rate of 73%. In each of 4 patients, 2 stents were inserted to ensure adequate biliary drainage. Ex-ternal nasobiliary drainage tubes were inserted in 2 patients initially and later converted into internal drainage. Among all 36 patients with initial successful endoscopic stenting, however, only 20 patients had satisfactory biliary drainage, resulting in an overall successful drainage rate of 41% among all 49 patients with attempted endoprosthesis insertion. Therefore, despite successful stenting, 16 patients (33%), of whom 14 had type III or type IV obstruction, had inadequate relief of cholestasis.

Early complications occurred in 14 patients, resulting in an early complication rate of 25% (Table 2). Three patients (5%) died of procedure-related complications. Two of those patients developed severe biliary sepsis after attempted endoprosthesis insertion and failed salvage procedure either by percutaneous drainage (1 patient) or by operative drainage (1 patient). In the third patient the endoscopic procedure was complicated by severe necrotizing pancreatitis and required repeated laparotomy for drainage and necrosectomy. He finally died of multiorgan failure. The 30-day mortality rate was 18%. Complete follow-up was achieved in all patients. The median survival time for all patients was 19 weeks (range, 0-290 weeks) from the first attempted drainage procedure. The causes of death were cachexia (41 patients [74%]), biliary sepsis (12 patients [22%]), postpapillotomy pancreatitis (1 patient [2%]), and postoperative liver failure (1 patient [2%]).

Median patency of the first endoprostheses inserted was only 1 week (Table 3). The median patencies of the second and third endoprostheses were much longer, probably because of patient selection and insertion of a wider caliber of stent. Among all 16 patients with successful biliary drainage by endoscopic endoprosth-
COMMENT

Although Klatskin tumor, or hilar cholangiocarcinoma, is a relatively rare tumor of the hepatobiliary system, it presents a major management challenge to clinicians. Most of these tumors are small and slow growing, and only infrequently metastasize by blood to other organs. However, because of this carcinoma’s great propensity for early local invasion of adjacent vital structures by neural, perineural, subepithelial, and lymphatic spread, the prognosis of these patients is usually guarded. In about 10% of the patients who are considered suitable for curative resection, the value of routine preoperative drainage is largely disputed. Although 3 prospective randomized trials in jaundiced patients with a heterogeneous level and nature of biliary obstruction showed no benefits in reducing hospital morbidity and mortality, few major hepatic resections were included in these trials. Comparison of patients in these trials therefore should not be made directly with patients with Klatskin tumors, as major hepatectomies are often required in these patients. Routine percutaneous transhepatic biliary drain insertion has been recommended by many authors as standard preoperative preparation in patients with Klatskin tumors and has gained much popularity. On the other hand, the use of an endoscopic stent as a means for preoperative biliary drainage for patients with Klatskin tumors is considered inadvisable. In 1994, Lai et al reported a randomized trial showing a significant risk of cholangitis and ineffective decompression following endoscopic drainage for patients with malignant hilar lesions. The argument is further supported by the results of endoscopic stenting in the present study on patients with Klatskin tumors. The successful drainage rate in this study was only 41% and procedure-related morbidity and mortality were 25% and 5%, respectively. One of the major drawbacks we experienced of the preoperative endoscopic procedure was conversion of tumors that were potentially resectable to being very difficult or impossible to resect after acute cholangitis or acute pancreatitis had complicated the endoscopic procedure.

In about 90% of patients with Klatskin tumors who are considered unsuitable or unfit for curative resection at presentation because of advanced disease or concomitant illness, palliative treatment seems worthwhile because the quality of life can be improved considerably by relief of the pruritus and nausea of cholestasis. Surgical palliation, however, is associated with a high morbidity and mortality in these patients. Even in the best hands, surgical bypass procedures were reported to have a 33% operative mortality, while surgical intubation carried a 60-day postoperative morbidity of 26% and a mortality of 30%. Nonoperative drainage, either percutaneous or endoscopic, has been recommended as the treatment of choice for palliation in patients with malignant hilar biliary obstruction that includes Klatskin tumor, especially in patients with high operative risk and limited life expectancy. Endoscopic endoprosthesis insertion has been reported to result in a success rate of 89% and a cumulative successful drainage rate of 82% in a heterogeneous group of 190 patients with malignant hilar biliary obstruction, including 101 patients (53%) with cholangiocarcinoma and 112 patients (59%) with type I...
or type II biliary strictures. The successful endoprosthesis insertion rate (73%) and successful drainage rate (41%) were much lower in the present study than in the one by Polydorou et al. The discrepancies could be explained by the differences in the primary disease and the types of biliary obstruction. All the patients in the present study had Klatskin tumors, about half (49%) of which were type III or type IV obstruction. In addition, having understood the possible complications of endoscopic stenting that includes the combined percutaneous-endoscopic technique, we seldom repeated attempts at endoscopic stenting for patients with difficult stricture in the present study. None of our patients underwent the combined percutaneous-endoscopic procedure before being switched to percutaneous drainage.

A high (19%) morbidity rate for endoscopic stenting and a procedure-related mortality of 3% have been reported in patients with malignant hilar biliary obstruction. Despite multiple stent insertions, early cholangitis was reported to occur in 17% of patients with type II and type III malignant strictures. These figures were not much different from those in the present study—an early complication rate of 25% and a procedure-related mortality of 5%. When compared with patients with distal bile duct obstruction, however, the outcome of palliative treatment of patients with Klatskin tumors by endoscopic stenting was significantly worse, as our previous experience also showed.

In contrast to patients with distal bile duct obstruction who can usually be adequately palliated with a single endoscopic stent, patients with Klatskin tumors often have segmental bile duct involvement, and complete biliary drainage is often impossible despite the insertion of multiple stents. Ineffective drainage of segmental ducts including the caudate branch may result in sepsis, especially after opacification during endoscopic examination. In patients in whom initial satisfactory biliary drainage is achieved, progressive tumor growth can occur, producing segregation of segmental ducts and thus resulting in poor long-term palliation by endoscopic stenting.

In summary, ERCP and endoscopic endoprosthesis insertion for drainage had a low success rate, were associated with high morbidity and procedure-related mortality, and had a limited role in long-term palliation in patients with Klatskin tumors. Endoscopic retrograde cholangiopancreatography and endoscopic endoprosthesis insertion has a limited value in the management of patients with Klatskin tumors.

**Corresponding author:** Chi-leung Liu, MB, BS, FRCS(Edin), Department of Surgery, University of Hong Kong Medical Centre, Queen Mary Hospital, 102 Pokfulam Rd, Hong Kong, People’s Republic of China.

**REFERENCES**