

Klatskin tumor—palliative therapy: the jury is still out or may be not yet in...

Klatskin tumor, the perihilar cholangiocarcinoma that involves the biliary confluence, accounts for 60% to 80% of bile-duct carcinomas seen in tertiary-referral centers¹ and mostly is seen an advanced incurable stage amenable only to palliative therapy. Patients with advanced Klatskin tumor and cholangitis often have segmental intrahepatic biliary involvement, and complete biliary drainage may be impossible, in spite of using multiple stents to drain obstructed liver segments. In the absence of cholangitis, the dominant liver segment could be drained with a single stent.^{2,3} Both endoscopic and transhepatic biliary drainage, and, in some cases, rendezvous or a combined approach, has been proven effective and safe when using plastic or self-expandable metal stents (SEMS) to achieve biliary drainage. Successful bilateral stenting with more than 2 stents has been associated with longer survival in patients with unresectable hilar disease, but adequate drainage has been achieved in 65% to 78% of cases.^{4,5} Initial complications have occurred in 11% of patients after ERCP and in 33% after percutaneous cholangiography (PTC), with a 5% 30-day mortality. It is interesting to note that, of the 5 patients who required PTC after an ERCP, 3 died within 30 days.⁵ The study by Deviere et al⁶ recommends that all accessible ducts are individually drained, with reduction of cholangitis from 38% to 17%. Liu et al⁷ reported their results of endoscopic therapy in 55 patients with hilar malignancy by attempting multiple stentings, as required, with a cumulative initial success rate of 73% and achieving effective biliary drainage in 41%. Procedure-related morbidity, such as pancreatitis, bleeding, and cholangitis, occurred in 25%, and there was 5% procedure-related mortality. The median patency of the initial stents was 1 week (range 0–8 weeks), whereas the 30-day mortality was 18%.⁷ In a randomized study of 20 patients with Klatskin tumors, Wagner et al⁸ demonstrated a significant decrease in the number of endoscopic procedures, the length of hospitalization, and the cost by using SEMS compared with plastic biliary stents. Duma et al⁹ described an endoscopic technique that simultaneously introduced 2 guidewires to facilitate bilateral biliary SEMS placement. Sang et al¹⁰ compared endoscopic with PTC drainage in patients with Klatskin tumors. The ini-

tial success rate of effective biliary drainage was lower for ERCP drainage in Bismuth types III and IV. Cholangitis occurred more frequently with ERCP compared with PTC, and this was related to the difficulty in selective stenting and contrast injection into segments that could not be endoscopically drained. Adequate initial relief of jaundice was achieved in 91%.¹⁰ Mansfield et al¹¹ concluded that endoscopic drainage should be avoided if possible, because of failure to achieve effective drainage in 29% of patients and required additional PTC. Multiple, mostly nonrandomized studies recommended either the endoscopic or percutaneous

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drainage, without reaching a consensus. Typically, endoscopic drainage was recommended for Bismuth type II and III lesions and a percutaneous approach for type IV lesions.⁶⁻¹⁰

In a retrospective multicenter study in this issue of *Gastrointestinal Endoscopy*, Paik et al¹² describe the palliative treatment of patients with advanced type III or IV hilar cholangiocarcinoma by using biliary SEMS and comparing the endoscopic with the percutaneous approach. The purpose of the study was to compare the 2 methods in terms of short-term and long-term outcomes of biliary drainage. Eighty-five patients who did not undergo previous therapy were included in the review. Forty-four patients were treated by endoscopy, and 41 patients were treated by the percutaneous method with insertion of biliary SEMS. Only 7 patients in the endoscopy group (16%) and 22 in the percutaneous group (54%) had 2 stents placed. Effective relief of cholestasis was achieved in 92.7% in the percutaneous group compared with 77.3% in the endoscopic group, with an overall successful drainage in 84.7%. The overall

complication rate was 30.6%, with no difference in the rate of procedure-related complications between the 2 groups, whereas the procedure-related mortality was 1 (1.2%), in a patient who developed cholangitis after endoscopic biliary stenting. Of interest, the patient died of sepsis, despite undergoing additional percutaneous drainage. The mean hospital stay was significantly shorter in the endoscopy group. Of the 72 patients who had successful initial drainage (84.7%), 3-month and 6-month patency rates were 69.4% and 44.4%, respectively. The median duration of stent patency was 9.8 months in the endoscopy group and 11 months in the percutaneous group, but this did not reach statistical significance. On multivariable analysis, long-term patency was not affected by the Bismuth type or single versus double stenting. Biliary reintervention was required in 40.3% patients, 38.2% in the endoscopic group and 42.1% in the percutaneous group, which was successful in the majority of patients, but this also did not reach significance. Overall survival was 7.9 months. Although survival seemed longer in the percutaneous group (8.7 vs 6.2 months), this was not statistically significant ($P = .125$). Median survival of patients with successful initial biliary drainage, regardless of the procedure, was significantly longer than those in whom initial drainage failed (median 8.7 vs 1.8 months). In a subanalysis that compared patients with successful biliary drainage and normal to near-normal bilirubin levels, there was significant survival advantage to those with normal bilirubin (median 10.9 vs 5.7 months). The investigators recommend that PTC with SEMS placement be the first palliative intervention in patients with Bismuth types III and IV hilar strictures because of a higher rate of successful initial biliary drainage. Moreover, patients who had a failed initial drainage had significantly shorter survival, despite undergoing subsequent PTC drainage (median 5.6 weeks).

One needs to keep in mind that this was a relatively small, retrospective, multicenter chart review of patients with advanced hilar cholangiocarcinoma in which patients were selected from a database between 1996 and 2006, and follow-up was obtained from medical records, cancer registry, and telephone contact with patients or family. Although the results are interesting, these are also the limiting factors of the study.

When patients undergo endoscopic or percutaneous biliary drainage with SEMS placement, patient selection and local expertise biases are likely. Although our initial reflex as endoscopists is to perform endoscopic biliary drainage, the study raises some important issues that need to be considered:

1. SEMS should be used for biliary drainage, because they are safe and effective.
2. Successful initial drainage, regardless of the procedure, is the most powerful factor that affects survival.
3. The goal of drainage should be normalization and not just improvement of the bilirubin levels, because drainage offers significant survival benefit.
4. PTC drainage has a higher success of initial biliary drainage when compared with ERCP.
5. The survival after a failed initial biliary decompression is significantly shorter, despite rescue percutaneous drainage.
6. Once biliary drainage is accomplished, there is no difference between the 2 methods with regard to complications and survival.
7. The only mortality is related to failed ERCP drainage, complicated by biliary sepsis.
8. Stent patency is limited, and reintervention should be expected.
9. In most patients, reintervention will likely succeed.
10. It is still not clear whether there is a benefit from single compared with multiple stenting. This issue is important because of the related risks and cost of placing multiple SEMS.

THE FUTURE

One-step EUS-guided biliary drainage, similar to that performed in endoscopic pseudocyst drainage, was described in a few reports. Under EUS guidance, the intrahepatic duct is punctured via a linear scope, followed by biliary placement of a plastic or metal stent. Although exciting, this technique is limited, however, because multiple stenting that may be required in these complex hilar strictures is not likely. EUS cannot accurately define such complex strictures that are usually present in these cases. Nevertheless, EUS may offer an alternative to the more invasive PTC in patients with Bismuth types I and II who have failed ERCP access.¹³⁻¹⁵

In summary, despite all the recent innovations in interventional endoscopy and radiology, palliative therapy of patients with advanced hilar malignant obstruction is still suboptimal, even when combined endoscopic and transhepatic biliary drainage is used; the overall survival remains poor, regardless of the palliation method used. Surgery should be offered to all patients whenever possible to provide any chance for a cure. In the past, these patients were assessed by ERCP, which was associated with the risk of cholangitis related to contrast injection and an inability to drain all injected liver segments. Today, MRCP should initially be performed in all patients to assess the biliary anatomy, before endoscopic or percutaneous intervention. In patients with type I and II strictures with advanced disease or who are unable to undergo surgery, endoscopic drainage should be offered. If ERCP access fails, then EUS-guided biliary stenting may be an alternative if local expertise exists. In patients with advanced type III and, certainly, type IV disease, the percutaneous approach should be considered. Also, available local expertise will be an important factor in choosing palliation in patients with advanced hilar cholangiocarcinoma.

DISCLOSURE

The author reports that there are no disclosures relevant to this publication.

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Abbreviations: PTC, percutaneous transhepatic cholangiography; SEMS, self-expandable metal stent.

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