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Current Status of Endoscopic Treatment of Advanced Hilar Cholangiocarcinoma

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Abstract

Cholangiocarcinoma is a high-mortality primary hepatic malignancy. A higher incidence of cholangiocarcinoma was reported in Asia, especially Southeast Asia, than in Western countries. Hilar cholangiocarcinoma is a specifc type of extrahepatic cholangiocarcinoma that involves the hepatic hilum and has a worse prognosis. More than half of the patients with jaundice are inoperable at the time of frst diagnosis. Therefore, biliary drainage is the mainstay of palliative treatment in these patients. Endoscopic biliary drainage via endoscopic retrograde cholangiopancreatography, the modality of choice, for the advanced hilar type is more diffcult and complex than those in distal cholangiocarcinoma. Endoscopists should consider many factors before selecting the most appropriate treatment for each patient. Here we discuss the factors systematically. In cases of transpapillary approach failure, other therapeutic modalities should be considered. Percutaneous transhepatic biliary drainage is the most popular method in such cases. At the present, endoscopic ultrasound-guided biliary drainage, especially hepaticogastrostomy, is an alternative procedure with the same effcacy and low complications when it was carried out in the expert hands. Furthermore, recent locoregional therapies for tumor control including trans-luminal photodynamic therapy and radiofrequency ablation also benefit these patients.

Keywords: Unresectable hilar cholangiocarcinoma; Inoperable hilar cholangiocarcinoma; Endoscopic treatment; Biliary stenting; Photodynamic therapy; Radiofrequency ablation; RFA; PDT

Introduction

Cholangiocarcinoma (CCA) is a fatal malignant tumor of the hepatobiliary system with a higher incidence in Eastern countries. e highest incidence of CCA was found in Southeast Asia, especially ailand, which was 71.3:100,000 in men and 31.6:100,000 in women [1], followed by China and some other countries in Southeast Asia [2], whereas data from the USA, Europe, and Australia showed overall incidences of 0.82:100,000, 0.9–5.5:100,000, and 0.8–1.0:100,000, respectively [3-5]. is discrepancy in disease incidence can be explained according to the pathogenesis of CCA, although cases of CCA were sporadic.

Strong risk factors for CCA include older age, male gender, chronic hepatobiliary tract in ammation such as primary sclerosing cholangitis, chronic hepatolithiasis, choledochal cyst, and chronic parasitic infestations such as Opisthorchis viverrini and Chlonorchis sinensis [6-8]. Other recently reported possible risk factors include chronic viral hepatitis infections such as hepatitis B and C, obesity, non-alcoholic steatohepatitis, and metabolic syndrome [9-13]. In the highest incidence area of CCA, viverrini

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had inoperable disease. is study provided the overall laparoscopy yield of 45% and accuracy of 71%. erefore, approximately two thirds of patients with CCA are in the advanced stage of the disease at the time of rst diagnosis.

Biliary drainage is the main palliative strategy for patients with advanced CCA. e advantages and disadvantages of endoscopic

lower rate of post-ERCP cholangitis in patients who underwent CO_2 cholangiography compared to a conventional contrast study (5.6% vs. 33.3%, p=0.04). us, we recommend the use of air or CO_2 cholangiography for the treatment of type IV hilar lesions.

Should plastic stents or self-expandable metal stents (SEMS) be selected?

To answer this question, endoscopists who perform the procedures must know the advantages and limitations of both stent types. Plastic stents are less expensive and technically easier to insert, remove, an exchange if stent malfunction or occlusion occurs. SEMS, which are composed of either stainless steel or nickel shape-retaining titanium (Nitinol), are designed and produced in many di erent styles and have advantages such as better stent patency than plastic stents as well as t ability to drain the side branches through the mesh. However, SEMS are much more expensive than plastic stents.

Prior to selecting a stent, endoscopists should consider patient life expectancy, cost e ectiveness, stent patency, and the need for stent revision. e patency of SEMS and plastic stents in hilar cholangiocarcinoma were previously reported in many studies as 3.4–5.5 months and 1.2–1.86 months, respectively [21,36]. A meta-analysis by Hong et al. [37,38] demonstrated that SEMS had a higher successful drainage rate with an odds ratio (OR) of 0.26 and 95% con dence interval (CI) of 0.16–0.42, lower early complication OR of 2.92 (95% CI, 1.65-Id [(dra)9(in)3(a)5(g)8(e ra)19(t)na1.65-Id [(dra)9(in)3(a)5(g)8u

system approach is the rst priority as stent insertion is easier because of less angulation. However, for type III hilar tumors, adequate drainage requires at least two stents, bilateral for type IIIb and bilateral or multi-segmented–unilateral stenting into the right system for type IIIa hilar tumors. For type IV lesions, stents should be inserted into at least two di erent intra-hepatic segments. e percutaneous approach might also bene t in cases where drainage by the transpapillary route has failed. Adequate cholangiography for complete evaluation of the entire biliary system is also essential.

e use of complete cholangiography in a conventional contrast study in patients with Klatskin type IV might be associated with a higher risk of post-procedural cholangitis. However, there have been few studies on the bene t of using air or carbon dioxide in ation instead of contrast agent. An air cholangiogram is shown in Figure 5. e usefulness of air cholangiography was rst reported by Sud et al. [34] in 2010. Zhang et al. [35] recently demonstrated a signi cantly

skillful endosonographers and is not yet a standard approach. In cases of failure of all interventional options, surgical bypass should be considered the last rescue procedure.

Locoregional Tumor Control

Photodynamic therapy (PDT)

PDT is a relatively new therapeutic approach for local tumor control. Based on the mechanism that the photosensitizing agent concentrates in the lesion, the photosensitizer is activated by non-thermal laser light of an appropriate wavelength, which leads to subsequent damage of the neoplastic tissue by generated free oxygen radicals [51]. Four photosensitizing agents are currently used for CCA. e most

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