Published online: 2020-01-22

Preoperative biliary drainage in hilar cholangiocarcinoma: when and how?

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DOI https://doi.org/10.1055/a-0990-9912 |
Endoscopy International Open 2020; 08: E211–E213

eISSN 2196-9736

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Cholangiocarcinoma (CCA) is the second most common primary hepatobiliary cancer after hepatocellular carcinoma. Approximately half the cases are located at the main confluence of the hepatic ducts. Magnetic resonance tomography (MRT) and computed tomography allow assessment of tumor location and extension, liver parenchyma, the hepatic vascular system and the volume of segments.

Hilar biliary stenoses should be classified according to Bismuth and Corlette because of important therapeutic implications. In this respect, magnetic resonance cholangiopancreatography (MRCP) is the diagnostic method of choice and provides detailed information on involvement of the biliary tree.

The need for histological or cytological confirmation of CCA should be discussed in a hepatobiliary tumor board. Endoscopic ultrasound allows fine-needle aspiration or biopsies of a hilar tumor mass. However, this approach is not recommended in operable patients because of the potential risk of seeding tumor cells. In most cases, endoscopic retrograde cholangiopancreatography (ERCP)-guided tissue acquisition is used for confirmation of CCA and differentiation from benign hilar stenoses. However, the sensitivity of ERCP-guided biopsies or brush cytology is limited with rates of less than 60 % [1]. Fluorescence in situ hybridization (FISH) probes for detection of pancreatobiliary tract cancer are promising in improving the accuracy of cytology brush samples [2]. Peroral cholangioscopy facilitates targeted biopsies and the latest technologies promise higher accuracy than ERCP-guided tissue acquisition [3]. In addition, cholangioscopy provides identification of intraductal extension of CCA, which has an impact on the indication for and extension of surgical resection [4].

Resection of hilar cholangiocarcinoma (HCCA) remains the gold-standard treatment. However only 25 % to 35 % of patients are candidates for radical resection. The majority of cases are diagnosed in an advanced tumor stage or are functionally inoperable. Surgical treatment of HCCA is associated with a potentially high risk of postoperative morbidity and mortality. Hyperbilirubinemia is regarded as the most important and modifiable risk factor for negative early postoperative outcomes. A recent retrospective single-center study reconfirmed that preoperative bilirubin concentration is a significant risk factor for postoperative morbidity and mortality with optimal cut-off levels of 2.5 mg/dL and 6.2 mg/dL, respectively [5]. These results may aid in decision-making with respect to preoperative biliary drainage. Other risk factors for surgery include cholangitis, malnutrition, need for portal vein embolization and predicted future liver remnant volume ≤ 30 % following surgery. Preoperative biliary drainage should be considered for these cases but the selection criteria and route for preoperative biliary drainage remain controversial. Routine preoperative drainage is not recommended [6, 7].

MRT and MRCP seem to be mandatory for assessment of location and extension of hilar obstruction and selection of the future liver remnant that is considered for preoperative biliary drainage in patients with HCCA. Interventional access to liver segments planned for resection usually should be avoided to minimize risk of cholangitis. Endoscopic drainage as well as percutaneous transhepatic biliary drainage (PTBD) are technically much more difficult for HCCA than for distal malignant biliary strictures. Therefore, they should be performed in high-volume centers with a multidisciplinary hepatobiliary team [6]. Percutaneous access should be promptly available in case of failed or incomplete endoscopic drainage.

Comparative studies on endoscopic versus percutaneous biliary drainage of hilar obstruction show conflicting results. Two meta-analyses of up to four retrospective non-randomized studies reported a similar or higher procedure-related morbid-

ity for ERCP versus PTBD [8, 9]. On the other hand, a more recent, retrospective study found that major postoperative morbidity was more frequent after percutaneous versus endoscopic drainage before major hepatic resection [10]. However, it should considered that only 30 patients were exclusively managed with endoscopic biliary drainage and 141 of 171 patients underwent at least one PTBD. There is only one multicenter, randomized controlled trial (RCT) that compared endoscopic versus percutaneous biliary drainage in patients with resectable HCCA [11]. Patients who require major liver resection and who had biliary obstruction of the future liver remnant (defined as a bilirubin concentration > 2.9 mg/dL) were randomly assigned (1:1) to receive endoscopic biliary drainage or PTBD. The primary outcome was the number of severe complications between randomization and surgery in the intention-to-treat population. The study was prematurely closed because of higher mortality in the PTBD group (41 % of 27 patients) than in the endoscopic biliary drainage group (11 % of 27 patients) with a relative risk of 3.7 ($P = 0.03$). The rate of patients who required additional PTBD after endoscopic biliary drainage was 56 %.

In this issue of the journal, Ba et al. report on a retrospective cohort study in 180 patients with HCCA (bismuth type II, III and IV) who underwent endoscopic (n = 99) or percutaneous transhepatic preoperative biliary drainage (n = 81) [12]. Only patients with risk factors for major hepatic resection were included. The authors did not report if MRCP was part of preinterventional imaging for guidance of drainage. Selection criteria for deciding between both routes were not mentioned. There were no significant differences in patient characteristics between the groups. The main goal of intervention was drainage of the future remnant liver lobe. Endoscopic drainage was done with unilateral (n = 34) or bilateral (n = 46) endoprostheses or nasobiliary drainage (n = 19). PTBD was performed with external (n = 49) or internal-external drainage (n = 32).

The results showed no significant difference in decrease in bilirubin between ERCP- and PTC-guided drainage. Compared with the PTBD group, the ERCP group had a higher incidence of procedure-related cholangitis (38 % vs. 22 %, $P = 0.028$) and pancreatitis (17 % vs. 2 %, $P = 0.001$); required more salvaged biliary drainage (18 % vs. 6 %, $P = 0.029$), and incurred higher costs ($P < 0.05$). Patients with type III and IV HC in the ERCP group had more cholangitis than those in the PTBD group (37 % vs. 18 %, $P = 0.018$). The rate of cholangitis in patients who received endoscopic bilateral biliary stents insertion was higher than in patients with unilateral stenting (50 % vs. 26 %, $P = 0.034$). PTBD internal-external drainage was associated with a higher incidence of cholangitis than was only external drainage (34 % vs. 14 %, $P = 0.034$). No significant difference in the rate of cholangitis was observed between the endoscopic unilateral stenting group and the endoscopic nasobiliary drainage group. The authors conclude that PTBD should be the preferred method for preoperative drainage in HCCA because of significantly lower rates of adverse events (AEs) and lower hospitalization costs compared to ERCP.

What does the study contribute to our current knowledge about preoperative biliary drainage in patients with HCCA and risk factors for major hepatic resection? Interpretation of the results is difficult for several reasons. The criteria for selecting patients in the ERCP or PTBD groups were not reported. ERCP may have been preferred for tissue acquisition followed by drainage. MRCP was not routinely performed for guidance of drainage. This may increase risk of cholangitis, particularly in the ERCP group because of unintended opacification of liver segments that have otherwise not to be drained. Tissue acquisition, lack of MRCP or lack of expertise could explain why bilateral stents were implanted by ERCP in 58 % of the cases. In contrast, PTBD was performed with placement of a single catheter for drainage of future remnant liver lobe in all cases. ERCP-guided bilateral stenting doubled risk of cholangitis compared to unilateral stenting. Interestingly, incidence of cholangitis after unilateral stenting was similar to that for PTCD-guided drainage (26 % vs 22 %). It also remains unclear why 18 % of patients in the ERCP group had to undergo salvage biliary drainage in spite of a high success rate and frequent placement of two or more stents.

The authors of the study discuss other limitations of their study, in particular, in terms of the retrospective and non-randomized design and lack of long-term clinical outcomes. They emphasize that a large, prospective, RCT is needed to compare ERCP- with PTC-guided preoperative drainage in patients with HCCA. However, as already mentioned, such a trial was prematurely closed because of a higher mortality in the PTBD group. It seems unlikely that another large-scale prospective controlled trial will be performed in the near future.

Conclusion

In conclusion, recommendations for indications and techniques for preoperative biliary drainage in patients with HCCA are based on a weak level of evidence. Patients should be referred to centers with expertise in hepatic surgery and endoscopic as well as radiological advanced interventional procedures. Imaging findings, tumor resectability, patient-specific risk factors and indications for tissue acquisition should be discussed by a multidisciplinary team. ERCP with or without cholangioscopy is the most accurate modality for tissue acquisition that may be considered as part of the diagnostic approach. Drainage of obstructed opacified liver segments has to be performed subsequently to reduce risk of cholangitis. If major hepatic surgery is planned without preoperative histological or cytological confirmation of HCCA, biliary drainage of the future liver remnant should be strongly considered in patients with risk factors. The route depends on local expertise in ERCP or PTBD and the ductal anatomy demonstrated by MRCP. ERCP-guided drainage seems to be as effective but safer than the percutaneous transhepatic approach according to results of the only RCT. However, important technical details should be considered to reduce risk of AEs, in particular, in terms of cholangitis. They include separate cannulation and subsequent drainage of the obstructed future liver remnant. Any approach to liver segments considered for resection should be avoided. Prophylactic antibiotic treatment is mandatory. PTBD for salvage drainage should be limited to failures of decompression of targeted liver segments or segments filled with contrast media that cannot

be drained by ERCP. The substantial risks of any preoperative biliary intervention must be carefully balanced against the potential benefits under close collaboration between experts in interventional radiology and endoscopy.

Competing interests

None

References

[1] Navaneethan U, Njei B, Lourdusamy V et al. Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis. Gastrointest Endosc 2015; 81: 168 – 176

[2] Barr Fritcher EG, Voss JS, Brankley SM et al. An optimized set of fluorescence in situ hybridization probes for detection of pancreatobiliary tract cancer in cytology brush samples. Gastroenterology 2015; 149: 1813 – 1824

[3] Navaneethan U, Hasan MK, Kommaraju K et al. Digital, single-operator cholangiopancreatoscopy in the diagnosis and management of pancreatobiliary disorders: a multicenter clinical experience (with video). Gastrointest Endosc 2016; 84: 649 – 655

[4] Tyberg A, Raijman I, Siddiqui A et al. Digital pancreaticocholangioscopy for mapping of pancreaticobiliary neoplasia: can we alter the surgical resection margin? J Clin Gastroenterol 2019; 53: 71 – 75

[5] Wronka KM, Grat M, Stypułkowski J et al. Relevance of preoperative hyperbilirubinemia in patients undergoing hepatobiliary resection for hilar cholangiocarcinoma. J Clin Med 2019; 8: 458

[6] Dumonceau JM, Tringali A, Papanikolaou IS et al. Endoscopic biliary stenting: indications, choice of stents, and results: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline – Updated October 2017. Endoscopy 2018; 50: 910 – 930

[7] Celotti A, Solaini L, Montori G et al. Preoperative biliary drainage in hilar cholangiocarcinoma: Systematic review and meta-analysis. Eur J Surg Oncol 2017; 43: 1628 – 1635

[8] Hameed A, Pang T, Chiou J et al. Percutaneous vs. endoscopic preoperative biliary drainage in hilar cholangiocarcinoma – a systematic review and meta-analysis. HPB (Oxford) 2016; 18: 400 – 410

[9] Al Mahjoub A, Menahem B, Fohlen A et al. Preoperative biliary drainage in patients with resectable perihilar cholangiocarcinoma: is percutaneous transhepatic biliary drainage safer and more effective than endoscopic biliary drainage? A meta-analysis J Vasc Intervent Radiol JVIR 2017; 28: 576 – 582

[10] Kishi Y, Shimada K, Nara S et al. The type of preoperative biliary drainage predicts short-term outcome after major hepatectomy. Langenbecks Arch Surg 2016; 401: 503 – 511

[11] Coelen RJS, Roos E, Wiggers JK et al. Endoscopic versus percutaneous biliary drainage in patients with resectable perihilar cholangiocarcinoma: a multicentre, randomised controlled trial. Lancet Gastroenterol Hepatol 2018; 3: 681 – 690

[12] Ba Y, Yue P, Leung J et al. Percutaneous transhepatic biliary drainage may be the preferred preoperative drainage method in hilar cholangiocarcinoma. Endoscopy International Open 2019; 08: E203 – E210