



Editorial on “Perihilar Cholangiocarcinoma—Novel Benchmark Values for Surgical and Oncological Outcomes From 24 Expert Centers”

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Cholangiocarcinoma (CCA) is a rare and very aggressive malignancy arising from the biliary tract. Based on the location of the tumor, CCA can be divided in intrahepatic cholangiocarcinoma (iCCA), perihilar cholangiocarcinoma (pCCA) and distal cholangiocarcinoma (dCCA). Many other characteristics differentiate these groups, including pathological features, oncological approach and surgical techniques, which in turn influences patient outcomes.

Resection of hilar CCA is one of the most technically difficult and demanding operations in hepatopancreatobiliary surgery. This stems from the sacrifice of a large amount of liver parenchyma for a small tumor located at the biliary hilum, the potential need for preoperative biliary drainage and the condition of the liver that may have cholangitis. In addition, the proximity of the tumor to the inflow vasculature of the porta hepatis may require a portal vein resection and reconstruction in addition to the bilioenteric anastomosis with the risk of leakage and stenosis of the anastomosis (1). The choice of resection sidedness typically depends on the biliary extent as dictated by the Bismuth-Corlette staging system (2) as well as vascular involvement or lobar atrophy as predicted by the Blumgart classification (3). Anatomically, the left hepatic duct has a longer extrahepatic course and the location of the left hepatic artery in the umbilical fissure typically spares it from envelopment by a hilar tumor. Conversely, the right hepatic duct is quite short and the right hepatic artery typically courses

either anterior or posterior to the biliary hilum precisely where the tumor is located. Therefore, the most common operation that is performed is a right hemi-hepatectomy or right trisectionectomy. As the left lateral section and segment can be small, many patients will require a portal vein embolization if the liver volumes are predicted to be under 30% (4). If a true Bismuth II lesion at the hilum does not invade either the right hepatic artery or portal vein, then a left hepatectomy can be performed. This can be advantageous as it leaves behind the entire right liver for the patient resulting in a less morbid operation. However, depending on the extent of the tumor, it may require separate anastomoses to the right anterior and posterior bile ducts. In addition, if the anterior ducts or artery is involved, an extended left hepatectomy may be required with future liver remnant consisting of the right posterior section which is typically >30% of the total volume.

The only chance of cure is a surgical resection, however the minority of patients are candidates. For those who are explored and resected, post operative mortality rates can vary from 3–18% (5). Additionally, the morbidity rates after hepatectomy for pCCA can be as high as 60% (6). Postoperative outcomes demonstrate heterogeneity between specialty centers and also between Western and Asian cohorts. Since pCCA is a rare cancer and limited hospitals are considered to be large volume (>10 cases per year), it is valuable to identify reference values which

enable personalized decision making for the best choice of treatment. Also it is importance to understand the differences in patient outcome between the West and East. Investigating the risk factors in each patient cohort provides insight into co-morbidity and complexity of the different populations.

Mueller *et al.* (7) published a study in *Annals of Surgery* on a benchmark approach for pCCA for surgical and oncological outcome. The paper included patients from 24 expert centers and investigated 21 clinically relevant outcome variables named “benchmarks”. The benchmarking values were defined into surgical outcome predictors such as bile leakage or liver failure after surgery and oncological outcome predictors like resection margin, amount of lymph nodes and overall survival and disease free survival.

Over a period of 5 years patients were included with locally advanced and resectable pCCA, without distant metastasis. Also, patients with major co-morbidities [cardiovascular disease, diabetes, obesity, chronic pulmonary and renal disease and American Society of Anesthesiologists (ASA) >3] were excluded in order to create a comparable group of patients. In total, 1,829 patients underwent surgical resection for pCCA of which only 39% met the benchmark criteria. More than 60% of the patients suffered from medical comorbidities or needed complex surgery with vessel reconstruction confounding the interpretation of the results.

First, the overall complication rate after surgery was 80.5%, while severe complications were reported in 58.1% of patients. The mean mortality rates was 4.7% for in hospital death and 7% at 3 months. Bile leakage of 18.4% at the anastomosis and 15.3% at the resection margin were reported. Post-operative liver failure occurred in 17.9% of patients. Readmissions were observed in 14.4% of patients of which 9% needed re-laparotomy. Median overall survival was 56 months (95% CI: 47–65) and the disease free survival was 27 months (95% CI: 24–30). The overall survival at 1, 3 and 5 years was 85.1%, 60.7% and 47.3%, respectively.

The study concluded that improved outcomes were significantly correlated with centers familiar with complex liver surgery and or transplantation. This indicates that referral of patients eligible for a resection to liver expert centers is of critical importance for patients. Comparable outcomes were shown in a Dutch national study (8).

Another important observation was a better outcome was observed in Asian centers, consistent with previous literature (9,10). Interestingly, while the benchmarking approach excluded patients in need of complex vascular

reconstructions and high morbidity, the difference in patient outcome was clearly illustrated. Patients operated in Asian centres showed a longer survival compared to the Western cohorts. The reasons behind this are a more precise surgical approach with significant longer operation time and a higher yield of lymph nodes.

The authors suggest that the results of this benchmark study can be widely implemented in clinical decision making and may serve as a reference for treatment performance in pCCA. However, since more than 60% of the patients did not meet the benchmark criteria, these results apply to a subgroup of patients. The choice for personalized treatment options will still depend on many factors as co-morbidity and the need for high complex surgery.

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Footnote

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