Impact of portal vein resection on oncologic long-term outcome in patients with hilar cholangiocarcinoma

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Background. *Liver resection (LR) for hilar cholangiocarcinoma (HCA) remains challenging because of the occurrence of unanticipated vascular and longitudinal bile duct invasion. Operative strategies to achieve negative resection margins vary, and the benefit of routine portal vein resection (PVR) is discussed controversially.*

Methods. *The data of 60 consecutive patients who underwent LR for HCA were analyzed. Twenty-one patients (35.0%) underwent LR plus PVR and 39 (65.0%) LR only. Clinicopathologic data were evaluated by the use of uni- and multivariate analyses.*

Results. *The majority of resections was performed for Bismuth–Corlette type III/IV tumors (97.3%). Hepatectomy involved trisectionectomies in 41 patients (68.3%). R1 resection margin status was identified as adverse prognosis factor for survival (hazard ratio 3.61;* P = *.003). PVR increased the perioperative morbidity (*P = *.04). The 90-day mortality rate was comparable between both groups (*P = *.70). Negative resection margin status was similar between groups (*P = *.70). The lymph node clearance was equal (*P = *.86). PVR was not associated with a beneficial long-term outcome, the 5-year and disease-free survival were comparable (LR only 17.8% vs LR plus PVR 20.0% [*P = *.89] and LR only 10.6% vs LR plus PVR 21.4% [*P = *.63]). PVR was no prognostic factor for tumor-dependent or disease-free survival (hazard ratio 0.64;* P = *.26 and hazard ratio 0.76;* P = *.47).*

Conclusion. *The presented data indicate that simultaneous PVR has no beneficial impact on oncologic long-term outcome in patients undergoing LR for HCA. Because it increases the perioperative morbidity, a recommendation for routine application cannot be given. (Surgery 2015;158:1252-60.)*

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Liver resection (LR) is the only curative treatment for hilar cholangiocarcinoma (HCA). The surgical management of HCA has evolved drastically.[1,2] Nowadays, hepatectomy combined with extrahepatic bile duct resection is the standard treatment in tertiary centers because it improves the rates of radical resections and shows clear impact on the oncologic long-term survival.[3-6] The rate of advanced HCA with Bismuth type III or IV tumors in previous studies was varied greatly, between 31 and 100%[7-12]; however, recurrence rates up to 75% illustrate the need to obtain clear resection margins.[13]

Because the special tumor biology with longitudinal intra-ductal tumor extension and the risk of vascular encasement, the achievement of negative resection margins remains challenging. Different strategies regarding the extent of LR have been advocated.[13] The role of simultaneous portal vein resection (PVR) is source of a heated debate. A recent multi-institutional study reported on microscopic portal vein involvement in 32% of patients and direct invasion of the main portal vein in 11%.[10] Although some centers advocate a PVR as standard for a no-touch resection technique in all

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patients, others recommend it only when it is unavoidable to achieve negative resection margins.[10,14-17] Conflicting results regarding the risk of perioperative morbidity and mortality caused by PVR have been reported. Information regarding the effect of a simultaneous PVR on the oncologic long-term outcome is heterogeneous.[14,18-22] Our aim was to determine the influence of PVR on perioperative and oncologic long-term outcome.

METHODS

Patients. All patients who underwent LR in addition to extrahepatic bile duct resection and regional lymphadenectomy for a histologically confirmed HCA between 2001 and 2012 were identified from a prospectively collected database. Patients with intrahepatic cholangiocarcinoma, distal cholangiocarcinoma, and/or patients with concomitant extrahepatic disease were excluded. Informed consent was obtained before operative treatment. Data collection and analysis were performed according to the Declaration of Helsinki. Preoperative assessment comprised clinical evaluation and contrast-enhanced angio-computed tomography scanning of thorax and abdomen and a magnetic resonance cholangiopancreatography. Endoscopic retrograde cholangiopancreatography with biliary drainage procedures was performed in most patients. Percutaneous transhepatic drainage of the biliary tree was performed on the side of the future liver remnant in patients with signs of cholangitis or malnutrition, marginal performance status, or when a previously inserted drain proved to be inadequate, ie, the level of serum bilirubin had to be $\leq$ 14 mg/dL before LR.

The type of LR to be performed was determined after abdominal exploration. The proximal bile duct was resected en bloc with the liver. The decision for PVR was based on both radiomorphologic evidence of tumor infiltration, which comprised a minority of patients ($n = 3$) or suspected intraoperative invasion of the portal vein. PVR was performed with either wedge resection or end-to-end anastomosis. Transection of the liver parenchyma was performed as previously described.[23] The bilioenteric continuity was re-established with an anastomosis of the draining bile duct(s) of the remnant liver with a Roux-en-Y jejunal limb without biliary drains. Portal vein embolization was performed in three patients of the study cohort ($n = 1$ in the LR only group and $n = 2$ in the LR plus PVR group). All of them underwent embolization of the right portal vein.

In summary of the currently available data, the use of adjuvant chemotherapy (cisplatin/gemcitabine) is considered in case of lymph node metastases (N1). On the basis of individual board decisions radiotherapy is considered for tumors with microscopically invaded resection margins (R1). Adjuvant chemotherapy was performed in 2 patients and adjuvant radiochemotherapy in 5 patients with R1 resection; however, this procedure was not routine. Operative complications were graded according to Clavien–Dindo classification and postoperative liver failure, hemorrhage, and bile leakage as previously described.[24-27] Postoperative liver failure was defined as the impaired ability of the liver to maintain its synthetic, excretory, and detoxifying functions, which are characterized by an increased international normalized ratio and concomitant hyperbilirubinemia (according to the normal limits of the local laboratory) on or after postoperative day 5. Posthepatectomy hemorrhage is defined as a decrease in hemoglobin level >3 g/dL postoperatively compared with the postoperative baseline level and/or any postoperative transfusion of packed red blood cells for a decreasing hemoglobin and/or the need for radiologic intervention (such as embolization) and/or relaparotomy to stop bleeding. Postoperative bile leakage was defined as bilirubin concentration in the drain fluid at least 3 times the serum bilirubin concentration on or after postoperative day 3 or as the need for radiologic or operative intervention resulting from biliary collections or bile peritonitis. Vascular invasion is classified as macrovascular, which is grossly recognizable (in large to medium vessels), or microvascular, which only is identifiable by microscopic observation (in small vessels in portal tracts, central veins in noncancerous liver tissue, and venous vessels in the tumor capsule).

Statistical analysis. SAS software (Release 9.1, SAS Institute, Inc, Cary, NC) was used for statistical analysis. The quantitative variables were expressed as median with interquartile range (IQR) or range. Odds ratios with the corresponding 95% confidence intervals were given. Outcome parameters were overall survival (data presented excluding the perioperative deaths) and disease-free survival (DFS) rates from date of LR. Survival rates and median survival times were calculated by the Kaplan–Meier estimate. All recurrences and tumor-related deaths were included as an event in the DFS analysis. The 1-, 3-, and 5-year survival rates are presented. The log-rank test was performed to compare survival curves. Patients alive at the last follow-up were censored, as were patients lost to follow-up after LR. To identify prognostic factors for survival and DFS, uni- and multivariate Cox regression analyses were performed. Hazard ratios with the corresponding 95% confidence intervals were presented.