Postoperative Liver Failure Risk Score: Identifying Patients with Resectable Perihilar Cholangiocarcinoma Who Can Benefit from Portal Vein Embolization

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BACKGROUND: Major liver resection for perihilar cholangiocarcinoma (PHC) is associated with a 22% to 33% postoperative liver failure incidence. The aim of this study was analyze the predictive value of future liver remnant (FLR) volume for postoperative liver failure after resection for PHC and to develop a risk score to improve patient selection for portal vein embolization.

STUDY DESIGN: A consecutive series of 217 patients underwent major liver resection for PHC between 1997 and 2014 at 2 Western centers; FLR volumes were calculated with CT volumetry; other variables included jaundice at presentation, immediate preoperative bilirubin, and preoperative cholangitis. The FLR volume was categorized as <30%, 30% to 45%, or >45%. A risk score for postoperative liver failure (grade B/C according to the International Study Group of Liver Surgery criteria) was developed using multivariable logistic regression with 5 predefined variables.

RESULTS: Postoperative liver failure incidence was 24% and liver failure-related mortality was 12%. Risk factors for liver failure were FLR volume <30% (odds ratio 4.2; 95% CI 1.77 to 10.3) and FLR volume 30% to 45% (odds ratio 1.4; 95% CI 10.6 to 3.4). In addition, jaundice at presentation (odds ratio 3.1; 95% CI 1.1 to 9.0), immediate preoperative bilirubin >50 μmol/L (>2.9 mg/dL) (odds ratio 4.3; 95% CI 1.7 to 10.7), and preoperative cholangitis (odds ratio 3.4; 95% CI 1.6 to 7.4) were risk factors for liver failure. These variables were included in a risk score that showed good discrimination (area under the curve 0.79; 95% CI 0.72 to 0.86) and ranking patients in 3 risk sub-groups with predicted liver failure incidence of 4%, 14%, and 44%.

CONCLUSIONS: The selection of patients for portal vein embolization using only liver volume is insufficient, considering the other predictors of liver failure in PHC patients. The proposed risk score can be used for selection of patients for portal vein embolization, for adequate patient counseling, and identification of other modifiable risk factors besides liver volume. (J Am Coll Surg 2017;225:387−394.

Radical resection is the preferred treatment for patients with perihilar cholangiocarcinoma (PHC). It often necessitates combined liver and biliary resection to obtain tumor-free margins.[1] Patients with PHC usually have obstructive cholestasis, and ultimately jaundice, due to the location of the tumor in the liver hilum.[2] The obstructive cholestasis impairs the regenerative capacity of the liver post-resection, which increases surgical risk, especially when the future liver remnant (FLR) is small.[3,4]

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Abbreviations and Acronyms

AUC = area under the curve
FLR = future liver remnant
FLRV = future liver remnant volume
PHC = perihilar cholangiocarcinoma
PHLF = post-hepatectomy liver failure
PVE = portal vein embolization

Preoperative biliary drainage is therefore used commonly, with the aim to decrease cholestasis and improve postoperative outcomes.[5]

Despite preoperative biliary drainage, liver failure and mortality rates after liver resection for PHC remain substantial. Mortality rates range from 5% to 18% in Western series[6,7] and post-hepatectomy liver failure (PHLF) is common, with a reported incidence of 22% to 33% and high mortality rates of 52% to 68%.[7-9] Strategies to increase FLR volume (FLRV) are expected to decrease the rate of PHLF and postoperative mortality. The current reference standard for increasing FLRV is preoperative portal vein embolization (PVE), as introduced in 1984[10] and used successfully in patients with PHC.[11]

Notably, the application of preoperative PVE in patients with resectable PHC differs greatly around the world. Portal vein embolization is reported sparsely in Western series[4,7,8] compared with application in up to 60% of patients in the largest series of PHC from Japan including 585 patients.[9] Most centers use a minimum FLRV as indication for PVE. Among several potential cutoff values, an FLRV <40% has gained most support among surgeons as an indication for PVE.[12] Despite this recommendation, evidence for an FLRV cutoff value specifically for PHC is lacking. Recent studies have shown that the risks for PHLF and mortality in patients with PHC are multifactorial,[4,7,8] rendering the value of a single binary cutoff to indicate PVE as uncertain. We aimed to examine the influence of FLRV on the incidence of PHLF in patients who underwent major liver resection for suspected PHC without PVE. The objective of this study was to determine which patients with resectable PHC have an elevated risk of PHLF and can benefit from PVE.

METHODS

Patient selection

All consecutive patients who underwent major liver resection (≥3 Couinaud liver segments) for suspected PHC between 1997 and 2014 at the Memorial Sloan Kettering Cancer Center in New York or the Academic Medical Center in Amsterdam were included. Suspected PHC was defined as a biliary stricture with malignant appearance between the segmental bile ducts and cystic duct. Patients who underwent PVE before liver resection were excluded. Patients were also excluded if no adequate preoperative CT or MRI was available that permitted FLR volumetry analysis. Patient management and workup have been described in detail previously.[4,7,13] The need for ethical approval and need for individual informed consent was waived by the Institutional Medical Ethics Committee.

Study variables

Total liver volume and FLRV were determined using Mx-View, version 3.52 (Philips Medical Systems) at Academic Medical Center in Amsterdam and Scout, version 1.5.1.1 (Pathfinder Technologies) at Memorial Sloan Kettering Cancer Center. All volumetric measurements were recalculated when the resection performed did not correspond to the preoperatively anticipated procedure. The FLRV was calculated by dividing the volume of the FLR by total liver volume and multiplying by 100%.

Preoperative cholangitis was considered present if, at any time in the preoperative course (before drainage, after drainage, or present at the time of operation), the patient had an episode of fever, abdominal symptoms, and leucocytosis requiring (additional) biliary drainage, as defined in clinical trials.[14,15]

Post-hepatectomy liver failure was defined, scored, and graded according to the International Study Group of Liver Surgery criteria.[16] Only grades B and C were considered as clinically relevant and scored. Biliary leakage[17] and hemorrhage[18] were defined and graded by the respective International Study Group of Liver Surgery criteria.

Statistical analysis

Categorical variables were analyzed using Fisher's exact or chi-square tests. Numerical variables were analyzed using Mann-Whitney U tests. The predictive value of FLRV for PHLF was determined using receiver operator characteristics curve analysis.

Univariable and multivariable analyses for PHLF were performed using binary logistic regression. The FLRV was entered as categorical variable with the categories <30%, >30% but <45%, and >45%. These values were chosen because 30% was previously suggested as the cutoff for FLRV[4] and 45% was revealed as the cutoff with a negative predictive value >90% in patients without cholangitis. For multivariable analysis, all predictors at univariable analysis with a p value ≤ 0.20 were included with backward selection. As demonstrated previously for mortality, there was no significant center-dependent difference in the current analyses and therefore no inter-center variable was included in the analyses.[4]