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Risk assessment for liver resection

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ABSTRACT

Background: In recent years, the profile for patients undergoing complex liver resections has changed, with mortality rates remaining generally stable. With these factors in mind, the objective of this study was to evaluate the variables associated with surgical outcomes after hepatectomy and identify groups at high risk for postoperative mortality.
Methods: The records of 1,796 patients who underwent liver resection of more than one liver segment at the Department of General and Transplantation Surgery, University Hospital Heidelberg, Germany, were analyzed. The primary end point was a 90-day in-hospital mortality. Logistic regression analyses were performed to identify risk factors associated with mortality. A risk score was created in accordance with weighted points based on the odds ratios obtained from multivariate logistic regression analyses. External validation of the score was performed, using data derived from 281 patients at the board-certified center for liver surgery in Karlsruhe, Germany.
Results: The overall patient morbidity rate (Clavien-Dindo Grade II or greater) was 32%. The 30- and 90-day mortality rates were 3.0% and 4.5%, respectively. In multivariate analysis, factors independently associated with risk for 90-day in-hospital mortality were age ≥60 years (OR 3.71), ASA classification III (OR 2.94), ASA IV (15.66), perihilar cholangiocarcinoma (OR 5.65), intrahepatic cholangiocarcinoma (OR 3.08), INR ≥ 1.1 (OR 2.43), g-GT ≥ 60 U/L (OR 2.86), platelet count ≤ 120/nL (OR 5.52), creatinine ≥ 2 mg/dL (OR 9.85), and right trisectionectomy (OR 2.88). The 90-day mortality-risk score that was created based on these factors effectively stratified patients into very low risk (0–1 points, 0.2% mortality rate in 662 patients), low risk (2–3 points, 2.9% mortality rate in 769 patients), medium risk (4–5 points, 14.7% mortality rate in 232 patients), and high risk (≥6 points, 33% mortality rate in 57 patients) groups ($P < .0001$). As a performance metric, the C-index for the proposed risk score for 90-day mortality was 0.86; whereas external validation revealed that this C-index was 0.89 ($P = .0002$).
Conclusion: Based on patient-related factors and procedure-specific variables, the proposed preoperative-risk score can be used to identify high-risk patients to determine 90-day mortality after liver resection.

Introduction

Given that the surgical indications for liver resection have expanded in recent years, patient profiles have been changing substantially. Simultaneously, operation safety and efficacy have seen notable improvements.[1–3] Major liver resection with concomitant biliary or vascular reconstruction has become a standard operative procedure in most tertiary centers and has been incorporated as part of a wider, multidisciplinary approach to treatment.[4,5] Quicker response rates in neoadjuvant therapies and the possibility to induce hypertrophy in the future liver remnants both mean that surgeons are confronted with older patients who meet the criteria for operative intervention, more comorbidities, and clinically important pathologic changes in the underlying liver parenchyma.[6–8] As a result, the complexity of liver surgery has generally increased throughout the years. When it comes to the ever-expanding indications for operative intervention, the most important issue facing surgeons today is patient safety. Mortality after liver resection is still far from ideal,[9] hence the need for surgeons to identify high-risk patients and to provide the appropriate counselling regarding the risks associated with the planned procedure. An accurate assessment of the safety of liver surgery may best be provided when objective outcome parameters from large data sets are analyzed. The 90-day mortality rate has now become the standard metric for outcome after liver resection.[10] As such, the aim of the current

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study was to identify patient-related factors and procedure-specific variables preoperatively that have direct influence on the perioperative outcome, as well as to establish a prognostic risk score for mortality after hepatectomy.

Methods

This analysis is focused on hepatectomy procedures performed between 2001 and 2013 at the Department of General and Transplantation Surgery, University Hospital Heidelberg, Germany. The institutional liver resection database contains anonymous information for about 2,317 cases, which represented more than 99% of all liver resections performed in the department. Patients who underwent liver resection for hepatobiliary trauma, as well as after liver transplantation, and patients who underwent resections in conjunction with other operations (such as pancreatoduodenectomy; laparoscopic resections; or the unroofing of simple or parasitic cysts, cystectomy, and necrosectomy) were excluded from the analysis. Resections performed in patients younger than 18 years of age were also excluded.

External validation was performed using data obtained from 281 patients who had undergone liver resection at the Städtisches Klinikum in Karlsruhe, Germany. The institution is a board-certified center that operates within the guidelines set by the German Society of General and Visceral Surgery (Supplement 1). Informed consent was obtained from patients who served as subjects of the investigation, and the study was approved by the ethical committee of both institutions.

End points

The primary end points of this analysis were 30-day mortality and 90-day in-hospital mortality. The 30- and 90-day mortality included all patient deaths that occurred within the hospitalization period (regardless of the duration of hospital stay), as well as all deaths that occurred after hospital discharge (up to 30 days postoperatively).

Statistical analysis

SAS software (Release 9.4, SAS Institute, Cary, NC, USA) was used for statistical data analysis. Categorical parameters were presented as absolute and relative frequencies. Differences among the subgroups of patients were analyzed using Fisher exact test. Continuous parameters were expressed as the median, with the interquartile range (IQR) or the mean with the standard deviation (SD), depending on the distribution of the data. With respect to the continuous parameters, comparisons among the subgroups of patients were performed using the Mann-Whitney *U* test. Logistic regression analyses were performed to identify the risk factors associated with 90-day mortality. The final logistic model for 90-day mortality was developed using backward selection, with a *P* value of less than .05 for inclusion. Odds ratios (ORs) with their corresponding 95% confidence intervals (CIs) are presented here. The receiver operating characteristic (ROC) curve was computed and the area under the curve (known as the C-index) was calculated to determine discriminations in the final logistic model. Predictive factors that had been identified in the multivariate analysis were selected for inclusion in a risk model based on the OR of these predictive factors. The resulting risk points were used to categorize patients into four groups: very low risk (0–1 point), low risk (2–3 points), medium risk (4–5 points), and high risk (>6 points). The 90-day mortality rates for each risk group are presented here. As a performance metric, the C-index for the ROC curve obtained from the risk points used to determine 90-day mortality was computed.

To conduct an external validation based on the data set obtained from Karlsruhe, the risk points for each patient were determined, and the 90-day mortality rates for each risk group were computed. The corresponding ROC curve with its C-index was calculated. Two-sided *P* values of less than .05 were considered statistically significant.

Results

Patient characteristics and risk profile

The median age of the study population was 61 years (IQR: 50.8 68.6 years), of whom 55.6% ($n = 999$) were male. The American Society of Anesthesiologists (ASA) classifications of I and II were determined in 57.2% ($n = 948$) of cases and classifications III to V were found in 47.3% ($n = 848$) of cases. A body mass index (BMI) of more than 30 was present in 11.9% ($n = 214$) of cases; whereas preoperative weight loss greater than 10% had occurred in 3.8% ($n = 69$). Alcohol abuse was noted in 9.6% ($n = 172$) of patients. The three most common, pre-existing comorbidities were cardiac disease (19.3%, $n = 346$), diabetes (12.1%, $n = 217$), and liver cirrhosis (7.0%, $n = 126$); whereas the three most common malignant primary diagnoses were colorectal liver metastases (37.5%, $n = 674$), noncolorectal liver metastases (17.8%, $n = 320$), and hepatocellular carcinoma (12.3%, $n = 221$). Benign lesions were resected in 10.1% ($n = 181$) of cases. The risk profile for the study population is presented in Table 1.

Hepatectomy and postoperative outcome

All hepatectomy procedures are presented in Table 2. Both left and right trisectionectomy were associated with greater 90-day mortality rates; whereas medial segmentectomy and resection of one or two segments had lesser mortality rates. A total of 109 patients (8.9%) underwent re-operation within 30 days. The most common operative-related complication was biloma (8.7%, $n = 156$); whereas the most common nonsurgical complication was pleural effusion (6.5%, $n = 117$). Complications that were classified as Clavien-Dindo Grade IIIa or greater occurred in 13.5% ($n = 241$) of cases. The overall morbidity rate of complications with a Clavien-Dindo Grade II classification or greater was 32% ($n = 575$). The incidence rates for major morbidities are presented in Table 3.

Hospital stay and mortality rates

The median duration of hospital stay was 10 days (IQR 7, 16 days). A total of 57% ($n = 1{,}034$) of all patients were admitted to the ICU with a median duration of stay of 1 day (IQR 1–2 days). The median duration of stay in the ICU and in the intermediate care unit (IMC) for those patients who died within the first 30 days was prolonged to 14 days in the 30-day population and to 16 days in the patients who died within the first 90 days. Admission rates to the ICU or the IMC and the durations are presented in Table 4. The overall 30-day mortality rate was 3.0% ($n = 54$), and the 90-day mortality rate was 5% ($n = 81$).

Analysis of predictive factors for postoperative mortality

Multivariate analysis revealed that for patients older than 60 years of age (OR 3.71), ASA classification III/IV (OR 15.66), intrahepatic cholangiocarcinoma (OR 3.08), perihilar cholangiocarcinoma (OR 5.65), right trisectionectomy (OR 2.88), international normalized ratio (INR) $\geq$ 1.1 (OR 2.43), g-GT $\geq$ 60 U/L (OR 2.86), platelet count $\leq$ 120/nL (OR 5.52), and creatinine levels $<$ 2 mg/dL (OR