Hepatic Parenchymal Preservation Surgery: Decreasing Morbidity and Mortality Rates in 4,152 Resections for Malignancy

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BACKGROUND: Liver resection is used to treat primary and secondary malignancies. Historically, these procedures were associated with significant complications, which may affect cancer-specific outcomes. This study analyzed the changes in morbidity and mortality after hepatic resection over time.

STUDY DESIGN: Records of all patients undergoing liver resection for a malignant diagnosis from 1993 to 2012 at Memorial Sloan Kettering were analyzed. Patients were divided into early (1993 to 1999), middle (2000 to 2006), and recent (2007 to 2012) eras. Major hepatectomy was defined as resection of 3 or more segments. Univariate and multivariate analyses were made with *t*-tests or Mann-Whitney tests.

RESULTS: There were 3,875 patients who underwent 4,152 resections for malignancy. The most common diagnosis was metastatic colorectal cancer ($n = 2,476$, 64% of patients). Over the study period, 90-day mortality rate decreased from 5% to 1.6% ($p < 0.001$). Perioperative morbidity decreased from 53% to 20% ($p < 0.001$). The percentage of major hepatectomies decreased from 66% to 36% ($p < 0.001$). The rate of perioperative transfusion decreased from 51% to 21% ($p < 0.001$). The spectrum of perioperative morbidity changed markedly over time, with abdominal infections (43% of complications) overtaking cardiopulmonary complications (22% of complications). Peak postoperative bilirubin (odds ratio [OR] 1.1, $p < 0.001$), blood loss (OR 1.5, $p = 0.001$), major hepatectomy (OR 1.3, $p = 0.031$), and concurrent partial colectomy (OR 2.4, $p < 0.001$) were independent predictors of perioperative morbidity. The mortality associated with trisectionectomy (6%) and right hepatectomy (3%) remained unchanged over time.

CONCLUSIONS: Morbidity and mortality rates after partial hepatectomy for cancer have decreased substantially as the major hepatectomy rate has dropped. Encouraging parenchymal preservation and preventing abdominal infections are vital for continued improvement of liver resection outcomes. (J Am Coll Surg 2015;220:471−479. © 2015 by the American College of Surgeons)

Liver resection is the most effective treatment for several malignant diseases and is used worldwide today. Historically, a major limitation of liver surgery has been the high morbidity and mortality related to blood loss and loss of functional liver. Recently, sharp reductions in perioperative mortality have been reported, from 10% in the 1980s to below 4%.[1-3] These improvements have resulted from better patient selection and perioperative management. The focus on intraoperative parenchymal preservation has led to substantial reductions in estimated blood loss (EBL), blood product transfusion, and postoperative liver failure.[4,5] This transformation in the safety profile of hepatic resection is largely responsible for its emergence as an effective cancer therapy.

However, the mortality rate for major liver resections such as right trisectionectomy remains as high as 9%.[3,6] Furthermore, there are serious complications associated

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Abbreviations and Acronyms
EBL = estimated blood loss
IQR = interquartile range
OR = odds ratio
PVE = portal vein embolization

with liver surgery, many of which are procedure-specific, but external factors play an increasingly important role. Comorbid medical conditions as well as the current trend of extensive preoperative systemic chemotherapy with its impact on perioperative outcome[7] are important examples. Continued efforts to improve perioperative morbidity rates are warranted. Also, there is evidence that perioperative morbidity is a powerful predictor and possible cause of adverse disease-specific survival.[8,9] In that light, reducing perioperative morbidity assumes even greater importance.

The type of morbidity seen after liver resection varies considerably, ranging from liver-specific, such as liver dysfunction or bile leak, to cardiopulmonary, gastrointestinal, renal, or infectious. Correcting this wide spectrum of complications is a challenge because multiple specific areas must be targeted. This report is an analysis of 4,152 hepatic resections for malignancy over 19 years at a single center, focusing on trends in perioperative outcomes variables and changes in practice.

METHODS

The liver resection database at Memorial Sloan Kettering (MSK) was queried to identify patients undergoing hepatectomy for malignancy from 1993 to 2012. The MSK Institutional Review Board provided a waiver from IRB review and HIPAA Authorization. Patients were divided into 3 groups of similar size according to time period (early [1993 to 1999], middle [2000 to 2006], and recent [2007 to 2012]).

The general approach to patients under consideration for liver resection has been previously documented.[10] Computed tomography, MR, or PET imaging were used for preoperative radiologic evaluations, and intraoperative ultrasonography was used in all cases. Portal inflow occlusion (Pringle maneuver) was used frequently, in 5- to 15-minute intervals. Control of portal, arterial, and biliary in-flow pedicles was performed extrahepatically or intrahepatically, depending on the resection planned, disease location, and surgeon preference. Low central venous pressure (<5 mmHg) was used in all cases when feasible. Parenchymal division was performed via a clamp-crushing technique with sutures or clips to control intrahepatic biliary and vascular structures; more recently, thermal bipolar devices were added. Postoperatively, patients were managed for 12 to 24 hours in the recovery room and then transferred to the surgical ward, unless clinical factors dictated a monitored setting. Red blood cell transfusions were guided by patient hemodynamic status in combination with hemoglobin level (<8 mg/dL).

Liver resections were quantified by number of segments resected using the Brisbane 2000 terminology of hepatic anatomy and resection[11]: enucleations (0), wedge resection and formal segmentectomy (1), sectionectomy (left lateral, right anterior or posterior, 2), left hepatectomy (3), right hepatectomy (4), and extended hepatectomy (5). Major hepatectomy was defined as resection of 3 or more segments. For our data, "perioperative" referred to the time period that included both operation and recovery room. Complications from 1993 to 2002 were identified retrospectively. From 2002 to 2012, complications were entered prospectively. All complications were graded using a score of 1 to 5.[12]

Complications were analyzed per patient and per resection. Major complications were defined as ≥grade 3. Liver dysfunction was defined by presence of at least 1 of the following: postoperative prolonged hyperbilirubinemia without obstruction or leak, prolonged coagulopathy, ascites (drainage >500 mL/day), or encephalopathy with hyperbilirubinemia.[5] Steatosis was defined as percentage of hepatocytes containing lipid vesicles divided by total number of hepatocytes. It was graded using the Kleiner-Brunt histologic scoring system,[13] in which moderate steatosis was defined as 5% to 33%. Mortality was determined at 90 days postprocedure.

Summary statistics are reported as median and interquartile range (IQR) for continuous variables, unless otherwise specified. Categorical variables are reported as percentages. Comparisons are made with *t*-tests or Mann-Whitney tests depending on type of distribution for continuous variables. Categorical variables are compared with chi-squared or Fisher's exact test, depending on number of observations. Multivariate analyses used logistic regression. All reported p values were 2-tailed and those ≤0.05 were considered significant. All analyses were conducted using Stata/IC 12.1 (StataCorp LP).

RESULTS

Patient demographics and pathology

There were 4,202 patients who underwent 4,480 hepatic resections for benign and malignant conditions from 1993 to 2012. Of these, 3,875 (92.2%) patients underwent 4,152 (92.7%) resections for malignancy (Table 1). The most common comorbidities were