Outcome of Right Hepatectomies in Patients Older Than 70 Years

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Hypothesis: The increasing number of elderly patients undergoing liver resections mandates updating of clinical outcomes on this specific population.

Design: Case series.

Setting: A tertiary care teaching hospital.

Patients: Twenty-three patients older than 70 years who underwent right hepatectomies (including 7 extended right hepatectomies) between January 1, 1995, and October 31, 2001 (group 1) and 99 patients younger than 70 years who underwent 64 right hepatectomies and 35 extended right hepatectomies during the same period (group 2) were included for a total sample population of 122.

Main Outcome Measures: Preoperative clinicopathological features, intraoperative factors, in-hospital mortality, postoperative complications, intensive care unit requirement, hospital stay, and course of main biochemical liver function test results of groups 1 and 2 were analyzed and compared.

Results: The 2 groups were similar for indications for surgery and the presence of underlying liver disease. Group 1 had a higher incidence of associated pulmonary diseases (21.7% vs 5%, P = .02) and patients with an American Society of Anesthesiologists score of III (ie, a patient with severe systemic disease limiting activity, but not incapacitating) (56.5% vs 26.3% of cases, P = .01). There were no differences in intraoperative requirement of packed red blood cells and in operation time. There were no in-hospital deaths in group 1; there were 2 deaths (2%) in group 2. Nine patients (39.1%) in group 1 and 32 patients (32.3%) in group 2 experienced postoperative complications (P = .53), of whom, respectively, 5 (21.7%) and 17 (17.2%) developed transient liver dysfunction (P = .56), and 4 (17.4%) and 5 (5.1%) required a supplementary intensive care unit stay (P = .06). The postoperative stay (mean [SD], 16 [14] days vs 13 [9] days, P = .88) and peak values of the aminotransferase level, total serum bilirubin level, and prothrombin time were similar in the 2 groups. The timing of the peak value of the total serum bilirubin level (mean [SD], 4.1 [4.8] days vs 2.5 [2.5] days, P = .28) and its period of normalization (mean [SD], 9.4 [10.8] days vs 6.7 [5.1] days, P = .67) were also similar for both groups. For patients with malignancies, the 3-year survival rate was 64.2% in group 1 and 53.9% in group 2 (P = .53).

Conclusion: Being older than 70 years should not be a contraindication for major hepatectomies, provided that liver cirrhosis and severe associated medical conditions are ruled out during the preoperative evaluation.

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The increasing age of patients with liver malignancies recently led several groups to specifically analyze the feasibility of hepatic resections in subjects older than 65 years. To date, sufficient evidence exists that hepatectomies can be safely performed in selected aged patients.

Regardless of the indications for surgery and the extent of planned liver resections, this population should be considered as more likely to suffer from associated diseases, such as diabetes mellitus and cardiac or pulmonary dysfunction, potentially affecting the postoperative outcome. Moreover, the amount of hepatic tissue that can be removed and the consequent capacity of regeneration are often difficult to be precisely assessed, although some recent studies have shown that aging itself does not affect liver function (as is the case with other organs) and that the grafts from donors older than 70 years can be used for liver transplantation with satisfactory results. Nevertheless, only a few reports have addressed the results of major hepatectomies in elderly patients.

A retrospective study was carried out at our institution to investigate the outcome of patients older than 70 years who underwent right hepatectomy (RH) or extended right hepatectomy (ERH) with various indications by comparing it with that obtained with the same procedures performed in subjects younger than 70 years during the same period.
From January 1, 1995, to October 31, 2001, a total of 16 RHs (removal of segments V through VIII, according to the Couinaud classification) and 7 ERHS (removal of segments V through VIII and segment IV—entirely or partially—or the whole caudate lobe) were performed in patients older than 70 years (median age, 73 years; age range, 70-78 years for group 1). The results of these operations were compared with 64 RHs and 35 ERHS performed in subjects younger than 70 years (median age, 57 years; age range, 16-68 years for group 2) in the same period. Sixteen men (69.6%) and 7 women (30.4%) composed group 1; 62 men (62.6%) and 37 women (37.4%) composed group 2. The total sample population was 122 patients.

The beginning of the study period was chosen on the basis of the standardization of surgical techniques and intraoperative care. These included a J-shaped incision as routine abdominal access, a slow and gentle hepatic dissection using Kelly forceps, with systematic ligatures of all intraparenchymal sizable vessels, close ultrasonographic guidance along the transection line, and the prevention of backflow bleeding by careful circulating volume and respiratory assistance monitoring during dissection to keep the central venous pressure as low as 5 mm Hg whenever possible.

The main indication for hepatectomy was metastases from various primary sites for groups 1 and 2. The indications are listed in Table 1.

The liver function was evaluated preoperatively by using the Child-Pugh classification and the lidocaine test in patients with underlying hepatic disease, as reported elsewhere. The presence of ascites and a lidocaine test value less than 25 µg/mL were considered an absolute contraindication for resection, as well as an abnormal total serum bilirubin (TSB) level and the presence of esophageal varices in cirrhotic subjects. One patient in group 1 and 3 in group 2 with hilar tumors causing obstructive jaundice were managed with preoperative placement of percutaneous transhepatic biliary drainage to lower the TSB level below 4 mg/dL (68 µmol/L). In cases of normal liver function, when the estimated remnant liver was judged to be less than 40% of the whole hepatic volume by computed tomographic volumetry, embolization of the right branch of the portal vein was performed 15 to 20 days before surgery. This was the case of 2 patients (both with liver metastases from colorectal cancer) in group 1 (8.7%) and 13 patients (5 with metastases from colorectal cancer, 3 with hepatocellular carcinoma [HCC] along with cirrhosis, 1 with HCC on chronic hepatitis, 3 with intrahepatic cholangiocellular carcinoma, and 1 with hilar tumor) in group 2 (13.1%).

The intraoperative vascular control was achieved either by a hemiepatic vascular occlusion inflow control of the right hepatic vein only, with or without ligature of the right hepatic vein before transection) or by Pringle maneuver (associated or not with hemiepatic vascular occlusion), or by total vascular exclusion. The main end point of the study was the analysis and comparison of the intraoperative data (ie, requirement of blood transfusions, type of vascular control, total clamping time, total operation time, need for associated procedures, and intraoperative complications), operative mortality (computed from the day of operation to the 30th postoperative day), in-hospital mortality, and postoperative complications of the 2 groups of patients. A secondary aim was the evaluation and comparison of peak values of aspartate aminotransferase, alanine aminotransferase, TSB, prothrombin activity, and activated partial thromboplastin time recorded in the first postoperative week, or later on in cases of liver failure. We also assessed and compared the timing of the peak values of TSB and prothrombin activity, and the period of postoperative normalization of the TSB level (<1.2 mg/dL [<20 µmol/L]).

Results are expressed as mean (SD) and compared with the Mann-Whitney test for continuous variables and the χ² test (or Fisher exact test, when appropriate) for categorical variables. Data were managed using an SPSS software package (SPSS Inc, Chicago, Ill). P<.05 were considered statistically significant.

### RESULTS

#### PREOPERATIVE CLINICOPATHOLOGICAL PROFILES

There were no differences between groups 1 and 2 for patients’ sex, indications for surgery, prevalence of diabetes mellitus, proportion of RHs and ERHS, and underlying liver disease. Among the associated medical conditions, there was a higher percentage of group 1 patients with some degree of respiratory dysfunction compared...
with group 2. Group 1 also showed a higher prevalence of cardiovascular diseases, although statistical significance was not reached. As a consequence, a greater proportion of older patients had an advanced American Society of Anesthesiologists (ASA) score (III) (Table 1). No specific indication for early postoperative intensive care unit (ICU) admission was posed based solely on age.

With special reference to parenchymal abnormalities, 3 patients (16.6%) of group 1 had chronic viral hepatitis with mild to moderate fibrosis, 1 (4.3%) had macrovesicular steatosis involving 10% of the hepatocytes, and 2 (82.6%) had a normal liver. In group 2, 8 patients (8.1%) had hepatitis with mild to moderate fibrosis, 2 (2%) had macrovesicular steatosis involving less than 10% of the hepatocytes, and 83 patients (83.8%) had no liver alterations.

### INTRAOPERATIVE AND POSTOPERATIVE OUTCOME FACTORS

Intraoperative and postoperative outcome factors are reported in Table 2 and Table 3. No substantial differences were found in these findings between group 1 and 2.

Most patients underwent hepatectomy with hemihepatic vascular occlusion as vascular inflow occlusion, although in some cases (with a prevalence in group 2) pedicle clamping was added or used as the sole vascular control. In a limited number of cases (1 in group 1 and 3 in group 2), total vascular exclusion was required because of neoplastic invasion of the caval wall and/or the confluence of the hepatic veins. However, a partial resection of the retrohepatic vena cava was performed in 2 patients (8.7%) in group 1 and 6 (6.1%) in group 2, whereas a partial resection of the diaphragm was needed owing to tumor infiltration in 2 (8.7%) and 17 (17.2%) cases, respectively.

In patients requiring total pedicle clamping, its mean duration was 33 minutes in group 1 and 30 minutes in group 2. Less than half the patients in both groups required intraoperative transfusions of packed red blood cells, with comparable mean amounts of infused units.

Mean operation time was 5 hours in both groups, while 1 patient (4.3%) in group 1 and 8 (8.1%) in group 2 had intraoperative complications. These consisted of bleeding, requiring transfusions of more than 1000 mL of packed red blood cells in all cases but 1 patient, in which a portal vein thrombosis misdiagnosed intraoperatively needed a second exploratory surgical procedure with successful thrombectomy on the first postoperative day.

There were no operative and in-hospital deaths in group 1; there were 2 operative deaths (2%) in group 2. In the early study period, one 65-year-old patient underwent ERH with resection of the caudate lobe for hilar tumor, without concomitant parenchymal abnormalities. She suffered from intraoperative bleeding requiring a transfusion of 1200 mL of packed red blood cells and, although the remnant left lobe of the hemiliver had been judged as giving a sufficient functional mass, she died of liver failure 18 days after being operated on. One 57-year-old patient who had undergone uneventful RH for a 14-cm HCC along with cirrhosis died on the second postoperative day owing to myocardial infarction without any other sign of organic decompensation. He had no history of cardiac disease and his preoperative cardiac profile showed no abnormality. No further in-hospital deaths occurred in group 2.

A higher number of group 1 patients were admitted to the ICU on the first and second postoperative days.

### Table 2. Intraoperative Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients Aged ≥ 70 y</th>
<th>Patients Aged &lt; 70 y</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Group 1: n = 23)</td>
<td>(Group 2: n = 99)</td>
<td></td>
</tr>
<tr>
<td>Vascular control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HH</td>
<td>18 (78.3)</td>
<td>55 (55.6)</td>
<td>.09</td>
</tr>
<tr>
<td>Pringle maneuver</td>
<td>4 (17.4)</td>
<td>41 (41.4)</td>
<td></td>
</tr>
<tr>
<td>TVE</td>
<td>1 (4.3)</td>
<td>3 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Pedicle clamping</td>
<td>33 (9) [23-45]</td>
<td>30 (19) [8-99]</td>
<td>.19</td>
</tr>
<tr>
<td>No</td>
<td>21 (91.3)</td>
<td>93 (93.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (8.7)</td>
<td>6 (6.1)</td>
<td>.64</td>
</tr>
<tr>
<td>Diaphragm involvement</td>
<td>21 (91.3)</td>
<td>82 (82.8)</td>
<td>.52</td>
</tr>
<tr>
<td></td>
<td>2 (8.7)</td>
<td>17 (17.2)</td>
<td></td>
</tr>
<tr>
<td>PRBCs transfusions</td>
<td></td>
<td></td>
<td>.85</td>
</tr>
<tr>
<td>No</td>
<td>13 (56.5)</td>
<td>58 (58.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (43.5)</td>
<td>41 (41.4)</td>
<td></td>
</tr>
<tr>
<td>Total PRBCs transfusions, mean (SD) [range], mL</td>
<td>389 (568) [0-2100]</td>
<td>323 (498) [0-3000]</td>
<td>.69</td>
</tr>
<tr>
<td>FFP transfusions</td>
<td></td>
<td></td>
<td>.47</td>
</tr>
<tr>
<td>No</td>
<td>14 (60.9)</td>
<td>68 (68.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 (39.1)</td>
<td>31 (31.3)</td>
<td></td>
</tr>
<tr>
<td>Total FFP transfusions, mean (SD) [range], mL</td>
<td>298 (372) [0-900]</td>
<td>274 (470) [0-3000]</td>
<td>.53</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>1 (4.3)</td>
<td>8 (8.1)</td>
<td>.99</td>
</tr>
<tr>
<td>Operation time, mean (SD) [range], min</td>
<td>311 (123) [180-750]</td>
<td>307 (113) [155-800]</td>
<td>.88</td>
</tr>
</tbody>
</table>

Abbreviations: FFP, fresh frozen plasma; HH, hemihepatic vascular occlusion; PRBCs, packed red blood cells; TVE, total vascular exclusion.

*Data are given as number (percentage) of patients unless otherwise indicated.
Liver dysfunction was the cause of death of 1 patient in group 2, whereas 2 patients in group 1 developed severe hepatic insufficiency requiring intensive medical treatment. One of them underwent ERH (including the caudate lobe) for metastases from colorectal cancer, and the postoperative hepatic failure was attributable to a more extended resection than planned preoperatively, in the attempt to achieve a sufficient tumor-free margin. Bile leakage from the resected surface required a reoperation, while the patient developed ascites and jaundice (peak TSB value, 16 mg/dL [273 µmol/L]), which gradually regressed. In the second patient, a 7-cm HCC was misinterpreted from the clinical history and preoperative imaging as metastases from colorectal cancer, the liver function being apparently normal. An RH was performed, as the gross aspect of liver seemed to confirm preoperative findings, even though the resected specimen showed features of chronic hepatitis with initial fibrosis. His postoperative course was characterized by transitory hyperbilirubinemia, which resolved spontaneously.

A bile leakage was the most frequent among other complications in both groups (3 and 5 cases, respectively). Two patients (8.7%) in group 1 and 3 (3%) in group 2 were reoperated on owing to complications. In group 1, one patient required hemostasis because of bleeding and an abdominal injury of the main hepatic duct during resection. The other biliostasis because of bile leakage from the cut surface of the liver. In group 2, one patient underwent thrombectomy for portal vein thrombosis (as described earlier), and 2 patients required delayed hepaticojejunostomy for accidental injury of the main hepatic duct during resection.

The mean hospital stay lasted around 2 weeks in the 2 study groups. The analysis of postoperative liver function revealed almost equal peak values of all the factors examined (aspartate aminotransferase level, alanine aminotransferase level, TSB level, prothrombin activity, and activated partial thromboplastin time).

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**Table 3. Postoperative Outcome of the 2 Study Groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients Aged ≥70 y (Group 1: n = 23)</th>
<th>Patients Aged &lt;70 y (Group 2: n = 99)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>0</td>
<td>2 (2)</td>
<td>.99</td>
</tr>
<tr>
<td>PO ICU admission</td>
<td>11 (47.8)</td>
<td>19 (19.2)</td>
<td>.004</td>
</tr>
<tr>
<td>PO ICU stay, mean (SD) [range], d</td>
<td>0.9 (1.2) [0-4]</td>
<td>0.3 (0.7) [0-4]</td>
<td>.002</td>
</tr>
<tr>
<td>PO complications</td>
<td>9 (39.1)</td>
<td>32 (32.3)</td>
<td>.53</td>
</tr>
<tr>
<td>Liver dysfunction</td>
<td>5 (21.7)</td>
<td>17 (17.2)</td>
<td>.56</td>
</tr>
<tr>
<td>PO TSB level &gt;5 mg/dL (&gt;85 µmol/L)</td>
<td>4 (17.4)</td>
<td>14 (14.1)</td>
<td>.74</td>
</tr>
</tbody>
</table>

Abbreviations: ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ellipses, not applicable; ICU, intensive care unit; PO, postoperative; TSB, total serum bilirubin.

SI conversion factors: To convert total serum bilirubin level to micromoles per liter multiply by 17.1.

*Data are given as number (percentage) of patients unless otherwise indicated.
Postoperative TSB and prothrombin activity values peaked within similar intervals in the 2 groups (group 1, 4.1 and 2.5 days, respectively; and group 2, 3.1 and 2.9 days, respectively). The period required for normalization of postoperative TSB values, although slightly longer for patients in group 1 (9.4 vs 6.7 days), did not significantly differ.

All patients carrying benign liver diseases are alive. There were no significant differences in 1- and 3-year survival rates between patients of groups 1 and 2 with malignant tumors (84.4% vs 82.2%, and 64.2% vs 53.9%, respectively; \( P = .53 \)).

The background allowing us to conduct the present study was the increasing age of patients undergoing liver resections for malignancies worldwide and the presumable high volume of elderly patients who will be evaluated for hepatectomies in our institution in the near future, given the progressive increase of age in recent years (Figure).

From our results, we could assume that advanced age itself should not be a contraindication for major hepatectomies, even in selected patients with hepatic alterations and/or carrying mild-degree-associated medical conditions. We demonstrated that the outcome of RHs and ERHs in patients older than 70 years was comparable to that of a younger population with similar indications for resection in the same period.

The 2 study groups were not different for any of the examined intraoperative factors, ie, blood and plasma consumption, duration of the operation, total clamping time, necessity of resecting the caval wall and/or a portion of the diaphragm, and intraoperative complications, which indicated a comparable complexity of the surgical procedure. The main issue, however, was the low perioperative mortality rate (1.6%), which was absent in elderly subjects, and the reduced incidence of postoperative complications, similar to (if not lower than) that reported in studies considering whichever type of resection and patients unselected for age.1-13,20

Several groups have investigated the feasibility of liver resections in patients older than 65 years, but only very recently have some results proved satisfactory, with an operative mortality rate less than 5%. Indeed, the experience in the late 1980s and early 1990s showed an operative mortality for all types of hepatectomy ranging from 6% to 40% in elderly populations.1,3 Excellent results in terms of operative deaths (not exceeding 5%) and complications (<30%) have been described by some subsequent studies,6,7,9,11,13 but most of them included different surgical procedures (ie, minor and major hepatectomies) and different percentages of patients with cirrhosis. Only 1 study reported no operative mortality in a series of octogenarians who underwent liver resections for HCC.13 In fact, advanced age still represents a major negative factor for the early outcome,10,12 with an operative mortality rate of up to 42%, in most cases attributable to liver failure in patients with cirrhosis.8

With the exception of 1 recent study,13 where 2 homogeneous groups of patients (>65 years or <40 years) with healthy livers undergoing RH were matched to define the selection criteria for elderly candidates for major hepatectomies, the previous reports were not comparable to the present one, solely addressing resections for HCC,1,2,3,6,8 or including all types of hepatectomies.3,7,9,11 None of them, in particular, specifically analyzed RHs or ERHs (ideally the least tissue-sparing procedures among major hepatectomies) in subjects older than 70 years.

The key points for referring aged subjects to major liver resections are a precise identification of associated medical diseases, a correct preoperative evaluation of the liver function, an accurate estimation of the residual functional hepatic mass, and a careful balancing of postoperative fluid infusion, but no limitations should be posed based exclusively on age. The first aspect has been widely investigated by others,4,6,9,11,13,20 focusing in particular on the ASA score. It has been found not to influence the postoperative mortality in 1 report,4 while advanced ASA score emerged as one of the most reliable predictors of postoperative complications and mortality in another study.9 Some authors have considered an ASA score higher than II (ie, a patient with mild to moderate systemic disease) as a contraindication for surgery for HCC11 or for major hepatectomies.13 We did not aim to weight the ASA score as an independent prognostic factor, even though older patients had a higher incidence of ASA III in our study. Despite the higher incidence of pulmonary and cardiovascular diseases, we did not indicate a routine admission to the ICU for them in the early postoperative period, although we observed a more frequent indication for ICU stay (precautionary or owing to complications) in elderly patients. However, only one among them was intensively treated for complications due to preoperative comorbidity.

The exact definition of the ASA is highly operator-dependent, and the already reported experience of postoperative deaths for causes unrelated to surgery (ie, myocardial infarction)2,13 in subjects with an unremarkable history of cardiac or pulmonary disease suggest that this score should be applied more selectively during the evaluation of elderly patients with underlying liver disease.
This latter element would lead to the exclusion of major hepatectomies in patients with cirrhosis, and the criteria for planning an adequate extent of the resection have already been reported. Together with the common tools used to exclude portal hypertension, we have adopted the lidocaine test for the assessment of functional reserve in subjects with cirrhosis, considering the value of 25 µg/mL as the lower limit to indicate a major resection. In fact, older patients in this series had chronic hepatitis, but none had cirrhosis, while in the younger group 8 had chronic hepatitis and 6 had cirrhosis. Among patients with cirrhosis, 3 had an uneventful postoperative course, 2 developed temporary mild liver failure, and 1 died of myocardial infarction on the second postoperative day. In 2 recent French studies, the presence of underlying liver disease has been envisaged as one criterion contraindicating RH in elderly subjects, whereas grade IV fibrosis (ie, cirrhosis) has been identified as the leading cause of postoperative liver failure and mortality after major liver resection. We agree that aged patients with liver disease can undergo RH or ERH only when the liver function is fully preserved, thus ruling out overt cirrhosis, and when the ASA score is less than III. The rate of hepatic steatosis allowing safe liver surgery is not yet clearly defined, although a moderate to severe steatosis (involving >30% of the hepatocytes) seems to affect both postoperative morbidity and mortality. None of our patients had high-degree liver steatosis. However, although it is impossible to exactly predict this feature before surgery without a liver biopsy specimen, this diagnostic tool should be considered when the presence of steatosis is suggested by imaging and a major resection is planned.

The adoption of techniques such as preoperative percutaneous biliary drainage to relieve jaundice, which has been envisaged as negatively affecting the postoperative outcome, or portal vein embolization to increase the volume of the remnant liver, led us to include 3 otherwise inoperable elderly patients, thus increasing the resectability rate. Although the 2 groups of patients in our study were not categorized according to a marked difference in age, we concluded that the postoperative recovery of hepatic function, as assessed by common biochemical factors (ie, transaminase levels, TSB level, prothrombin activity, and activated partial thromboplastin time) is not strictly age related, in accord with what is expressed in previous studies. Factors other than age (ie, hepatic diseases, temporary ischemia, or remnant liver volume) play the main role, although the slightly later collocation of the postoperative peak of the level of TSB seems to support the fact that older livers probably react to injuries with a more prolonged cholestasis.

In summary, major hepatectomies are feasible procedures in patients older than 70 years who have preserved liver function and controllable medical conditions, yielding 0% operative mortality and low morbidity rates in specialized tertiary centers.

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REFERENCES