Use of Vascular Clamping in Hepatic Surgery

Lessons Learned From 1260 Liver Resections

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Hypothesis: Several techniques have been introduced to minimize intraoperative bleeding in hepatic surgery. Ischemia-reperfusion injuries and intestinal congestion are the main drawbacks of vascular clamping. We hypothesized possible negative effects on early postoperative outcomes associated with different types of vascular clamping during liver resections and evaluated how attitudes have changed in the past 20 years.

Design: Retrospective review.

Setting: Academic research institute.

Patients: Patients who underwent 1260 consecutive liver resections, 338 of them (26.8%) in patients with cirrhosis.

Main Outcome Measures: Postoperative complications and mortality were analyzed relative to liver disease, blood transfusion, vascular clamping, and type of liver resection.

Results: Vascular clamping was applied in 594 patients (47.1%). Operative mortality was 4.4% in the vascular clamping group and 2.9% in the nonclamped group, a statistically nonsignificant difference. On multivariate analysis, blood transfusion, major hepatectomies, and the presence of cirrhosis were statistically significantly associated with postoperative complications. Among the overall cohort and among patients with cirrhosis, there was statistically significantly reduced use of vascular clamping and of blood transfusion during the past 20 years. The lowest incidences of severe complications occurred among cases of continuous or hemihepatic clamping. Among 338 patients with cirrhosis, 155 (45.9%) received some type of vascular control; morbidity and mortality rates were similar in the groups with vs those without vascular control. On multivariate analysis, only blood transfusion was statistically significantly associated with postoperative morbidity. Postoperative complications were statistically significantly reduced among patients receiving intermittent compared with continuous clamping.

Conclusions: Vascular clamping can be applied without additional risk during partial hepatectomy. Intermittent or hemihepatic clamping is preferable in patients with cirrhosis.


The effect of intraoperative bleeding during liver resections on postoperative morbidity is well known. Operative mortality increases, and the long-term prognosis can be poor in patients requiring intraoperative blood transfusion during partial hepatectomy for hepatocellular carcinoma and liver metastases. Therefore, resection with minimal blood loss remains a primary objective in hepatobiliary surgery. Pringle was the first to describe occlusion of the hepatic pedicle to control liver bleeding in patients with abdominal trauma.

Several techniques for minimizing blood loss have been introduced in the past 20 years, including hemihepatic vascular occlusion, intermittent pedicle clamping, total vascular exclusion (TVE), and hepatic vascular exclusion with caval flow preservation. Each has different advantages, hemodynamic consequences, and adverse effects. However, the major concern regarding ischemia-reperfusion injuries and intestinal congestion is associated with the application of vascular clamping that may compromise liver function, especially in patients with chronic liver diseases. As a result, some authors have suggested avoiding the use of vascular control, particularly in noncirrhotic patients. Controlled studies have compared the effect of different vascular clamping
methods on postoperative morbidity, mortality, and biochemical laboratory test results. However, no clear guidelines have been reported on when it is useful to apply vascular clamping during a surgical procedure or which type of clamping to apply. Consequently, application of vascular clamping remains controversial.21

The objective of this study was to review our experience with 1260 liver resections during 20 years to evaluate whether vascular clamping may be dangerous during liver resection and in which patients compared with the nonclamping approach. We also assessed how attitudes regarding vascular control have changed during the past 2 decades and which type of vascular clamping should be selected.

METHODS

From June 1, 1985, to September 30, 2005, 1260 consecutive liver resections were performed at the Department of Surgery and Transplantation, S Orsola Hospital, University of Bologna, Bologna, Italy. In 289 laparotomies for various malignant hepatobiliary diseases during the same period, it was impossible to perform curative liver resection because of the extent of disease.

At the time of admission to the hospital, the preoperative diagnosis was metastases in 418 patients (33.2%), hepatocellular carcinoma associated with cirrhosis in 338 patients (26.8%), benign tumors in 161 patients (12.8%), hepatocellular carcinoma in 130 patients (10.3%), cholangiocarcinoma in 71 patients (5.6%), and various other diseases in the remaining 142 patients (11.3%). The diagnostic workup in all patients included chest radiograph, abdominal ultrasonography, evaluation of liver function, measurement of tumoral markers, and abdominal spiral computed tomography. Other radiologic studies and liver biopsy were performed in only selected patients.

FOLLOW-UP ENDING IN DECEMBER 2005

There were 746 male patients (59.2%) and 514 female patients (40.8%). The mean (SD) age was 57.5 (13.3) years (age range, 15-82 years). The mean (SD) number of lesions was 1.5 (1.1) (range, 1-10). The mean (SD) diameter of the largest tumor was 6.0 (4.1) cm (range, 0.4-20 cm).

The type of procedure was defined according to the terminology of hepatic anatomy and resection proposed by the International Hepato-Pancreato-Biliary Association in 2000.24 Bi-sectectomy or more was defined as major hepatectomy; sectionectomy or less was defined as minor hepatectomy. Overall, 867 minor hepatectomies (68.8%) and 393 major hepatectomies (31.2%) were performed.

SURGICAL TECHNIQUE

Our standard laparotomy for hepatobiliary surgery was a right subcostal incision extended to the xiphoid process along the midline (J-shaped incision). Extension from a left subcostal incision (Mercedes logo-shaped laparotomy) was used in less than 5% of patients in the case of large tumors located in the left hemiliver or the left caudate lobe or in patients requiring application of TVE.

After lysis of any adhesions and sectioning of the lesser omentum, the hepatoduodenal ligament was encircled with tape. Generally, a vascular clamp (eg, a Shatinsky clamp) was applied until the arterial pulse disappeared in the case of continuous clamping or in the application of intermittent clamping. If a left hepatic artery emanating from the left gastric artery was present, it was isolated and clamped using a small vascular clamp (bulldog clamp). Fifteen minutes of intermittent clamping followed by 5 minutes without clamping was our standard intermittent approach.

Hemihepatic vascular occlusion requires selective clamping of the right or left hemiliver, avoiding ischemia of the remnant hemiliver and the common hemodynamic effects of pedicle occlusion.22 The hepatoduodenal ligament was encircled for safety. Ligation of the cystic duct and cholecystectomy were performed to facilitate exposure of the right branch of the hepatic artery and the portal vein posterolaterally to the cystic duct, minimizing bile duct skeletonization and biliary complications. Bifurcation of the portal vein was approached from the right side after isolation of the right branch of the hepatic artery and any right hepatic artery. The left branch of the portal vein was approached from the left side, taking care with the small branch of the caudate lobe; at the same time, the left branch of the hepatic artery was encircled. After this, the right or left branches could be clamped when ischemia of a hemiliver was required. Application of hemihepatic clamping is particularly advisable for minor resections (sectionectomy or less).

When TVE was required, complete mobilization of the liver from its right and left coronary ligament was necessary. The inferior vena cava was completely freed from the retroperitoneum and mobilized above and below the liver. Vascular clamping was applied on the hepatic pedicle, as already described, on the infrahepatic inferior vena cava, and finally on the suprahepatic inferior vena cava. This is not tolerated in almost 5% of patients because of the hemodynamic effects. For this reason, a trial period of 5 minutes is mandatory before applying the procedure. This technique has been described elsewhere.23,26

Liver transection was accomplished by kellyclasia (crushing progressively the liver parenchyma using a small Kelly clamp to identify the vascular pedicles, which are tied and sectioned) in most cases.23 During the past 3 years, an ultrasonic suction aspirator (Cavitron [CUSA]; Valleylab, Boulder, Colorado) has also been used during major hepatectomies, with the argon beam coagulator applied at the end of the transaction on the raw cut surface to reach hemostasis (for the same purpose, hemostatic agents such as oxidized cellulose [Surgicel or Tabotamp [Johnson & Johnson, New Brunswick, New Jersey] have been applied in the past 10 years). Most surgeons in the department apply a similar technique for hepatic resection that has been previously described.23 Based on a surgeon’s experience, vascular clamping was usually applied as soon as excessive bleeding was encountered to avoid severe hypotension and reduction of hemoglobin level requiring intraoperative blood transfusion (the type of clamping is arbitrarily chosen by the surgeon). Cholecystectomy was performed routinely only in case of hemihepatic clamping to facilitate the approach to the portal and arterial branches, as well as for technical reasons when the tumor was located close to the gallbladder. No patients receiving vascular clamping experienced any complications by the absence of cholecystectomy. Blood transfusion was administered in the event of excessive intraoperative bleeding when the hemoglobin level fell below 8 g/dL (to convert hemoglobin to grams per liter, multiply by 10.0) and the hematocrit was lower than .25% (to convert hematocrit to proportion of 1.0, multiply by 0.01), or when the hemoglobin level decreased more than 30% compared with the preoperative value.

AIM OF THE STUDY

Operative data were retrospectively reviewed from a prospectively collected database to evaluate which variables affect early
postoperative outcomes; in particular, postoperative complications and mortality were analyzed relative to liver disease, blood transfusion, vascular clamping, and type of liver resection. The same variables were related to the appearance of severe complications, including persistent ascites (requiring prolonged hospitalization and intensive therapy using diuretics and albumin transfusion), hepatic failure (defined as transient jaundice with a bilirubin level exceeding 5 mg/dL [to convert bilirubin to micromoles per liter, multiply by 17.104] associated with severe alteration of coagulation factors), and transient renal failure (defined as a serum creatinine level exceeding 2 mg/dL [to convert serum creatinine to micromoles per liter, multiply by 88.4] when the preoperative level was in the normal range [≤1.2 mg/dL]). Transfusion of more than 600 mL of red blood cells was arbitrarily considered an indirect index of massive bleeding.

Operative data were also reviewed to evaluate the use of vascular clamping methods during 3 different eras (group A [1985-1992], group B [1993-1998], and group C [1999-2005]). The 3 periods were arbitrarily divided to compare similar numbers and types of liver resections; 1992 was also selected as a cutoff because of the improvements in surgical and anesthesiology techniques previously reported.27,28 The percentages of patients with cirrhosis in groups A, B, and C were not statistically significantly different (27.5%, 27.7%, and 24.8%, respectively), nor were the mean (SD) numbers of nodules (1.38 [0.7], 1.53 [1.0], and 1.56 [1.3], respectively) or the mean (SD) tumor diameters (6.3 [4.1], 6 [3.7], and 5.9 [4.3] cm, respectively). Minor resections were performed in 299, 272, and 296 patients in groups A, B, and C, respectively; major hepatectomies were performed in 138, 135, and 120 patients, respectively.

By selecting patients requiring vascular clamping, postoperative morbidity and mortality were compared on the basis of the total length of vascular clamping (using 30 and 60 minutes as arbitrary cutoffs). Furthermore, the relationships among morbidity, mortality, and blood transfusion were also evaluated based on the different types of vascular control.

A further step was to select the patients with cirrhosis (the presence of cirrhosis was confirmed by final pathologic examination of resected specimens). Morbidity, mortality, and severe complications were analyzed relative to vascular clamping, blood transfusion, and Child classification. The use of different vascular clamping methods in groups A through C was also investigated.

### Table 1. Univariate Analysis of Different Prognostic Factors on Postoperative Complications and Mortality in the Overall Cohort

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Morbidity</th>
<th>P Value</th>
<th>Mortality</th>
<th>P Value</th>
<th>Ascites</th>
<th>P Value</th>
<th>Liver Failure</th>
<th>P Value</th>
<th>Renal Failure</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>Yes (n=338)</td>
<td>138 (40.8)</td>
<td>&lt;.001</td>
<td>18 (5.3)</td>
<td>.03</td>
<td>79 (23.4)</td>
<td>&lt;.001</td>
<td>14 (4.1)</td>
<td>.09</td>
<td>10 (3.0)</td>
</tr>
<tr>
<td></td>
<td>No (n=922)</td>
<td>209 (22.7)</td>
<td></td>
<td>27 (2.9)</td>
<td></td>
<td>37 (4.0)</td>
<td></td>
<td>29 (3.1)</td>
<td></td>
<td>13 (1.4)</td>
</tr>
<tr>
<td>Resection type</td>
<td>Minor (n=887)</td>
<td>213 (24.6)</td>
<td>&lt;.001</td>
<td>19 (21.9)</td>
<td>&lt;.01</td>
<td>83 (9.6)</td>
<td>.08</td>
<td>17 (2.0)</td>
<td>&lt;.01</td>
<td>14 (1.6)</td>
</tr>
<tr>
<td></td>
<td>Major (n=393)</td>
<td>132 (33.6)</td>
<td></td>
<td>28 (6.6)</td>
<td></td>
<td>32 (8.1)</td>
<td></td>
<td>27 (6.9)</td>
<td>&lt;.01</td>
<td>8 (2.0)</td>
</tr>
<tr>
<td>Vascular clamping</td>
<td>Yes (n=594)</td>
<td>180 (30.3)</td>
<td>.03</td>
<td>26 (4.4)</td>
<td>.06</td>
<td>56 (9.4)</td>
<td>.09</td>
<td>20 (3.4)</td>
<td>.09</td>
<td>13 (2.2)</td>
</tr>
<tr>
<td></td>
<td>No (n=666)</td>
<td>166 (24.9)</td>
<td></td>
<td>19 (2.9)</td>
<td></td>
<td>60 (9.0)</td>
<td></td>
<td>23 (3.5)</td>
<td></td>
<td>10 (1.5)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>Yes (n=496)</td>
<td>203 (40.9)</td>
<td>&lt;.001</td>
<td>34 (6.9)</td>
<td>&lt;.001</td>
<td>64 (12.9)</td>
<td>&lt;.01</td>
<td>31 (6.3)</td>
<td>&lt;.001</td>
<td>14 (2.8)</td>
</tr>
<tr>
<td></td>
<td>No (n=764)</td>
<td>153 (20.0)</td>
<td></td>
<td>11 (1.4)</td>
<td></td>
<td>52 (6.8)</td>
<td></td>
<td>12 (1.6)</td>
<td></td>
<td>9 (1.2)</td>
</tr>
<tr>
<td>Blood transfusion quantity, mL</td>
<td>0-600 (n=1024)</td>
<td>232 (22.7)</td>
<td>&lt;.001</td>
<td>23 (2.2)</td>
<td>&lt;.001</td>
<td>76 (7.4)</td>
<td>&lt;.01</td>
<td>40 (16.9)</td>
<td>&lt;.01</td>
<td>13 (1.3)</td>
</tr>
<tr>
<td></td>
<td>&gt; 600 (n=236)</td>
<td>114 (48.3)</td>
<td></td>
<td>22 (9.3)</td>
<td></td>
<td>40 (16.9)</td>
<td></td>
<td>10 (4.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) unless otherwise indicated.

### STATISTICAL ANALYSIS

Operative mortality was defined as death occurring within 90 days after the surgical procedure. Survival was considered from the day of surgery to the day of death or to the most recent follow-up visit.

The results are expressed as mean (SD). The χ² test was used to compare categorical variables, and the t test was used to compare continuous variables. Differences in survival were compared using the log-rank test. Multivariate analysis using Cox proportional hazards regression model was used for the prognostic factors analyzed at the univariate analysis. P < .05 was considered statistically significant. Statistical analysis was performed using commercially available software (SPSS, version 8.0; SPSS Inc, Chicago, Illinois).

### RESULTS

Vascular clamping was applied in 594 patients (47.1%); 666 patients (52.9%) did not require any vascular control. The 2 groups were comparable in mean age (57.2 [12.9] vs 58.2 [13.7] years), mean tumor diameter (6.2 [4.1] vs 6.0 [3.9] cm), mean number of nodules (1.5 [1.1] vs 1.6 [1.2]), and mean percentage of major (32.3% vs 31.2%) vs minor (67.3% vs 68.8%) hepatectomies. There was a higher percentage of patients with cirrhosis in the clamped group compared with the nonclamped group (29.6% vs 24.3%, P < .05).

Operative mortality was 4.4% in the vascular clamping group and 2.9% in the group that did not require vascular clamping, a difference that did not reach statistical significance (Table 1). Postoperative complications occurred more frequently in the group that required vascular clamping (180 patients) compared with the group that did not require vascular clamping (166 cases) (P = .03). Operative morbidity was statistically significantly higher in cases involving blood transfusion, major hepatectomies, and patients with cirrhosis. Morbidity and mortality rates statistically significantly increased with blood
transfusion exceeding 600 mL. On multivariate analysis, blood transfusion (odds ratio, 2.54), major hepatectomies (odds ratio, 1.95), and the presence of cirrhosis (odds ratio, 3.37) were statistically significantly associated with postoperative complications ($P < .001$ for all), while vascular clamping did not show a statistically significant correlation. Postoperative ascites, liver failure, and renal failure were statistically significantly associated with blood transfusion, but they were not affected by vascular clamping. Transient liver failure was associated with the type of resection, and ascites was associated with the presence of cirrhosis.

Considering the 3 different eras, vascular clamping was applied in 52.2% of the patients in group A, 53.1% in group B, and 36.0% in group C ($P < .01$ for group A vs group C and for group B vs group C). Blood transfusion was required in 66.4% of the patients in group A, 29.1% in group B, and 24.6% in group C ($P < .01$ for group A vs group B and for group A vs group C; $P = .06$ for group B vs group C).

Vascular clamping was applied in 160 (53.5%) of minor resections in group A, 144 (52.9%) in group B, and 98 (33.1%) in group C, with a statistically significant decrease in group C ($P < .05$ for group A vs group C and for group B vs group C). In contrast, there was no difference in vascular clamping applied in cases of major resections during the 3 periods (68 [49.3%] in group A, 73 [54.0%] in group B, and 51 [42.5%] in group C).

### PATIENTS WHO REQUIRED VASCULAR CLAMPPING

We identified 594 patients who received some kind of vascular control. No difference was noted in overall postoperative morbidity and mortality between patients receiving vascular clamping for less than 30 minutes vs those receiving vascular clamping for 30 minutes or longer (3.3% and 5.7%, respectively, for <30 minutes vs 29.3% and 33.6%, respectively, for ≥30 minutes). However, compared with patients receiving vascular clamping for less than 60 minutes, there was a tendency for greater mortality among patients receiving vascular clamping for 60 minutes or longer (13.3% vs 3.7%, $P = .06$), and morbidity was statistically significantly higher in this group of patients (66.7% vs 29.4%, $P = .004$). In particular, ascites was much more frequent among patients receiving vascular clamping for 60 minutes or longer compared with those receiving vascular clamping for less than 60 minutes (46.7% vs 9.0%, $P = .001$).

Among 594 patients who received some kind of vascular control, 319 (53.7%) did not require blood transfusion. Those who did not require blood transfusion had a statistically significantly lower incidence of postoperative complications compared with those receiving blood transfusion (19.1% vs 43.3%, $P < .001$). The incidences of mortality (5.1% vs 1.6%) and postoperative ascites (14.2% vs 5.3%) were statistically significantly higher among the patients receiving blood transfusion compared with the nontransfused patients.

Among 594 patients receiving vascular control, continuous clamping was applied in 339 patients, intermittent clamping in 132 patients, hemihepatic clamping in 94 patients, and TVE in 29 patients (Table 2). The longest duration of continuous clamping was 50 minutes, and the longest duration of intermittent clamping was 99 minutes. The mean duration of vascular clamping was 29 (18) minutes. There was statistically significantly increased use of intermittent clamping during the 3 eras, and it is the most frequent means of vascular control, being applied in almost half of the cases in which vascular control is necessary. In contrast, continuous clamping, which was applied in almost 90% of patients requiring vascular control before 1993, is used in less than 20% of them. Hemichepatic clamping has been applied in a constant number of patients, varying from 22% to 33% of cases in the past 10 years. More than two-thirds of hemichepatic clamping techniques in the present series were applied in cases of 1 or 2 segmentectomies. Total vascular exclusion has been progressively applied in fewer cases and in only 2 patients in the past 3 years. Seventy-five percent of TVE techniques were applied in cases of major hepatectomies.

The highest mortality among patients receiving vascular control (6.9%) was associated with TVE. However, there was no statistically significant difference in mortality rates among the different types of vascular clamping. Postoperative complications, transient liver failure, and transient renal failure were statistically signifi-

<table>
<thead>
<tr>
<th>Table 2. Type of Vascular Clamping During 3 Eras in the Overall Cohort and in Patients With Cirrhosisa</th>
</tr>
</thead>
<tbody>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>Continuous (n = 339)</td>
</tr>
<tr>
<td>Intermittent (n = 132)</td>
</tr>
<tr>
<td>Hemihepatic (n = 94)</td>
</tr>
<tr>
<td>Total vascular exclusion (n = 29)</td>
</tr>
<tr>
<td><strong>Patients With Cirrhosis</strong></td>
</tr>
<tr>
<td>Continuous (n = 89)</td>
</tr>
<tr>
<td>Intermittent (n = 44)</td>
</tr>
<tr>
<td>Hemihepatic (n = 22)</td>
</tr>
<tr>
<td>Total vascular exclusion (n = 0)</td>
</tr>
</tbody>
</table>

a Data are given as number (percentage) unless otherwise indicated.
cantly higher in the group of patients receiving TVE compared with the other types of vascular clamping. Transient liver failure was also statistically significantly more frequent in patients receiving intermittent clamping compared with those receiving continuous or hemihepatic clamping. The lowest incidences of severe complications were in the patients receiving continuous and hemihepatic clamping. The mean numbers of blood transfusions were statistically significantly higher in patients requiring TVE and intermittent clamping. Fewer blood transfusions were required among the patients requiring continuous and hemihepatic clamping (Table 3).

**Patients with Cirrhosis**

Among 338 patients with cirrhosis (276 with Child A classification and 62 with Child B classification), 155 (45.9%) received some type of vascular control, while 183 (54.1%) did not (Table 4). The percentages of major hepatectomies were similar in the 2 groups (8% vs 7.5%), as were morbidity and mortality rates. Postoperative complications were statistically significantly more frequent in cases of major resections, in patients with Child B classification, and in patients requiring blood transfusion. On multivariate analysis, only blood transfusion (odds ratio, 2.9) was statistically significantly associated with postoperative morbidity. Operative mortality was statistically significantly related to the amount of blood transfused, occurring in 2.5% of cases if blood transfusion was 600 mL or less and occurring in 16.4% of cases if blood transfusion exceeded 600 mL. Mortality was more frequent in major hepatectomies and was slightly more frequent in patients with Child B classification, although these did not reach statistical significance.

Among patients with cirrhosis, postoperative transient liver failure occurred in 14 patients and transient renal failure occurred in 10 patients. Transient liver failure was statistically significantly more frequent in cases of massive bleeding requiring transfusion of more than 600 mL of red blood cells, and postoperative ascites was statistically significantly associated with blood transfusion. Among 14 patients in whom postoperative tran-

### Table 3. Postoperative Complications and Mortality in the Overall Cohort Based on the Type of Vascular Clamping

<table>
<thead>
<tr>
<th>Variable</th>
<th>Continuous (n=339)</th>
<th>Intermittent (n=132)</th>
<th>Hemihepatic (n=94)</th>
<th>Total Vascular Exclusion (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>16 (4.7)</td>
<td>6 (4.5)</td>
<td>2 (2.1)</td>
<td>2 (6.9)</td>
</tr>
<tr>
<td>Overall morbidity</td>
<td>100 (29.5)</td>
<td>44 (33.3)</td>
<td>22 (23.4)</td>
<td>14 (48.3)</td>
</tr>
<tr>
<td>Ascites</td>
<td>31 (9.1)</td>
<td>15 (11.4)</td>
<td>7 (7.4)</td>
<td>3 (10.3)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>4 (1.2)</td>
<td>10 (7.6)</td>
<td>1 (1.1)</td>
<td>5 (17.2)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>3 (0.9)</td>
<td>7 (5.3)</td>
<td>0</td>
<td>3 (10.3)</td>
</tr>
<tr>
<td>Blood transfusion quantity, mL</td>
<td>157 (210)c</td>
<td>326 (417)c</td>
<td>148 (199)c</td>
<td>998 (772)</td>
</tr>
</tbody>
</table>

*a Data are given as number (percentage) unless otherwise indicated.  
*b P<.05 vs each of the other types of vascular clamping.  
c P<.05 vs total vascular exclusion.

### Table 4. Univariate Analysis of Different Prognostic Factors on Postoperative Complications and Mortality in Patients With Cirrhosis

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Morbidity</th>
<th>Mortality</th>
<th>Ascites</th>
<th>Liver Failure</th>
<th>Renal Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resection type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor (n = 311)</td>
<td>122 (39.2)</td>
<td>14 (4.5)</td>
<td>.02</td>
<td>72 (23.2)</td>
<td>.04</td>
</tr>
<tr>
<td>Major (n = 27)</td>
<td>16 (59.3 )</td>
<td>4 (14.8)</td>
<td>.04</td>
<td>6 (22.2)</td>
<td>.09</td>
</tr>
<tr>
<td><strong>Vascular clamping</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n = 155)</td>
<td>67 (43.2)</td>
<td>10 (6.5)</td>
<td>.08</td>
<td>35 (22.6)</td>
<td>.09</td>
</tr>
<tr>
<td>No (n = 183)</td>
<td>71 (38.8)</td>
<td>8 (4.4)</td>
<td>.08</td>
<td>44 (24.0)</td>
<td>.09</td>
</tr>
<tr>
<td><strong>Blood transfusion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n = 116)</td>
<td>68 (58.6)</td>
<td>13 (11.2)</td>
<td>.01</td>
<td>39 (33.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No (n = 222)</td>
<td>70 (31.5)</td>
<td>5 (2.3)</td>
<td>&lt;.001</td>
<td>40 (18.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Blood transfusion quantity, mL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-600 (n = 283)</td>
<td>100 (35.3)</td>
<td>8 (2.8)</td>
<td>.02</td>
<td>56 (19.8)</td>
<td>.02</td>
</tr>
<tr>
<td>&gt;600 (n = 55)</td>
<td>38 (69.1)</td>
<td>10 (18.2)</td>
<td>&lt;.001</td>
<td>23 (41.8)</td>
<td>.02</td>
</tr>
<tr>
<td><strong>Child classification</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>A (n = 276)</td>
<td>103 (37.3)</td>
<td>13 (4.7)</td>
<td>.01</td>
<td>22 (20.7)</td>
<td>.09</td>
</tr>
<tr>
<td>B (n = 62)</td>
<td>35 (56.5)</td>
<td>5 (8.1)</td>
<td>1</td>
<td>5 (8.1)</td>
<td>.1</td>
</tr>
</tbody>
</table>

*a Data are given as number (percentage) unless otherwise indicated.
sient liver failure developed, mortality at 90 days was 64.3% (9 patients), while 1 patient underwent successful salvage liver transplantation. The remaining 4 patients recovered completely.

Among 338 patients with cirrhosis, vascular clamping was applied in 70 patients in group A, in 61 patients in group B, and in 24 patients in group C. The decrease in the application of vascular clamping during the 3 periods was statistically significant (P < .01). The need for blood transfusion statistically significantly decreased during the same periods, as the percentages of transfused patients were 82% in group A, 26.5% in group B, and 13% in group C (P < .01). The mean numbers of nodules were similar in groups A, B, and C (1.4 [0.9], 1.2 [0.8], and 1.1 [0.4], respectively), as were the mean tumor diameters (4.4 [1.8], 4.5 [2.1], and 4.2 [3.0] cm, respectively).

After 1999, only 29.6% of patients with cirrhosis required the use of vascular clamping. Among them, intermittent clamping was the most applied vascular control, with statistically significantly increased use compared with previous eras (P < .05). Total vascular exclusion was never applied in patients with cirrhosis.

The mean numbers of nodules were similar among patients receiving continuous, intermittent, and hemihepatic clamping (1.1 [0.6], 1.2 [0.7], and 1.05 [0.2], respectively). Major hepatectomies were slightly more frequent among patients receiving intermittent clamping (6 of 44 [13.6%]) compared with those receiving continuous (7 of 89 [7.9%]) and hemihepatic (2 of 22 [9.1%]) clamping.

The incidence of postoperative complications was statistically significantly reduced among patients receiving intermittent clamping compared with those receiving continuous clamping. A tendency to lower (minor incidence) complications and mortality was seen among patients receiving intermittent and hemihepatic clamping. The least need for blood transfusion was among patients receiving hemihepatic clamping (Table 5). The mean blood transfusion among nonclamped patients was 209 (423) mL.

### Table 5. Postoperative Complications and Mortality in Patients With Cirrhosis Based on the Type of Vascular Clamping

<table>
<thead>
<tr>
<th>Variable</th>
<th>Continuous (n = 89)</th>
<th>Intermittent (n = 44)</th>
<th>Hemihepatic (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>6 (6.7)</td>
<td>3 (6.6)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Overall morbidity</td>
<td>46 (51.7)</td>
<td>13 (29.5)</td>
<td>8 (36.4)</td>
</tr>
<tr>
<td>Ascites</td>
<td>23 (25.8)</td>
<td>7 (15.9)</td>
<td>5 (22.7)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>5 (5.6)</td>
<td>2 (4.5)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1 (1.1)</td>
<td>2 (4.5)</td>
<td>0</td>
</tr>
<tr>
<td>Blood transfusion quantity, mean (SD), mL</td>
<td>382 (523)</td>
<td>375 (788)</td>
<td>80 (228)*</td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) unless otherwise indicated.

COMMENT

In a large Western series of liver resections, we observed that 3 main factors are associated with postoperative mortality, namely, blood transfusion, extent of resection, and the presence of cirrhosis, but not the application of vascular clamping. The same 3 factors were associated with overall morbidity on multivariate analysis. Major complications such as ascites, transient liver failure, and transient renal failure were statistically significantly more frequent in patients receiving blood transfusion and were unrelated to vascular control in the overall cohort and in patients with cirrhosis.

Up to a limit of 600 mL of blood transfusion, the morbidity and mortality rates were acceptable and were similar to those of nontransfused patients. However, in cases of massive bleeding requiring more than 600 mL of red blood cells, postoperative mortality and severe complications were statistically significantly increased. Because we cannot change the type of resection in patients with liver tumors, we should try to reduce the need for blood transfusion (particularly by avoiding massive bleeding) to improve early postoperative outcomes.

Several factors in the past 10 years have led to a progressive decrease in morbidity and mortality associated with liver surgery, including better knowledge of liver anatomy, improvement in surgical technique, tumor and residual liver mass localization, precise preoperative evaluation of hepatic function, routine use of intraoperative hepatic ultrasonography, and introduction of new devices (such as the ultrasonic suction aspirator and the harmonic scalpel) as well as achievements in anesthesiology management, in particular hemodilution and maintenance of central venous pressure at approximately 5 cm of water to reduce backflow bleeding. As a result, there has been a progressive reduction during several decades in the use of blood transfusion and pedicle clamping in patients with healthy livers and in patients with cirrhosis. Liver resections now can be safely performed without blood transfusion and without the use of vascular clamping in more than two-thirds of cases at a tertiary referral center. This is particularly true in the case of minor hepatectomies, which have been performed without vascular clamping in more than 80% of cases in the past 4 years.

To avoid the negative effects of ischemia-reperfusion injuries, investigators have emphasized the possibility of performing most liver resections without vascular clamping, with good results in terms of morbidity, mortality, and blood transfusion. However, persistent bleeding during surgery is much less tolerated than the use of vascular clamping. Liver parenchyma, particularly in cirrhotic livers, is more tolerant to prolonged normothermic ischemia due to vascular clamping than to consequences of bleeding or blood transfusion. Although we have progressively reduced the use of vascular clamping during the past 15 years (particularly in minor resections), we reported no increased risk by using vascular clamping, while we experienced a statistically significant increase in morbidity and mortality if blood transfusion exceeded 600 mL. Therefore, during liver surgery, the use of vascular clamping and its possible consequences should always be preferred over the conse-
quences of persistent bleeding, particularly if liver resections are performed in nonspecialized centers.

The Pringle maneuver (continuous clamping), which was the first technique applied to control bleeding during liver surgery, allows continuous hepatic pedicle inflow control. In the present study among 339 patients who underwent continuous clamping (one of the largest studies reported in the literature to date), the efficacy of continuous clamping was confirmed by the least necessity for blood transfusion among the overall cohort. The incidence of postoperative complications was similar to that among nonclamped patients, as well as to that among patients receiving other types of vascular clamping (or less). The longest duration of continuous clamping was 50 minutes.

The major concern about continuous clamping is warm ischemic injury, which may be poorly tolerated in diseased livers. To reduce the effect of ischemia-reperfusion damage, intermittent clamping has been increasingly applied during the past 10 years. A statistically significant decrease in ischemic injury has been reported in patients with cirrhosis by using intermittent clamping compared with continuous clamping during liver resections. Intermittent clamping induces a lower transaminase peak than continuous clamping and is better tolerated. Consequently, the longest reported duration of intermittent clamping is 322 minutes in healthy livers and 204 minutes in patients with cirrhosis. Tolerability of the intermittent method has also been confirmed in the case of partial hepatectomy for liver transplantation from living donors.

Despite the fact that major hepatectomies were performed more frequently in our series among the group of patients with cirrhosis receiving intermittent clamping, we reported a statistically significant lower incidence of postoperative complications in this group compared with those receiving continuous clamping. We have applied this technique more in the past 10 years, and it has almost completely replaced continuous clamping in patients with cirrhosis when vascular control is required.

Similarly, we have increasingly used intermittent clamping among all patients undergoing liver resection during the past 15 years. However, based on the results of this and other studies, continuous clamping may be preferred among noncirrhotic patients up to a limit of 60 minutes, in which case there is no evidence of possible advantages of the intermittent approach vs the continuous approach and no increased risk of complications.

Makuuchi et al first reported the use of hemihepatic vascular inflow occlusion to prevent ischemia-reperfusion injury in the nonclamped hemiliver and to avoid bleeding that occurs during the declamping period by applying intermittent clamping. We use this technique almost solely in patients with cirrhosis generally requiring the resection of 1 or 2 segments. In this setting, hemihepatic clamping statistically significantly reduced bleeding and major complications compared with the other methods of vascular clamping and compared with nonclamped patients. A disadvantage is that it is technically demanding because of the complex hilar dissection. A large Japanese study and subsequently other investigators reported routine application of hemihepatic inflow occlusion in liver resections. In a recent randomized study of 80 patients, Figueras et al reported reduced ischemic injury among patients with cirrhosis by using selective vascular clamping based on the measurement of aspartate aminotransferase and alanine aminotransferase levels (although no difference in morbidity rates was found between 2 study groups). We believe that routine use of this procedure is unnecessary but that it should be included in the available options to hepatobiliary surgeons and applied in selected patients with cirrhosis.

Total vascular exclusion has been applied to prevent bleeding from venous backflow that is not controlled by hepatic pedicle clamping. It has previously been reported that TVE should be used only in elective cases. Less than 3% of patients need TVE, and it is not applied in patients with cirrhosis; during the past 5 years, it was necessary in 2 only cases. Because of the complex procedures in which TVE is usually applied, it is associated with the highest morbidity and the greatest need for blood transfusion, as reported in other series. Indications for TVE are a tumor that is invading the inferior vena cava, a tumor located in the caudate lobe with massive intraoperative bleeding uncontrolled in any other way, or a tumor with invasion of the major hepatic veins requiring vascular reconstruction, usually associated with extended heptectomy.

In conclusion, there is no current evidence to avoid the use of vascular clamping, particularly in case of major hepatectomies, to reduce intraoperative bleeding requiring massive blood transfusion, which is the major cause of postoperative morbidity and mortality. Intermittent or hemihepatic clamping is preferable in patients with cirrhosis. Only in large experienced centers may most liver resections be performed safely without vascular clamping.

Accepted for Publication: December 21, 2006.
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Financial Disclosure: None reported.

Additional Contributions: Giovanni Varotti, MD, Alessandro Cucchetti, MD, and Francesco Tuci, MD, contributed to the data collection.

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