The Impact of New Technology on Hepatic Resection for Malignancy

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Hypothesis: Relatively high morbidity rates remain problematic in hepatic resection for malignant neoplasms. Technological innovations coupled with surgical expertise can ameliorate morbidity and mortality rates.

Design: Medical records survey.

Setting: Tertiary care university hospital.

Patients: Five hundred one patients underwent liver resection at our hospital from March 1, 1988, through November 30, 1999. Three hundred twenty-one patients (64.1%) had primary carcinoma, whereas 180 (35.9%) had metastatic disease, mainly colorectal secondary disease (83.3%). Morbidity and mortality rates were compared with those of a previous series in the same setting.

Main Outcome Measures: Special attention was paid to the impact of new technology (eg, newer imaging techniques, ultrasonic aspiration, intraoperative ultrasonography, argon beam coagulation, and autotransfusion) and improved anesthetic and surgical management on mortality and morbidity rates.

Results: Five patients died after liver resection and 93 patients had various complications, representing mortality and morbidity rates of 1.0% and 18.6%, respectively. These results compare favorably with the results of a previous unpublished series (mortality, 5/55 [9.1%]; morbidity, 28/55 [50.9%]). Intraoperative ultrasonography resulted in a change in operative strategy in 7 (17.5%) of a recent group of 40 patients.

Conclusions: Morbidity after major hepatic resection for malignancy can be reduced considerably by applying newer technologies to preoperative and intraoperative decision making. Advanced technology also assists in reducing intraoperative risk by minimizing bleeding during resection of the hepatic parenchyma.

Arch Surg. 2001;136:1307-1313

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RESULTS

INTRAOPERATIVE COMPLICATIONS

Severe bleeding resulted in shock in 5 patients (1.0%) and was fatal in 1 patient (0.2%). Three other patients who underwent extended right hepatectomy had an injury of the left hepatic duct, which was repaired by the placement of a small T tube; the tube was removed 3 weeks later after cholangiography. Recovery was uneventful for all 3 patients. The rate of severe intraoperative complications was 1.6% (Table 2).

POSTOPERATIVE COMPLICATIONS

In group 1, 85 postoperative complications were encountered (a rate of 17.0%). The most severe were hepatic failure in 6 patients (1.2%), 2 of whom died; acute respiratory distress syndrome in 5 (1.0%), 1 of whom died; and myocardial infarction in 2 (0.4%), 1 of whom died. The total rate of complications was 18.6% (Table 2).
PATIENTS AND METHODS

Five hundred one patients (group 1) underwent liver resection for primary and secondary hepatic tumors at the Second Department of Surgery, Athens University, Athens, Greece, from March 1, 1988, through November 30, 1999, since one of us (J.D.P.) was appointed director of the department. Morbidity and mortality rates in group 1 were compared with those of 55 other patients (group 2) who underwent similar surgery in the same setting before 1986 and before new technological innovations were available (A.C.F. and A.A.P., unpublished data, 1999). The results were statistically analyzed using the χ² test. All surgical procedures were performed by us.

The age distribution and sex variables of the study cohort are shown in the following tabulation:

<table>
<thead>
<tr>
<th>Patient Features</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>55 (11.0)</td>
</tr>
<tr>
<td>51-65</td>
<td>301 (60.1)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>145 (28.9)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>246 (49.1)</td>
</tr>
<tr>
<td>Female</td>
<td>255 (50.9)</td>
</tr>
</tbody>
</table>

Liver malignancies were distributed almost equally between male and female patients.

Of the 501 patients in the study cohort, 321 (64.1%) underwent resection for primary tumors and 180 (35.9%) for metastases. The mean hospitalization times were 7 and 14 days for groups 1 and 2, respectively.

PREOPERATIVE EVALUATION

The clinical manifestations in the patients with liver tumors are shown in Figure 1. In addition to clinical examination, preoperative evaluation included liver function tests (Figure 2), ultrasonography, computed tomographic (CT) scan, whole-body radioisotope scanning, and, when indicated, CT portography (Figure 3) and selected angiography. More recently, helical CT scanning (Figure 4) and magnetic resonance imaging (Figure 5) have tended to be the standard preoperative imaging procedures. In nearly half (250/501) of our cases, the diagnosis was confirmed by means of CT-guided fine-needle aspiration biopsy (Figure 6). Patients with Child A cirrhosis, and Child B cirrhosis for limited excisions, were included in the study.

HEPATIC RESECTION TECHNIQUE

The most common approach was bilateral subcostal incision with an upper midline extension, when needed; a thoracic extension never proved to be necessary. The types of surgical excision are shown in the following tabulation:

<table>
<thead>
<tr>
<th>Type of Operation</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extra-anatomic resection</td>
<td>125 (25.0)</td>
</tr>
<tr>
<td>Anatomic resection</td>
<td>376 (75.0)</td>
</tr>
<tr>
<td>Segmentectomy</td>
<td>120 (24.0)</td>
</tr>
<tr>
<td>Hepatectomy</td>
<td>240 (47.9)</td>
</tr>
<tr>
<td>Right</td>
<td>194 (38.7)</td>
</tr>
<tr>
<td>Left</td>
<td>46 (9.2)</td>
</tr>
<tr>
<td>Extended right hepatectomy</td>
<td>16 (3.2)</td>
</tr>
</tbody>
</table>

In the 376 patients for whom an anatomic excision was performed, after ruling out the possibility of extrahepatic metastases, the type of hepatectomy was planned. Complete mobilization of the liver and dissection of the hepatic hilar structures were of paramount importance. The right or left hepatic vein was ligated and divided mostly extrahepatically. However, the intrahepatic approach of the hepatic vein was useful in some cases when the extrahepatic length of the vein was too short. When all relevant structures were divided, liver transection was usually performed using an ultrasonic dissection device.

MORTALITY

In group 1, 5 patients died (1.0%). We should, however, stress that in the most recent 110 patients enrolled, there have been no deaths. In group 2, 5 patients (9.1%) died within 30 days following the operation. The difference between groups was statistically significant (P<.001).

HISTOLOGICAL FINDINGS

Of the 501 liver tumors, 321 (64.1%) were primary and 180 (35.9%) were secondary. Cirrhosis was present in 201 (62.6%) patients with primary liver tumors. Of the 321 primary tumors, 261 (81.3%) were hepatocellular carcinomas; 32 (10.0%), cholangiocarcinomas; 19 (5.9%), sarcomas; and 9 (2.8%), hepatoblastomas. In 150 (83.3%) of the 180 patients with metastatic disease, the sites of the primary lesion were the colon and rectum; in 30 (16.7%), various other primary lesions, eg, breast, kidney, melanoma, leiomyosarcoma, and neuroendocrine, were involved.
ULTRASONIC SURGICAL ASPIRATOR

From January 1, 1990, through December 31, 1994, a prospective study was undertaken to evaluate the impact of an ultrasonic surgical aspirator (Cavitron, System 200; Valley Laboratories, Boulder, Colo) on perioperative blood loss. Ninety-two patients (Table 1) who underwent major liver resection were divided into the following 2 groups: 49 patients undergoing ultrasonic dissection, and 43 patients undergoing the finger-fracture method (Table 1). Median perioperative blood loss was 50% to 56% less in the ultrasonic dissection group (P<.01). Minor bleeding was stopped using fine polypropylene (Prolene) sutures or light diathermy and/or argon beam.

Only exceptionally were gross sutures used to compress the cut surface of the liver.

INTRAOPERATIVE ULTRASONOGRAPHY

This diagnostic modality is more helpful than palpation and preoperative imaging procedures in identifying lesions. In 40 patients in whom intraoperative ultrasonography (Aloka 550-1400; Mitaka-Shi, Tokyo, Japan) was used, 7 additional lesions (17.5%) were identified (Figure 7A-B). Moreover, by visualizing the vascular anatomy and its relation to the tumor (Figure 8), the surgeon is able to perform more accurate dissection.

LAPAROSCOPIC ULTRASONOGRAPHY

During the past year, we have used this diagnostic procedure in a limited number of patients with secondary liver deposits. In 3 of 11 patients, 2 to 4 additional lesions measuring 0.4 to 1.0 cm were detected; in 2 of these patients, the lesions were located in the contralateral lobe, and the patients avoided unnecessary surgery.

Curative hepatectomies were performed in 193 (60.1%) patients with primary tumors and in 120 patients (66.7%) with secondary tumors.

ANESTHETIC MANAGEMENT

Anesthetic management included general endotracheal anesthesia with controlled ventilation. Anesthesia was based on opioids (fentanyl citrate) and inhalation agents (isoflurane or sevoflurane) with an air-oxygen mixture. In addition, noninvasive monitoring by means of electrocardiography, blood pressure and temperature measurement, and pulse oximetry as well as invasive techniques for direct monitoring of arterial and central venous pressures were used. Pulmonary artery pressure was used to record a detailed hemodynamic profile for patients with limited cardiovascular reserves. Laboratory studies for the analysis of arterial blood gases and coagulation profile (platelet count, prothrombin time, partial thromboplastin time, levels of fibrinogen and ionized calcium, and thromboelastography) were performed on demand. Facilities for rapid transfusion were always available.

The maintenance of normal renal function is important. Crystalloids, dopamine hydrochloride (2-3 µg/kg per minute), and furosemide (3-10 mg/hr) were administered only if the aforementioned measures coupled with autotransfusion were inadequate in maintaining sufficient diuresis and central venous pressure equal to 8 to 10 mm Hg. Body temperature was always carefully monitored and maintained at normal levels.

Early extubation of the patient was attempted as soon as the patient was able to maintain normal blood gas levels. During the postoperative period, a transient elevation of aspartate aminotransferase, serum bilirubin, and prothrombin levels was not uncommon, but levels returned to normal within a few days.

AUTOTRANSFUSION

Of the 110 patients who underwent surgery during the last 20 months, no banked blood was used in 58 (52.7%). All of these patients donated 1 to 2 U of blood a few days before surgery. Five patients who received epoetin alfa 15 days before the operation were able to donate 3 to 5 U of blood before surgery. In cases of excessive bleeding, a cell-saver apparatus (Cell Saver 4; Haemonetics Corporation, Braintree, Mass) was applied.

Curative hepatectomies were performed in 193 (60.1%) patients with primary tumors and in 120 patients (66.7%) with secondary tumors.

Since the first reported hepatic resection a century ago,11,12 this procedure remained rare for many years.13,14 Because of a high mortality rate,15,16 hepatectomy was restricted to selected cases.

As experience and new technology contributed to improved results, hepatic resection became a common operation, and the mortality rate was reduced to less than 5%,6,9 Nonetheless, morbidity remained a problem.7,9

Innovations in technology and integral action on the part of the surgical and anesthetic teams have contributed to the achievement of better results. Morbidity and mortality rates (18.6% and 1.0%, respectively) in group 1 (patients undergoing resection during the past 14 years, when new technology was used) compared favorably with those of group 2 (patients undergoing resection before 1986) (50.9% and 9.1%, respectively).

In 2 multivariate logistic regression studies,17,18 the amount of blood loss during the operation was shown to be one of the most important factors predisposing to complications. Autotransfusion is a safe and effective method for replacing blood loss,19 and it has been used extensively in nonmalignant diseases.20 Because of concern regarding contamination with malignant cells, surgeons were reluctant to use this method in patients with tumors. It has been shown that autotransfusion is not responsible for recurrence when a cell-saver apparatus is used in patients with hepatocellular carcinoma.19,22 Autologous blood can be obtained by means of preoperative donation and/or intraoperative salvage using a cell-saver apparatus.

By using autotransfusion in our most recent 110 patients, we were able to avoid the use of banked blood in 58 patients (52.7%).

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ULTRASONIC DISSECTION ASPIRATOR

This device is designed to aspirate the hepatic parenchyma while leaving the intrahepatic blood vessels and bile ducts intact. This facilitates the ligation of any intact structure. In contrast, when using the finger-fracture technique, small vessels are torn and bleeding results. By using the ultrasonic dissection device in a group of 92 patients, blood requirements were reduced by 50% in cases of extra-anatomic excision and by 56% in anatomic excisions, compared with blood requirements when the finger-fracture technique was used.

Figure 2. Biochemical tests in patients with liver tumor. In hepatocellular carcinoma, the most common finding was elevation of the α-fetoprotein (AFP) level. AST indicates aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; Bil, bilirubin; Hb, hemoglobin; and PT, prothrombin time.

Figure 3. Computed tomographic portography shows a lesion in the right lobe.

Figure 4. Spiral computed tomography indicates a 3-cm tumor in the left hepatic lobe before (A) and after (B) intravenous contrast.

Figure 5. Magnetic resonance imaging shows a lesion in the right lobe of the liver. A, Axial T1-weighted image after intravenous injection of gadopentetic acid, dimeglumine salt (0.2 mL/kg) shows a low-signal-intensity mass. B, Axial STIR (short T1 inversion recovery) image after intravenous injection of ferumoxides (15 µmol/kg) shows a high-signal-intensity mass.
In liver surgery, continuous oozing from the capillaries of the cut surface that are too small to be ligated may occasionally pose a real problem. To control bleeding of this origin, various methods have been used. Light diathermy (Licht Koagulator LC 250; Lumed, Munich, Germany) seems to have several advantages, ie, it is cheap, effective, and easy to use. Argon laser coagulation has also been used during the past 4 years, and it appears to be an efficient device, contributing to the achievement of hemostasis while causing only moderate tissue reaction.

Intraoperative ultrasonography has been shown to be the most sensitive method of detecting hepatic metastases of colorectal cancer. Patients with colorectal cancer have occult liver metastases that are not palpable at the time of the operation, due either to their small size or to their location deep in the parenchyma. Intraoperative ultrasonography is capable of diagnosing more lesions than are preoperative imaging procedures. In 40 recent patients, 7 additional lesions (17.5%) were detected. Furthermore, ultrasonography is valuable in providing information regarding the relationship of the tumor to the portal and hepatic veins; this is extremely helpful in deciding operative strategy.

Laparoscopic liver ultrasonography seems to improve the selection process in determining candidates for surgery. In 3 of 11 recent patients, 2 to 4 more deposits were detected. In 1 case, these deposits were confirmed by means of intraoperative ultrasonography and proved histologically to be malignant. In 2 cases, the lesions were located in the contralateral lobe, thus obviating the need for laparotomy.

At present, in an otherwise healthy liver, technical problems in performing resections are rare. It has been stressed that blood loss in noncirrhotic patients undergoing hepatic resection is very low and merely accidental.

Cirrhotic patients present a serious problem, since excessive bleeding may follow hepatic resection. In addition, hepatic failure may threaten the life of a cirrhotic patient, as regeneration of a cirrhotic liver depends on the grade of the cirrhosis. In our series, cirrhosis was present in 62.6% of the group of patients with primary liver tumor; 2 potentially fatal complications of hepatic resection, ie, bleeding and hepatic failure, were related to concomitant cirrhosis. In our study cohort, 3 of 5 patients who experienced bleeding were cirrhotic, and hemorrhagic shock was the cause of death in 1 of these patients. Hepatic failure occurred in 6 cirrhotic patients, 2 of whom died. However, cirrhosis does not necessarily exclude a patient from hepatic resection. In our series,
In addition to decreasing mortality and morbidity, new technology is valuable in making hepatic resection cost-effective. The median hospital stay has been reduced from 13 to 6 days,2 and in our series from 14 to 7 days.

In our series, the following forms of new technology have helped to reduce morbidity after hepatic resection to an acceptable level:

1. Autotransfusion by means of either preoperative donation by the patient or the use of a cell-saver apparatus intraoperatively can eliminate complications due to transfusion with banked blood.

2. The use of ultrasonic dissection aspirator devices, light diathermy, and argon laser coagulation reduces blood loss and, consequently, transfusion needs.

3. The preoperative use of laparoscopic ultrasonography may reduce the rate of unnecessary surgery by detecting more inoperable lesions in cases of secondary malignant liver tumors.

4. Intraoperative ultrasonography is very helpful in deciding operative strategy in that it provides useful information vis-à-vis the real extent of the tumor margin and the relation of the tumor to the branches of the portal and hepatic veins.

We thank Dimitris Papadimitriou, biologist, for preparing the graphs used in this report.

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Table 2. Complications in Hepatic Resection

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. (%) of Cases</th>
<th>No. (%) of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding, shock</td>
<td>5 (1.0)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Injury hepatic duct</td>
<td>3 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Postoperative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>2 (0.4)</td>
<td>0</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>6 (1.2)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Bile leakage</td>
<td>11 (2.2)</td>
<td>0</td>
</tr>
<tr>
<td>Gastrointestinal tract bleeding</td>
<td>1 (0.2)</td>
<td>0</td>
</tr>
<tr>
<td>Suprahepatic collection</td>
<td>4 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Infrad hepatic abscess</td>
<td>4 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>3 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td>Infection</td>
<td>10 (2.0)</td>
<td>0</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome</td>
<td>1 (0.2)</td>
<td>0</td>
</tr>
<tr>
<td>Aspects</td>
<td>16 (3.2)</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (0.4)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Thrombosis in the inferior vena cava</td>
<td>1 (0.2)</td>
<td>0</td>
</tr>
<tr>
<td>Ileus</td>
<td>4 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>2 (0.4)</td>
<td>0</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>14 (2.8)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>93 (18.6)*</td>
<td>5 (9.1)*</td>
</tr>
<tr>
<td><strong>Group 2 total</strong></td>
<td>28/55 (50.9)</td>
<td>5 (9.1)*</td>
</tr>
</tbody>
</table>

*P<0.01, χ² test.

patients with Child A cirrhosis were included in hepatic resection, and those with Child B cirrhosis underwent minor liver resection. Nonetheless, avoidance of bleeding is of utmost importance, as it reflects the rate of complications.7,27,31 To reduce intraoperative bleeding, some investigators32-34 advocate the cross-clamping technique (the Pringle maneuver).35 However, the question of a potential ischemic injury to the cirrhotic liver remains, although it has been reported that controlled ischemia is less harmful to the cirrhotic liver than is increased blood loss.33

A careful selection of patients, strict adherence to the principles of anatomic resection of the liver, and use of special equipment all decrease the risk for intraoperative bleeding and thus improve the results of surgical treatment of malignant neoplasms of the liver.

**REFERENCES**