Simultaneous Colorectal and Hepatic Resections for Colorectal Cancer: Postoperative and Longterm Outcomes

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BACKGROUND: Our goal was to analyze the results of resection of colorectal cancer and liver metastases in one procedure.

STUDY DESIGN: Between June 1982 and July 1998, 522 patients underwent liver resection for colorectal metastases. Liver resection was performed simultaneously with colorectal resection in 71 cases, representing the population in this study. Morbidity, mortality, overall survival, and disease-free survival times were analyzed. Median followup time was 29 months (range 6 to 162 months). Prognostic factors and their influence on outcomes were analyzed.

RESULTS: The median hospital stay was 8 days (range 5 to 23 days). Morbidity was 21% and included nine pleural effusions, seven wound abscesses, four instances of hepatic failure, three systemic infections, three intraabdominal abscesses, and one colonic anastomosis leakage. Operative mortality was 0%. Recurrence rate was 57.7% (41 or 71), and progression of disease was detected in 33.8%. Overall and disease-free survivals at 1, 3, and 5 years were 88%, 45%, and 38% and 67%, 17%, and 9%, respectively. Prognostic factors with notable influence on patient outcomes were nodal stage as per TNM classification, number of liver metastases, diameter (smaller or larger than 5 cm), liver resection specimen weight (lighter or heavier than 90 g), and liver resection margin (smaller or larger than 1 cm).

CONCLUSIONS: Simultaneous resection of colorectal cancer and liver metastases can be performed with low morbidity and mortality rates, avoiding a second surgical procedure. (J Am Coll Surg 2002; 195:196–202. © 2002 by the American College of Surgeons)

Surgical resection has become the standard therapy for colorectal metastases confined to the liver.1-5 It is a potentially curative option in this group of patients with 25% to 35% 5-year survival, but it is associated with 90% tumor recurrence, usually in the liver, lungs, and peritoneal cavity.6-9 About half of the patients who develop metastases will have them discovered at the time that the primary tumor is diagnosed. For most of these patients, this fact has meant undergoing two major abdominal procedures in close proximity. In the past most series presented results of delayed hepatic resection performed 2 to 3 months after colorectal procedures.10-13 Although a few authors have commented on simultaneous resection of a colorectal primary and a liver secondary tumor,14-16 large case series that allow evaluation of the safety and effectiveness of this approach are not available. The purpose of this study is to present the results of one such large case series with very favorable results.

METHODS

The present series analyzes the outcomes of 71 patients who underwent simultaneous colorectal and hepatic resection between June 1982 and June 1998. They represent 13.6% of the 522 hepatic resections and 2.6% of
the 2,700 colorectal operations for cancer performed during this period. The analysis was performed using data prospectively obtained. Median age of the population was 65 years (range 35 to 83 years); 49 patients were men (69%), and 22 were women (31%).

Preoperative staging and patient selection
Preoperative staging included physical examination, measurement of CEA and Ca19-9 colonoscopy or barium enema plus rectoscopy, abdominal imaging with ultrasonography or CT scan, and chest imaging by routine chest radiographs or CT scan. Brain CT scan was performed only when neurologic symptoms were present. Bone scan was performed to rule out widespread disease.

All 186 patients with colorectal cancer and synchronous liver metastasis were evaluated as candidates for simultaneous resection. Liver resection was contraindicated in 107 because of one of the following: performance status, advanced cirrhosis, bowel occlusion, gross bilobar tumor, multicentricity, and distal or peritoneal metastases. Intraoperatively, the following criteria for performance of liver resection were applied: primary colorectal resectable tumor with negative margins, absence of extrahepatic disease with the exception of the primary, and ability to resect all liver tumor with negative margins, yet leave an adequate amount of residual liver tissue. Based on these criteria, liver resection was ruled out intraoperatively in eight patients: because of peritoneal spread in three patients, because of hepatic hilar node metastasis in four patients, and because of failure to perform resection of the primary tumor in one patient. In summary, simultaneous liver resection was performed in 71 of 186 (38.1%) patients. The locations of the colorectal tumor were right colon in 23 patients (32.4%), left colon in 24 (33.8%), and rectum in 24 (33.8%). The median value of preoperative CEA was 69 ng/mL (range 2.1 to 150 ng/mL).

Preoperative preparation
Patients were admitted to the hospital 24 hours before operation. Mechanical bowel preparation was achieved with 90 mL of phosphate solution. Antibiotic prophylaxis consisted of one oral dose of 750 mg ciprofloxacin administered 1 hour before operation and one IV dose of 1 g ornidazole given during induction of anesthesia.

Table 1. Colorectal Operations Performed in This Series

<table>
<thead>
<tr>
<th>Operation Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>High anterior resections</td>
<td>21</td>
</tr>
<tr>
<td>Right hemicolectomies</td>
<td>20</td>
</tr>
<tr>
<td>Low anterior resections</td>
<td>16</td>
</tr>
<tr>
<td>Segmental colectomies</td>
<td>5</td>
</tr>
<tr>
<td>Left hemicolectomies</td>
<td>4</td>
</tr>
<tr>
<td>Abdominoperineal resections</td>
<td>4</td>
</tr>
<tr>
<td>Subtotal colectomy</td>
<td>1</td>
</tr>
</tbody>
</table>

Surgical technique
The initial approach was through a long median laparotomy that enabled adequate exploration of the abdominal cavity. Resection of the colorectal tumor was performed first to be sure that a margin-negative resection could be achieved. Colorectal operations performed are described in Table 1. After the colorectal procedure was finished, the surgical instruments and drapes were changed.

Next, the falciform ligament was divided to perform ultrasonic evaluation of the liver. The number of metastases was one in 38 patients (54%), two in 15 patients (21%), three in 13 patients (18%), and four in 5 patients (7%). After it was determined that resection was possible, the abdominal incision was transversely enlarged to the right if the liver metastases were located in segments VI or VII according to the Couinaud classification.

We used the cavitation ultrasonic aspirator (Valley Inc, Boulder, CO) for liver transection. Pringle’s maneuver was used only when needed to decrease intraoperative bleeding, to avoid the splanchnic edema that might jeopardize the synthesis of the colon anastomosis.

In cases of multiple metastases that did not involve large vessels, we used nonanatomic resections with a margin of healthy parenchyma larger than 1 cm. An argon beam coagulator was used for the final hemostasis of raw surfaces with the addition of a biologic adhesive (Tissucol, Immuno, Inc, Vienna, Austria). We placed one to three suction catheters, which were removed after 3 to 5 days if no bile leak developed.

The hepatic resections performed are listed in Table 2. Other associated surgical procedures were performed in nine patients: two hysterectomies, two adrenalectomies, two ileostomies, two bilateral oophorectomies, and one partial duodenal resection. In 62 of 71 patients (87.3%), adjuvant chemotherapy was administered during the postoperative period.
Followup
We performed physical examination, ultrasound or CT scan, and laboratory parameters including CEA and CA19-9 tumor markers every 4 months. We modified the frequency of each screening according to the evolution of each individual patient. Median followup was 29 months (range 6 to 162 months).

Statistical analysis
Continuous data are expressed as median and range. Overall and disease-free survival rates were calculated with the Kaplan-Meier method. Survival times were expressed as median, and the 95% confidence interval (CI) was calculated. Survival curves were compared using the log-rank test. The different variables were evaluated using intervariance analysis. Correlation studies between survival and the different prognostic factors were analyzed using Pearson’s coefficient. Results were considered to be statistically significant at a p level of 0.05 or less.

RESULTS
The median operation time was 4 hours (range 3 to 7 hours). The Pringle maneuver was used during hepatectomy in 7 of 71 patients (9.8%), with a median duration of 11 minutes (range 5 to 22 minutes). During operation, 26 of 71 patients (36.6%) required red blood cell transfusion, and 19 of 71 (26.8%) required frozen fresh plasma, with medians of 2 IU (range 1 to 5 IU) and 2 IU (range 1 to 4 IU), respectively. Median hospitalization time was 8 days (range 5 to 23 days). Twenty-six patients required admission to the intensive care unit (36.6%), with a median length of stay of 56 hours (range 12 to 216 hours) and a median period of mechanical ventilation of 12 hours (range 3 to 48 hours). Patients with prolonged operative times required more mechanical ventilation during the postoperative period (p < 0.05).

Morbidity was 21% and is shown in Table 3. These complications resolved with medical and interventional treatment in all cases, except for one patient who required an ileostomy and drainage of a pelvic collection caused by dehiscence of the colorectal anastomosis. There was no postoperative mortality (within 30 days of operation). During the followup period, recurrence occurred in 41 of 71 patients (57.7%). Sites of recurrence were hepatic in 38 cases (79%), pelvic in 8 (17%), and abdominal wall in 2 (4%). Progression of disease was detected in 24 of 71 cases (33.8%) in the following locations: lung in 18 (25.3%), peritoneum in 6 (8.4%), and bone in 1 patient (1.4%). No correlation was found between the location of the primary tumor and the presence of tumor recurrence. At the end of followup, 23 of 71 patients were alive (32.4%), representing an overall mortality of 67.6%. The causes of death were related to progression or recurrence of colorectal cancer in 40 patients and unrelated in 8 patients.

The median overall and disease-free survival times were 21 months (95% CI 18 to 24) and 17 months (95% CI 14 to 20), respectively. Overall survival of the population at 1, 3, and 5 years was 88%, 45%, and 38%, respectively, and disease-free survival at 1, 3, and 5 years was 67%, 17%, and 9%, respectively (Fig. 1). The overall survival time (OST) varied according to the primary tumor location: right colon 20 months (95% CI 13 to 27), left colon 24 months (95% CI 19 to 29), and rectum 26 months (95% CI 22 to 30). These differences did not reach statistical significance (p < 0.29).

Study of the colorectal specimen showed the following T stages: 1 T1, 3 T2, 56 T3, and 11 T4. N stages were as follows: 22 N0, 31 N1, 3 N2, and 5 N3. The OST and disease-free survival time (DFST) were statistically shorter in patients with a more advanced node stage according to the TNM classification (Fig. 2). Patients with N0 had a median OST of 33 months (95% CI 13 to 27), left colon 24 months (95% CI 19 to 29), and rectum 26 months (95% CI 22 to 30). These differences did not reach statistical significance (p < 0.29).

Study of the colorectal specimen showed the following T stages: 1 T1, 3 T2, 56 T3, and 11 T4. N stages were as follows: 22 N0, 31 N1, 3 N2, and 5 N3. The OST and disease-free survival time (DFST) were statistically shorter in patients with a more advanced node stage according to the TNM classification (Fig. 2). Patients with N0 had a median OST of 33 months (95% CI 27 to 39), those with N1 had 21 months (95% CI 12 to 39), and patients with N2 or N3 had an OST of Table 2. Hepatic Resections Performed in This Series

<table>
<thead>
<tr>
<th>Type of Resection</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonanatomic resections</td>
<td>48</td>
</tr>
<tr>
<td>Segmentectomies</td>
<td>15</td>
</tr>
<tr>
<td>Right hepatectomies</td>
<td>4</td>
</tr>
<tr>
<td>Left hepatectomy</td>
<td>1</td>
</tr>
<tr>
<td>Right trisectionectomy</td>
<td>1</td>
</tr>
<tr>
<td>Left trisectionectomy</td>
<td>1</td>
</tr>
<tr>
<td>Right hepatectomy with contralateral segmentectomy</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3. Postoperative Complications Observed in the Population That Underwent Simultaneous Liver and Colorectal Resection

<table>
<thead>
<tr>
<th>Type of Complication</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural effusions</td>
<td>9</td>
</tr>
<tr>
<td>Wound abscesses</td>
<td>7</td>
</tr>
<tr>
<td>Hepatic failures</td>
<td>4</td>
</tr>
<tr>
<td>Systemic infections</td>
<td>3</td>
</tr>
<tr>
<td>Hepatic abscess</td>
<td>1</td>
</tr>
<tr>
<td>Pelvic abscess</td>
<td>1</td>
</tr>
<tr>
<td>Subdiaphragmatic abscess</td>
<td>1</td>
</tr>
<tr>
<td>Anastomotic fistula</td>
<td>1</td>
</tr>
</tbody>
</table>
16 months (95% CI 8 to 23; p < 0.01); median DFSTs were 28 (95% CI 12 to 34), 19 (95% CI 12 to 28), and 11 months (95% CI 6 to 23; p < 0.01), respectively.

The median weight of the hepatic resection specimen was 275 g (range 5 to 1,785 g), and the median diameter of the resected hepatic metastases was 2 cm (range 0.3 to 17 cm). Patients with hepatic tumors larger than 5 cm in diameter had OST and DFST of 17 months (95% CI 12 to 23) and 14 months (95% CI 11 to 18), respectively, and patients with tumors measuring less than 5 cm had median OST and DFST of 26 months (95% CI 22 to 33) and 22 months (95% CI 17 to 27), respectively (p < 0.01 for OST and p < 0.05 for DFST, Fig. 3).

The number of metastases markedly affected the DFST. In solitary liver masses, the median was 26 months (95% CI 22 to 30), but it was 16 months (95% CI 9 to 23) for two liver masses and 6 months (95% CI 4 to 8) for patients with three or more metastases (p < 0.001, Fig. 4). The hepatic resection margin was less than 1 cm in 12 patients (16.9%) and 1 cm or more in 59 patients (83.1%). Patients with less than 1 cm of normal liver margin had median OST and DFST of 12 months (95% CI 8 to 17) and 6 months (95% CI 3 to 11), respectively, and OST and DFST were 32 months (95% CI 22 to 39) and 24 months (95% CI 19 to 29) for resection margins of 1 cm or larger (p < 0.01 for OST and p < 0.05 for DFST, Fig. 5).

Patients who underwent resection of liver specimens weighing less than 90 g had median OST and DFST of 30 months (95% CI 23 to 36) and 22 months (95% CI 17 to 27), and those with heavier liver specimens resected had 14 months (95% CI 10 to 19) and 9 months (95% CI 4 to 17), respectively (p < 0.05 in both cases, Fig. 6).

On univariate and multivariate analyses, the number
of liver metastases, tumors greater than 5 cm in diameter, hepatectomy specimens weighing more than 90 g, and resection margins of less than 1 cm were prognostic factors related to the liver disease that showed statistically significant differences and had an influence on OST and DFST.

DISCUSSION
When a hepatic metastasis is diagnosed during a laparotomy for resection of colorectal cancer, the best approach is not clearly defined. In 1993, Foster\textsuperscript{13} recommended that if the patient's condition, type of incision, and the surgeon's experience allow for an easy local resection of a single and peripheral lesion, such resection should be performed simultaneously with that of the primary tumor.\textsuperscript{13} Nonetheless, most authors believed that it would be best to postpone hepatic resection for several weeks.\textsuperscript{13} Some of the reasons mentioned by those who discourage performance of a simultaneous resection are increase in operative mortality, the association of a contaminating procedure with a clean one, the risk of an anastomotic fistula, and the lack of complete intraoperative oncologic staging.\textsuperscript{14-16} Other series have demonstrated that simultaneous resection of hepatic metastases and colorectal cancer in synchronous disease does not differ from resections performed in a delayed fashion with regard to survival time at 5 years.\textsuperscript{16-20} The present large study shows that simultaneous resection is a safe procedure in selected patients and confirms that it is as effective as staged resection.

Certain important steps are required to make combined simultaneous resection successful. In patients in whom the diagnosis of hepatic metastases is made during the preoperative evaluation, a staging with thorax, abdomen, and pelvis CT scan and a bone scintigram is recommended to avoid hepatic resections in patients with lung or bone metastases. When diagnosis of metastases is made during operation, histologic confirmation of malignancy using an ultrasound-guided needle biopsy is very often necessary.\textsuperscript{21} Also, it is very important that the colorectal surgery team be certain about the curative nature of the procedure performed before continuing with the liver operation. If residual disease is left behind in the pelvis or abdomen of these patients, survival will not increase, even if liver metastases are resected.\textsuperscript{9,16,22,23} Similarly, if hepatic lesions are not totally resected, or if the oncologic margin is insufficient, the natural course of the metastatic disease will not change.\textsuperscript{24,25} For these reasons, intraoperative ultrasound staging, which detects more lesions than the preoperative assessment or the surgeon's manual exploration, is essential if a complete liver resection is to be performed.\textsuperscript{21}

The impact of specialization in colorectal and liver operation is demonstrated by the improvement in immediate and longterm results and in a decrease in global hospital costs.\textsuperscript{26,27} The present series reports the results obtained by trained colorectal and hepatic surgeons with more than 2,500 colorectal and 700 hepatic oncologic surgeries working at a single institution.

It has been stated that a major hepatectomy should ideally be performed with less than a 5% mortality rate, a hospital stay of 6 to 10 days, blood transfusion in less than 50% of the patients, and only minor changes in hepatic enzymes.\textsuperscript{28} When a colorectal procedure is asso-
citated, this statement should still hold true, adding an acceptable rate of anastomosis dehiscence. The hospital stay, rate of patients undergoing transfusion, and morbidity of the present series compared well with other series of synchronous and delayed hepatectomy.\textsuperscript{2,14–16}

Although some reports mention an increased risk of anastomotic leakage when a hepatic resection is associated,\textsuperscript{6} our rate (1.4\%) is still low and similar to the 1.9\% rate of dehiscence in 790 elective IP anastomoses performed at our hospital since 1970 and to rates reported by other authors.\textsuperscript{13–15}

The rate of overall survival obtained (32\%) is comparable with that reported by other authors with simultaneous and delayed resections, ranging from 25\% to 40\% and with similar followup periods.\textsuperscript{12,29–31} The liver and the lungs were the more frequent sites of recurrence and progression of the colorectal cancer, respectively. In our population, the primary cause of death was related to local or distal cancer recurrence, as is reported by several series.\textsuperscript{15–19}

The fact that 57.7\% of patients experienced recurrences during followup and that 53.5\% of recurrences were hepatic demonstrates the presence of microscopic residual disease that was not detected during operation. This provides the rationale for the use of adjuvant therapies during the postoperative period or PET scan for preoperative staging.

Conclusion

Simultaneous resection of colorectal cancer and its hepatic metastases can be performed with low rates of morbidity and mortality, avoiding a second surgical procedure.

Acknowledgment: The authors thank Dr Steven Strasberg for his assistance and contributions with this manuscript.

REFERENCES


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