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## Resection of the Liver for Colorectal Carcinoma Metastases:

### A Multi-institutional Study of Long-term Survivors

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### Abstract

In this review of a collected series of patients undergoing hepatic resection for colorectal metastases, 100 patients were found to have survived greater than five years from the time of resection. Of these 100 long-term survivors, 71 remain disease-free through the last follow-up, 19 recurred prior to five years, and ten recurred after five years. Patient characteristics that may have contributed to survival were examined. Procedures performed included five trisegmentectomies, 32 lobectomies, 16 left lateral segmentectomies, and 45 wedge resections. The margin of resection was recorded in 27 patients, one of whom had a positive margin, nine of whom had a less than or equal to 1-cm margin, and 17 of whom had a greater than 1-cm margin. Eighty-one patients had a

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solitary metastasis to the liver, 11 patients had two metastases, one patient had three metastases, and four patients had four metastases. Thirty patients had Stage C primary carcinoma, 40 had Stage B primary carcinoma, and one had Stage A primary carcinoma. The disease-free interval from the time of colon resection to the time of liver resection was less than one year in 65 patients, and greater than one year in 34 patients. Three patients had bilobar metastases. Four of the patients had extrahepatic disease resected simultaneously with the liver resection. Though several contraindications to hepatic resection have been proposed in the past, five-year survival has been found in patients with extrahepatic disease resected simultaneously, patients with bilobar metastases, patients with multiple metastases, and patients with positive margins. Five-year disease-free survivors are also present in each of these subsets. It is concluded that five-year survival is possible in the presence of reported contraindications to resection, and therefore that the decision to resect the liver must be individualized.

## Keywords

Hepatic metastases; Cancer; Colorectal neoplasms; Hepatic resection

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Liver Metastases are found in over 70 percent of patients dying from carcinoma of the colon and rectum. The only currently available curative treatment for this condition is hepatic resection, which has a five-year survival rate of 33 percent.<sup>1</sup> Though this treatment has an impressive survival rate and carries with it a mortality of only about 5 percent,<sup>2-5</sup> there remains a reluctance among physicians to refer patients for this procedure.

The purpose of this report is to discuss long-term survivors from this procedure collected in a multi-institutional retrospective review. The authors present these data to confirm that long-term survival is not only possible, but common following hepatic resection for colorectal metastases, and to examine the characteristics of these five-year survivors to evaluate the indications and contraindications for this procedure.

## Materials and Methods

The methods of data collection have been described in a previous report.<sup>1</sup> Briefly, the records of 859 patients who had undergone hepatic resection for colorectal carcinoma metastases between 1948 and 1985 were reviewed. Patients who died in the postoperative period, and patients who had gross tumor left *in situ* have been excluded. Consecutive patients from each of 24 recording institutions were reviewed and entered into a single data base. Approximately two thirds of the patient charts were reviewed by a single author (K.S.H.), and this author also reviewed all data sheets completed by other authors prior to entry into the computer.

Five-year survivors included any patient who was known to be alive at five years after liver resection. One hundred patients met this criteria. Characteristics of these patients were determined from the computer data base.

In order to look at a comparable group who did not survive five years, a second analysis was performed using only those patients operated on prior to 1981. This allowed almost complete five-year follow-up. In order to determine the characteristics by which the survivors differed significantly from those surviving less than five years, chi-square tests (for categorical variables) and *t* tests (for continuous variables such as age) were used. However, the comparison of the two groups based on multiple variables requires caution in interpretation, as significant results can occur by chance when statistical tests are performed using measurements that may be correlated.

## Results

One hundred patients survived five years after hepatic resection for colorectal metastases (Table 1). The mean age at the time of liver resection was 56 years, with a range of 18 to 83 years. The male-to-female ratio of the five-year survivors was 1.1 to 1. The length of survival ranged from 5 to 35+ years.

### Disease Status

Of the 100 survivors, 71 (71 percent) remained disease-free through the last follow-up, 19 (19 percent) had recurrences before five years, and ten (10 percent) had recurrences more than five years after liver resection.

### Age at Time of Liver Resection

Ninety-five of the 100 five-year survivors had age recorded at the time of liver resection. Twelve were less than age 40, 68 were between 40 and 70 years old, and 15 were over 70 years old. The youngest patient was 18 at the time of resection, and he remains alive and disease-free 13 years later at age 31. The oldest patient was 83 at the time of resection, and remains alive and disease-free six years later at age 89.

### Type of Resection

Ninety-eight of the five-year survivors had the extent of liver resection recorded. Forty-five had undergone a wedge resection (32 remain disease-free), 26 had undergone a right lobectomy (22 remain disease-free), six had undergone a left lobectomy (five remain disease-free), 16 had undergone a left lateral segmentectomy (seven remain disease-free), and five had undergone a trisegmentectomy (three remain disease-free).

### Margin of Resection on Liver Specimen

The margin was recorded in 27 of the 100 five-year survivors. The margin was histologically positive in one patient (he remains disease-free), was less than or equal to 1 cm in nine patients (4 remain disease-free) and was greater than 1 cm in 17 patients (14 remain disease-free).

### Number of Metastases

The number of metastases was recorded as an integer in 96 of the five-year survivors, and was recorded as “multiple” in only three of the five-year survivors. Eighty-one had a solitary metastasis resected (58 remain disease-free), 11 had two metastases resected (eight remain disease-free), one had three metastases resected (he has had a recurrence), and three had four metastases resected (one remains disease-free).

### Distribution of Multiple Metastases

The distribution of metastases was recorded in 16 of the five-year survivors who had multiple metastases. Thirteen had multiple, unilobar metastases (nine remain disease-free), and three had multiple, bilobar metastases (two remain disease-free).

### Stage of Primary Cancer

Primary cancer stage was recorded in 71 of the five-year survivors. Thirty had mesenteric node involvement (21 remain disease-free) and 41 did not have mesenteric node involvement (30 remain disease-free).

### Size of Solitary Metastases

Twelve of the five-year survivors had a solitary metastasis greater than 8 cm in greatest diameter resected (ten remain disease-free).

### Disease-free Interval

The disease-free interval was recorded in 98 of the five-year survivors. Sixty-five had a disease-free interval less than or equal to one year, and 34 had a disease-free interval greater than one year.

### Comparison of Five-year Survivors with Patients Surviving Less than Five Years (resected prior to 1981)

By limiting this analysis to those patients resected prior to 1981, the authors were able to have almost complete five-year follow-up. Three hundred seventy-seven patients had isolated liver metastases resected prior to 1981. In this group there were 91 five-year survivors (the other nine five-year survivors were excluded since five were resected in 1981, and four had resection of both liver and extrahepatic metastases). The actual five-year survival was 91 of 377 (24 percent). A comparison of these 91 survivors with the 286 who did not survive five years with respect to number of metastases, mesenteric node involvement, distribution of multiple metastases, disease-free interval, type of resection, margin of resection, sex, and age is shown in Table 2.

Nineteen of the five-year survivors had multiple metastases, compared with 31 percent of those who survived less than five years ( $P < .05$ ). Fifty-one percent of the five-year survivors but only 36 percent of the nonsurvivors had disease-free intervals of greater than one year ( $P < .025$ ). Of the 243 patients for whom the stage of the primary cancer is known, 56 percent of the 63 five-year survivors had negative mesenteric nodes, but only 38 percent of the nonsurvivors had negative mesenteric nodes ( $P < .025$ ).

## Discussion

Hepatic resection is the only curative treatment currently available for hepatic metastases. However, physicians remain skeptical as to whether any patient with hepatic metastases can be cured. In addition, there is a feeling that hepatic resection carries too high a mortality to be used widely. Many series have addressed the mortality of hepatic resection, and have consistently found it to be in the range of 5 percent.<sup>2-5</sup> This is a very acceptable mortality for patients who have no alternative treatment.

Many series have also addressed the indications and results of this procedure. Though a five-year survival of greater than 25 percent<sup>2-7</sup> is a generally accepted figure following resection, there remains a certain degree of skepticism. Many physicians believe that survival and cure are not possible once a patient has hepatic metastases, and these physicians feel that the 25 percent survivals recorded are statistical aberrations or the result of statistical predictions based on short follow-up.

This report presents a collected series of 100 patients who have survived five years after liver resection. In reviewing the literature, there are only 14 patients reported to survive greater than five years after the detection of liver metastases without resection,<sup>8-9</sup> and only seven of these were biopsy-proven metastases. The comparison of 100 five-year survivors from this collected series vs. the 14 five-year survivors without resection in the literature is very suggestive that hepatic resection does extend survival, and is probably curative in certain cases.

This analysis of the actual survival of those resected prior to 1981 tends to confirm previous reports. It appears that those patients with a smaller number of metastases, more localized primary disease, and longer disease-free interval do have a survival advantage. The effect of margin on survival did not reach statistical significance, but since this factor was only recorded in 25 percent of patients, it should not be discounted yet. It appears that the distribution of multiple metastases, sex, age, type of procedure, size of metastases, and contiguous spread are of less importance in determining prognosis.

An important result of this study is that there are a finite number of five-year survivors in each of the poor prognosis subgroups. There is one five-year survivor with a positive margin on the liver specimen, three with bilobar metastases, 30 with stage C primary cancers, and 12 with solitary metastases, 8 cm or greater in diameter. Though survival in the poor prognosis subgroups is possible, it appears less likely, and decisions regarding surgery must be individualized.

The authors recommend hepatic resection in any patient with one or two isolated liver metastases if these can be removed with a low mortality. A 1-cm margin should be obtained if possible. Prognosis will be affected by the stage of the primary cancer, the disease-free interval, and probably by the margin, but these factors alone should not be regarded as contraindications to resection. Patients with three or four metastases should be considered for resection on an individual basis.

Five-year survival following the resection of hepatic metastases is not only possible, but common. The authors recommend that the prognostic factors be considered in determining who should undergo this procedure, but since five-year survival does occur despite these factors, the final decision to resect must be made on an individual basis.

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**TABLE 1**

## Five-Year Survival Following Hepatic Resection for Colorectal Metastases

| Characteristics                               | Number | Percent* |
|---|--------|----------|
| Number of metastases                          |        |          |
| 1   | 81     | (81)     |
| 2   | 11     | (11)     |
| 3   | 1      | (1)      |
| 4   | 3      | (3)      |
| > 4   | -      |          |
| Multi <sup>†</sup>                            | 1      | (1)      |
| Mesenteric nodes involved from primary cancer |        |          |
| No  | 41     | (57)     |
| Yes   | 30     | (42)     |
| Distribution for multiple metastases          |        |          |
| Unilobar                                      | 13     | (81)     |
| Bilobar                                       | 3      | (19)     |
| Disease-free interval                         |        |          |
| < 1 year                                      | 64     | (65)     |
| > 1 year                                      | 34     | (35)     |
| Type of resection                             |        |          |
| Wedge   | 45     | (46)     |
| Right lobectomy                               | 26     | (27)     |
| Left lateral segmentectomy                    | 16     | (16)     |
| Left lobectomy                                | 6      | (6)      |
| Trisegmentectomy                              | 5      | (5)      |
| Margin in liver specimen                      |        |          |
| Positive                                      | 1      | (4)      |
| Neg, but < 1 cm                               | 9      | (33)     |
| > 1 cm  | 17     | (63)     |

\* Percent of patients who had this characteristic.

<sup>†</sup> Exact number of metastases not recorded.



TABLE 2

Actual Five-Year Survival of 377 Patients Undergoing Hepatic Resection for Isolated Colorectal Metastases Prior to 1981

| Characteristics                               | Survivors/<br>Total | Actual 5 Year<br>Survival<br>(Percent) | <i>P</i> |
|---|---------------------|--|----------|
| Number of metastases                          |                     |  |          |
| 1   | 73/267              | 27                                     | <.05*    |
| 2   | 10/55               | 18                                     |          |
| 3   | 1/18                | 5                                      |          |
| 4   | 3/11                | 27                                     |          |
| > 4   | 0/6                 | -                                      |          |
| Mesenteric nodes involved from primary cancer |                     |  |          |
| No  | 35/103              | 34                                     | <.025    |
| Yes   | 28/140              | 20                                     |          |
| Distribution of multiple metastases           |                     |  |          |
| Unilobar                                      | 11/60               | 18                                     | N.S.     |
| Bilobar                                       | 2/23                | 9                                      |          |
| Disease-free interval                         |                     |  |          |
| < 1 year                                      | 45/228              | 20                                     | <.025    |
| > 1 year                                      | 46/149              | 31                                     |          |
| Type of resection                             |                     |  |          |
| Major   | 47/187              | 25                                     | N.S.     |
| Minor   | 44/190              | 23                                     |          |
| Margin on liver specimen                      |                     |  |          |
| < 1 cm  | 9/46                | 20                                     | N.S.     |
| > 1 cm  | 14/47               | 30                                     |          |
| Sex   |                     |  |          |
| Male  | 44/194              | 23                                     | N.S.     |
| Female  | 43/170              | 25                                     |          |
| Age   |                     |  |          |
| < 70  | 74/315              | 24                                     | N.S.     |
| > 70  | 17/62               | 27                                     |          |

\*  $P < .05$  for 1 metastasis vs. multiple metastases.