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Pattern of Recurrence in Liver Resection for Colorectal Secondaries

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The pattern of relapse and factors influencing the site of recurrent disease were studied in 68 patients subjected to liver resection of colorectal metastases. Fifty-three (78%) patients had recurrence. Liver, lungs, and peritoneal cavity were most frequently involved, and all patients with relapse had recurrence in one or more of these sites. Intraabdominal relapse occurred in 50 (74%) patients (94% of patients with relapse). The liver was involved in 44 (65%) patients and was the only site of recurrence in 19 (28%). Extrahepatic metastases developed in 34 (50%) patients. Four or more liver tumors, a resection margin of less than 10 mm, and extrahepatic disease were the main determinants of hepatic recurrence. Bilateral intrahepatic spread, as compared to unilateral disease, major liver resection, as compared to wedge resection, and percent liver tumor volume were also associated with an increased risk of liver recurrence. The presence of extrahepatic disease before resection was the only factor that could be demonstrated to increase the risk of (further) extrahepatic spread. It is concluded that the number of liver metastases, the resection margin, and the presence or absence of extrahepatic disease helps in predicting the risk of hepatic recurrence after resection for colorectal liver cancer. No variable presently available is of any help, however, in predicting the extrahepatic recurrence affecting about half of the patients having no evidence of extrahepatic disease before liver resection. This finding should urge improved evaluation of candidates for liver resection and should influence adjuvant treatment protocols.

After resection of colorectal liver metastases, some three-quarters of the patients die of recurrent disease [1, 2]. This is the reason why the present study investigates the pattern of recurrence and factors influencing the site of recurrent disease in patients subjected to resection of colorectal liver metastases. Such information is sparse and would aid in selecting patients for resection and would aid also in tailoring follow-up and postresection adjuvant treatment regimens.

Material and Methods

This is a retrospective analysis of a consecutive series of 68 liver resections for colorectal liver metastases from 1971 to 1984. Another 4 patients were operated on during this period but were excluded from the present analysis because they died before discharge from the hospital (0–130 days after liver resection; operative mortality: 5.6%).

Thirty-four patients were male and 34 female with a median age of 62 (range 27–76) years. The operations consisted of 13 (19%) wedge resections, 10 (15%) segmentectomies, 8 (12%) left lobectomies, 1 (1%) extended left lobectomy, 32 (47%) right lobectomies, and 9 (13%) extended right lobectomies. Complete dissection of the hepatoduodenal ligament with removal of lymph nodes for microscopic examination was performed in 30 patients.

Nine patients were reoperated on during the postoperative phase because of bleeding (2), abscess (4), bile leakage (2), and mechanical obstruction (1). Transitory hepatic insufficiency was encountered in 3 patients. Minor complications, infectious or respiratory, were encountered in 20 patients.

Enumeration of the liver tumors was based on histopathological and/or laparotomy findings. The margin of resection was determined from the histopathological review alone. The extent of liver involvement, in percent of the total liver volume, was determined from preoperative angiograms in 50 patients and from laparotomy findings in 22 patients, most of whom were treated with wedge resections.

The median follow-up time was 20 (range 3–167) months. Follow-up was standardized and based on clinical examination with rectoscopy and laboratory tests, including liver function tests and carcinoembryonic antigen (CEA), after 3, 6, 9, 12, 18, and 24 months and then at yearly intervals. Barium enema and/or colonoscopy and x-ray of the lungs were performed routinely after 1, 3, and 5 years. When the clinical or laboratory investigations suggested liver metastases, scintigraphy, ultrasonography, and/or computed tomography (CT) combined with fine-needle biopsy were performed. Other investigations, such as bone scintigraphy and CT of the pelvis, were carried out only when symptoms or laboratory findings indicated recurrent disease.

In each patient, extent of recurrence was determined on the basis of clinical, laboratory, and radiologic investigation. In 23 (34%) patients it was based also on laparotomy findings at the time of initial relapse. Autopsy was performed in only 6 patients and did not give any new information with respect to the recurrence pattern.

Fifty-three patients had recurrence after a median disease-free period of 9 (range 1–36) months. Forty-six (68%) patients died of disease. Seven (10%) patients were living with disease, median 9 (range 4–25) months after resection, and 15 (22%)

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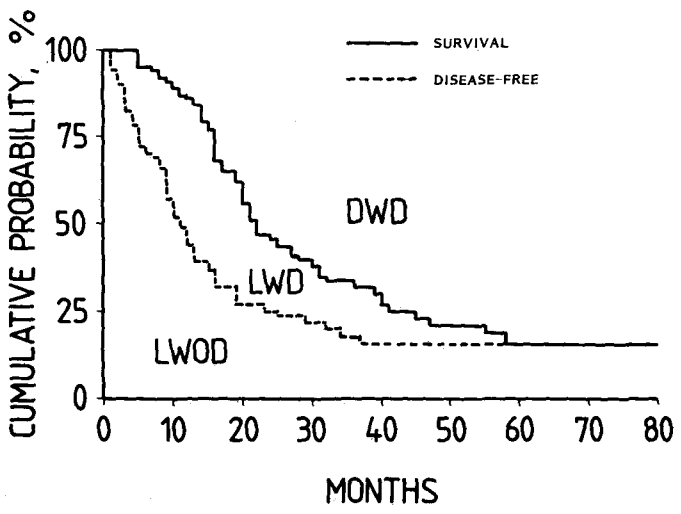

Fig. 1. Cumulative probability of survival (—) and of disease-free interval (- - -) after liver resection of colorectal metastases (n = 72). LWOD = living without disease, LWD = living with disease, DWD = dead with disease.

patients were disease-free after 47 (median) months (range 3–167). The proportions of patients dead with disease, and living with or without disease, at different time points are shown in Fig. 1. The median actuarial survival was 22 (0–167) months.

Graphs of the disease-free interval were constructed with the life-table technique. Possible determinants of recurrence (Table 1) were tested both separately and simultaneously. The Generalized Wilcoxon test [3] was used to analyze the influence of isolated variables on recurrence. In the multivariate analysis, the Cox proportional hazards model [4] was used to determine the importance of each variable at the same time as the influence of the other possibly interrelated variables was taken into account. In this analysis, all variables were entered and selected stepwise in order of statistical significance. Values are stated as medians and ranges.

Results

The frequency of recurrent disease in different organs is summarized in Table 2. Fifty-three (78%) patients had relapse. The liver, lungs, and peritoneal cavity (intraabdominal lymph nodes, peritoneal surface) were most frequently involved and all patients with relapse had recurrence at one or more of these sites. Fifty (74%) patients (94% of those with relapse) had intraabdominal recurrence, in the liver, peritoneal cavity, or at the colorectal resection site. The liver was affected in 44 (65%) patients (83% of those with recurrent disease) and solely in 19 (28%) patients. Extrahepatic metastases were encountered in 34 (50%) patients and were unassociated with liver recurrence in 9 (13%) patients. The lungs were the most common site of extrahepatic recurrence and were affected in 15 (22%) patients. Three patients had pulmonary metastases only.

It is noteworthy that 8 (12%) patients had local failure. Four patients with colonic carcinoma had anastomotic recurrence 14 months (range 8–35) after the primary operation (10 months after liver resection, range 6–20 months). The other 4 patients had perineal and/or pelvic relapse 20 months (range 10–30) after resection of a rectal carcinoma (10 months after liver resection, range 5–14 months). Five of the patients with local recurrence had liver secondaries synchronous with the primary tumor.

Liver recurrence was diagnosed 9 months (range 1–57) after liver resection (within a year in 68% of the cases and within 2 years in 89%). Lung metastases occurred after 17 months (range

Table 1. Variables in uni- and multivariate analyses (n = 68).

Variable	Definition	Patients n (%)
Primary tumor		
Site	Colon	48 (71)
	Rectum	20 (29)
Differentiation	Well	7 (10)
	Moderate	54 (79)
	Low	7 (10)
Dukes' classification	A	3 (4)
	B	18 (26)
	C	47 (69)
Liver metastases		
Timing	Synchronous	40 (59)
	Metachronous	28 (41)
Intrahepatic spread	Unilateral	52 (76)
	Bilateral	16 (24)
Number of tumors	Single	34 (50)
	Multiple	34 (50)
	1, 2, or 3	55 (81)
	4 or more	13 (19)
Tumor diameter (largest)	<4 cm	28 (41)
	≥4 cm	40 (59)
Liver tumor volume	<25%	41 (60)
	25–49%	22 (32)
	50–74%	5 (7)
Type of operation	Wedge resection	13 (19)
	Major resection	55 (81)
Margin of resection	≥10 mm	27 (40)
	<10 mm	29 (43)
	No margin	12 (18)
Extrahepatic disease		
Extrahepatic disease	Not present	56 (82)
	Present	12 (18)
Hilum node metastases	Negative biopsy	24 (35)
	Positive biopsy	6 (56)

Table 2. Sites of recurrence.

Site	No. of patients	Percent of all patients (n = 68)	Percent of patients with recurrence (n = 53)
Liver (all)	44	65	83
Liver only	19	28	36
Extrahepatic (all)	34	50	64
Extrahepatic only	9	13	17
Lungs (all)	15	22	28
Lungs only	3	4	6
Local recurrence	8	12	15
Peritoneum[a]	12	18	23
Bone[b]	4	6	8
Skin[b]	4	6	8
Brain[b]	2	3	4
Extraabdominal lymph nodes[b]	1	1	2

[a]Peritoneal surface and/or intraabdominal lymph nodes.
[b]Always combined with recurrence in the liver and/or other extrahepatic sites.

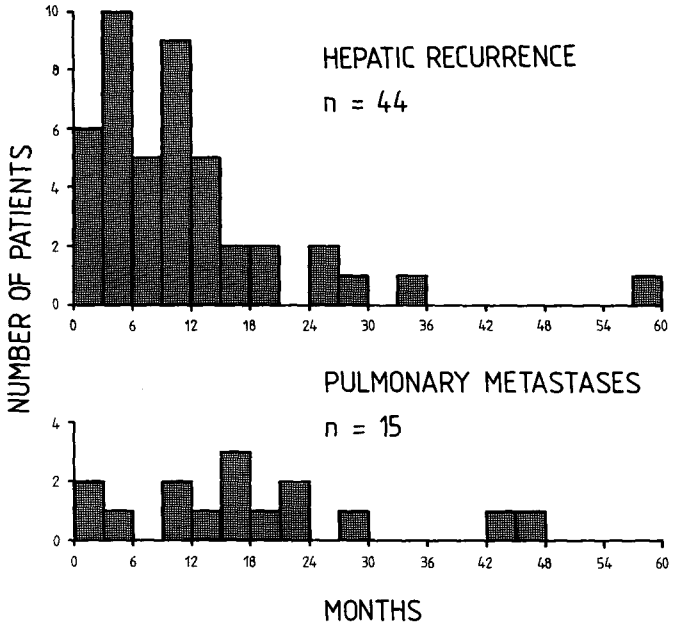

Fig. 2. Relapse in the liver and lungs at different time points after liver resection.

3–48): within a year in 33% and within 2 years in 67% (Fig. 2). Peritoneal recurrence was diagnosed after 14 months (range 5–37). Patients with only extrahepatic metastases had the relapse after 16 months (range 3–36). No patient developed recurrent disease more than 3 years after liver resection.

All variables that correlated significantly with the disease-free interval in the single variable analyses are given in Table 3. The prognosis was unfavorable if there were multiple liver tumors and especially if the number of liver tumors was 4 or more. Bilateral hepatic disease was accompanied by earlier recurrence than unilateral disease. The difference was reduced, but still significant, when patients with multiple metastases only (n = 34) were considered (median 5 and 12 months, respectively; $p = 0.05$). A similar difference was seen also in patients with <4 tumors although the 3- or 5-year disease-free rates were only slightly higher in unilateral than in bilateral disease.

The extent of liver involvement by tumor influenced the disease-free interval, especially when the liver involvement was 50% or more. A tumor-free margin of less than 10 mm as well as absence of extrahepatic metastases was of great importance. Patients operated on with wedge resection had a longer disease-free interval than the other patients.

The following variables did not show any statistically significant variation with disease-free interval ($p > 0.15$ and no substantial difference in median values): site of primary tumor, Dukes' classification, histologic differentiation of the primary, synchronous or metachronous metastases, and liver tumor size.

The results of the multivariate analysis agreed with those of the single-variable analysis and are shown in Table 4. The following variables, arranged in order of statistical importance, were associated with early recurrence: extrahepatic disease, major liver resection, number of tumors being 4 or more, resection margin of <10 mm, bilateral intrahepatic spread, and liver tumor volume of ≥25%. Each variable increased the risk

Table 3. Recurrence: single variable analyses.

Variable	No. of patients	Disease-free interval Median (mo)	3-yr (%)	5-yr (%)	p value
No. of tumors					
Single	34	16	24	24	0.01
Multiple	34	9	12	8	
1, 2, or 3	55	13	22	20	0.01
4 or more	13	7	0	0	
Intrahepatic spread					
Unilateral	52	13	20	17	0.01
Bilateral	16	5	13	13	
<4 tumors					
Unilateral	44	16	24	21	0.04
Bilateral	11	5	18	18	
Liver tumor volume					
<25%	41	11	25	22	0.03 (1 versus 2)
25–49%	22	13	9	9	0.03 (1 versus 3)
50–74%	5	3	0	0	
Margin of resection					
≥10 mm	27	19	31	31	0.08 (1 versus 3)
<10 mm	29	12	12	6	0.05 (2 versus 3)
No margin	12	8	0	0	
Extrahepatic disease					
Not present	56	13	22	20	0.01
Present	12	6	0	0	
Hilum node metastases					
Negative biopsy	24	12	22	18	0.03
Positive biopsy	6	5	0	0	
Type of operation					
Wedge resection	13	17	34	22	0.06
Major resection	55	11	15	15	

of recurrence 2–4 times. If the number of tumors was classified as single or multiple, instead of <4 versus ≥4, liver tumor number did not significantly affect disease-free interval. It is noteworthy that major liver resection, as compared to wedge resection, was accompanied by early recurrence also in this analysis.

The distribution of disease with respect to the demonstrated determinants of recurrence is shown in Table 5. Patients with fewer than 4 tumors had a lower frequency of hepatic or hepatic-only recurrence as compared to patients with 4 or more tumors (chi-squared test; $p < 0.01$ in both cases). Presence or absence of extrahepatic disease, resection margin, and type of operation also varied with risk of recurrence in the liver; however, none of the variables was related to the frequency of extrahepatic recurrence.

Forty-five patients had fewer than 4 tumors and no extrahepatic disease; 21 (47%) of these patients had hepatic recurrence. Of the remaining 23 patients who had more than 3 tumors or extrahepatic disease, 23 (100%, $p < 0.001$) had hepatic recurrence. Development of extrahepatic metastases, however, was equally frequent in both groups: 49% and 52%, respectively.

The multivariate analysis was repeated for hepatic recurrence. The outcome was almost identical to that shown in Table 4 with the exception that the resection margin (<10 mm versus ≥10 mm, relative risk 4.2; $p = 0.0002$) and the number of tumors (≥4 versus <4, relative risk 3.1; $p = 0.002$) were the two most important risk factors. In the multivariate analysis for extrahepatic recurrence, the presence of extrahepatic disease

Table 4. Determinants of recurrence (Cox proportional hazards model, n = 68).

Variable	Example Status 1	Status 2	Relative risk 1:2[a]	Coefficient[b]	*p* value
Extrahepatic disease	Yes	No	3.9	1.37	0.0005
Type of operation	Major	Wedge	3.3	1.20	0.01
No. of tumors (≥4 versus <4)	≥4	<4	2.8	1.03	0.005
Resection margin (<10 versus ≥10 mm)	<10	≥10	2.4	0.88	0.02
Intrahepatic spread	Bilateral	Unilateral	2.0	0.70	0.03
Liver tumor volume (≥25% versus <25%)	≥25%	<25%	2.0	0.69	0.06

Included are variables with $p < 0.25$.
[a]A relative risk 1:2 means that a patient with status 1 has a correspondingly greater risk of recurrence than a patient with status 2, provided that all other variables in this analysis are kept constant.
[b]Coefficient of the hazard function.

Table 5. Distribution of recurrent disease.

Variable	Recurrence				
	Hepatic	Hepatic only	Extra-hepatic	Extra-hepatic only	Total
No. of hepatic tumors					
<4 (n = 55)	31 (56)[a]	11 (20)[a]	29 (53)	9 (16)	40 (73)[b]
≥4 (n = 13)	13 (100)	8 (62)	5 (38)	0 (0)	13 (100)
Extrahepatic disease					
Not present (n = 56)	32 (57)[a]	15 (27)	26 (46)	9 (16)	41 (73)[b]
Present (n = 12)	12 (100)	4 (33)	8 (67)	0 (0)	12 (100)
Resection margin					
≥10 mm (n = 27)	13 (48)[b]	4 (15)	14 (52)	5 (19)	18 (67)
<10 mm (n = 41)	31 (76)	15 (37)	20 (49)	4 (10)	35 (85)
Type of operation					
Wedge resection (n = 13)	6 (46)	1 (8)[b]	7 (54)	2 (15)	8 (62)
Major resection (n = 55)	38 (69)	18 (33)	27 (49)	7 (13)	45 (82)
Intrahepatic spread					
Unilateral (n = 52)	31 (60)	13 (25)	26 (50)	8 (15)	39 (75)
Bilateral (n = 16)	13 (81)	6 (38)	8 (50)	1 (6)	14 (88)
Liver tumor volume					
<25% (n = 41)	27 (66)	10 (24)	19 (46)	3 (7)	29 (71)
≥25% (n = 27)	17 (63)	9 (33)	15 (56)	6 (23)	24 (89)

Figures within parentheses denote percentages.
[a]$p < 0.01$, refers to lesser risk of recurrence (chi-squared test).
[b]$p < 0.05$, refers to lesser risk of recurrence (chi-squared test).

before resection increased the risk of relapse (relative risk 5.6; $p = 0.0006$). No other variable could be demonstrated to vary with the risk of extrahepatic recurrence.

Analysis of the survival data has been presented elsewhere [5]. Briefly, the analysis indicated that resection is worthwhile only when there are fewer than 4 liver tumors (even if bilateral), no extrahepatic disease is present, and a resection margin of at least 10 mm can be obtained. Factors such as type of operation (major resection versus wedge resection), uni- or bilateral disease, and liver tumor volume could not be demonstrated to influence survival significantly and were not considered to help in electing or rejecting patients for liver resection.

Discussion

This study showed that margin of resection, number of tumors, presence or absence of extrahepatic disease, type of operation, intrahepatic distribution, and liver tumor volume were determinants of hepatic recurrence after liver resection for colorectal secondaries. In contrast, extrahepatic disease before resection was the only variable that could predict dissemination to (other) extrahepatic sites. The liver, lungs, and peritoneal cavity were the most frequent areas of failure, and all patients with relapse had disease at one or more of these sites. Ninety-four percent of patients with relapse had intraabdominal recurrence.

It is true that there is not much to offer a patient whose disease recurs after liver resection; however, some patients may benefit from adjuvant postresection chemotherapy, especially if effective drugs are developed. In testing existing and future drugs, it is essential to know where and when the disease is likely to recur.

After operation of the primary colorectal cancer, relapse is most frequent in the liver, elsewhere in the peritoneal cavity, and at the colorectal resection site [6, 7]. Recurrence in the liver alone is reported to occur in 4.5–19% [7–9]. From 5 previous reports on resection of liver colorectal metastases, comprising a total 168 patients [10–14], it may be calculated that 34% of the patients had liver recurrence and that 40% of the patients had extrahepatic recurrence. Analysis of these 5 reports also reveals that of patients with relapse, slightly more than half (58%) had liver recurrence, one-third had relapse in the liver alone, two-thirds had extrahepatic recurrence, and almost half of the

patients (46%) had extrahepatic recurrence alone. These figures agree with ours except that we had a higher frequency of hepatic recurrence (83% of all patients with relapse) and, accordingly, a lower proportion of patients with extrahepatic relapse alone (17%). Similarly, liver recurrence alone or in combination with extrahepatic relapse was relatively more common in our liver resection material (36% and 83% of patients with relapse) than in the primary resection material (19% and 54%) reported by Willet et al. [7]. The higher frequency of liver recurrence in our patients may reflect the fact that we resected patients with relatively advanced hepatic disease. In the previous reports, about 30% of the patients had multiple liver metastases [11, 12], as compared to 50% in our material.

After colorectal resection, the risk of hepatic, peritoneal, and local recurrence has been demonstrated to vary with the histological differentiation of the primary tumor and Dukes' stage [7, 15, 16]; however, those factors did not seem to play any prognostic role after liver resection. The risk of hepatic recurrence was determined mainly by the number of tumors (<4 versus ≥ 4) and by the absence or presence of extrahepatic disease. It should be emphasized that biopsy of liver hilum lymph nodes is an important step in prognosticating the disease.

The risk of extrahepatic relapse was 50% and was not affected by the characteristics of the liver involvement or by any other variable except for the presence or absence of extrahepatic disease at the time of liver resection. Although we have some means to identify patients with a relatively low risk of hepatic recurrence, i.e., patients with <4 liver tumors and no extrahepatic disease, about half (47%) of these patients will still get extrahepatic disease. These results have obvious implications for preoperative evaluation and selection of candidates for liver resection as well as for adjuvant treatment protocols. Since relapse is common both in the liver and at extrahepatic sites, it is rational to try to achieve effective drug levels in both hepatic inflow and systemic blood. Considering that many of the extrahepatic recurrences are situated within the abdominal cavity, intraperitoneal chemotherapy is a logical choice [17]. It should be remembered that clinical series underestimate the frequency of recurrence in the peritoneal cavity unless routine exploratory laparotomy is performed and that the frequency of peritoneal surface and intraabdominal or retroperitoneal lymph gland relapse is higher in necropsy series [8]. Intraperitoneal administration would achieve high levels of the drug in the peritoneal cavity and also relatively high concentrations in the portal vein. Provided that the fractional hepatic extraction of the drug is different from zero or that the liver is not the only site of elimination, this should give a first-pass effect on the liver that makes this approach advantageous to systemic delivery also with respect to the effect on the liver [18]. In order to obtain maximal effect on extrahepatic sites, the dose chosen should give systemic levels that are close to those considered optimal after intravenous treatment.

In an adjuvant study, patients with no margin of resection, evidence of liver hilum lymph node metastases or extrahepatic disease elsewhere, or patients having 4 or more liver tumors (even if diagnosed first at microscopic examination) should be excluded. It is obviously difficult to control for differences in the risk of extrahepatic recurrence. In contrast, it is possible to control some of the risk for hepatic recurrence by stratification for type of operation (major resection versus wedge resection), margin of resection (<10 mm versus ≥ 10 mm), and intrahepatic distribution (bilateral versus unilateral disease), in that order of priority.

The observation that major liver resection was accompanied by a higher risk of recurrence than wedge resection deserves comment. Although it cannot be excluded that this was a result of inadequate control of nontreatment variables, it should be observed that anesthesia and surgery has been reported to affect the immune system adversely with a risk that immunoreactivity against cancer is depressed and that dormant metastases escape destruction [19].

After resection of the primary cancer, failure at the colorectal resection site occurs in 15–63% of patients with relapse [7, 9, 15, 16]. Up to about half of the local failures (20–45%) occur more than 2 years after the primary resection [15, 16], which means that the risk of local recurrence is substantial also in patients operated on for metachronous liver metastases. In our material, 8 patients (15%) had recurrence at the site of bowel resection, and 5 of them had liver metastases synchronous with the primary cancer. This is an unacceptably high rate of local recurrence in patients subjected to liver resection and emphasizes the need for improved preoperative evaluation and selection of patients.

Résumé

Le mode de récidive et les facteurs qui influencent le siège de la récidive ont été étudiés chez 68 malades soumis à résection hépatique pour des métastases d'origine colo-rectale. Cinquante trois (78%) patients présentèrent une nouvelle récidive. Ces récidives se situèrent le plus souvent au niveau du foie, des poumons, et de la cavité péritonéale. Tous les malades présentaient une ou plusieurs récidives au niveau d'un ou de plusieurs de ces éléments. La récidive intra-abdominale fut observée chez 50 (74%) malades soit 94% des malades avec récidive. Le foie fut concerné chez 44 (65%) malades et fut le siège unique de la récidive chez 19 (28%) d'entre eux. Les métastases extra-hépatiques concernèrent 34 (50%) malades. Les causes de la récidive furent les suivantes: 4 ou plus de 4 métastases hépatiques lors de l'intervention initiale, marge de résection inférieure à 10 mm, maladie extra-hépatique. Les autres facteurs de risque furent les suivants: bilatéralité des métastases colo-rectales, importance de la résection du parenchyme hépatique, volume de la masse tumorale. L'existence d'une affection extra-hépatique avant la résection fut le seul facteur retrouvé pour expliquer le risque de dissémination extra-hépatique. On peut conclure de ces faits que le nombre des métastases hépatiques, la marge de résection, et la présence ou l'absence d'une maladie extra-hépatique sont des facteurs de risque de récidive au niveau du foie après résection des métastases hépatiques d'origine colo-rectale. Aucun élément n'est actuellement disponible pour permettre de prédire la récidive extra-hépatique qui affecte la moitié des malades indemnes d'affection extra-hépatique avant la résection hépatique. Ce fait, essentiel, doit inciter à mieux évaluer les candidats aptes à la résection hépatique et à influencer les protocoles thérapeutiques complémentaires.

Resumen

El patrón de recurrencia y los factores que influencian el sitio de la enfermedad recurrente fueron estudiados en 68 pacientes sometidos a resección de metástasis hepáticas de cáncer colorrectal. Cincuenta y tres pacientes (78%) presentaron recurrencia. El hígado, los pulmones, y la cavidad peritoneal fueron los lugares más frecuentemente afectados, y todos los pacientes con relapso de la enfermedad presentaron recurrencia en uno o más de estos sitios. La recurrencia intraabdominal occurió en 50 (74%) de los pacientes (94% de los pacientes con recurrencia). El hígado apareció afectado en 44 (65%) pacientes y fue el único lugar de recurrencia en 19 (28%). Se presentaron metástasis extrahepáticas en 34 (50%) pacientes. Los principales factores determinantes de recurrencia hepática fueron la presencia original de 4 o más tumores hepáticos, un márgen de resección de menos de 10 mm, y enfermedad extrahepática. Otros factores que también aparecieron asociados con un mayor riesgo de recurrencia hepática fueron la invasión intrahepática bilateral (en comparación con enfermedad unilateral), resección hepática mayor (en comparación con resección en cuña), y el porcentaje del volumen tumoral hepático. La presencia de enfermedad extrahepática antes de la resección fue el único factor demostrable capaz de aumentar el riesgo de ulterior extensión extrahepática. Se llega a la conclusión de que el número de las metástasis hepáticas, el margen de resección, y la presencia o ausencia de enfermedad extrahepática ayudan a predecir el riesgo de recurrencia hepática después de la resección de metástasis hepáticas de cáncer colorrectal. Sin embargo, ninguna variable actualmente disponible es de utilidad para la predicción de la recurrencia extrahepática que afecta a aproximadamente la mitad de los pacientes que no exhiben evidencia de enfermedad extrahepática antes de la resección hepática. Este hallazgo indica la urgencia de una mejor valoración de los candidatos a resección hepática y debe influenciar los protocolos de terapia adyuvante.

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Invited Commentary

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Following the watershed clinical reviews of hepatic resection for metastatic colon and rectum carcinoma by Foster and Berman [1] and Wilson and Adson [2], and the anatomic expositions of Starzl et al. [3] in the mid-1970's, hepatic resection for primary and metastatic disease has flourished. Initial reports and later series present a clear message: (a) resection of up to 75–85% of the liver can be performed with an expected mortality rate of ≤5% [4–7]; (b) a small subset of patients with colon and rectum cancers that have metastasized to the liver will have no extrahepatic disease and will be resectable for cure; (c) between 25 and 35% of such patients, depending on the selection process involved, will be free of any evidence of re-recurrent disease from 5 to 10 years after hepatic resection.