Int J Clin Oncol (2005) 10:86–96
DOI 10.1007/s10147-005-0475-z

REVIEW ARTICLE

Kenzo Yasui · Yasuhiro Shimizu

Surgical treatment for metastatic malignancies. Anatomical resection of liver metastasis: indications and outcomes

Received: January 5, 2005

Abstract Hepatectomy may be the only treatment modality for the cure of colorectal liver metastasis. However, whether to perform nonanatomical resection or anatomical resection remains unclear. Original articles in English on liver metastasis, including reports that dealt with case series of more than 50 curative hepatectomies, were reviewed, and the current status of surgical treatment for colorectal liver metastasis was summarized, with a special emphasis on the relevance, indications, and outcomes of anatomical hepatectomy. Anatomical hepatic resection was performed in 63% of the patients. For patients who were treated by curative hepatectomy, including both anatomical and nonanatomical resection, the morbidity rates, mortality rates, 5-year survival rates, and rates of hepatic recurrence were 23%, 3.3%, 34%, and 41.2%, respectively. In 73 articles that each analyzed more than 50 patients treated with potentially curative hepatectomy, the incidence of anatomical resection exceeded 50% in 56 series, while anatomical resection was performed in fewer than 50% of the patients in 17 series. A comparison between these two groups naturally revealed a remarkable difference in the incidence of anatomical resection (72% versus 34%), but no difference in terms of morbidity; mortality; survival rates at 3, 5, and 10 years; or rate of hepatic recurrence. The profile of liver metastasis related to prognosis was generally advantageous to patients treated with nonanatomical resection, and this may have nullified the survival advantage of anatomical hepatectomy over nonanatomical resection. Anatomical resection provides a higher probability of coresecting microscopic invasions that are predictable but undetectable, and can be recommended as a standard procedure for locally advanced metastatic liver cancer.

Key words Colorectal liver metastases · Hepatic resection · Anatomical hepatectomy · Indication · Prognosis

K. Yasui (✉) · Y. Shimizu
Department of Gastroenterological Surgery, Aichi Cancer Center, 1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681, Japan
Tel. +81-52-752-6111; Fax +81-52-764-2967
e-mail: kenyasui@aichi-cc.jp

Introduction

There has been remarkable progress in the treatment of metastatic liver cancer during the past four decades. Woodington and Waugh[1] treated patients with colorectal liver metastasis by hepatectomy and, in 1963, reported a 5-year survival rate of 20%, although these data apparently came from a highly selected population of patients. In 1967, Flannagan and Foster[2] attained a 5-year survival rate of 26% with 45 patients with colorectal liver metastasis. In 1967, Wilson and Adson,[3] of the Mayo Clinic, reported that 8 of 54 patients with colorectal liver metastasis survived disease-free for 10 years after hepatectomy. In 1986, Butler et al.,[4] of Memorial Sloan-Kettering, claimed 5-year and 10-year survival rates of 26% and 21%, respectively, for a series of 62 patients who underwent resection of liver metastasis from colon cancer, and demonstrated for the first time that colorectal liver metastasis was actually a curable disease. Since then, the 10-year survival rates have been reported[5–12] to be in the range of 20% to 42%. D'Angelica et al.[13] analyzed 96 patients who survived for more than 5 years, and concluded that disease-free survival for 5 years after liver resection most likely implies cure.

Given these encouraging data, there is little doubt that surgical resection is the only treatment modality for colorectal liver metastasis with solid evidence for a reasonable possibility of cure. However, whether to perform nonanatomical resection or anatomical resection for this disease entity remains controversial.

Methods

An electronic search of the Medline Database was undertaken, using the search terms of "hepatectomy or liver resection", "colorectal cancer", and "liver metastasis". Here, original articles in English on liver metastasis that dealt with case series of more than 50 curative hepatectomies are reviewed, and the current status of surgical treatment for

colorectal liver metastasis is summarized, with a special emphasis on the relevance, and indications, and outcomes of anatomical hepatectomy.

Indications for surgical resection of colorectal liver metastasis: history and current status

The past two decades have seen remarkable progress regarding the surgical techniques and postoperative management of major hepatic surgery. Consequently, the indications for hepatectomy, now a safe and accomplished procedure, have been markedly extended. This trend was further prompted by accumulating reports[10,14–25] in the literature claiming operative mortality of zero following hepatectomies for colorectal liver metastasis.

In the early era of hepatic surgery, the indication for the surgical resection of colorectal liver metastasis was defined as small solitary metastasis appearing later after resection of a colon tumor, without mesenteric lymph node involvement. Adson and Van Heerden[26] and Adson et al.,[27] of the Mayo Clinic, later extended the indication to include multiple metastatic lesions and lesions with large diameters that call for major hepatectomy. With further accumulation of data from several case series of colorectal liver metastases treated with surgery, the safety and efficacy of hepatectomy became widely accepted. More recently, hepatectomy has come to be considered and attempted even for patients with extrahepatic recurrences,[28–33] or hepatic node metastases[22,34–40] to the hepatic hilum, which, in the past, had not been indicated for surgical resection. Such an aggressive approach, however, is not currently shared by all investigators. At some institutions, metastasis to the hepatic lymph nodes, extrahepatic disease, and multiple metastases, of four or more, are considered to be contraindications[41] to hepatic resection.

In 1996, Bismuth et al.[42] performed hepatectomy for 53 patients with colorectal liver metastases initially considered unresectable because of mal-location, large tumor size, multiplicity, or extrahepatic disease. These lesions were downstaged by systemic chronomodulated chemotherapy with 5-fluorouracil, folinic acid, and oxaliplatin, to the point that operation could be performed, and surgery led to a remarkable 5-year survival rate of 40%, demonstrating the potential of a multimodal approach to expand the indication for hepatic resection.

Recurrence to the remnant liver following previous hepatic resection affects prognosis, but may be amenable to repeat rsection.[43] In 1994, Nordlinger et al.[44] reported that, in a series including 116 patients, from 85 institutions treated by repeat hepatectomy, the actuarial survival rate was 33% at 3 years. In 1997, Adam et al.[45] reported a 5-year survival rate of 41% for 64 patients treated by repeat liver resection, which is comparable to that observed following primary liver resections. Thus, patients with recurrence limited to the liver following previous hepatic resection have come to be treated by repeat surgery,[7,8,10,45–64] as long as general indications for hepatic surgery are met, and this principle has led to the enhanced overall survival of patients with colorectal liver metastasis.

Although hepatectomy is now considered as the first choice in the treatment of colorectal liver metastasis, the aims of and eligibility for hepatic resection in modern clinical practice can be classified into the following three categories:

(i) Hepatectomy intended for cure. This applies to patients whose metastatic lesions are completely dissected along with local invasion. Patients who fall into this category should have no metastatic or recurrent disease, other than hepatic metastasis, and this must be resected completely with the associated local invasion.
(ii) Hepatectomy intended for palliation but that could result in cure. This applies to patients who have extrahepatic metastatic lesions, such as lung, locoregional, or peritoneal metastasis, that can be coresected with the liver metastasis.
(iii) Hepatectomy for palliation. This applies to patients with extensive liver metastasis or extrahepatic metastasis that cannot be resected completely, including patients with systemic disease whose survival is still likely to depend on the progression of liver metastasis and those whose metastatic lesions have been downstaged and have become respectable after chemotherapy.

For each category, accurate assessment of the disease status, including the size of the metastasis, the location in relation to the main vascular pedicles, and the extent of lymph node metastasis and vascular invasion, is mandatory. In addition, surgery can only be considered as the first choice when it can be preformed adequately, with low morbidity and mortality rates, along with other components of multidisciplinary treatment.

Selection of the extent of surgical resection for hepatectomy with curative intent

According to Penna and Nodlinger,[65] the decision of whether or not to perform surgical resection for liver metastases should be based on the patient's condition, the extent of the metastatic disease, and the liver functional reserve. The type of liver resection depends on the size, number, and location of the metastases, their relation to the main vascular and biliary pedicles, and the volume of the liver parenchyma that can be preserved after surgery. Small metastases located near the liver capsule can be resected by nonanatomical wedge resection, while major anatomical resection is more often required for a large lesion. These comments more or less summarize the selection criteria for surgical resection and the extent of hepatectomy at most institutions.

The actual numbers of each type of surgery performed were assessed from 73 articles,[4–13,16,19–22,34–38,41,54–56,66–114] each of which described the outcome of curative treatment of more than 50 patients, and presented the proportions of

anatomical resections among all hepatectomies performed (Table 1). Anatomical hepatic resection was performed in 63% of the patients (range, 16%–100%). Curative hepatectomy, including both anatomical and nonanatomical resections, resulted in a morbidity rate of 23% (range, 6%–37%), a mortality rate of 3.3% (range, 0–10%), and 3-year and 5-year survival rates of 50% (range, 30%–66%) and 34% (range, 15%–59%), respectively. The rate of recurrence in the liver following primary curative hepatectomy was 41.2% (range, 21.3%–74%).

Thus, anatomical resection was more commonly performed for colorectal liver metastasis, compared with nonanatomical resection. As a logical outcome, this suggests that more than half of the patients with colorectal liver metastases diagnosed at most institutions either had large tumor size or had multiple lesions that necessitated anatomical resection. In contrast, institutions that showed lower rates of anatomical liver resection were considered simply to have had a higher proportion of lesions that were either small enough in size or located near the capsule to be treated with nonanatomical resection.

Outcome after anatomical resection

Because no official stage classification exists for metastatic liver cancer, it is not possible currently to make an adequate comparison of survival between different types of liver resection. In the 73 case series that each analyzed more than 50 patients treated with potentially curative hepatectomy, the incidence of anatomical resection exceeded 50% in 56 series, while anatomical resection was performed in fewer than 50% of the patients in 17 series. To evaluate the difference in outcome between the two types of surgery, 51 sets of data were extracted from the 73 reports in order that the same patients from the same institution were not included (Table 2). A comparison between these two groups naturally revealed a remarkable difference in the incidence of anatomical resection (72% versus 34%), but no difference in terms of morbidity; mortality; survival rates at 3, 5, and 10 years; or rate of hepatic recurrence (Table 2). From these findings, some investigators may conclude that the extent of liver resection is not, by itself, a prognostic factor.

Scheele et al.[5] reported that the size of metastatic lesions ranged from 8 to 32 cm (median, 18.5 cm) for those treated with anatomical resection, from 7 to 28 cm (median, 14 cm) for those treated with segmental resection, and from 1 to 17 cm (median, 5 cm) for those treated with wedge resection. According to Kokudo et al.,[91] the mean diameter of tumors treated with anatomical resection was 5.81 cm, whereas that of tumors treated with nonanatomical wedge resection was 2.69 cm. These data are representative of several others, in that anatomical resection is apt to be performed for large or multiple lesions, while wedge resection is applied mainly for smaller metastases located near the liver capsule.

From studies describing the natural history of unresected metastases,[115,116] it is clear that the prognosis of colorectal liver metastasis depends on the size and number of the metastatic lesions. In addition, several investigators have found, in their series, that the prognosis of the patients depended on the number,[5,10,16,19,20–22,34,40,41,71,80,110,111,117] and size[8,9,12,34,36,37,66,67,80,97,99,102,103,118] of the metastases, the proportion of hepatic parenchyma involved, or the number of lobes involved.[12,19,22,34,76,112,119] Because the size and number of the metastatic lesions increase in accordance with the time elapsed from the establishment of metastasis, and the doubling time of the tumor cells, there is little doubt that the size and number reflect survival. Even in the report from Kokudo et al.,[91] demonstrating a lack of difference in survival between patients treated with anatomical resection and those treated with nonanatomical resection, tumor size was also larger among the subset treated with anatomical resection. Large and multiple metastatic lesions usually lead to poor prognosis after hepatectomy but, again, it seems as though these disadvantages have been nullified by the anatomical resection. In the subset of patients treated with anatomical resection 15.7% of the patients also had extrahepatic metastasis, as opposed to 4% in the subset treated with nonanatomical resection. Despite these differences in patient demographics that are advantageous to nonanatomical resection, no difference in survival was observed between the two subsets. In addition, it must be borne in mind that recurrence in the liver following nonanatomical resection has a greater chance for repeat hepatectomy which could contribute to improve the survival of the subset treated with nonanatomical resection,[8,44] and this advantage may have been nullified by the anatomical resection. In order to accurately evaluate the prognostic significance of the procedure, comparisons of anatomical and nonanatomical resection, with both survival and the incidence of recurrence in the liver as endpoints, should be made among patients with colorectal liver metastasis at similar clinical stages.

In the current review, survival data from some investigators were in favor of anatomical resection,[5,16,76,102,120–122] while survival data in other studies were in favor of nonanatomical resection.[8,13,112] Scheele et al.[102] analyzed 350 patients who underwent potentially curative hepatectomy and found that the 5-year survival rate was 41% among patients who underwent anatomical resection as opposed to 24% among those treated with nonanatomical resection. Hughes et al.[41] analyzed 798 patients treated at 24 United States institutions, and found that anatomical resection had a survival advantage over nonanatomical resection among a subset of patients with solitary liver metastasis of more than 4 cm diameter. On the other hand, Fong et al.[8] found, in an analysis of 1001 cases of colorectal liver metastasis, that the 5-year survival rate was 39% for patients treated with nonanatomical resection and 33% for those treated with anatomical resection. However, this result reflects in part, the fact that 108 of 132 patients (82%) who had recurrence to the liver were treated with repeat resection, and this significantly affected survival for this subset.

The profile of liver metastases, including their size and number of metastases, was generally advantageous to patients treated with nonanatomical resection, and this may have nullified the survival advantage of anatomical hepatectomy over nonanatomical hepatectomy.

Table 1. Summary of 73 articles on hepatectomy for hepatic metastasis, each describing the outcome of curative treatment of more than 50 patients, and providing the proportions of anatomical resections

Article no.	Year	Author	Years of analysis	Institute/Place	No. of patients (curative) treatment	Anatomical resection	Morbidity	Mortality	Survival		Hepatic recurrence
									3-Year	5-Year	
1	1984	Fortner[82]	1971–1982	M. Sloan-Kettering	75	87%	27%	4%	57%	40%	
2	1986	Butler[4]	1950–1981	M. Sloan-Kettering	62	43.50%	26%	10%	50%	34%	67%
3	1988	Fortner[81]	1971–1985	M. Sloan-Kettering	77	89.60%			65%	49%	
4	1997	Fong[80]	1985–1991	M. Sloan-Kettering	410	73.50%	24%	2.80%		38%	48%
5	1997	D'Angelica[13]	1985–1991	M. Sloan-Kettering	96	53%					
6	1998	Chan[73]	1991–1996	M. Sloan-Kettering	379	63%	25.60%	3.20%			
7	1999	Fong[8]	1985–1998	M. Sloan-Kettering	1001	86%	31%	2.80%	57%	37%	28.80%
8	2000	DeMatteo[75]	1985–1998	M. Sloan-Kettering	267	55.40%	17%	0.40%	62%	43%	
9	2003	Martin[94]	1997–2001	M. Sloan-Kettering	260	100%					
10	1986	Ekberk[34]	1971–1984	Lund, Sweden	72	82%	15%	5.60%	30%	16%	
11	1987	Ekberk[35]	1971–1984	Lund, Sweden	68	80.90%					65%
12	1998	Ohlsson[55]	1971–1995	Lund, Sweden	111	77%		3.60%	37%	25%	58%
13	1986	Iwatsuki[16]	1975–1985	Pittsburgh, USA	60	95%	13.30%	0%	53%	45%	30%
14	1994	Gayowski[19]	1981–1991	Pittsburgh, USA	184	83.30%		0%	49%	38%	
15	1988	Hughes[41]	1984–1985	24 Institutes, USA	798	53.10%				33%	
16	1990	Scheele[103]	1960–1987	Erlangen, Germany	173	72.30%		5.50%		40%	69.80%
17	1991	Scheele[5]	1960–1988	Erlangen, Germany	219	62.60%		5.60%		39%	
18	1995	Scheele[102]	1960–1992	Erlangen, Germany	350	74.60%	16%	4.40%		39.30%	
19	1990	Schlag[104]	1981–1989	Heidelberg, Germany	122	77%	34%	4.10%			
20	1991	Fregiz[83]	Not described	7 Institutes, Italy	212	46.70%		6.80%		24%	
21	1991	Steele[106]	1984–1988	15 Institutes, USA	69	78.30%	13%	2.70%	52%		74%
22	1991	Doci[76]	1980–1989	Milan, Italy	100	50%	11%	5%		30%	
23	1995	Doci[77]	1980–1992	Milan, Italy	208	42.30%	35%	2.40%			
24	1991	Lise[92]	1975–1990	Podova, Italy	64	59.70%	16.90%	3%		32%	37.50%
25	1991	Petrelli[98]	1963–1988	Rosewell Park CC	62	63%	30%	8.10%		28%	
26	1992	Rosen[100]	1960–1987	Mayo Clinic	280	53.00%		1.80%	47%	25%	
27	1997	Jamison[6]	1960–1987	Mayo Clinic	280	54.60%		2%	46%	27%	
28	1992	van Ooijen[111]	1979–1989	15 Institutes, Holland	118	78%	34.70%	7.60%		21%	
29	1993	Zieren[114]	1982–1991	Cologne, Germany	90	73%	26%	3%	45%	32%	30%
30	1993	Sugihara[109]	1978–1989	NCC, Japan	109	25%		1.30%	57%	48%	31.20%
31	1999	Yamamoto[56]	1992–1994	NCC, Japan	96	24%			61%	51%	
32	2000	Minagawa[10]	1980–1997	NCC, Japan	218	41.70%		0%	51%	38%	41.70%
33	2001	Sugawara[108]	1985–1997	NCC, Japan	304	20.70%					
34	1994	Pedersen[97]	1978–1991	Holland	50	74.20%	28.80%	7.60%	36%		24%
35	1995	Jatzko[87]	1984–1992	Graz, Germany	66	37.90%	19.70%	4.50%		30%	
36	1995	Fuhraman[84]	1988–1992	M.D. Anderson	107	69%		2.80%		44%	
37	1995	Yasui[36]	1983–1994	ACC, Japan	64	100%		2.40%			31.30%
38	1997	Yasui[37]	1983–1995	ACC, Japan	81	83.60%		2%		41.70%	41.80%
39	1996	Wanebo[112]	1978–1994	Virginia, USA	74	68.90%	17.60%	5.40%		24%	
40	1997	Beckhurts[68]	1987–1994	Munich, Germany	119	27.70%	21%		34%	15%	
41	1997	Nadig[95]	1988–1992	St. Louis, USA	275	32.40%		4%		26%	
42	1997	Jenkins[88]	1975–1993	Chicago, USA	107	64.10%	26.20%	3.80%	42%	25%	

Table 1. Continued

Article no.	Year	Author	Years of analysis	Institute/Place	No. of patients (curative) treatment	Anatomical resection	Morbidity	Mortality	Survival		Hepatic recurrence
									3-Year	5-Year	
43	1997	Jaeck[86]	1959–1991	85 Institutes, France	720	63.30%		3.60%		26%	
44	1997	Nuzzo[96]	1984–1995	Rome, Italy	58	88%	24%	1.70%	36%	17%	
45	1997	Taylor[20]	1977–1993	Toronto, Canada	123	76.40%		0%		34%	
46	1997	Rees[99]	1986–1996	Winchester, UK	89	94%	6%	1%		37%	39.30%
47	1998	Bakalakos[66]	1978–1993	Ohio, USA	238	20.20%	17.20%	1.10%		28.80%	
48	1998	Bakalakos[67]	1985–1993	Ohio, USA	210	16%		1.40%			
49	1998	Lorenz[93]	1991–1996	26 Institutes, Germany	218	67%		5%		35%	34.90%
50	1998	Cady[71]	To 1996	Boston, USA	223	70%	16%	3.60%		20%	
51	1998	Elias[78]	1984–1996	Villejuif, France	233	70%		2%		24.70%	
52	1998	Elias[54]	1984–1996	Villejuif, France	136	73%		1.50%		28%	21.30%
53	1999	Ambiru[38]	1984–1997	Chiba, Japan	168	95.20%	30%	3.50%	42%	26%	46%
54	1999	Wigmore[113]	1988–1998	Edinburgh, UK	84	87%		6%			25%
55	2004	Stewart[107]	1988–2001	Edinburgh, UK	137	100%					
56	1999	Nakamura[7]	1978–1998	Hamamatsu, Japan	79	60.80%	15%	2.50%		49%	33.70%
57	1999	Jourdan[89]	1987–1997	New Zealand	53	80%	37.10%	5.70%	62%	27%	
58	1999	Harmon[9]	1978–1998	Seattle, USA	110	66.40%	34%	4%		46%	
59	2000	Seifert[105]	1985–1996	Mainz, Germany	103	30.60%	28.30%	5.80%		35%	39.80%
60	2000	Ueno[110]	1985–1996	Saitama, Japan	85	59%		3.40%		27.90%	
61	2000	Bolton[70]	To 1999	New Orleans, USA	165	79.40%		6%		36%	
62	2001	Nakajima[21]	1985–1996	Nara, Japan	70	47.10%		0%	56.20%	35.50%	60%
63	2001	Kokudo[91]	1980–1999	Cancer Institute, Japan	174	55.20%	9.80%	1.10%	56.70%	43.20%	
64	2002	Belli[69]	1986–2000	Naples, Italy	181	31%	10.50%	2.80%	55.30%	39.80%	29.30%
65	2002	Jaeck[22]	1988–1998	Strasbourg, France	160	34.30%	33%	0%	56%	42%	
66	2002	Choti[74]	1984–1999	Johns Hopkins	226	71.20%	18.60%			40%	
67	2002	Sasaki[101]	1982–2000	Oita, Japan	67	67.20%		5.30%		33.40%	40.30%
68	2003	Cavallari[72]	1986–2000	Bologna, Italy	246	61.40%	20%	0.80%		40% (DFS)	30.10%
69	2003	Nagakura[11]	1982–2000	Niigata, Japan	102	29.80%		1.70%		40%	39.20%
70	2003	Kato[90]	1992–1996	18 Institutes, Japan	585	54%				39.20%	41.40%
71	2004	Imamura[85]	1994–2002	Tokyo University, Japan	116	59.80%					51%
72	2004	Fernandez[79]	1995–2002	St. Louis, USA	100	98%		1%	66%	58.60%	46.20%
73	2004	Tanaka[12]	1985–2000	Yokohama, Japan	189	59.10%	26.30%	0.52%	46.30%	42.60%	45.50%

M. Sloan-Kettering, Memorial Sloan-Kettering; Rosewell Park CC, Rosewell Park Cancer Center; NCC, National Cancer Center; ACC, Aichi Cancer Center; DFS, disease free survival

Table 2. Morbidity, mortality, cumulative survival, and rate of hepatic recurrence in series showing different incidences of anatomical hepatic resection

	Anatomical resection performed in 50% or more patients (n = 39)	Anatomical resection performed in fewer than 50% of patients (n = 12)
Anatomical resection	72% (53–98)	34% (18–47)
Morbidity	23% (6–37)	22% (11–33)
Mortality	3% (0–8)	3% (0–7)
3-Year survival rate	48% (34–66)	52% (34–56)
5-Year survival rate	34% (17–59)	32% (15–46)
10-Year survival rate	26% (13–43)	26%
Rate of hepatic recurrence	41% (21–74)	43% (29–60)

To evaluate the difference in outcome between the two types of surgery, 51 sets of data were extracted from the 73 articles (see Table 1) in order that the same patients from the same institution were not included
Figures in parentheses are ranges

Recurrence in the liver following primary hepatectomy

Recurrences in the liver following primary hepatectomy may be explained either as growth following a dormant metastasis from the primary colorectal cancer, or as secondary metastasis as a consequence of the local invasion of the primary liver metastasis. The prognosis of synchronous liver metastasis has been reported by several investigators[5,9–10,22,41,68,69,96,102,103,109,110,123–127] as being worse than that of metachronous metastasis, while several others postulate that clinical stage[4,10,16,27,41,61,76,83,86,87,90,96,103,123,126,128–130] or lymph node metastasis[8,23,38,40,41,80,86,89,90,96,118,131–136] of the primary colorectal cancer is also reflected in the prognosis of liver metastasis. Theoretically, it is unlikely that the clinical stage of the primary affects the survival of the metastatic lesion in a patient with metachronous liver metastasis that was detected long after surgery for the primary, which may have been cured locally by that time. This means that the clinical stage of the primary colorectal cancer influences the outcome only in patients with concurrent metastasis and if the metastases are found shortly after surgery for the primary cancer.

For patients whose primary cancer has been completely cured, minimal residual disease disseminated from the metastatic liver tumor may be the cause of recurrence in the liver, which, in turn, may affect the prognosis after hepatectomy.[15] Repeat hepatectomy may, in such cases, be a useful option to improve survival.[7,10,43–46,48,55,56,61,64,80,137–140] However, adequate selection of the type of surgery at the time of primary hepatectomy may be of even greater importance if this can avoid recurrence in the liver.

Minagawa et al.[10] postulated that the use of intraoperative ultrasound could detect potential residual cancer during surgery, and they noted that resection reflecting this information resulted in a good prognosis, regardless of the type of hepatectomy the surgeon considered as a standard procedure. Indeed, surgery based on diagnostic imaging should be able to completely avoid locoregional recurrences, if all metastatic lesions can be visualized and resected. In reality, however, the incidence of recurrence to the liver in their series was as high as 41.7%, and almost half of the recurrences were subsequently treated with repeat hepatectomy.

Needless to say, complete detection of all minimal metastatic foci and vessel invasion by preoperative imaging studies, including a unified computed tomography (CT) and angiography system,[141] magnetic resonance imaging (MRI), and F-18 fluorodeoxyglucose-positron emission tomography (FDG-PET),[79,142] and intraoperative ultrasound would result in an accurate decision regarding the extent of liver resection. If this could be accomplished, patients would never suffer from locoregional recurrence and could be cured if no other dissemination from the primary colorectal cancer had occurred. This goal, however, has not been achieved, even with combinations of various modern diagnostic modalities. In order to decrease the incidence of recurrence in the liver, therefore, it is of paramount importance that an adequate selection of the extent and type of hepatectomy be made, so as to minimize the chances of leaving minimal residual disease unresected.

Patterns of local invasion that may provide criteria for the selection of the type of hepatic resection

Understanding the clinicopathological behavior of liver metastasis that can be described in terms of various patterns of local invasion is a prerequisite for adequate selection of the type of hepatic resection. How to minimize the incidence of locoregional recurrence is an issue of great importance for those performing hepatectomy which, after all, is an option for local control.

In the histopathological evaluation of hepatic metastasis, the following patterns of local invasion from the metastatic liver tumor have been reported; these types of invasion could affect prognosis or hepatic recurrence if unresected: intrahepatic portal vein invasion,[8,36,37,56,82,143–149] hepatic vein invasion,[36,37,56,143–148,150] intrahepatic bile duct invasion,[36,37,143–145,147,148,151,152] perineural invasion,[101,143,146] satellite lesions,[5,6,20,54,55,100,102,103,144,145,153,154] invasion to adjacent organs,[8,36,37] and nodal metastasis to the hepatoduodenal ligament.[6,8,10,11,15,22,34–41,54,66–68,80,82,86,90,100,101,105,108,117,128,154–158]

Okano et al.[146] performed thorough histopathologic examinations of liver metastases from 149 patients, and found microinvasion of the bile duct in 58% of the tumors, while macroscopic invasion of the bile duct was observed only in

12%. In fact, patients with macroscopic findings of bile duct invasion had an excellent 5-year survival rate, of 80%, whereas the finding of microscopic bile duct invasion did not seem to affect survival. However, such an excellent survival result could not be attained unless a precise diagnosis of the extent of the lesion and sufficient excision of the liver could be achieved, with the patients being fortunate enough not to have extrahepatic metastasis.

According to Yasui et al.,[36] macroscopic findings of one or more patterns of local invasion were observed in 0% of lesions less than 3 cm in diameter, in 19.2% of lesions with a diameter of 3 to 6 cm, and in 22.6% of lesions over 6 cm in diameter, after meticulous examination of the resected specimens. The 5-year survival rates were inversely correlated with the incidence of local invasion in all anatomically hepatectomized patients. Because the incidence of local invasion correlates with the size of the tumor, it seems rational to perform anatomical resection for tumors with a diameter of 3 cm or more, to remove potential sources of local invasion that cannot be detected preoperatively by current diagnostic modalities.

One of the reasons that the local recurrence rate is comparatively high among patients treated with partial resection[8] is that microscopic invasion of the vessels and bile ducts may not necessarily be restricted to within a limited distance from the margin of the tumor.[145] Although Yamamoto et al.[143] claimed that such microscopic invasion rarely reached beyond 10 mm from the liver metastasis, cancer cells that are disseminated into these vessels are mobile and can travel along the vessels, in accordance with the movement of the diaphragm, to establish micrometastases in regions that are distant from their origins. This means that the chance of completely resecting microscopic tumor deposits (which cannot be recognized perioperatively) is decreased considerably by surgical procedures that do not allow sufficient clearance between the tumor and the cut section of the liver.

Hepatic lymph node metastases and extrahepatic metastases

In 1985, August et al.[15] reported on seven patients who had lymph node metastasis from a metastatic liver tumor, and they declared that these patients were not indicated for hepatectomy. After this report, nodal metastasis was recognized as an important indicator of poor prognosis. While several investigators[15,68,112,131,159] postulate, that because of the dismal outcome, hepatectomy should not be performed for this group of patients, there are recent reports from other investigators who perform lymphadenectomy in addition to hepatectomy, to prevent obstructive jaundice and to improve survival, even if the patients will eventually die of the disease.[31,36,39,40,138] In 1996, Elias et al.[155] reported, in a prospective study of patients treated with curative hepatectomy, that microscopic lymph node involvement of the hepatic pedicle was found in 23.5% of 63 patients who were treated with anatomical resection and in 5.4% of 37 patients who underwent partial resection. This indicated that advanced metastatic cancer that calls for anatomical resection is associated with a high incidence of nodal metastasis. Yasui et al.[36] reported, in 1995, that the incidence of node metastasis correlated with the size of the tumor (0% for tumors with a diameter of less than 3 cm, 3.8% for those that ranged from 3 to 6 cm, and 22.6% for those with diameters greater than 6 cm).

Nakamura et al.[7] reported 2 of 7 patients with lymph node metastasis to have survived more than 5 years. Yasui et al.[37] performed routine lymphadenectomy for 81 patients with colorectal liver metastasis, including 11 patients (13.6%) who actually had nodal metastasis, and achieved a 5-year survival of 41.7%. Bakalakos et al.[67] experienced 3 patients with nodal involvement who survived for 3 to 4 years after surgery, and concluded that the favorable survival in these patients may illustrate how patients with seemingly poor prognostic features may still benefit from hepatic resection. Recently, Laurent et al.[40] emphasized, from a completely different viewpoint, that lymphadenectomy should be performed routinely in order to evaluate the biology of metastatic liver cancer to a greater depth and to more precisely predict survival.

Although whether or not to perform lymphadenectomy for metastatic liver cancer remains controversial, the addition of this procedure to hepatectomy would not actually significantly increase risk to the patients.[39] As mentioned earlier in this review, nodal metastasis represents one of several patterns of local invasion from liver metastasis, and lymphadenectomy may have a place as part of curative surgery for metastatic liver cancer similar to the place it has for cancer of the stomach or the pancreas. In other words, lymphadenectomy may contribute to improving survival, while it definitely results in more precise staging.

There is a similar controversy regarding resectable extrahepatic metastases, in that resection could result in cure, although the prognosis of this subset of patients as a whole is inevitably poor. Although patients with colorectal liver metastasis with extrahepatic lesions had not previously been considered as candidates for surgery,[5,27,41,80] recent improvements in surgical techniques and postoperative care have prompted several investigators[29,31,32,54] to attempt surgery for this subset. Elias et al.[31] reported that the 5-year survival rate after hepatectomy for 75 patients with extrahepatic disease was 28%, and this was not much lower than that of 33% for 219 patients without extrahepatic metastasis. Consequently, they concluded that extrahepatic disease in colorectal cancer patients with liver metastases should no longer be considered as a contraindication to hepatectomy.

Conclusions

Articles on colorectal liver metastasis in English were reviewed to explore the outcomes of and the indications for anatomical resection, with special emphasis on survival data and the incidence of intrahepatic recurrence according to the type of surgery. In addition, the association between

several patterns of local invasion and the outcome of patients treated with hepatectomies of varying extent was described.

The advantage of anatomical resection over partial resection is that, with anatomical resection, there is a higher probability of coresecting extratumoral vessel or bile duct invasions that cannot be detected preoperatively. The resection lines are based on the anatomy of the Glisson sheath, so that ischemia or congestion in any part of the remaining hepatic parenchyma would rarely occur. In addition, skeletonization and dissection of major vascular pedicles at the hepatic hilum allows better control of perioperative hemorrhage. The process of skeletonization also facilitates lymphadenectomy along the hepatoduodenal ligament. One drawback of anatomical resection could be that the removal of more hepatic parenchyma might result in an increased risk of post-resectional hepatic failure.

Needless to say, nonanatomical resection is quite feasible for small metastases with little risk of microscopic local invasion. However, locally advanced liver metastases have a higher risk of local invasion, such as vessel invasion, bile duct invasion, nodal metastasis, and invasion to the adjacent structures. Anatomical resection, which allows a better clearance between tumor deposits and the cut section of the liver, provides a higher probability of coresecting microscopic invasions that are predictable but undetectable, and can be recommended as a standard procedure for metastatic liver cancer.

References

1. Woodington GF, Waugh JM (1963) Results of resection of metastatic tumors of the liver. Am J Surg 105:24–29
2. Flannagan L, Foster JH (1967) Hepatic resection for metastic cancer. Am J Surg 113:551–557
3. Wilson SM, Adson MA (1976) Surgical treatment of hepatic metastases from colorectal cancers. Arch Surg 111:330–334
4. Butler J, Attiyeh FF, Daly JM (1986) Hepatic resection for metastases of the colon and rectum. Surg Gynecol Obstet 162:109–113
5. Scheele J, Stangl R, Altendorf-Hofmann A, et al. (1991) Indicators of prognosis after hepatic resection for colorectal secondaries. Surgery 110:13–29
6. Jamison RL, Donohue JH, Nagorney DM, et al. (1997) Hepatic resection for metastatic colorectal cancer results in cure for some patients. Arch Surg 132:505–511
7. Nakamura S, Suzuki S, Konno H (1999) Resection of hepatic metastases of colorectal carcinoma: 20 years' experience. J Hepatobiliary Pancreat Surg 6:16–22
8. Fong Y, Fortner J, Sun RL, et al. (1999) Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. Ann Surg 230:309–321
9. Harmon KE, Ryan JA, Biehl TR, et al. (1999) Benefits and safety of hepatic resection for colorectal metastases. Am J Surg 177:402–404
10. Minagawa M, Makuuchi M, Torzilli G, et al. (2000) Extension of the frontiers of surgical indications in the treatment of liver metastases from colorectal cancer. Ann Surg 231:487–499
11. Nagakura S, Shirai Y, Yokoyama N, et al. (2003) Major hepatic resection reduces the probability of intrahepatic recurrences following resection of colorectal carcinoma liver metastases. Hepatogastroenterology 50:779–783
12. Tanaka K, Shimada H, Ohta M, et al. (2004) Procedures of choice for resection of primary and recurrent liver metastases from colorectal cancer. World J Surg 28:482–487
13. D'Angelica M, Brennan MF, Fortner JG, et al. (1997) Ninety-six 5-year survivors after liver resection for metastatic colorectal cancer. J Am Coll Surg 185:554–559
14. Taylor B, Langer B, Falk RE, et al. (1983) Role of resection in the management of metastases to the liver. Can J Surg 26:215–217
15. August DA, Sugarbaker PH, Ottow RT, et al. (1985) Hepatic resection of colorectal metastases. Influence of clinical factors and adjuvant intraperitoneal 5-fluorouracil via Tenckhoff catheter on survival. Ann Surg 200:210–218
16. Iwatsuki S, Esquivel CO, Gordon RD, et al. (1986) Liver resection for metastatic colorectal cancer. Surgery 100:804–810
17. Iwatsuki S, Starzl TE (1988) Personal experience with 411 hepatic resections. Ann Surg 208:421–434
18. Cole DJ, Ferguson CM (1992) Complications of hepatic resection for colorectal carcinoma metastasis. Am Surg 58:88–91
19. Gayowski T, Iwatsuki S, Madariaga JR, et al. (1994) Experience in hepatic resection for metastatic colorectal cancer: analysis of clinical and pathologic risk factors. Surgery 116:70–710
20. Taylor M, Forster J, Langer B, et al. (1997) A study of prognostic factors for hepatic resection for colorectal metastases. Am J Surg 173:467–471
21. Nakajima Y, Nagao M, Ko S, et al. (2001) Clinical predictors of recurrence site after hepatectomy for metastatic colorectal cancer. Hepatogastroenterology 48:1680–1684
22. Jaeck D, Nakano H, Bachellier P, et al. (2002) Significance of hepatic pedicle lymph node involvement in patients with colorectal liver metastases: a prospective study. Ann Surg Oncol 9:430–438
23. de Santibanes E, Lassalle FB, McCormack L, et al. (2002) Simultaneous colorectal and hepatic resections for colorectal cancer: postoperative and longterm outcomes. J Am Coll Surg 195:196–202
24. Chua HK, Sondenaa K, Tsiotos GG, et al. (2004) Concurrent vs staged colectomy and hepatectomy for primary colorectal cancer with synchronous hepatic metastases. Dis Colon Rectum 47:1310–1316
25. Shimada H, Tanaka K, Masui H, et al. (2004) Results of surgical treatment for multiple (≥5 nodules) bi-lobar hepatic metastases from colorectal cancer. Langenbecks Arch Surg 389:114–121
26. Adson MA, Van Heerden AV (1980) Major hepatic resections for metastatic colorectal cancer. Ann Surg 191:576–583
27. Adson MA, van Heerden JA, Adson MH, et al. (1984) Resection of hepatic metastases from colorectal cancer. Arch Surg 119:647–651
28. Smith JW, Fortner JG, Burt M (1992) Resection of hepatic and pulmonary metastases from colorectal cancer. Surg Oncol 1:399–404
29. Nagakura S, Shirai Y, Yamato Y, et al. (2001) Simultaneous detection of colorectal carcinoma liver and lung metastases does not warrant resection. J Am Coll Surg 193:153–160
30. Bellon N, Pignon JP, Pocard M, et al. (2003) Extrahepatic disease does not contraindicate hepatectomy for colorectal liver metastases. Br J Surg 90:567–574
31. Elias D, Sideris L, Pocard M, et al. (2004) Results of R0 resection for colorectal liver metastases associated with extrahepatic disease. Ann Surg Oncol 11:274–280
32. Ferrero A, Polastri R, Muratore A, et al. (2004) Extensive resections for colorectal liver metastases. J Hepatobiliary Pancreat Surg 11:92–96
33. Yoshidome H, Kimura F, Ambiru S, et al. (2004) Surgical treatment for extrahepatic recurrence after hepatectomy for colorectal metastases. Hepatogastroenterology 51:1805–1809
34. Ekberk H, Tranberg KG, Andersson R, et al. (1986) Determinants of survival in liver resection for colorectal secondaries. Br J Surg 73:727–731
35. Ekberk H, Tranberg KG, Andersson R, et al. (1987) Pattern of recurrence in liver resection for colorectal secondaries. World J Surg 11:541–547
36. Yasui K, Hirai T, Kato T, et al. (1995) Major anatomical hepatic resection with regional lymph node dissection for liver metastases from colorectal cancer. J Hepatobiliary Pancreat Surg 2:103–107

37. Yasui K, Hirai T, Kato T, et al. (1997) A new macroscopic classification predicts prognosis for patients with liver metastases from colorectal cancer. Ann Surg 226:582–586
38. Ambiru S, Miyazaki M, Isono T, et al. (1999) Hepatic resection for colorectal metastases: analysis of prognostic factors. Dis Colon Rectum 42:632–639
39. Elcolani G, Grazi GL, Ravaioli M, et al. (2004) The role of lymphadenectomy for liver tumors. Further considerations on the appropriateness of treatment strategy. Ann Surg 239:202–209
40. Laurent C, Cunha AS, Rullier E, et al. (2004) Impact of microscopic hepatic lymph node involvement on survival after resection of colorectal liver metastasis. J Am Coll Surg 198:884–891
41. Hughes KS, Simon R, Songhorabodi S, et al. (1988) Resection of the liver for colorectal carcinoma metastases. A multi-institutional study of indications for resection. Surgery 103:278–288
42. Bismuth H, Adam R, Levi F, et al. (1996) Resection of nonresectable liver metastases from colorecal cancer after neoadjuvant chemotherapy. Am Surg 224:509–520
43. Tomas-de la Vega JE, Donahue EJ, Doolas A, et al. (1984) A 10-year experience with hepatic resection. Surg Gynecol Obstet 159:223–228
44. Nordlinger B, Vallant J, Guiguet M, et al. (1994) Survival benefit of repeat liver resections for recurrent colorectal metastases: 143 cases. J Clin Oncol 12:1491–1496
45. Adam R, Bismuth H, Castaing D, et al. (1997) Repeat hepatectomy for colorectal liver metastases. Ann Surg 225:51–60
46. Huguet C, Bona S, Nordlinger B, et al. (1990) Repeat hepatic resection for primary and metastatic carcinoma of the liver. Surg Gynecol Obstet 171:398–402
47. Griffith KD, Sugarbaker PH, Chang AE (1990) Repeat hepatic resections for colorectal metastases. Surgery 107:101–104
48. Fong Y, Blumgart LH, Cohen A, et al. (1994) Repeat hepatic resection for metastatic colorectal cancer. Ann Surg 220:657–662
49. Pinson CW, Wright JK, Chapman WC, et al. (1996) Repeat hepatic surgery for colorectal cancer metastasis to the liver. Ann Surg 223:765–773
50. Di Carlo V, De Nardi P, Ferrari G, et al. (1997) Repeated hepatectomy for colorectal metastasis. Ann Ital Chir 68:775–780
51. Adam R, Delvart V, Pascal G, et al. (2004) Rescue surgery for unresectable colorectal liver metastases downstaged by chemotherapy: a model to predict long-term survival. Ann Surg 240:644–657
52. Chu QD, Vezeridis MP, Avradopoulos KA, et al. (1997) Repeat hepatic resection for recurrent colorectal cancer. World J Surg 21:292–296
53. Elias D, Lasser P, Hoang JM, et al. (1993) Repeat hepatectomy for cancer. Br J Surg 80:1557–1562
54. Elias D, Cavalcanti A, Sabourin J, et al. (1998) Results of 136 curative hepatectomies with a safety margin of less than 10 mm for colorectal metastases. J Surg Oncol 69:88–93
55. Ohlsson B, Stenram U, Tranberg KG (1998) Resection of colorectal liver metastases: 25-year experience. World J Surg 22: 268–277
56. Yamamoto J, Shimada K, Kosuge T, et al. (1999) Factors influencing survival of patients undergoing hepatectomy for colorectal metastases. Br J Surg 86:332–337
57. Sugarbaker PH (1999) Repeat hepatectomy for colorectal metastases. J Hepatobiliary Pancreat Surg 6:30–38
58. Aramaki M, Kawano K, Kai T, et al. (2000) Postoperative complications of repeat hepatectomy for liver metastasis from colorectal carcinoma. Hepatogastroenterology 47:478–480
59. Muratore A, Polastri R, Bouzari H, et al. (2001) Repeat hepatectomy for colorectal liver metastases: a worthwhile operation? J Surg Oncol 76:127–132
60. Suzuki S, Sakaguchi T, Yokoi Y, et al. (2001) Impact of repeat hepatectomy on recurrent colorectal liver metastases. Surgery 129:421–428
61. Yamada H, Katoh H, Kondo S, et al. (2001) Repeat hepatectomy for recurrent hepatic metastases from colorectal cancer. Hepatogastroenterology 48:828–830
62. Nagakura S, Shirai Y, Suda T, et al. (2002) Multiple repeat resections of intra- and extrahepatic recurrences in patients undergoing initial hepatectomy for colorectal carcinoma metastases. World J Surg 26:141–147
63. Petrowsky H, Gonen M, Jarnagin W, et al. (2002) Second liver resections are safe and effective treatment for recurrent hepatic metastases from colorectal cancer: a bi-institutional analysis. Ann Surg 235:863–871
64. Takahashi S, Inoue K, Konishi M, et al. (2003) Prognostic factors for poor survival after repeat hepatectomy in patients with colorectal liver metastases. Surgery 133:627–634
65. Penna C, Nordlinger B (2002) Colorectal metastasis (liver and lung). Surg Clin N Am 82:1075–1090
66. Bakalakos EA, Young DC, Martin EW Jr (1998) Radioimmunoguided surgery for patients with liver metastases secondary to colorectal cancer. Ann Surg Oncol 5:590–594
67. Bakalakos EA, Kim JA, Young DC, et al. (1998) Determinants of survival following hepatic resection for metastatic colorectal cancer. World J Surg 22:399–405
68. Beckhurts KTE, Hoelscher AH, Bollschweiler E, et al. (1997) Significance of lymph node involvement at the hepatic hilum in the resection of colorectal liver metastases. Br J Surg 84:1081–1084
69. Belli G, D'Agostino A, Ciciliano F, et al. (2002) Liver resection for hepatic metastases: 15 years of experience. J Hepatobiliary Pancreat Surg 9:607–613
70. Bolton JS, Fuhrman GM (2000) Survival after resection of multiple bilobar hepatic metastases from colorectal carcinoma. Ann Surg 231:743–751
71. Cady B, Jenkins RL, Steele GD, et al. (1998) Surgical margin in hepatic resection for colorectal metastasis: a critical and improvable determinant of outcome. Ann Surg 227:566–571
72. Cavallari A, Vivarelli M, Bellisci R, et al. (2003) Liver metastases from colorectal cancer: present surgical approach. Hepatogastroenterology 50:2067–2071
73. Chan ACW, Blumgart LH, Wuest DL, et al. (1998) Use of preoperative autologous blood donation in liver resections for colorectal metastases. Am J Surg 175:461–465
74. Choti MA, Sitzmann JV, Tiburi MF, et al. (2002) Trends in long-term survival following liver resection for hepatic colorectal metastases. Ann Surg 235:759–766
75. DeMatteo RP, Palese C, Jarnagin WR, et al. (2000) Anatomic segmental hepatic resection is superior to wedge resection as an oncologic operation for colorectal liver metastases. J Gastrointest Surg 4:178–184
76. Doci R, Gennari L, Bignami P, et al. (1991) One hundred patients with hepatic metastases from colorectal cancer treated by resection: analysis of prognostic determinants. Br J Surg 78:797–801
77. Doci R, Gennari L, Bignami P, et al. (1995) Morbidity and mortality after hepatic resection of metastases from colorectal cancer. Br J Surg 82:377–381
78. Elias D, Cavalcanti A, Sabourin JC, et al. (1998) Resection of liver metastases from colorectal cancer: the real impact of the surgical margin. Eur J Surg Oncol 24:174–179
79. Fernandez FG, Drebin JA, Linehan DC, et al. (2004) Five-year survival after resection of hepatic metastases from colorectal cancer in patients screened by positron emission tomography with F-18 fluorodeoxyglucose (FDG-PET). Ann Surg 240:438–450
80. Fong Y, Cohen AM, Fortner JG, et al. (1997) Liver resection for colorectal metastases. J Clin Oncol 15:938–946
81. Fortner JG (1988) Recurrence of colorectal cancer after hepatic resection. Am J Surg 155:378–382
82. Fortner JG, Silva JS, Golbey RB, et al. (1984) Multivariate analysis of a personal series of 247 consecutive patients with liver metastases from colorectal cancer. I. Treatment by hepatic resection. Ann Surg 199:306–316
83. Fregiz G, Bezzi M, De Angelis R, et al. (1991) Hepatic resections for colorectal metastases: the Italian multicenter experience. J Surg Oncol Suppl 2:144–154
84. Fuhrman GM, Curley SA, Hohn DC, et al. (1995) Improved survival after resection of colorectal liver metastases. Ann Surg Oncol 2:537–541
85. Imamura H, Seyama Y, Kokudo N, et al. (2004) Single and multiple resections of multiple heaptic metastases of colorectal origin. Surgery 135:508–517
86. Jaeck D, Bachellier P, Guiguet M, et al. (1997) Long-term survival following resection of colorectal heaptic metastases. Br J Surg 84:977–980

87. Jatzko GR, Lisborg PH, Stettner HM, et al. (1995) Hepatic resection for metastases from colorectal carcinoma—a survival analysis. Eur J Cancer 31A:41–46
88. Jenkins LT, Millikan KW, Bines SD, et al. (1997) Hepatic resection for metastatic colorectal cancer. Am Surgeon 63:605–610
89. Jourdan JL, Cannan R, Stubbs R (1999) Hepatic resection for metastases in colorectal carcinoma. N Z Med J 112:91–93
90. Kato T, Yasui K, Hirai T, et al. (2003) Therapeutic reults for hepatic metastasis of colorectal cancer with special reference to effectiveness of hepatectomy. Dis Colon Rectum 46:522–531
91. Kokudo N, Tada K, Seki M, et al. (2001) Anatomical major resection versus nonanatomical limited resection for liver metastases from colorectal carcinoma. Am J Surg 181:153–159
92. Lise M, Da Pian PP, Nitti D, et al. (1991) Colorectal metastases to the liver: present results and future strategies. J Surg Oncol Suppl 2:69–73
93. Lorenz M, Muller HH, Gassel HJ, et al. (1998) Randomized trial of surgery versus surgery followed by adjuvant hepatic arterial infusion with 5-fluorouracil and folinic acid for liver metastases of colorectal cancer. Ann Surg 228:756–762
94. Martin RC, Jarnagin WR, Fong Y, et al. (2003) The use of fresh frozen plasma after major hepatic resection for colorectal metastasis: is there a standard for transfusion? J Am Coll Surg 196: 402–409
95. Nadig DE, Wade TP, Fairchild RB, et al. (1997) Major hepatic resection. Indications and results in a national hospital system from 1988 to 1992. Arch Surg 132:115–119
96. Nuzzo G, Giuliante F, Giovannini I, et al. (1997) Resection of hepatic metastases from colorectal cancer. Hepatogastroenterology 44:751–759
97. Pedersen IK, Burcharth F, Roikjaer O, et al. (1994) Resection of liver metastases from colorectal cancer. Indications and results. Dis Colon Rectum 37:1078–1082
98. Petrelli N, Gupta B, Piedmonte M, et al. (1991) Morbidity and survival of liver resection for colorectal adenocarcinoma. Dis Colon Rectum 34:899–904
99. Rees M, Plant R, Bygrave S (1997) Late results justify resection for multiple hepatic metastases from colorectal cancer. Br J Surg 84:1136–1140
100. Rosen CB, Nagorney DM, Taswell HF, et al. (1992) Perioperative blood transfusion and determinants of survival after liver resection for metastatic colorectal carcinoma. Ann Surg 216:493–505
101. Sasaki A, Aramaki M, Kawano K, et al. (2002) Prognostic significance of intrahepatic lymphatic invasion in patients with hepatic resection due to metastases from colorectal carcinoma. Cancer 95:105–111
102. Scheele J, Stang R, Altendorf-Hofmann A, et al. (1995) Resection of colorectal liver metastases. World J Surg 19:59–71
103. Scheele J, Stangle R, Altendorf-Hofmann A (1990) Hpeatic metastases from colorectal carcinoma: impact of surgical resection on the natural history. Br J Surg 77:1241–1246
104. Schlag P, Hohenberger P, Herfarth C (1990) Resection of liver metastases in colorectal cancer – competitive analysis of treatment results in synchronous versus metachronous metastases. Eur J Surg Oncol 16:360–365
105. Seifert JK, Bottger TC, Weigel TF, et al. (2000) Prognostic factors following liver resection for hepatic metastases from colorectal cancer. Hepatogastroenterology 47:239–246
106. Steele G, Bleday R, Mayer RJ, et al. (1991) A prospective evaluation of heaptic resection for colorectal carcinoma metastases to the liver: Gastrointestinal Tumor Study Group Protocol 6584. J Clin Oncol 9:1105–1112
107. Stewart GD, O'Suilleabhain CB, Madhavan KK, et al. (2004) The extent of resection influences outcome following hepatectomy for colorectal liver metastases. Eur J Surg Oncol 30:370–376
108. Sugawara Y, Yamamoto J, Yamasaki S, et al. (2001) Estimating the prognosis of hepatic resection in patients with metastatic liver tumors from colorectal cancer with special concern for the timing of hepatectomy. Surgery 129:408–413
109. Sugihara K, Hojo K, Moriya Y, et al. (1993) Pattern of recurrence after hepatic resection for colorectal metastases. Br J Surg 80: 1032–1035
110. Ueno H, Mochizuki H, Hatsuse K, et al. (2000) Indications for treatment strategies of colorectal liver metastases. Ann Surg 231:59–66
111. van Ooijen B, Wiggers T, Meijer S, et al. (1992) Hepatic resections for colorectal metastases in The Netherlands. A multiinstitutional 10-year study. Cancer 70:28–34
112. Wanebo HJ, Chu QD, Vezeridis MP, et al. (1996) Patient selection for hepatic resection of colorectal metastases. Arch Surg 131:322–329
113. Wigmore SJ, Madhavan K, Currie EJ, et al. (1999) Does the subspecialty of the surgeon performing primary colonic resection influence the outcome of patients with hepatic metastases referred for resection? Ann Surg 230:759–765
114. Zieren HU, Muller JM, Zieren J, et al. (1993) The impact of patient's age on surgical therapy of colorectal liver metastases. Int Surg 78:288–291
115. Wood CB, Gillis CR, Blumgart LH. (1976) A retrospective study of the natural history of patients with liver metastases from colorectal cancer. J Clin Oncol 2:285–288
116. Bengtsson G, Carlsson G, Hafstroem L, et al. (1981) Natural history of patients with untreated liver metastases from colorectal cancer. Am J Surg 141:586–589
117. Jarnagin WR, Fong Y, Ky A, et al. (1999) Liver resection for metastatic colorectal cancer: assessing the risk of occult irresectable disease. J Am Coll Surg 188:33–42
118. Nordlinger B, Giuguet M, Vaillant JC, et al. (1996) Surgical resection of colorectal carcinoma metastases to the liver. A prognostic scoring system to improve case selection, based on 1568 patients. Cancer 77:1254–1262
119. Hughes KS, Simon R, Songhorabodi S, et al. (1986) Resection of the liver for colorectal carcinoma metastases: a multi-institutional study of patterns of recurrence. Surgery 100:278–284
120. Cady B, Monson DO, Swinton NW (1970) Survival of patients after colonic resection for carcinoma with simultaneous liver metastases. Surg Gynecol Obstet 131:697–700
121. Baden H, Andersen B (1975) Survival of patients with untreated liver metastases from colorectal cancer. Scand J Gastroenterol 10:221–223
122. Adson MA (1979) Hepatic resection. Dis Colon Rectum 22:366–369
123. Fegiz G, Ramacciato G, D'Angelo F, et al. (1991) Patient selection and factors affecting results following resection for hepatic metastases from colorectal carcinoma. Int Surg 76:58–63
124. Scheele J, Altendorf-Hofmann A (1999) Resection of colorectal liver metastases. Langenbecks Arch Surg 384:313–327
125. Hananel N, Garzon J, Gordon PH (1995) Hepatic resection for colorectal liver metastases. Am Surgeon 61:444–447
126. Sato T, Konishi K, Yabushita K, et al. (1998) The time interval between primary colorectal carcinoma resection to occurrence of liver metastases is the most important factor for hepatic resection. Analysis of total course following primary resection of colorectal cancer. Int Surg 83:340–342
127. Irie T, Itai Y, Hatsuse K, et al. (1999) Does resection of small liver metastases from colorectal cancer improve survival of patients? Br J Radiol 72:246–249
128. Dworkin MJ, Earlam S, Fordy C, et al. (1995) Importance of hepatic artery node involvement in patient with colorectal liver metastases. J Clin Pathol 48:270–272
129. Wang JY, Chiang JM, Jeng LB, et al. (1996) Resection of liver metastases from colorectal cancer: are there any truly significant clinical prognosticators? Dis Colon Rectum 39:847–851
130. Fujita S, Akasu T, Moriya Y (2000) Resection of synchronous liver metastases from colorectal cancer. Jpn J Clin Oncol 30:7–11
131. Weber JC, Nakano H, Bachellier P, et al. (2001) Is a proliferation index of cancer cells a reliable prognostic factor after hepatectomy in patients with colorectal liver metastases? Am J Surg 182:81–88
132. Mala T, Bohler G, Mathisen O, et al. (2002) Hepatic resection for colorectal metastases: can preoperative scoring predict patient outcome? World J Surg 26:1348–1353
133. Yamada H, Katoh H, Kondo S, et al. (2002) Mesenteric lymph nodes status influencing survival and recurrence pattern after hepatectomy for colorectal liver metastases. Hepatogastroenterology 49:1265–1268
134. Wagner JS, Adson MA, Van Heerden JA, et al. (1984) The natural history of hepatic metastases from colorectal cancer. A comparison with resective treatment. Ann Surg 199:502–508

135. Hardy KJ, Fletcher DR, McL. Jones R. (1998) One hundred liver resections including comparison to non-resected liver-mobilized patients. Aust N Z J Surg 68:716–721
136. Heslin MJ, Medina-Franco H, Parker M, et al. (2001) Colorectal hepatic metastases: resection, local ablation, and hepatic artery infusion pump are associated with prolonged survival. Arch Surg 1136:318–323
137. Lind DS, Parker GA, Horsley JS 3rd, et al. (1992) Formal hepatic resection of colorectal liver metastases. Ploidy and prognosis. Ann Surg 215:677–683
138. Nakamura S, Yokoi Y, Suzuki S, et al. (1992) Results of extensive surgery for liver metastases in colorectal carcinoma. Br J Surg 79:35–38
139. Fernandez-Trigo V, Shamsa F, Sugarbaker PH (1995) Repeat liver resections from colorectal metastasis. Surgery 117:296–304
140. Tuttle TM, Curley SA, Roh MS (1997) Repeat hepatic resection as effective treatment of recurrent colorectal liver metastases. Ann Surg Oncol: 4:125–130
141. Inaba Y, Arai Y, Kanematsu M, et al. (2000) Revealing hepatic metastases from colorectal cancer: value of combined helical CT during arterial portography and CT hepatic arteriography with a unified CT and angiography system. Am J Roentgenol 174:955–961
142. Selzner M, Hany TF, Wildbrett P, et al. (2004) Does the novel PET/CT imaging modality impact on the treatment of patients with metastatic colorectal cancer of the liver? Ann Surg 240:1027–1036
143. Yamamoto J, Sugihara K, Kosuge T, et al. (1995) Pathologic support for limited hepatectomy in the treatment of liver metastases from colorectal cancer. Ann Surg 221:74–78
144. Shirabe K, Takenaka K, Gion T, et al. (1997) Analysis of prognostic risk factors in hepatic resection for metastatic colorectal carcinoma with special reference to surgical margin. Br J Surg 84:1077–1080
145. Nanko M, Shimada H, Yamaoka H, et al. (1998) Micrometastatic colorectal cancer lesions in the liver. Surg Today 28:707–713
146. Okano K, Yamamoto J, Moriya Y, et al. (1999) Macroscopic intrabiliary growth of liver metastases from colorectal cancer. Surgery 126:829–834
147. Koike M, Yasui K, Torii A, et al. (2000) Prognostic significance of entrapped liver cells in hepatic metastases from colorectal cancer. Ann Surg 232:653–657
148. Kubo M, Sakamoto M, Fukushima N, et al. (2002) Less aggressive features of colorectal cancer with liver metastases showing macroscopic intrabiliary extension. Pathol Int 52:514–518
149. Tada K, Kokudo N, Seki M, et al. (2003) Hepatic resection for colorectal metastasis with microscopic tumor thrombus in the portal vein. World J Surg 27:299–303
150. Miyazaki M, Ito H, Nakagawa K, et al. (1999) Aggressive surgical resection for hepatic metastases involving the inferior vena cava. Am J Surg 177:294–298
151. Povoski SP, Klimstra DS, Brown KT, et al. (2000) Recognition of intrabiliary hepatic metastases from colorectal adenocarcinoma. J Hepatobiliary Pancreat Surg 11:383–390
152. Takamatsu S, Teramoto K, Kawamura T, et al. (2004) Liver metastasis from rectal cancer with prominent intrabile duct growth. Pathol Int 54:440–445
153. Coboum CS, Makowka L, Langer B, et al. (1987) Examination of patient selection and outcome for hepatic resection for metastatic disease. Surg Gynecol Obstet 165:239–246
154. Gibbs JF, Weber TK, Rodriguez-Bigas MA, et al. (1998) Intraoperative determinants of unresectability for patients with colorectal hepatic metastases. Cancer 82:1244–1249
155. Elias D, Saric J, Jaeck D, et al. (1996) Prospective study of microscopic lymph node involvement of the hepatic pedical during curative hepatectomy for colorectal metastases. Br J Surg 83:942–945
156. Kokudo N, Sato T, Seki M, et al. (1999) Hepatic lymph node involvement in resected cases of liver metastases from colorectal cancer. Dis Colon Rectum 42:1285–1290
157. Imamura H, Kawasaki S, Miyagawa S, et al. (2000) Aggressive surgical approach to recurrent tumors after hepatectomy for metastatic spread of colorectal cancer to the liver. Surgery 127: 528–535
158. Weber SM, Jarnagin WR, DeMatteo RP, et al. (2000) Survival after resection of multiple hepatic colorectal metastases. Ann Surg Oncol 7:643–650
159. Hughes K, Scheele J, Sugarbaker PH (1989) Surgery for colorectal cancer metastatic to the liver. Optimizing the results of treatment. Surg Clin N Am 69:339–359