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Indications for Resection of Metastatic Liver Lesions

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Table 2. — Results of Nonsurgically Treated Colorectal Cancer Metastasis

Reference (year)	No. of Patients	Median Survival (mos)	5-yr Survival (%)
Pestana[23] (1964)	353	9.0	3
Cady[24] (1970)	269	13.0	1
Lahr[25] (1983)	175	6.1	1
Wagner[9] (1984)	252	19.0	2
Adson[26] (1987)	70	–	<5
Wood[27] (1976)	113	10.6	–
Scheele[12] (1990)	921	6.9	0
Stangl[28] (1994)	677	7.5	1
Rougier[29] (1995)	318	5.7	–
Scheele[30] (1995)	964	–	0
Kato[31] (2003)	178	–	3.4

Results of Resection of Metastatic Tumors of the Liver

GEORGE F. WOODINGTON, M.D. AND JOHN M. WAUGH, M.D.,* *Rochester, Minnesota*

From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

SURGICAL resection of a portion of the liver for primary or metastatic lesions is not new. In 1849 Rokitansky classified tumors of the liver and distinguished between primary and secondary neoplasms of this organ. Keen [1] found that between 1886 and 1897 partial hepatectomy had been performed in fifty-nine patients, with an operative mortality of 15.5 per cent. Resection of the liver as a planned operative procedure was first performed by

supplies 40 per cent of the blood; a low-pressure portal venous system, which is also afferent and carries 60 per cent of the blood to the liver; and a complex biliary circulation. Careful dissection based on thorough knowledge of the anatomic arrangement of these circulatory systems has resulted in considerable reduction in the hazard of hemorrhage. With regard to infection, the normal human liver, in contrast to that of a dog, is sterile, and therefore little more danger of infection is present than in other operations on abdominal viscera.

* Doctor Waugh died August 12, 1962.

Hepatic Resection

Results in 39 Patients Operated Upon During the 11-Year Period From 1952 to 1963

H. GANS, MD; SUK-KYUNG KOH, MD; AND J. B. AUST, MD, MINNEAPOLIS

OPERATIVE surgery on the liver is by no means a recent development. Successful resections of liver tissue have been reported by Burckhardt (1887),[1] Von Bergmann (1893),[2] Auvray (1897),[3] Langenbuch (1897),[4] Keen (1899),[5] Thompson (1899),[6] and others. Although both Langenbuch [4] and Keen [5] realized as early as 1900 that there were relatively avascular planes in the liver along which resections could be carried out safely, most surgeons refrained from attacking lesions of the liver because of the threats of air embolism, operative and postoperative hemorrhage, and bile peritonitis.

1955 [10]; Couinaud, 1957 [11]). An additional advance was decompression of the biliary tract as an added safety measure against cholerrhagia (Wangensteen, 1945).[12]

As a result of these developments in the last decade, there have been many publications on successful hepatic resections for a variety of liver lesions. The information confirmed previous speculations that these techniques may be lifesaving in the treatment of extensive and deep lacerations and neoplasms of the liver.

Notable contributions to hepatic surgery for neoplasms have been made by Rayan

Table 1. — Results of Colorectal Liver Metastasis Resection

Reference (year)	No. of Patients	Operative Mortality (%)	Survival (%)				Median Survival (mos)
			1-yr	3-yr	5-yr	10-yr	
Foster[8] (1974)	168	5.0	–	–	20	–	–
Wilson[3] (1976)	60	–	–	–	25	–	–
Wagner[9] (1984)	116	–	–	–	25	–	–
Adson[10] (1984)	141	3.0	82	40	25	–	24
Hughes[11] (1986)	859	–	–	–	33	–	–
Scheele[12] (1990)	173	5.5	–	–	40	27	–
Schlag[13] (1990)	122	4.0	85	35	25	–	32
Rosen[14] (1992)	280	4.0	84	47	25	–	–
Gayowski[15] (1994)	204	0.0	91	43	32	–	–
Scheele[16] (1995)	434	4.0	85	45	23	18	40
Jamison[17] (1997)	280	4.0	84	–	27	20	33
Fong[18] (1999)	1001	2.8	89	57	37	22	42
Choti[19] (2002)	226	1.0	93	57	40	26	46
Abdalla[20] (2004)	190	–	–	73	58	–	21
Mutsaerts[21] (2005)	102	3.0	71 (2-yr)		29	–	–

Hepatic Resection for Colorectal Metastases

Value for Risk Scoring Systems?

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Introduction: Predictors of outcome in patients with metastatic colorectal cancer remain inconsistent. We aimed to identify predictors of outcome in these patients, to develop a prognostic scoring system, and to assess the general applicability of the current major risk scoring systems.

Materials and Methods: Following IRB approval, medical records of 662 consecutive patients undergoing resection of colorectal metastases to the liver during 1960 to 1995 were reviewed. Clinicopathologic and outcome data were assessed from records and mailed questionnaire. Clinicopathologic variables were tested using univariate and multivariate analyses; best-fit models were then generated to study the effect of each independent risk factor on outcome. To validate existing scoring models, our independent data set was applied to those scores. The relative concordance probability estimates were calculated for these models and compared with that of the proposed Mayo model.

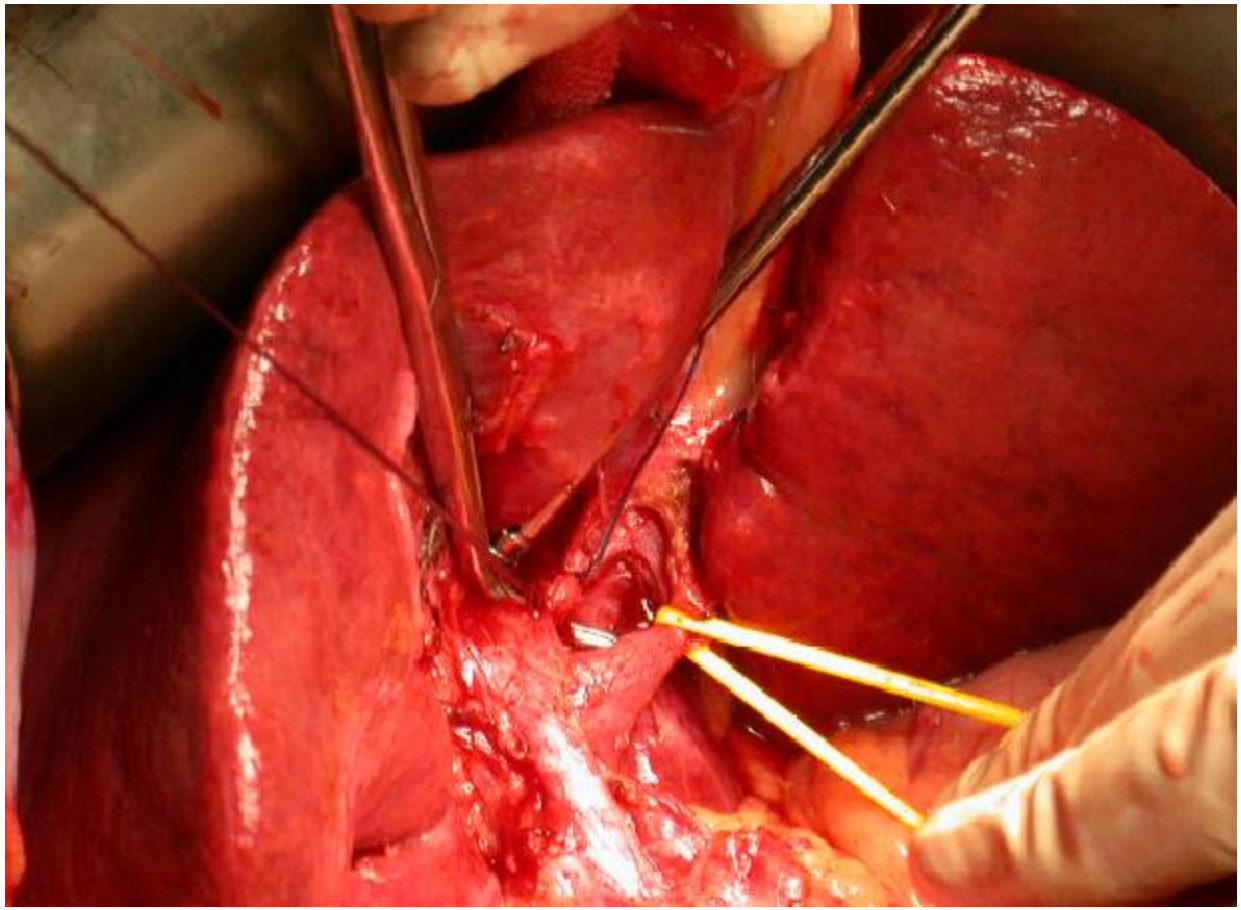
Results: The overall and disease-specific 5-year survival rates were 37% and 42%, respectively. The probability of recurrence at any site was 65% at 5 years. Perioperative blood transfusion and positive hepatoduodenal nodes were the major determinants of survival and recurrence. To assess the general applicability of the proposed risk scoring systems, we imported the data from our patient population into 3 other scoring systems. Neither survival nor recurrence among our patients was stratified discretely by any of the scoring systems. Based on probability estimates, all models were only marginally better than chance alone in predicting outcome.

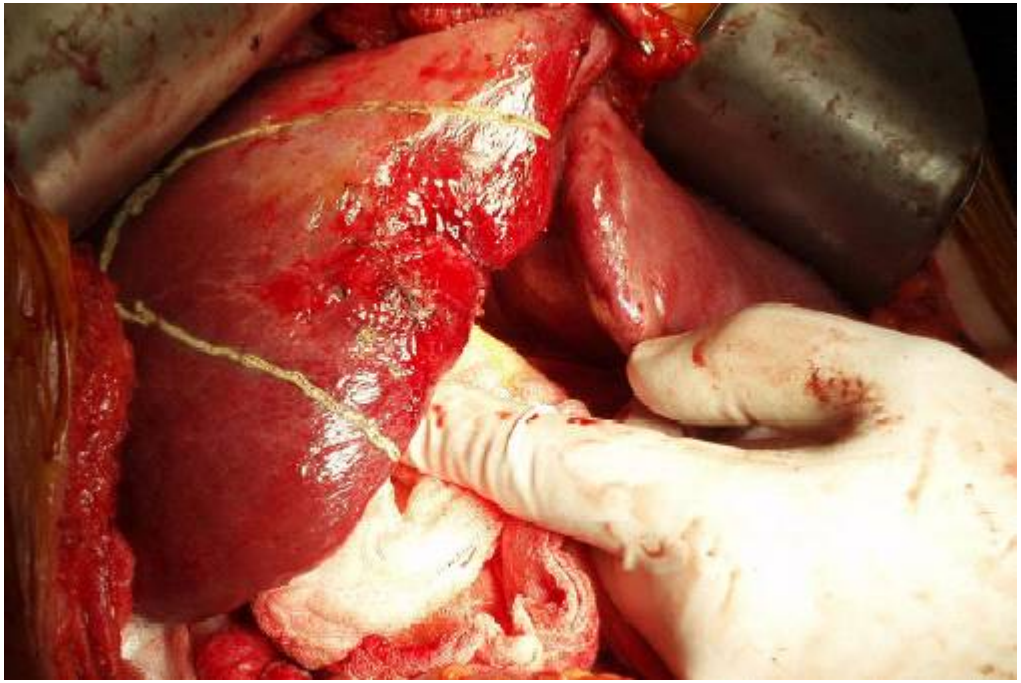
Conclusion: Broad application of risk scoring systems for patients with metastatic colorectal cancer has limited clinical value and refinement and external validation should be undertaken before utilization.

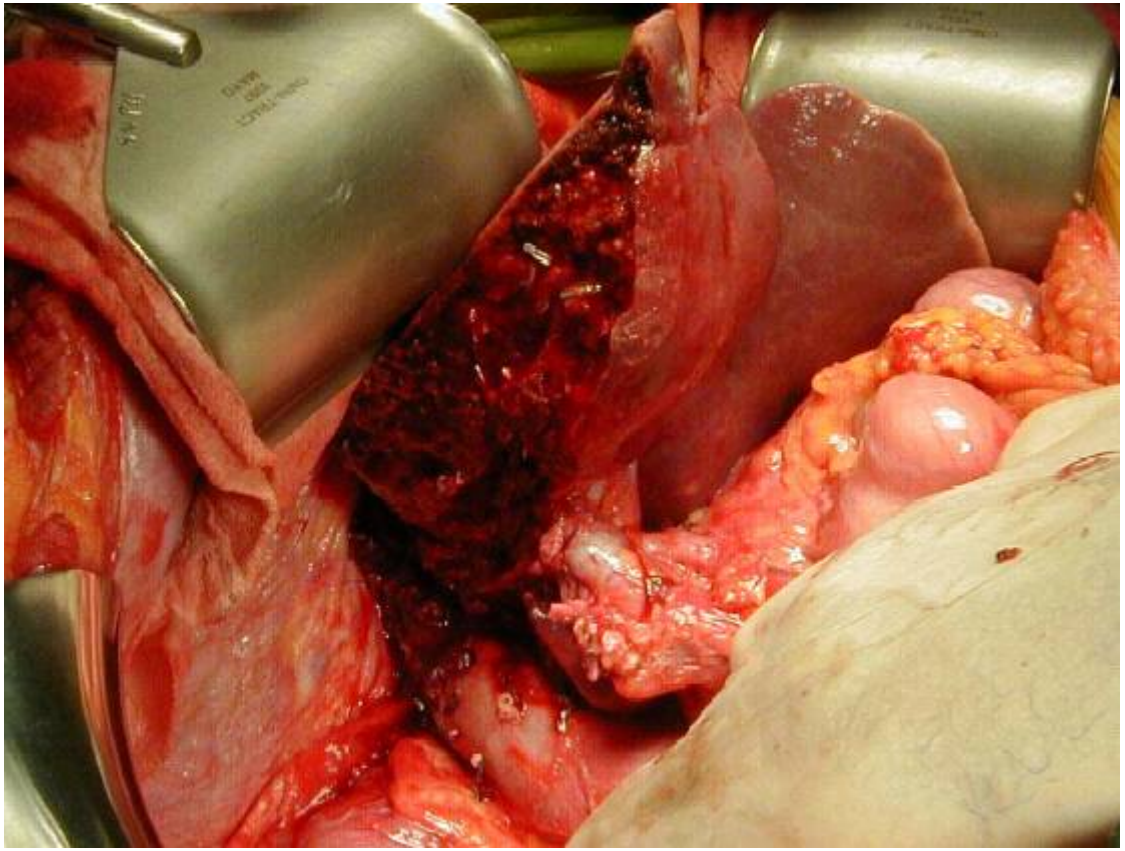
(*Ann Surg* 2007;246: 183–191)

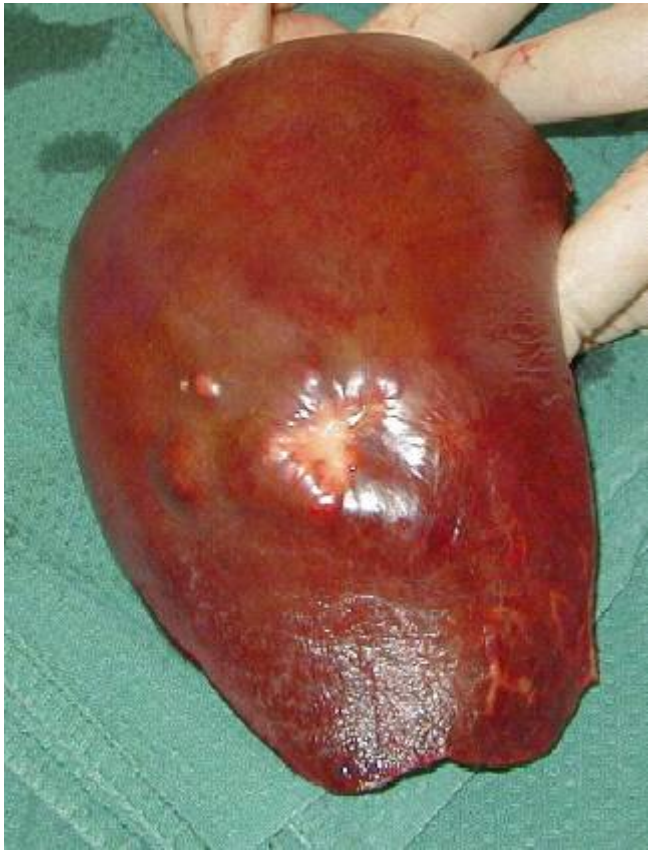
TABLE 1. Type and Frequency of Hepatic Resection in Patients With Metastatic Colorectal Cancer

Type of Resection	n	%
Wedge	243	36.7
Right hepatectomy	108	16.3
Left hepatectomy	31	4.7
Extended right hepatectomy	101	15.3
Extended left hepatectomy	8	1.2
One segment ± wedge	41	6.2
Two segments ± wedge	72	10.8
Three or 4 segments ± wedge	58	8.8









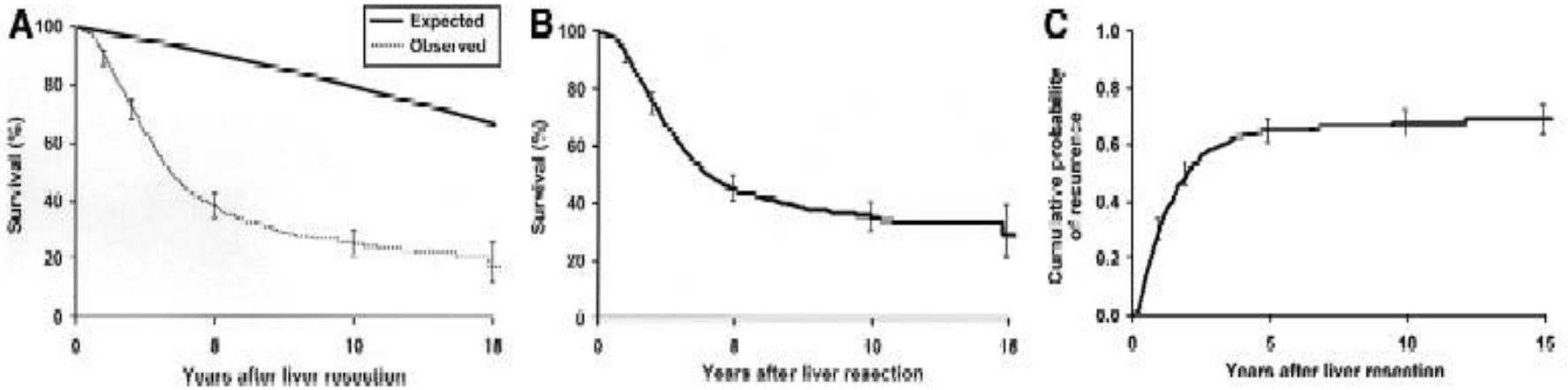


FIGURE 1. Overall expected and observed survival (A) and disease-specific survival (B) of patients undergoing hepatic resection for colorectal metastases. C, Recurrence of patients undergoing hepatic resection for colorectal metastases.

TABLE 3. Correlation of Clinical and Pathologic Factors to Disease-Specific Survival and Recurrence: Multivariable Analysis

	Survival			Recurrence		
Variable	Hazard Ratio	95% CI	*P*	Hazard Ratio	95% CI	*P*
Metastasis diameter >8 cm	1.4	1.0–1.8	0.03			
Interval to metastases <30 mo	1.4	1.0–1.9	0.03			
Hepatoduodenal lymph node	2.8	1.8–4.4	0.0001	2.4	1.6–3.6	0.0001
Transfusions	1.5	1.2–2.0	0.0002	1.3	1.1–1.6	0.009
Primary cancer regional lymph node				1.3	1.1–1.6	0.01
No. metastases ≥2				1.3	1.1–1.6	0.01

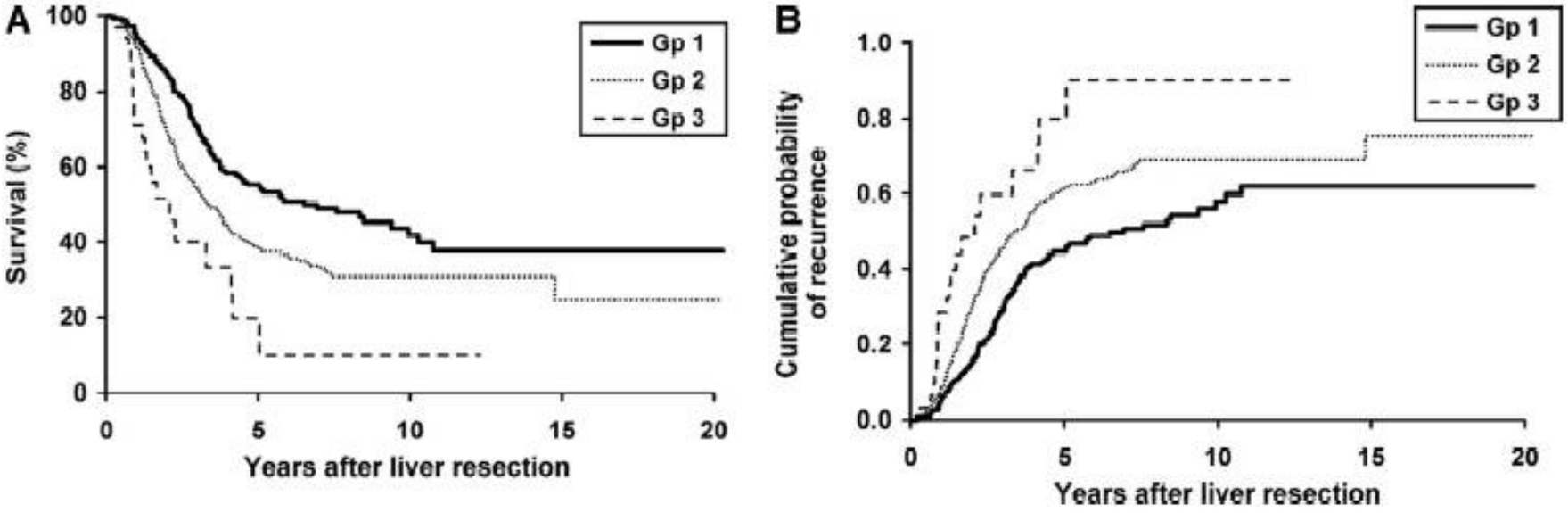


FIGURE 2. Mayo Risk Groups. (A) Disease-specific survival (A) and recurrence (B) of patients undergoing hepatic resection for colorectal metastases using best fit models.

TABLE 5. Concordance Probability Estimates

	Concordance Estimates (95% CI)	
Model	**Disease-Specific Survival**	**Recurrence**
Mayo	0.61 (0.57, 0.64)	0.58 (0.55, 0.61)
Nordlinger	0.55 (0.51, 0.59)	0.56 (0.52, 0.59)
Fong	0.56 (0.50, 0.62)	0.58 (0.54, 0.63)
Iwatsuki	0.53 (0.50, 0.56)	0.55 (0.53, 0.58)

Table 6. — Results of Repeat Hepatic Tumor Resections for Cure

Reference (year)	No. of Patients	Operative Mortality (%)	Median Survival (mos)	Survival (%)		
				1-yr	3-yr	5-yr
Bozzetti[49] (1992)	11	9	23		36	–
Vaillant[48] (1993)	16	6.2	33		57	30
Nordlinger[47] (1994)	116	–	–		33	–
Fong[46] (1994)	25	0	30		–	–
Fernandez[45] (1995)	170	–	34		45	32
Tuttle[44] (1997)	23	0	40		55	32
Adam[53] (1997)	64	0	46	87	60	41
Yamamoto[54] (1999)	75	0	30	48	31	
Muratore[43] (2001)	29	3.4	–		35	–
Suzuki[42] (2001)	26	0	31		62	32
Petrowsky[52] (2002)	126	1.6	37	86	51	34

Strategies to achieve an R0 resection

- Staged resection
- Portal vein embolization
- Hepatic artery infusion / chemoembolization
- Focused radiotherapy
- Radiofrequency ablation
- Neoadjuvant chemotherapy

Laparoscopic evaluation of patient with colorectal liver metastases

- Lymph node positive primary
- CEA > 200 ng/ml
- Disease free interval < 12 months
- > 1 liver metastasis
- Metastasis > 8 cm

Patients with 2 or more factors have 30% chance of extrahepatic intraperitoneal disease

Grobmyer *Arch Surg* 2004; 139: 1326-1330

Table 5. — Results for Neoadjuvant Therapy Prior to Resection

Reference (year)	No. of Patients	Chemotherapy Regimen	Resectability	5-Year Survival
Bismuth[79] (1996)	330	Oxaliplatin/FU/LV	46 (14%)	40%
Giacchetti[108] (1999)	151	Oxaliplatin/FU/LV	58 (38%)	
Adam[109] (2001)	701	Oxaliplatin/FU/LV	95 (13.5%)	35%
Wein[110] (2001)	53	Infusional FU/LV	6 (11%)	
Rivoire[111] (2002)	131	Oxaliplatin/FU/LV	57 (43%)	
Adam[112] (2004)	1104	Oxaliplatin/irinotecan/FU/LV	128 (12.5%)	
Pozzo[113] (2004)	40	CPT/FU/LV	11 (27.5%)	
Delaunoit[114] (2005)	795	Oxaliplatin/irinotecan/FU/LV	24 (3.3%)	

Neuroendocrine liver metastases

- Untreated 5 year survival rate 30%
- Best option: complete resection of primary lesion and liver metastasis – 5YSR 46-93%
- Octreotide may control growth and symptoms
- Octreotide linked therapies may target lesions
- Incomplete resection may reduce symptoms
- Transplantation possible in select situations
- Adjuvant chemotherapy not indicated

Non-colorectal, non-neuroendocrine (NCNN) metastases

- Autopsy studies show 10 -15% of patients with NCNN mets have disease confined to the liver
- Mathematical analysis of the frequency of mets in various tissues suggest liver, lung and bone are staging sites for further spread
- Liver mets appear to be less sensitive to chemotherapy than lesions elsewhere

Non-colorectal, non-neuroendocrine liver metastectomy			
Study PI (year)	No. patients	5 yr survival	Favourable prognostic factors
Harrison (1997)	96	37%	Ro, non-GI primary, DFI>36m
Elias (1998)	127	40%	Ro, non-GI, non-melanoma
Lang (1999)	127	25%	Ro
Hemming (2000)	37	45%	Ro, non-GI primary
Laurent (2001)	39	35%	DFI>24m
Cordera (2005)	64	30%	DFI>24m
Weitz (2005)	141	36%	Ro, reproductive tract, DFI>24m
Ercolani (2005)	142	34%	Ro, non-GI

Adapted from *Advanced Therapy in Surgical Oncology* 2008 Pollock, Curley, Ross, Perrier (eds)

Non-colorectal, non-neuroendocrine (NCNN) metastases

- Ro resection more important than number of lesions
- Disease free interval > 24 months
- Resected NCNN mets with prognosis similar to colorectal mets: gynecological, urological, breast and sarcoma
- Resected NCNN mets with poor prognosis: biliary, pancreatic, gastric, esophageal
- Multimodality treatment (assume micrometastases elsewhere)