

Surgical Treatment of Colorectal Metastases to the Liver

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Introduction

Colorectal cancer develops in more than 138,000 patients and is responsible for more than 55,000 deaths in the United States every year.¹ Up to one fourth of patients diagnosed with colorectal cancer present with liver metastases.² In addition, liver metastases are detected in many more patients after diagnosis, such that by the time of death up to 70 percent of patients with colorectal cancer have metastatic disease to the liver.³

Since the first systematic attempts to treat liver metastasis from colorectal cancer by surgical excision three decades ago,⁴ this aggressive approach has gained general acceptance. A large number of studies have demonstrated that resectional therapy of colorectal liver metastasis is not only safe, but also potentially curative.⁵⁻¹⁰ The rationale for the surgical approach was based on two important assumptions that have been verified by data. First, isolated liver metastasis to the liver can occur without tumor growth elsewhere, and second, surgical removal of liver tumors can be performed with low morbidity and mortality.

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This summary starts with a review of the natural history of colorectal liver metastases and results of systemic chemotherapy as treatment in this clinical setting. A review of surgical results follows, starting with surgical resection and concluding with alternative surgical options that are available. It is clear that at present surgical excision is the standard therapy for resectable liver metastases from colorectal primaries.

Natural History of Colorectal Liver Metastasis

Colorectal cancer metastatic to the liver was long presumed incurable, and data from studies during the late 1960s to the early 1980s provide a glimpse of the natural history of colorectal metastasis to the liver (Table 1). Certain conclusions are clear from these data. First, colorectal metastasis to the liver is common. As many as 25 percent of patients presenting with colorectal primaries will be found to have synchronous liver metastasis.² In addition, after treatment of the primary as many as 50 percent of patients will recur with metachronous liver metastasis.^{11,12} Given the estimate of 138,000 new cases of colorectal cancer each year in the United States, at least 46,000 of these patients will present for evaluation of liver metastases during the course of the disease. Second, survival for untreated colorectal metastases to the liver can be measured in months, and five-year survival after discovery of such disease is less than two percent.^{2,13-15}

Many of the natural history studies have been criticized for lack of data on extent of liver involvement. In two of the series presented,^{14,16} the authors attempted to distinguish potentially resectable from unresectable disease. In the study from Wood et al at the Glasgow Royal Infirmary, 26 of the 113 patients reported were thought retrospectively to have potentially resectable disease. In this group the one-year survival for untreated but resectable disease was 46 percent (compared with six percent for the unresectable cohort); three-year survival was 12 percent (compared with zero percent) and five-year survival was three percent.¹⁴ In the study from Wagner et al, the three-year survival for untreated resectable disease was 14 percent (compared with four percent for unresectable disease) and two percent at five years (compared with two

therapy for resectable liver disease. However, it is clear that for most chemotherapeutic regimens, less than one third of patients with liver metastases have shown any response. It is unfortunate that the most recent trials for what is currently the standard chemotherapeutic regimen, namely 5-FU and leucovorin, do not indicate the percentage of patients with isolated liver tumors that respond to this regimen. Given that the overall response to these regimens is 26 to 44 percent, it is unlikely that liver-specific responses are significantly greater than this.

Surgical Resections

Given the poor outcome of unresected metastatic colorectal cancer to the liver, it is understandable that an increasingly aggressive surgical approach has been un-

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percent). From these data, it appears that although solitary lesions or unilobar disease appear to have better prognosis, the five-year survival was still consistently less than three percent. Liver metastasis from colorectal cancer is therefore common and has a uniformly poor outcome when untreated.

Results of Medical Treatment of Isolated Liver Metastatic Disease

Many systemic chemotherapeutic regimens have been tested for metastatic colorectal cancer. The most consistently active agent for this disease has been 5-fluorouracil (5-FU), and most regimens have been based on this agent (Table 2).¹⁷⁻²⁵ Few studies, and certainly none of the most recent studies, have specifically examined the role of systemic chemo-

dertaken in the last two decades for treatment of this disease. This aggressive resectional approach coincided and partly produced improvements in the understanding of liver anatomy, in surgical techniques, and in anesthetic support for liver resection. The result is overwhelming evidence that not only is surgical resection a safe option, it is also a rational and potentially curative treatment for hepatic metastatic disease from colorectal tumors.

RESULTS

The results of six surgical series with 100 or more patients each are presented in Table 3. These surgical results are typified by an operative mortality of less than six percent.⁵⁻¹⁰ All studies reporting results of resections to date are retrospec-

Table 1
Natural History of Liver Metastasis from Colorectal Cancer

Study	Number of Patients	Number of Liver Metastases (Percent)	Survival			
			Mean (Months)	1 Year (Percent)	3 Year (Percent)	5 Year (Percent)
Benchmark and Hafstrom ² (1969)	173	40 (23)	5.7	—	0	0
Oxley and Ellis ¹³ (1969)	640	112 (18)	—	27	4	1
Wood et al ¹⁴ (1976)	—	113	6.6	15	3	1
Bengtsson et al ¹⁵ (1981)	155	25 (16)	4.5	12	0	0

tive studies and contain no control group of untreated patients. Nevertheless, the reported results of five-year survival of 25 to 39 percent and median survival of over two years are significantly better than prior results for untreated patients or those treated with systemic chemotherapy. The study by Hughes et al represents collected data from a large number of surgeons from 24 institutions in North America and Europe.⁶ The results emphasize that favorable results reported for surgical treatment of liver metastasis are not limited to the experience of a few surgeons.

The favorable results of resectional treatment for colorectal metastases to the liver are not restricted to minor liver resections. In most recent series (Table 3), nearly one half of the resections reported are of one half the liver or more (lobectomy or more).⁷⁻⁹ While major resections generally have higher perioperative mortality and morbidity than minor resections, most series report a mortality less than eight percent for major hepatic resections.^{5,7-9} In a recent series of 100 liver resections from our institution, minor resections were not associated with any operative mortality. A lobectomy was associated with a six percent operative mor-

tality, and an extended hepatectomy (resection of greater than 70 percent of the liver parenchyma) was associated with an operative mortality of four percent.²⁶ Thus, even extensive liver resections can be performed safely.

Even though the mortality associated with liver resection is less than five percent, the complexity of such resections and the physiologic stress of losing a significant portion of such a metabolically and immunologically important organ is associated with a complication rate of at least 25 percent. Complications, such as myocardial infarction (one percent),^{8,9} pneumonia (five to 10 percent),^{7,8} and pulmonary embolism (one percent),^{9,26} are expected after any major upper abdominal surgery.

Patients offered liver resection should also be warned of certain major complications specifically associated with liver surgery. The most ominous of these is liver failure, occurring in three to eight percent of all major resections.^{7,9,26} Though most often transient, liver failure may be chronic and may be a cause of subsequent mortality. Significant intraoperative hemorrhage occurs in two to five percent of resections.^{8,9} Intra-abdominal

Table 2
Results of Systemic Chemotherapy for Metastatic
Colorectal Cancer

Study	Drug Regimen	Number of Patients	Liver Metastases (Percent)	Overall Response (Percent)	Liver Response (Percent)	Median Survival (Months)
Baker et al ¹⁷ (1976)	5-FU	42	26	10	0	—
MacDonald et al ¹⁹ (1976)	Methyl-CCNU/5-FU	25	52	40	31	8
Buroker et al ²⁰ (1978)	Methyl-CCNU/5-FU	133	70	16	18	9.7
Grage et al ¹⁸ (1979)	5-FU	31	100	23	23	13.3
Petrelli et al ²⁵ (1987)	5-FU/leucovorin	30	80	40	—	12
Nordic GI Tumor Group ²⁴ (1989)	Methyl-FU/leucovorin	119	71	17	18	11.5
Kemeny et al ²¹ (1990)	Interferon/5-FU	35	69	26	29	—
Doroshov et al ²³ (1990)	5-FU/leucovorin	36	67	44	—	14.2

5-FU = 5-fluorouracil
Methyl-CCNU = methyl-1-ornustine
GI = gastrointestinal

collections either due to bile leak (four percent)^{8,9} or perihepatic abscess (five to 10 percent)^{7,11} may also occur.

The complexity of the operations and of the postoperative care prompts the recommendation that major liver resections be performed at centers specializing in such procedures. Despite the myriad potential problems, in 100 consecutive resections performed in the last year at the Memorial Sloan-Kettering Cancer Center, including 52 trisegmentectomies, the median hospital stay has been 13 days; admission to the intensive care unit was required for only four patients; and the mortality was three percent.²⁶

PATIENT SELECTION AND RISK FACTORS FOR RECURRENCE

Investigators have been attempting to further increase the long-term outcome of liver resection by improving patient selection for surgical treatment. Parameters that have been examined as potential risk factors for poor long-term outcome can be categorized into three groups: general medical risk factors, characteristics of the primary tumor that may predict early recurrence, and characteristics of the liver metastasis that may predict early recurrence. Analysis of some of these parameters is summarized in Table 4.

General medical risk factors that are contraindications to liver surgery (e.g., severe coronary artery disease or pulmonary disease) are the same as those for any major upper abdominal surgery. There has been concern that age may be a significant risk factor for poor outcome. In a large study by Hughes et al, age more than 70 years was found to be a risk factor.²⁷ Two separate studies of liver resection for hepatocellular cancers have suggested that advanced age may be associated with a significant increase in the rate of poor recovery.^{28,29} At our institution, we have performed over 100 major liver resections in patients older than

sixty-five years in the last two years and have found no significant increased risk associated with age. Advanced age alone should not be considered a contraindication to liver resection.

The tumor characteristic most closely correlated with poor outcome is the stage of the primary tumor.^{5,8,9,27} The number of metastases more than three^{11,27} and tumor size²⁷ are also thought to correlate with poor prognosis. A negative surgical margin is correlated with improved long-term results,^{9,27} but what this surgical margin should be is not clear. Scheele et al analyzed their data according to a 1-cm margin,⁹ while other investigators were satisfied with a grossly negative margin.

A number of studies have suggested that outcome correlates with the preoperative level of carcinoembryonic antigen.

Surgical excision is the standard therapy for resectable liver metastases from colorectal primaries.

Cady et al have reported that none of 18 patients with preoperative levels of carcinoembryonic antigen over 200 ng/ml remained disease free for two years after liver resection,³⁰ but there are no confirming studies to support this.

It is controversial whether a liver tumor presenting synchronously with the primary colorectal tumor is associated with worse outcome than a tumor presenting metachronously. Some studies have found a correlation,^{7,9,27} while others have not.^{5,8,10} Bilobar liver distribution of tumors does not appear to influence outcome^{5,8,9} as long as the disease is resectable. In multivariate analyses, the most consistent predictors of long-term outcome have been stage of primary tumor,

Table 3
Results of Hepatic Resection for Metastatic Colorectal Cancer

Study	Number of Patients	Lobectomy or More* (Percent)	Operative Mortality		Survival				Median (Months)
			Overall (Percent)	Lobectomy or More (Percent)	1 Year (Percent)	3 Year (Percent)	5 Year (Percent)		
Adson et al ⁵ (1984)	141	33	2	4	82	40	25	24	
Hughes et al ⁶ (1986)	607	—	—	—	—	—	33	—	
Schlag et al ⁷ (1990)	122	57	4	7	85	40	30	32	
Doci et al ⁸ (1991)	100	50	5	8	—	—	30	28	
Scheele et al ⁹ (1991)	219	43	6	6	—	—	39	—	
Rosen et al ¹⁰ (1992)	280	—	4	—	84	47	25	34	

*Percentage of all hepatic resections that were a lobectomy or more.

Table 4
Predictors of Recurrence after Hepatic Resection for Metastatic Colorectal Cancer

Study	Patient Age	Primary Stage	Metastases				Surgical Margin
			Synchronous	Size	Number	Percent	
Adson et al ⁵ (1984)	—	YES	NO	NO	NO	NO	—
Hughes et al ²⁷ (1988)	—	YES	YES	YES	YES	YES	YES
Schlag et al ⁷ (1990)	—	—	YES	—	—	—	—
Doci et al ⁸ (1991)	NO	YES	NO	NO	NO	YES	—
Scheele et al ⁹ (1991)	NO	YES	YES	NO	NO	—	YES
Rosen et al ¹⁰ (1992)	—	NO	NO	NO	NO	—	NO

total percentage of liver involvement,⁸ and complete resection.^{5,8,11,31}

From these results, it appears that a medically fit patient, regardless of age, with metastatic disease that can be encompassed by a surgical resection should be considered for resective surgical therapy. Particularly favorable results should be expected in patients with less than four metastases and a node-negative primary lesion. However, long-term survival can be obtained despite bilobar metastases and in patients with node-positive primary lesions.

ADJUVANT THERAPY

Most patients who undergo liver resection for metastatic colorectal cancer eventually die of recurrent disease,^{11,12} indicating that subclinical disease undetected at the time of surgery is responsible for failures. No prospective study has examined the use of adjuvant systemic chemotherapy after complete resection of liver tumors. In the retrospective studies, the results are equivocal. In the large collected series of Hughes et al, patients who received postoperative chemotherapy had a better overall survival.²⁷ No other study has confirmed this. At present, a role for postoperative chemotherapy after liver resection for metastatic colorectal cancer has yet to be proven. Standard care after complete resection must at present be considered observation alone.

In patients who recur after liver resection, over one half recur within the liver.^{11,12} This has led investigators to wonder whether adjuvant hepatic artery infusional therapy may provide benefit. Only one randomized trial has examined this.³² Unfortunately, this study only includes a small number of patients (n=36) separated into four groups, making definitive conclusions impossible. Nevertheless, the results are interesting. In this study the 11 patients with solitary metastasis were separated into two groups, re-

section alone or resection followed by hepatic artery infusional (HAI) chemotherapy. None of the five patients with adjuvant HAI treatment developed liver recurrence. The 25 patients with multiple metastasis were randomized to resection and adjuvant HAI or HAI alone. In the 10 patients in the multiple metastasis group treated by resection and HAI, no patient recurred in the liver first. Although one cannot conclude from this small study that adjuvant HAI after liver resection is beneficial, the data certainly suggest that local disease in the liver is controllable by HAI. A recent single-arm study using adjuvant HAI after liver resection provides further encouragement

Liver metastasis from colorectal cancer is common and has a uniformly poor outcome when untreated.

for definitive trials in this area.³³ At the Memorial Sloan-Kettering Cancer Center, we are currently randomizing patients after complete tumor resection to receive or not receive adjuvant HAI chemotherapy in combination with systemic chemotherapy.

Other Surgical Options

CRYOSURGERY

It has long been recognized that the freeze-thaw process produces significant destruction of tissues. Over the last 50 years, these destructive properties have been harnessed as a method for treatment of liver tumors. Early attempts were crude and involved direct application of liquid nitrogen to tumors or to metallic instruments in contact with the tumors. Only in the last decade with the development of sophisticated ultrasound units to guide placement of cryosurgical probes

Table 5
Results of Intra-arterial Infusional Chemotherapy
using FUDR for Metastatic Colorectal Cancer

Study	Number of Patients	Prior Chemotherapy (Percent)	Response (Percent)	Median Survival (Months)
Cohen et al ³⁷ (1983)	50	36	51	—
Johnson et al ³⁸ (1983)	40	—	47	12
Niederhuber et al ³⁹ (1984)	70	45	83	25
Kemeny et al ⁴⁰ (1984)	41	43	42	12
Shepard et al ⁴¹ (1985)	53	42	32	17

FUDR = 5-fluorouracil deoxyribonucleoside.

Table 6
Results of Randomized Trials Comparing Intra-arterial with
Systemic Chemotherapy for Colorectal Metastasis to the Liver

Study	Number of Patients	Regimen HAI/IV	HAI Response (Percent)	IV Response (Percent)	Probability
Kemeny et al ⁴⁷ (1987)	162	FUDR/FUDR	52	20	0.001
Chang et al ⁴² (1987)	143	FUDR/FUDR	42	10	0.0001
Hohn et al ⁴³ (1989)	64	FUDR/FUDR	62	17	0.003
Wagman et al ⁴⁴ (1990)	41	FUDR/5-FU	56	0	—
Martin et al ⁴⁵ (1990)	69	FUDR/5-FU	48	21	0.02
Rougier et al ⁴⁶ (1992)	163	FUDR/5-FU	49	14	—

HAI = hepatic artery infusional therapy IV = intravenous therapy
 FUDR = 5-fluorouracil deoxyribonucleoside 5-FU = 5-fluorouracil

and mass-manufactured delivery systems with well-insulated freezing probes has this technique become widely accessible for the treatment of liver cancer.

Cryoablation has been used extensively for primary hepatocellular carcinoma. The experience with metastatic colorectal cancer is preliminary, and in this

setting, cryoablative surgery must still be considered experimental. Three groups have had most of the experience in using cryosurgery for the treatment of otherwise unresectable colorectal metastasis.

Morris et al have treated 67 patients with as many as 13 colorectal metastases to the liver.³⁴ They have demonstrated

that the method is safe, with no perioperative mortality. They have also demonstrated effectiveness of this method for local control of disease, because 10 of the last 13 failures have been in distant organs (lung or bone). However, long-term survival data are not available. Furthermore, because they routinely use intra-arterial infusional chemotherapy in conjunction with the cryosurgery, it is difficult to separate the relative contributions of cryoablation from those of chemotherapy.

Ravikumar et al at the New England Deaconess Hospital have reported their experience with cryoablation for 24 patients with metastatic colorectal cancer to the liver.³⁵ All patients had less than six tumors and no evidence of extrahepatic disease. There were no operative deaths. With a median follow-up of two years, nine patients have died (37 percent), seven patients are disease free (29 percent), and eight patients are alive with recurrence (34 percent). The median survival in this group of patients is greater than two years. Furthermore, only two of the 17 recurrences have been at the original cryoablation site.

Onik et al at the Allegheny Hospital in Pittsburgh have also presented results of cryoablation for 18 patients with metastatic colorectal cancer to the liver.³⁶ Patients had as many as 12 tumors within the liver, but none were found to have extrahepatic tumor. Mean survival for this group was 21 months. At a mean follow-up of 29 months, four of the patients (22 percent) are disease free.

Although mortality rates in these early reports are low, this type of surgery is not without significant complications. Myoglobinuria and renal failure resulting from by-products of tumor necrosis have been reported.³⁶ In addition, cracking of the liver during the freeze-thaw process and direct impalement of major vessels and bile ducts may occur, leading to significant bleeding or to a biliary fistula.³⁶ This type of surgery should only be per-

formed by surgeons familiar with hepatic anatomy and surgery. It is clear that cryoablation can ablate and control local tumors. Whether this will translate into a survival benefit awaits controlled randomized studies.

REGIONAL INFUSIONAL THERAPY

The liver derives its nutrient blood supply from two vascular sources, the hepatic artery and the portal vein. Regional infusional chemotherapy has been directed at delivery of chemotherapeutic agents to each of these vessels. It has become clear, however, that tumors greater than 3 mm in size derive most of their blood supply from the hepatic artery, and the intraportal approach has largely been abandoned. Currently, intra-arterial infusional chemotherapy appears to be an effective method for treatment of unresectable metastatic disease isolated to the liver.³⁷⁻⁴¹

Percutaneous catheters placed through the femoral artery have been used as a method to deliver chemotherapy into the hepatic artery. However, this method of delivery has been associated with a high incidence of gastrointestinal complications due to perfusion of the stomach or duodenum by branches of the hepatic artery. This problem can be remedied by using surgically placed ports,³³ because small arteries from the hepatic artery to the gastrointestinal tract can be meticulously ligated during the surgical procedure. These arterial ports, however, are associated with frequent thrombosis and occlusion and have the inconvenience of requiring an external pump. Currently, most groups using intra-arterial delivery of chemotherapy to the liver use subcutaneously implanted pumps. This method allows continuous infusion of the chemotherapeutic agent without any external device. Trials from the mid-1980s have shown this to be a safe and effective treatment for colorectal metastasis (Table 5). In most studies, well over one third of the patients responded

Table 7
Dearterialization and Colorectal Metastasis

Study	Number of Patients	Type	Adjuvant Chemotherapy	Mortality (Percent)	Response (Percent)	Survival (Months)
Ramming et al ⁴⁸ (1976)	9	HAL	5-FU	—	56	7.2 (mean)
El-Domeiri and Mojab ⁵¹ (1978)	9	Transient occlusion	FUDR	—	—	12.2 (mean)
Taylor ⁴⁹ (1978)	6	HAL	No	17	—	3.1 (mean)
	7	HAL	5-FU ip and HAI	14	—	9.8 (mean)
Berjian et al ⁵² 1980	12	HAL	Yes	13	50	14 (median)
Petrelli et al ⁵⁰ (1984)	97	HAL	No	2	—	9.5 (median)

HAL = hepatic artery ligation
 FUDR = 5-fluorouracil deoxyribonucleoside
 HAI=hepatic artery infusion

5-FU = 5-fluorouracil
 ip = intraperitoneally

to the chemotherapy, and the median survival was 12 to 26 months. This is remarkable, given that a large proportion of patients entering these early trials had failed systemic chemotherapy.

Based on these encouraging data, at least six randomized trials comparing hepatic infusional chemotherapy with systemic therapy have been performed (Table 6). It is clear that intrahepatic chemotherapy is an effective therapy and is associated with a significantly higher number of responses than systemic chemotherapy.⁴²⁻⁴⁷ The response rates for HAI were 48 to 62 percent, compared with zero to 21 percent for intravenous therapy. Critics have pointed out that this increase in response rate has translated to increased survival in only one study.⁴² In this study from the National Cancer Institute, if patients with portal lymph nodes positive for metastatic cancer are not included, the two-year survival for intra-arterial chemotherapy was 47 percent,

while systemic chemotherapy resulted in a survival of 13 percent ($p=0.03$).

Two problems in the design of these trials have limited the study of survival. First, most trials have only studied small populations. Second, in the two largest trials, crossover in therapy was allowed. Patients failing systemic chemotherapy were switched to HAI chemotherapy.^{43,47} In the study at the Memorial Sloan-Kettering Cancer Center, 60 percent of patients randomized to systemic chemotherapy eventually crossed over to HAI.⁴⁷ As a possible testimony to the effectiveness of HAI, those patients who crossed over from systemic chemotherapy to HAI had a median survival of 18 months, while those who could not crossover because of technical reasons had a median survival of eight months. Similarly, in the study by Hohn et al, 43 percent of patients randomized to systemic therapy eventually crossed over to the HAI arm.⁴³

Even though the operative mortality

for placement of infusional pumps is less than one percent in most series,^{37,40} potential complications associated with arterial infusional therapy are numerous. Complications associated with the initial surgery include bleeding, infection, and incomplete liver perfusion or extrahepatic perfusion. Chemotherapeutic complications include chemical hepatitis, sclerosing cholangitis (five to 10 percent),⁴⁷ and gastrointestinal ulcerations/erosions (10 to 20 percent).⁴⁷ Nevertheless, these side effects occur at an acceptable rate in experienced hands. Hepatic infusional therapy clearly provides an improved response rate when compared with systemic chemotherapy. There is suggestive evidence survival is improved. A multicenter trial without crossover will begin in 1995.

VASCULAR INTERRUPTION

Vascular interruption includes hepatic artery ligation (HAL) and intermittent occlusion of the hepatic artery using implantable occlusive cuffs. The rationale for these modes of therapy is based on the finding that when hepatic metastatic disease becomes grossly apparent, the tumor nodules derive most of their blood supply from the hepatic artery, while normal liver tissues derive most nutrient supply from the portal vein. Theoretically, occlusion of the hepatic artery would have a significantly greater detrimental effect on the tumor than on normal liver.

Early preliminary studies demonstrated significant necrosis of metastatic tumors after HAL.⁴⁸ A number of studies have used this modality in the treatment of metastatic colorectal cancer, but most are plagued by significant design flaws. Representative studies are summarized in Table 7.⁴⁸⁻⁵² Most are small studies, and only one offers a randomized comparison.⁴⁹ Furthermore, a large number of the studies combined hepatic artery interruption with either intraportal chemotherapy or intra-arterial chemotherapy, thus pre-

venting the distinction of effects of arterial interruption from effects of chemotherapy.

Two studies deserve particular attention. Taylor conducted a randomized study involving hepatic arterial interruption for metastatic colorectal cancer to the liver.⁴⁹ The patients (n=24) were randomized to four arms: no treatment, HAL, HAL and subsequent intraportal infusional therapy with 5-FU, or HAL followed by intra-arterial and intraportal infusion of 5-FU. The mean survivals were 3.1, 3.0, 4.1, and 9.8 months respectively. The author concluded that HAL followed by a combination of intra-arterial and intraportal infusional chemotherapy was promising. The number of patients were clearly too small to derive definitive conclusions.

Petrelli et al examined 97 patients with metastatic disease to the liver treated with HAL alone.⁵⁰ Operative mortality was two percent, and median survival was 9.5 months. No other study has duplicated these results. Furthermore, this study contains many patients who otherwise may have been resectable, so that without an adequate control group it is impossible to assess the value of this approach.

At present, arterial interruption must still be regarded as experimental and certainly inferior to resection for resectable lesions. It has no better record of efficacy than that shown for intra-arterial infusional chemotherapy.

Conclusion

Data for the last three decades have defined an important role for surgical therapy in the treatment of metastatic colorectal cancer to the liver. In patients with resectable disease, complete resection is effective and can be curative. In unresectable disease, implantable devices for hepatic artery infusional chemotherapy may be an effective therapy. The role for adjuvant chemotherapy after curative resections is not yet defined. Ongoing stud-

ies will determine the role for other surgical therapy, such as cryoablation. Most importantly, available data emphasize the

importance of a multidisciplinary approach in the study and treatment of patients with metastatic disease to the liver.

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