

REVIEW ARTICLE

Liver resections in metastatic gastric cancer

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Abstract

Background: The 5-year survival of patients receiving standard-of-care chemotherapy for metastatic gastric cancer (MGC) to the liver is <2%. This review examines the published data on liver resections for MGC and analyses the rationale for potentially aggressive surgical management.

Methods: A search of the PubMed and Scopus databases was used to identify studies published in English from 1990 to 2009 that reported on 10 or more patients who underwent liver resections for MGC. All available clinicopathologic data were analysed. In particular, we examined longterm survival and the characteristics of individuals surviving for >5 years.

Results: Nineteen studies reported on 436 patients. Median 5-year survival was 26.5% (range: 0–60%). Overall, 13.4% (48/358) of patients were alive at 5 years and studies with extended follow-up reported that 4.0% (7/174) of patients survived for >10 years. Overall in-hospital mortality was 3.5% (12/340 patients); however, the median mortality rate across the studies was 0%. No prognostic factor was found to be consistently statistically significant across these small studies.

Conclusions: Despite the limitations of any analysis of retrospective data for highly selected groups of patients, it would appear that liver resections combined with systemic therapy for MGC can result in prolonged survival.

Keywords

gastric cancer, liver metastases

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Introduction

Gastric cancer is the fourth most common cancer worldwide and has an incidence of 989 598 and an annual mortality close to 738 069.¹ In the USA, the incidence of gastric cancer has steadily declined in recent years and it now represents the 14th most common cancer, and accounts for 1.5% of all new diagnoses and 5.2% of all cancer deaths.^{2,3} Approximately 21 130 people will develop gastric cancer in the USA this year and an estimated 10 620 individuals will die from the disease.^{2,3}

At the time of diagnosis, 35% of patients present with evidence of distant metastases and 4–14% have metastatic disease to the liver.^{4–6} In patients who undergo gastric resection with curative intent, hepatic recurrences are common. A study from the Memorial Sloan-Kettering Cancer Center (MSKCC) described patterns

of recurrence in completely resected gastric adenocarcinomas in a large series of patients ($n = 1172$) and found liver-specific recurrence rates of 37%.⁷

There are no adequate large prospective studies detailing the natural history of metastatic gastric carcinoma and longterm survival. However, two small randomized trials compared best supportive care vs. combination chemotherapy and found that no patients treated with supportive care lived for >1 year.^{8–11} Survival data for patients with metastatic gastric cancer (MGC) to the liver only are also limited. In a study analysing 643 patients enrolled in five separate chemotherapy trials by the Japanese Clinical Oncology Group (JCOG), 5-year survival for patients with metastases confined to the liver and treated with systemic therapy alone was 1.7%.¹² Palliative chemotherapy using various regimens has been widely used as the treatment of choice, but only modest

improvements in overall survival have been observed, with median survival increasing from approximately 3 months to 7–15 months. Longterm survival is rarely reported.^{8–13}

Liver resection is now a routine procedure at specialty centres around the world. Improvements in the understanding of anatomy, physiology, perioperative care and surgical technique have reduced operative mortality in most tertiary referral cancer centres to <2%.¹⁴ For hepatic colorectal metastases, retrospective studies involving thousands of patients show that surgical resection can yield 5-year survival rates of 35–61%.¹⁵ Similar results have been observed following resections of hepatic metastases from primary neuroendocrine tumours.¹⁶ Thus, surgical management of metastatic disease is now considered the standard of care for these two malignancies.

Identifying the patients who are most likely to benefit from surgery is critical to improving treatment options for patients with MGC. Therefore, the aim of this review was to examine the current evidence for longterm survival following hepatic resections for metastatic gastric adenocarcinomas and to determine factors that may be used in a prospective fashion to identify the patients who are most likely to benefit from operative management.

Materials and methods

A comprehensive PubMed and Scopus database search was performed to identify all studies published in English from 1990 to 2009 reporting on liver resections for MGC. A total of 26 studies were identified, from which studies reporting on <10 patients and studies lacking longterm outcome or survival data were excluded, leaving 21 studies for analysis (Fig. 1).^{17–37} Data from Miyazaki

*et al.*³³ and Sakamoto *et al.*²⁴ were not used in calculating the total number of patients or survival statistics because more recent follow-up data on the same patient populations were reported by Ambiru *et al.*²⁹ and Koga *et al.*,²² respectively.

Data were collected and evaluated on the size of the series, the year and country of publication, patient and primary tumour characteristics, whether hepatic surgeries were completed in synchronous (together with gastrectomy) or metachronous (after gastrectomy) fashion, the type of operative intervention (wedge resections, anatomic segmentectomies or hepatectomies), and operative morbidity and mortality. Longterm outcome evaluations included 1-, 3- and 5-year actuarial survival based on Kaplan–Meier curves, along with the number of patients alive for 5 years at the time of reporting, excluding duplicated data (Fig. 1). Detailed profiles of individuals surviving for >5 years were analysed and used to generate potential selection criteria for patients who might benefit from liver resection in MGC.

Results

Patients

Between 1990 and 2008, 436 patients at multiple institutions in seven countries were reported in 21 studies to have undergone liver resection for metastatic gastric adenocarcinoma (Table 1).^{17–37} These included 279 patients (64%) from Japan, 114 patients (26%) from Europe, 33 patients (8%) from South Korea, and only 10 patients (2%) from the USA. Patient gender was defined for 375 patients, including 284 males (76%) and 91 females (24%). The median age of patients by series ranged from 55 years to 67 years.

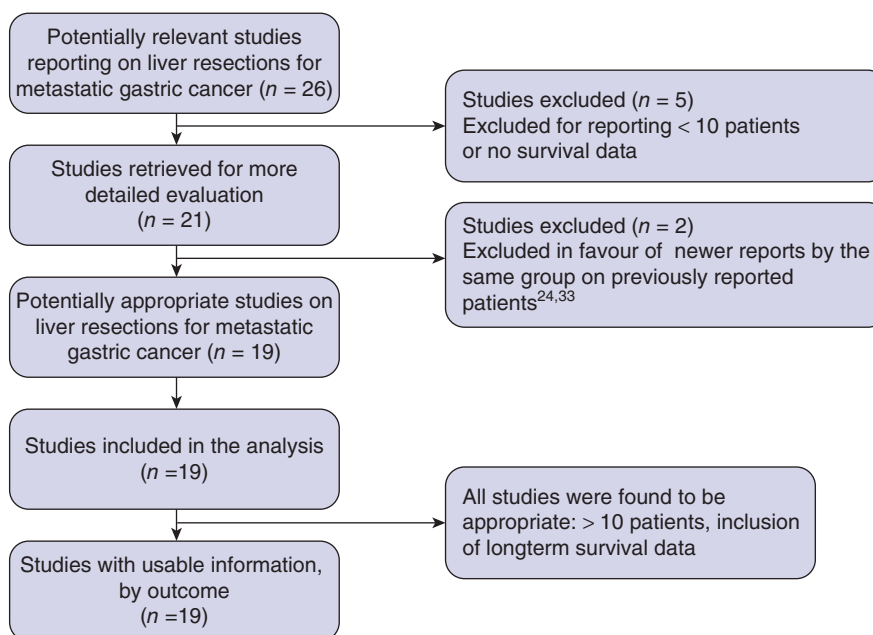


Figure 1 Flow chart showing details of the PubMed article selection process

Table 1 Longterm survival of patients after resection of hepatic metastases from gastric adenocarcinomas

Authors	Country	Year	Patients, n	Survival, months		Survival rate, %			Alive at 5 years, n	Mortality, n
				Median	Mean	1-year	3-year	5-year		
Morise <i>et al.</i> ¹⁷	Japan	2008	18	13	–	56	27	27	3 ^a	0
Thelen <i>et al.</i> ¹⁸	Germany	2008	24	–	–	53	22	15	2	1
Cheon <i>et al.</i> ¹⁹	S. Korea	2008	22	17	–	77	30	23	3	1
Ueda <i>et al.</i> ^{b20}	Japan	2008	15	–	–	80	60	60	3	0
Sakamoto <i>et al.</i> ²¹	Japan	2007	37	31	–	–	–	11	2	0
Koga <i>et al.</i> ²²	Japan	2007	42	34	–	76	48	42	8	2
Adam <i>et al.</i> ³⁶	France	2006	64	15	–	–	–	27	–	–
Hirai <i>et al.</i> ³⁷	Japan	2006	14	–	–	–	–	42	–	0
Roh <i>et al.</i> ²³	S. Korea	2005	11	19	–	73	38	38	1	0
Shirabe <i>et al.</i> ²⁵	Japan	2003	36	–	–	64	26	26	4	0
Okano <i>et al.</i> ²⁶	Japan	2002	19	21	–	77	34	34	3	0
Saiura <i>et al.</i> ²⁷	Japan	2002	10	25	27	50	30	20	2	3
Zacherl <i>et al.</i> ²⁸	Austria	2002	15	9	16	36	29	–	0	1
Ambiru <i>et al.</i> ²⁹	Japan	2001	40	12	–	–	–	18	6	0
Imamura <i>et al.</i> ³⁰	Japan	2001	17	–	–	47	22	0	0	0
Fujii <i>et al.</i> ³¹	Japan	2001	10	16	–	60	20	10	1	1
Elias <i>et al.</i> ³²	France	1998	11	–	–	90	35	–	4	–
Ochiai <i>et al.</i> ³⁴	Japan	1994	21	–	–	–	–	–	4	–
Bines <i>et al.</i> ³⁵	USA	1993	10	–	–	45	–	30	2	3
Total		–	436	–	–	–	–	–	48 (13.4%)	12 (3.5%)

^aAlive at 4 years at time of follow-up

^bThree patients received microwave ablation therapy

Table 2 Clinicopathologic features of primary gastric adenocarcinomas

Depth	Lymph node	Lymphatic invasion	Venous invasion	Differentiation	Synchronous
17–19,21–23,26–31	8,17–19,21–23,26–31,34	17–19,21–23,25–31	17–19,21–23,25–31	17–19,21–23,26–31,35	16–31,33,34
T1–T2	N0–N1	No	No	Poor–moderate	No
56% (114/202)	48% (80/166)	32% (31/97)	37% (43/115)	83% (86/104)	42% (145/342)
T3–T4	N2–N3	Yes	Yes	Well	Yes
44% (88/202)	52% (86/166)	68% (66/97)	63% (72/115)	15% (16/104)	58% (197/342)

Development of hepatic metastases from gastric cancer

Rates of synchronous and metachronous disease varied depending on the particular definitions applied by each study. Commonly, synchronous disease was defined as metastases found either at the time of primary tumour diagnosis or within 1–6 months of the primary gastric resection. Data on the occurrence of hepatic gastric cancer metastases were reported in 16 studies.^{17–23,25–31,34,35} Overall, 58% (197/342) of patients had synchronous metastatic disease; proportions of patients with synchronous metastatic disease in individual studies lay in the range of 42–100% (Table 2).

The median time to first diagnosis of metachronous disease (median disease-free interval [DFI]) to the liver was 12.5 months (range: 10.1–21 months).^{18,19,22,23,26–28,31,34,35}

Clinicopathologic features of the primary gastric adenocarcinoma

Clinicopathologic features of the primary gastric cancer are summarized in Table 2.

Clinicopathologic features of hepatic metastases from gastric cancer

Clinicopathologic features of the hepatic metastases are shown in Table 3.

Adjuvant therapy

Nine studies^{19,21,22,26,27,29,32,34,35} reported on adjuvant therapy specifically to treat hepatic disease. Overall, 48% (119/248) of patients received some form of liver-specific adjuvant systemic

Table 3 Clinicopathologic features of hepatic metastases

Lesions, <i>n</i>	Distribution	Surgical procedure		
		Wedge	Segment	Lobe
17–19,21–23,26–31	17–19,21–23,26–31	17–19,21–23,25,26,28–31,34,35	17–19,21–23,25,26,28–31,34,35	17–19,21–23,25,26,28–31,34,35
1	Unilobar	50% (119/240)	31% (76/240)	19% (45/240)
61% (162/265)	77% (172/222)			
>1	Bilobar			
39% (103/265)	23% (50/222)			

chemotherapy, 15% (37/248) of patients received hepatic arterial infusion (HAI), and 1% (2/248) of patients underwent concurrent intraoperative radiation. Four studies^{19,21,27,35} reported on the specific agents used, which included 5-fluorouracil (5-FU),^{21,27,29,35} cisplatin,^{19,21} anthracylin,¹⁹ aclarubicin²⁹ and mitomycin C⁹ through HAI.

Patterns of recurrence

Nine studies reported on disease recurrence.^{18,19,21–23,25,26,29,31} Detailed site-specific recurrence data were not available in most reports. However, high rates of recurrent disease at any site were uniformly described in all studies (64–91%). Overall, the recurrence rate at any site was 76% (183/241 patients) and the hepatic-specific recurrence rate was 56% (136/241 patients). Data on whether recurrences were localized to the resection site were not specified.

Morbidity and mortality after liver resection

Mortality rates were reported in 16 studies (Table 1).^{17–23,25–31,35,37} Nine studies (207 patients) had no deaths in their series.^{17,20,21,23,25,26,29,30,37} The median mortality rate across the studies was 0% (range: 0–30%). Analysis of all patients indicated that overall in-hospital mortality was 3.5% (12/340 patients) and 30-day mortality was 0.9% (3/340 patients). Minimal data regarding the morbidity of these operations were provided. Thelen *et al.*¹⁸ reported that four of 24 patients developed postoperative complications consisting of liver insufficiency (one patient), pneumonia (one patient) and pleural effusion (two patients). Zacherl *et al.*²⁸ reported on seven of 15 patients who developed postoperative complications. Only four of these patients were categorized as demonstrating major complications, but no further details were available. Two of these patients were re-operated for multiple complications such as bleeding, anastomotic failure, pancreatitis and peritonitis. Excluding three patients who were counted as in-hospital mortalities, Bines *et al.*³⁵ reported three of 10 patients who developed complications (pulmonary embolus, pleural effusion with arrhythmia, wound infection) after hospital discharge.

Survival rates

Actuarial 1-, 3- and/or 5-year survival rates were reported in 18 studies (Table 1).^{17–23,25–32,35–37} Longterm 5-year survival was

reported in 16 studies.^{17–23,25–27,29–31,35–37} Eleven studies reported 5-year survival rates of $\geq 20\%$ ^{17,19,20,22,23,25–27,35–37} and three studies reported 5-year survival rates of 10–19%.^{21,29,31} If data from all the studies are combined, the median 1-, 3- and 5-year survival rates are 62.0%, 30.0% and 26.5%, respectively. Seventeen studies^{17–22,25–32,34,35} provided information about the number of patients still alive 5 years after surgical resection of metastatic liver disease. Although follow-up was not complete, 13.4% (48/358) of patients were still alive 5 years after surgery. Seven studies reported a median survival of >15 months.^{19,21–23,26,27,31} The median survival across the studies was 17 months.

Detailed analyses of data for a total of 29 patients who survived for >5 years were reported by eight studies.^{20,22,23,25,27,31,34,35} Interestingly, 17 of the 29 patients had synchronous lesions, which suggests that longterm survival may be attainable despite advanced disease presentation in highly selected individuals. Of the 29 long-term survivors, 26 had a single lesion resected and only three patients had multiple metastatic nodules removed. No strong patterns were observed regarding patient sex, tumour differentiation status, lymph node status or type of surgery performed. Seven of the 29 patients survived for ≥ 10 years. All patients who survived for 10 years had only one lesion removed and four of six presented with a well-differentiated histological grade and four of five patients had a T1–T2 primary lesion. Surprisingly, six of the seven 10-year survivors initially presented with synchronous disease. Two patients underwent wedge resections, two had formal lobectomies, one had a segmentectomy and for one patient the specific liver resection was not clearly documented.

Prognostic factors

Ten studies^{17,18,21,22,25,26,28,29,31,34} evaluated various prognostic factors for patients undergoing liver resections for gastric adenocarcinomas. The categories analysed were demographics (age, gender), primary tumour characteristics (size, location, depth of invasion, tumour grade, lymphatic invasion, venous invasion, presence of tumour lymphocytes, fibrous pseudocapsule, lymph node involvement), characteristics of liver metastases (size, number, distribution, timing of resection, type of resection, resection margin, DFI), preoperative carcinoembryonic antigen (CEA) level, and use of liver-specific adjuvant therapies.

Univariate analysis showed a positive resection margin to be a significant predictor of poor outcome in two studies ($P = 0.005$,

Table 4 Prognostic factors significant on multivariate analysis

Variable	P-value and study reference
Primary tumour lymphatic invasion	0.0475 ²⁵
Primary tumour venous invasion	0.001 ²⁵
Primary tumour serosal invasion	0.02 ²²
Resection margins	0.023 ¹⁸
Unilobar vs. bilobar metastases	0.003 ²¹
Number of metastases	0.005 ²² 0.0035 ²⁵
Tumour size (<4 cm vs. ≥4 cm)	0.006 ²¹
Synchronous vs. metachronous	0.031 ²⁹

$P = 0.024$).^{18,29} Primary tumour characteristics such as increased depth of invasion (T-stage) were significant in three studies ($P = 0.02$, $P = 0.06$, hazard ratio 5.60 [1.42–22.15])^{17,22,34} and a higher degree of lymphatic invasion ($P = 0.002$, $P = 0.0001$)^{17,25} and venous invasion ($P = 0.02$, $P = 0.0069$)^{21,25} were significant in two. A moderate or poorly differentiated primary tumour histologic grade ($P = 0.015$)²⁶ also predicted worse outcome in one study. By contrast, the presence of lymphocytic aggregation ($P = 0.026$)³¹ and a fibrous pseudocapsule ($P = 0.02$)²⁶ on primary tumours predicted improved outcome in single reports.

Characteristics of gastric liver metastases that predicted worse outcomes in at least two studies by univariate analysis included the presence of disease in both hemi-livers ($P = 0.004$, $P = 0.001$)^{21,28} and increased size ($P = 0.02$, $P = 0.035$)^{21,31} and number ($P = 0.03$, $P = 0.0004$)^{22,25} of metastatic deposits. One study reported poorer outcomes for patients with DFIs of <1 year for metachronous presentation ($P = 0.014$)³¹ and only one study reported the presence of synchronous disease as a predictor of worse outcome ($P = 0.0078$).²⁹

Multivariate analysis to determine independent prognostic factors was performed in five studies (Table 4).^{18,21,22,25,29} Factors found to significantly predict worse outcome in single reports included positive resection margins ($P = 0.023$),¹⁸ primary tumour serosal invasion ($P = 0.02$),²² primary tumour venous invasion ($P = 0.0001$)²⁵ and lymphatic invasion ($P = 0.0475$).²⁵ For hepatic metastases, independent predictors of worse outcome in single studies were disease in both hemi-livers ($P = 0.002$),²¹ increased number of tumour deposits ($P = 0.005$, $P = 0.0035$),^{22,25} metastatic deposits ≥4 cm in size ($P = 0.006$)²¹ and synchronous presentation ($P = 0.031$).²⁹

Discussion

Hepatic metastases are relatively common in patients with gastric cancer. Up to 14% of all patients will have MGC to the liver at diagnosis and, after curative resection for gastric cancer, over a third of all patients will eventually develop liver-specific recurrences.^{4–7} Currently, systemic chemotherapy is considered the standard of care, but longterm survival with chemotherapy

alone is rare. Although recent advancements with newer regimens for this disease have led to modest improvements, longterm survival beyond 5 years is rarely reported.^{38–40}

Based on estimates from published reports and known gastric cancer incidence rates, nearly 2100 people in the USA and 99 000 individuals worldwide will present this year with hepatic metastases. Additionally, a number of patients will eventually develop liver metastases amenable to surgery after undergoing a primary gastric resection. For these patients, even modest improvements in survival compared with the survival afforded by chemotherapy alone will represent a significant advancement in the management of MGC. The role of liver resection for patients with MGC is not clearly defined and resection is rarely offered to these patients. We therefore performed a thorough review of the literature and identified 19 studies published after 1990 in English reporting on 436 gastric adenocarcinoma patients undergoing liver resection with curative intent.

In retrospective analyses, biases can be introduced by selecting patients who present with favourable prognostic factors. However, once metastatic disease develops, it is thought to supersede the value of primary tumour prognostic factors. In these series, although 56% of the patients presented with small primary gastric tumours (T1 or T2), 44% of these tumours were poorly differentiated and over half had significant lymphatic and/or vascular invasion with at least one positive lymph node involved. Thus, although these series were highly selected, they represent a group of patients with unfavourable biology at presentation.

Synchronous disease is a known prognostic factor representative of aggressive biology. Overall, more than half of all patients had synchronous hepatic disease. This is higher than the 4–14% previously reported in the literature and can be potentially explained by the broad time range used to define synchronous disease in these studies (up to 6 months after gastrectomy) or the fact that these reports describe a highly selected subset of the entire population of patients with MGC. The remainder of the patients developed metachronous liver metastases after a median DFI of 12.5 months. Favourable tumour biology based on the DFI is unlikely to solely account for the encouraging outcomes observed in this group.

Low-volume and/or localized metastatic disease may represent a more favourable biology. Nearly two-thirds of patients in these series underwent resection of a solitary hepatic metastasis and in over three-quarters of cases this was localized to one hemi-liver. This represents a biased selection of patients with relatively low-volume and localized disease for liver resection and may explain the unusually favourable outcomes. However, almost half of all patients had lesions measuring >3 cm in size and several median tumour sizes of >5 cm were reported. Additionally, the more recent of these studies reported multiple hepatic lesions resected in 47%, 52% and 53% of patients, respectively.^{28–30} These may mitigate the selection biases based on low-volume and localized disease in one hemi-liver. It is possible that the improvements in hepatic surgical techniques and perioperative care utilized in the

more recent reports led to a more aggressive approach for MGC. Nonetheless, the selection of patients with low-volume liver disease (e.g. with single, isolated lesions measuring <5 cm, localized to one hemi-liver) represents a bias that may account for the favourable outcomes.

The potential benefits of liver resection in MGC should be weighed against the small but not negligible risks in liver resection. In these series, a variety of liver resections were undertaken with acceptable mortality. The combined overall 30-day operative mortality was 3.5% (12/340 patients), but the median mortality rate across studies was 0% and nine institutions reported no perioperative deaths. These results compare favourably with published mortality rates of <4% for hepatic resections in general during the same time period.¹⁴ Although morbidity is a significant factor in any cancer treatment and, in particular, in liver resections, the available data were insufficient to perform an adequate analysis.

Prognostic factors can be used to select similar patients for this aggressive approach to treating MGC to the liver. In these series of patients undergoing hepatic resections for MGC, the following were found to be negative prognostic factors on uni- and multivariate analyses in individual reports: synchronous presentation; DFI from primary resection of <1 year; the presence of multiple or larger metastases, and bilobar disease. However, it should be noted that although these factors were found to be significant in one or two studies, findings in most reports examining the same parameters did not reach statistical significance. Based on this analysis and the nature of this retrospective review, no definitive conclusions can be made regarding negative prognostic factors.

Although systemic therapy is considered to be the standard of care for MGC, fewer than half of these patients received systemic or liver-directed chemotherapy following hepatic resection. Any improvement in survival in MGC is small with chemotherapy alone, but it does, nevertheless, result in an increase in overall survival compared with no treatment at all. Therefore, the survival data reported here may potentially be underestimated. These issues will be better addressed in a prospective randomized trial, but no conclusions can currently be drawn regarding the value of adjuvant chemotherapy after liver resection in MGC.

Longterm survival and the maintenance of good quality of life are paramount in the evaluation of any modality of cancer treatment. The 5-year survival of patients with gastric metastases confined to the liver who are treated with systemic therapy alone is reported to be 1.7%.¹² Median survival in individual studies in this series ranged from 9 to 34 months, and the median 5-year actuarial survival was 26.5% (range: 0–60%). Despite the limited follow-up, 13.4% (48/358) of all patients were reported as still alive 5 years following hepatic resection. Several studies with more extended follow-up reported that 4.0% (7/174) of patients survived for >10 years. An examination of the 29 patients who survived for >5 years found that the majority had small (T1–T2; 18/26 patients), moderately to well-differentiated (20/25 patients) tumours and underwent the removal of a single isolated meta-

static liver lesion (26/29 patients), suggesting that favourable biology of the primary tumour in patients with a low metastatic burden may have contributed to prolonged survival following metastasectomy. Nonetheless, 17 of 29 patients underwent resection of synchronous lesions, including six of the seven patients who lived for >10 years. Furthermore, only one of the studies in this series found synchronous disease to be predictive of poor outcome on multivariate analysis. Drawing conclusions from this group of patients is difficult. However, these results suggest that survival could potentially be prolonged in a similar highly selected group of patients, even in those who present with synchronous hepatic MGC. Currently, all of these patients would be considered non-operable by standard-of-care criteria.

The application of an aggressive surgical approach in MGC should also be evaluated in terms of recurrence and disease-free survival and not only in terms of overall survival. Early or high recurrence rates translate into prolonged periods of systemic therapy and a potentially reduced quality of life. These will mitigate any short-term advantage resulting from liver resection in MGC. It is not surprising that over three-quarters of the patients in these series experienced a recurrence and over half (56%) suffered hepatic recurrence. Based on these recurrence rates, liver resection in MGC is less appealing. However, in these series the majority of patients did not receive adjuvant chemotherapy after liver resection. Given the biology and systemic nature of MGC, this may partially account for the high recurrence rates. Recent reports on novel chemotherapy regimens for MGC such as the FOLFOXIRI regimen (5-fluorouracil, leucovorin, oxaliplatin and irinotecan) are encouraging.^{39,40} Trials using this regimen, although they were non-randomized and of Phase II status, achieved for the first time a median overall survival of 15 months. It is not unreasonable to assume that recurrence rates after liver resection in MGC could potentially decrease with the addition of these new regimens as adjuvant therapies.

In conclusion, the merits of liver resection in MGC should not be dismissed reflexively simply because we have no prospective, randomized data. For patients with hepatic disease amenable to surgical resection, treatment alternatives include systemic chemotherapy, locoregional ablative therapies with or without systemic treatment or surgical resection with or without systemic treatment. Based on this review, it is not unreasonable to consider liver resections in MGC in highly selected patients as part of multidisciplinary care for this malignancy. Potential patients should be good operative candidates with favourable tumour biology, such as small (<5 cm) or isolated disease, long DFIs (>1 year), lesions amenable to resection with negative margins, and no extrahepatic disease. To better address the question of whether systemic therapy in combination with resection in limited MGC prolongs survival, the National Cancer Institute (NCI) at the National Institutes of Health (Bethesda, MD, USA) is currently accruing patients for the GYMSSA trial, which will compare gastric resection and metastasectomy plus FOLFOXIRI with FOLFOXIRI alone in patients with MGC (ClinicalTrials.gov ID NCT00941655).⁴¹

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Conflicts of interest

None declared.

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