Original article

Hepatic resection for colorectal metastases – a national perspective

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Background: Many consultant surgeons are uncertain about peri-operative assessment and postoperative follow-up of patients for colorectal liver metastases, and indications for referral for hepatic resection. The aim of this study was to assess the views the consultant surgeons who manage these patients.

Methods: A postal questionnaire was sent to all consultant members of the Association of Coloproctology of Great Britain and Ireland and of the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland. The questionnaire assessed current practice for pre-operative assessment and follow-up of patients with colorectal malignancy and timing of and criteria for hepatic resection of metastases. Number of referrals/resections were also assessed.

Results: The response rate was 47%. Half of the consultants held joint clinics with an oncologist and 89% assessed the liver for secondaries prior to colorectal resection. Ultrasound was used by 75%. Whilst 99% would consider referring a patient with a solitary liver metastasis for resection, only 62% would consider resection for more than 3 unilobar metastases. The majority (83%) thought resections should be performed within the 6 months following colorectal resection. During follow-up, 52% requested blood CEA levels and 72% liver ultrasound. Half would consider chemotherapy prior to liver resection and 76% performed at least one hepatic resection per year with a median number of 2 resections each year.

Conclusions: A substantial proportion of patients are assessed for colorectal liver metastases pre-operatively and during follow-up though there is spectrum of frequency of assessment and modality for imaging. Virtually all patients with solitary hepatic metastases are considered for liver resection. Patients with more than one metastasis are likely to be not considered for resection. Many surgeons are carrying out less than 3 resections each year.

Key words: Liver metastases – Colorectal cancer

Colorectal cancer remains the second commonest cause of cancer-related mortality resulting in over 19,000 deaths each year in the UK.¹ Approximately a quarter of these patients have liver metastases at

presentation^{2,3} and another 20% will develop liver metastases following apparently curative surgery.⁴ The 5-year survival of patients with untreated liver metastases is less than 3%.^{5–7}

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Hepatic resection for colorectal liver metastases has been shown to provide a significant survival benefit with 5-year survival approaching 40%, with an operative mortality of less than 5%.^{8–12} The indications for resection of colorectal metastases have been extended over the last decade. Whilst some studies have shown that multiple metastases are a predictor of a less favourable outcome,¹² other studies have demonstrated that the outcome can still be satisfactory provided all the disease is resected.^{8,9,13} Thus multiple and even bilateral hepatic metastases could be resected, provided there is adequate residual liver.

Ten years ago, it was found that screening for colorectal hepatic metastases was patchy and that there was no general consensus amongst consultant surgeons as to which patients would benefit from hepatic resection for colorectal metastases.¹⁴ Of surgeons, 62% stated that they would consider hepatic resection if the secondary deposit was solitary and 29% said that they screened patients postoperatively for recurrent liver disease.

In view of the developments in hepatic resection for colorectal metastases over the last decade, the aim of the study was to re-assess the current attitude of consultant gastrointestinal surgeons towards screening for and treatment of colorectal hepatic metastases.

Methods

In 2000, a questionnaire and covering letter was sent to all consultant members of the Association of Coloproctology of Great Britain and Ireland and of the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland. The questions were as shown in Appendix 1 and addressed: (i) the colorectal practice of the consultant; (ii) their current practice regarding pre-operative assessment and follow-up of colorectal cancer patients; (iii) their indications for hepatic resection of colorectal metastases; and (iv) the number of hepatic resections performed personally or referred during the preceding year.

Results

Treatment of colorectal cancer

Of 714 questionnaires sent, 302 were completed and returned. Sixty-six consultants are members of both Associations and, therefore, the response rate was 47%. The following results are based on the replies of the 283 consultants who treated patients with colorectal cancer of whom 68% worked in district general hospitals, 31% in teaching hospitals, and 1% in private practice. The proportion of their practice that was colorectal ranged from 10% to 100% with a median value of 60%. The median hospital catchment area was estimated as 300,000.

Approximately 31% performed less than 30 colorectal resections per year, 35% 30–60 resections per year, and 34% more than 60 resections per year. Of the consultants, 52% took part in combined oncology clinics with an oncologist.

Screening

Pre-operative screening for liver metastases prior to colonic resection was performed by 88% of consultants. Ultrasound screening was used by 75%, CT scanning by 63%, liver function tests by 60%, and MRI by 6%. During routine follow-up of colorectal cancer patients, 72% of consultants routinely performed liver ultrasound, 52% performed blood carcinoembryonic antigen (CEA) levels, and 33% abdominal/pelvic CT scanning.

Criteria for hepatic resection

Of the consultants, 99% would consider excision of colorectal liver metastases if there were a solitary metastasis present. If there were less than 3 unilobar metastases, 93% of consultants would resect; 62% if unilobar and greater than 3 metastases; 56% if bilobar and less than 3 metastases; and 26% if bilobar and greater than 3 metastases. With regards to the timing of hepatic resection for colorectal metastases, when a solitary hepatic metastasis is detected pre-operatively, 46 consultants (15%) considered that it would be optimum to perform the resection synchronously with the colorectal resection, 232 consultants (76.7%) within 6 months of the colorectal resection, and 25 consultants (8.3%) more than 6 months after the colonic resection.

Resectable extrahepatic disease was considered to be a contra-indication to hepatic resection of colorectal metastases by 126 consultants (45%). Previous liver resection was considered a contra-indication to further resection by 54 consultants (19%), and 142 (51%) considered impaired liver function a contra-indication to resection. The presence of a solitary pulmonary metastasis was considered to be a contra-indication to hepatic resection by 36% of consultants.

Additional therapy

Half of the responding consultants would routinely consider the use of chemotherapy prior to hepatic resection of colorectal metastases and 47% would consider the use of chemotherapy to downstage hepatic metastases in order to allow resection.

Number of hepatic resections performed/referred

In all, 210 surgeons (76%) had performed 753 liver resections during the previous year. The number of resections ranged

Figure 1 Hepatic resections performed per surgeon each year.

from 1 to 15 (Fig. 1) with a median of 2 resections per surgeon each year. The type of resection was not assessed. Forty-eight surgeons referred their patients elsewhere for hepatic resection.

Discussion

Ten years ago, the concept of hepatic resection for colorectal metastases was still relatively new, but since that time it has become established practice with a large number of reports of complete resection of liver metastases resulting in a 5-year survival of a third of patients.^{8,11,12} For patients with colorectal cancer to receive optimum treatment with respect to liver metastases, adequate pre-operative assessment and follow-up is essential. Of surgeons, 88% assess for liver secondaries pre-operatively, with a substantial proportion using either ultrasound or CT scanning and in keeping with published guidelines.¹⁵

The value of intensive follow-up has been addressed by a number of studies which failed to show any real benefit for intensive follow-up over symptomatic follow-up.^{16–18} Most of these studies were done before the advent of safe liver resection. This intervention has shown a quantifiable survival advantage and may, therefore, be the one area where earlier detection of recurrence may be beneficial. Serum CEA is a reliable marker of recurrent colorectal cancer¹⁹ but, as the level is related to tumour mass, it may identify recurrence at a stage too late for intervention.²⁰ It is interesting to note that while approximately half of surgeons routinely check serum CEA, over 70% routinely perform liver ultrasound, an increase from only 17% ten years ago. Routine follow-up with liver ultrasound has yet to demonstrate a survival benefit in a randomised controlled trial but the substantial application is encouraging and needs critical evaluation.

There has been a major change over the last decade with respect to the type and number of colorectal liver metastases that are considered feasible for resection. Provided all the metastases can be removed with clear margins and with adequate functioning liver remaining, resection is an appropriate option.^{8,12,13} This may involve segmental and/or bilateral resections to both lobes of the liver.²¹ That virtually all the responding surgeons would consider hepatic resection for a solitary metastasis is encouraging as this is an increase from 62% ten years ago.¹⁴

However, the proportion of surgeons considering resection decreased as the number or extent of the metastases increased. It is of interest to note that only just over half the surgeons would consider resection if the metastases were bilateral and less than 3 in number. Patients with 3 or more metastases are more likely to be unresectable. In the hands of an experienced liver surgeon, however, some might be resectable and, therefore, some patients are not being offered potentially curative surgery. Uncertainty over resectability might be avoided if appropriate liver imaging was reviewed by an experienced hepatic surgeon, provided there were no other physiological contra-indications to resection.

It is of interest that only half of surgeons would consider the use of chemotherapy to downstage hepatic metastases as a prelude to resection. This was not available at the time of the original survey in 1988. The role of oxaliplatin-based advanced chemotherapy protocols to reduce the size of metastases is now well recognised and should be standard practice. In 1996, Bismuth *et al.*²² published a series of 53 patients with colorectal liver metastases who presented with extensive hepatic disease initially deemed unresectable. Following the use of a combination of systemic chronomodulated chemotherapy (chronotherapy) based on 5-fluorouracil, folinic acid and oxaliplatin, initially inoperable disease was rendered operable and hepatic resection carried out. In 5 of the 53 patients, a staged hepatectomy was carried out. In this entire group of patients, the cumulative 3- and 5-year survival rates were 54% and 40%, respectively.²² As more than half of surgeons would not consider downstaging liver metastases by chemotherapy, many patients in the UK are disadvantaged. In 2000, Bismuth and coworkers further published their results with 872 patients referred with colorectal liver metastases. Of these, 171 (19.6%) were resected immediately. The remaining 701 patients were treated with oxaliplatin-based chronotherapy with sufficient downstaging in 95 (10.9%) to render their hepatic disease operable. These 95 patients were also offered resection with a 5-year survival of 34%.²³ Thus, overall, nearly 30% of patients were offered resection. It may be estimated that about 10,000 patients develop colorectal liver metastases each year.^{1–4} In this survey, it would appear that the resected fraction is less than 10%.

None of the possible contra-indications to resection enquired about would be considered absolute contra-indications by hepatic surgeons. Whilst the majority of gastrointestinal surgeons justifiably do not consider previous hepatic resection as a contra-indication, it is striking that about 20% of surgeons unfortunately do. The literature shows that in about 20% of patients who do develop further hepatic metastases, re-resection is possible with up to 40% 5-year survival.²⁴ With the use of neo-adjuvant chemotherapy, the 20% fraction undergoing re-resection might be improved. Many patients are, therefore, not receiving optimum treatment.

Just over half the consultants (51%) consider resectable extrahepatic disease a contra-indication to resection. This remains controversial. The presence of limited pulmonary or respectable intra-abdominal disease should not be considered a contra-indication. However extrahepatic portal nodal disease remains a strong contra-indication. A recent review of hepatic resection with lymph node involvement showed that there were few 2-year survivors,²⁵ and no longer-term survivors.

Surprisingly, this survey shows that 131 surgeons are performing 3 or less liver resections each a year. Hepatic resection for colorectal metastases can only be justified if the morbidity and mortality is low.²⁶ In the hands of the occasional liver surgeon, the risk of major haemorrhage and possible death from liver resection may be higher than expected. We did not anticipate the large numbers of occasional operators and our study did not enquire as to complications or mortality from such activity. Whilst a substantial number of hepatic resections appear to be performed each year, it is uncertain as to whether these represent 'classical' resections of lobes or segments or whether they are merely wedge resections. Classical resections with adequate clear margins have been shown to improve survival, whilst non-anatomical wedge resections have been associated with an increased incidence of positive margins⁸ and thus a worse survival. The question as to whether it is appropriate for the occasional hepatic operator to carry out anatomical resections must be asked.

Conclusions

There is no doubt that hepatic resection for colorectal liver metastases has become an established part of surgical practice over the last decade and surgical practice does appear to show increased acceptance of this. However, follow-up criteria and ultrasound evaluation need to be defined more rigidly. Criteria for hepatic resection need to be further defined so that all patients with metastatic colorectal cancer involving the liver are offered optimum management for palliation and possible cure.

Acknowledgement

This work was presented in part as a poster at AUGIS, Edinburgh, September 2001.

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APPENDIX 1

Questionnaire

1. Do you treat patients with colorectal cancer?	Yes	No
2. What type of hospital do you work in?	DGH	Teaching
3. Do you have combined oncology clinics?	Yes	No
4. What proportion of your practice is colorectal?		%
5. How large is the catchment population for your hospital?		
6. How many colorectal resections have you performed in the last year?	< 30 30–60 > 60	
7. Do you assess for liver secondaries prior to colonic resection?	Yes	No
By what method?		
Liver function tests	Yes	No
Ultrasound	Yes	No
CT	Yes	No
Other		
8. When would you consider surgical excision of liver secondaries from colorectal cancer?		
(a) Never	Yes	No
(b) Only if solitary	Yes	No
(c) Unilobar and < 3	Yes	No
(c) Unilobar and > 3	Yes	No
(d) Bilobar and < 3	Yes	No
(e) Bilobar and > 3	Yes	No
9. If you detected a solitary resectable colorectal liver metastasis pre-operatively in a patient due to undergo colonic resection, what would you consider to be the optimum timing for liver resection? (please ring one answer only)		
Never	Yes	No
Synchronous with the colorectal resection	Yes	No
Within 6 months after colorectal resection	Yes	No
More than 6 months after colorectal resection	Yes	No
10. During colorectal cancer follow-up, do you routinely perform the following?		
Blood CEA level	Yes	No
Liver ultrasound	Yes	No
Abdominal/pelvic CT	Yes	No
11. Would you consider any of the following a contra-indication to liver resection for colorectal metastases?		
(a) Extrahepatic disease even if resectable	Yes	No
(b) Previous liver resection for colorectal metastases	Yes	No
(c) Impaired liver function	Yes	No
(d) Solitary pulmonary metastasis	Yes	No
12. Would you routinely consider the use of chemotherapy prior to liver resection for colorectal metastases?	Yes	No
13. Would you ever use chemotherapy to attempt to downstage liver metastases to allow attempted resection?	Yes	No
14. How many cases of surgical excision of liver secondaries from colorectal cancer have you performed in the last year?	Yourself	Referred