Guidelines for resection of colorectal cancer liver metastases

O J Garden, M Rees, G J Poston, D Mirza, M Saunders, J Ledermann, J N Primrose and R W Parks

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GUIDELINES

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1.0 INTRODUCTION

There has been increasing recognition of the potential benefits of liver resection for colorectal metastases in the UK although this treatment has been established more widely in other Western countries. There are no randomised studies assessing outcome following resection compared with no treatment or other therapeutic modalities in patients with known resectable liver metastases as it is generally considered unethical not to offer surgery for resectable disease. There has been increased interest in more aggressive chemotherapy regimens that have been reported to not only control metastatic disease but also to render some advanced liver metastases resectable.[1–4] Furthermore, other new modalities have become available that allow safe ablation of liver metastases without the need for surgical intervention. There is therefore a need to produce clear guidelines on the appropriate management of patients with colorectal cancer who have been shown to have hepatic metastases.

These guidelines are intended to address a number of issues:

(a) the principles under which patients with hepatic metastases should be managed;
(b) which patients who have undergone attempted curative resection of the primary colorectal tumour should be offered surveillance;
(c) what investigations are required to determine appropriate management; and
(d) which treatment modality is most appropriate in a given clinical context.

2.0 FORMULATION OF GUIDELINES

The process of formulating any clinical guidelines requires a guideline development group, a search strategy with review of the relevant literature, synthesis of evidence (and consensus methods for topics when evidence is lacking), followed by external review. A multidisciplinary meeting with representation from a number of interested bodies involving surgeons, gastroenterologists, oncologists, diagnostic and interventional radiologists, pathologists, general practitioners, clinical nurse specialists, nurse practitioners, and patients was held in the Pelican Centre in Basingstoke on 2–4 October 2003 (see appendix 1). The Appraisal of Guidelines Research and Evaluation (AGREE) instrument was used to provide a framework for assessing the quality of the clinical practice guidelines. At this initial meeting, discussion resulted from individual presentations on aspects of hepatic metastases, a literature review, and expert re-evaluation. The literature review has been published in the *British Journal of Cancer*.[5] An initial group consensus was reached and a preliminary document produced before this was further refined by the group on 12 March 2004. This document has undergone subsequent expert external review and been amended accordingly.

This guideline is not intended to serve as a standard of care as such standards are determined on the basis of all clinical data available for the individual case. It is recognised that they are subject to change with advances in scientific knowledge and technology and as patterns of care evolve. These parameters of clinical practice should be considered as guidelines only. The critical judgement regarding a particular clinical procedure or treatment plan has to be made by the doctor and the multidisciplinary team, following discussion of the options with the patient, and in the light of the diagnostic and therapeutic choices available. However, it is advised that significant departures from these guidelines be documented in the patient's case records at the time the relevant decision is taken.

This guideline was issued in 2005 and will be reviewed periodically and no later than 2008 to reflect any new evidence. The strength and evidence used in these guidelines was that used by the Agency for Health Policy Research (1992).

3.0 CATEGORIES OF EVIDENCE

- Ia: evidence from meta-analysis of randomised controlled trials.
- Ib: evidence from at least one randomised controlled trial.
- IIa: evidence from at least one controlled study without randomisation.
- IIb: evidence from at least one other type of quasi-experimental study.
- III: evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case control studies.
- IV: evidence from expert committee reports or opinions and/or clinical experience of respected authorities.

4.0 DERIVED STRENGTHS OF RECOMMENDATION

- A: directly based on category I evidence.
- B: directly based on category II evidence or extrapolated recommendation from category I evidence.

Abbreviations: MDT, multidisciplinary meeting; CT, computed tomography; CEA, carcinoembryonic antigen; MRI, magnetic resonance imaging; FDG, F-18 fluorodeoxyglucose; PET, positron emission tomography; CLOCC trial, chemotherapy + local ablation versus chemotherapy trial

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- C: directly based on category III evidence or extrapolated recommendation from category I or II evidence.
- D: directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence.

5.0 SUMMARY OF RECOMMENDATIONS

5.1. General

- Patients under consideration of treatment of hepatic metastases should be discussed at a multidisciplinary meeting which has experience in the management of liver metastases.
- A hepatobiliary multidisciplinary team (MDT) which carries out liver resection should be based in a cancer centre serving a population of at least two million. When two or three networks cooperate to create a single joint team, there should be explicit arrangements for referral between networks. (Category of evidence II ; strength of recommendation B)
- Consideration of patients for resection of liver metastases should be carried out at a single high volume centre. (Category of evidence II; strength of recommendation B)

5.2 At time of presentation of primary colorectal cancer

- Patients with primary colorectal cancer should have a computed tomography (CT) scan of the abdomen and pelvis performed with intravenous contrast and ideally a maximum collimation of 5 mm. This should be performed preoperatively or, in the case of an emergency, as soon as practical thereafter. (Category of evidence II; strength of recommendation B)
- A chest CT is ideal to assess the presence of pulmonary metastases but a chest *x* ray is considered satisfactory. (Category of evidence III; strength of recommendation C)
- The whole of the colon should be visualised to ensure a ''clean colon''. (Category of evidence II; strength of recommendation B)
- A baseline measurement of carcinoembryonic antigen (CEA) should be performed. (Category of evidence III; strength of recommendation C)

5.3 Following curative resection of primary colorectal cancer

- Following treatment of the primary disease, some patients will prove to be unfit or unwilling to have further treatment and in such cases follow up is inappropriate.
- Other patients will prove to have metastatic disease at presentation. Some of these will have isolated liver metastases and should be managed as described in these guidelines.
- Patients undergoing R0 colorectal resection may be candidates for adjuvant chemotherapy and a further abdominal contrast enhanced CT (or magnetic resonance imaging (MRI)) should be performed following completion of chemotherapy. (Category of evidence III; Strength of recommendation C)
- Where possible patients over the age of 50 years should be considered for randomisation to the FACS trial, the UK NCRN trial of follow up strategies (synopsis in appendix 2).
- If the patient is ineligible for trial inclusion, does not wish to participate in the randomised trial, or if the unit is not recruiting to the trial, the following follow up schedule is appropriate[6]:

(a) CT scan of the abdomen and pelvis should be undertaken as a minimum in the two years following completion of treatment of the primary disease. (Category of evidence III; strength of recommendation C)

(b) Colonoscopy repeated after five years.

(c) The case for routine serial CEA measurements is unproven. (Category of evidence III; strength of recommendation C)

5.4 Further staging investigation to detect extrahepatic involvement in patients with colorectal liver metastases

- For a patient discovered to have isolated liver metastases, CT of the chest, abdomen, and pelvis should be performed by the liver surgery unit or using protocols agreed with that unit. The liver surgery centre will also often perform liver specific imaging by local protocol.
- Biopsy of hepatic lesions should not be performed without discussion with the regional hepatobiliary unit. (Category of evidence III; strength of recommendation C)
- Patients with ''high risk'' primary disease (T4 (perforated); C2 (apical node)) should have careful preoperative investigations that might include positron emission tomography (PET) and laparoscopy. (Category of evidence III; strength of recommendation C)

5.5 Liver resection for colorectal metastases

- The aim of liver resection (resectability) is to remove all macroscopic disease with clear (negative) margins and leave sufficient functioning liver. (Category of evidence II; strength of recommendation B)
- Patients with solitary, multiple, and bilobar disease who have had radical treatment of the primary colorectal cancer are candidates for liver resection. (Category of evidence III; strength of recommendation C)
- The ability to achieve clear margins (R0 resection) should be determined by the radiologist and surgeon in the regional hepatobiliary unit. (Category of evidence III; strength of recommendation C)
- The surgeon should define the acceptable residual functioning volume, approximately one third of the standard liver volume, or the equivalent of a minimum of two segments. (Category of evidence III; strength of recommendation C)
- The liver surgeon and anaesthetist should take the clinical decision regarding fitness for surgery. (Category of evidence III; strength of recommendation C)
- If deemed medically unfit for surgery, patients should be considered for ablative therapy. (Category of evidence IV; strength of recommendation D)
- Patients with extrahepatic disease that should be considered for liver resection include:

(1) resectable/ablatable pulmonary metastases;

(2) resectable/ablatable isolated extrahepatic sites—for example, spleen, adrenal, or respectable local recurrence; and

(3) local direct extension of liver metastases to, for example, diaphragm/adrenal that can be resected. (Category of evidence IV; strength of recommendation D)

- Normal contraindications to liver resection would include uncontrollable extrahepatic disease such as:

– non-treatable primary tumour;
– widespread pulmonary disease;
– locoregional recurrence;
– peritoneal disease;
– extensive nodal disease, such as retroperitoneal, mediastinal or portal nodes; and
– bone or CNS metastases. (Category of evidence II; strength of recommendation B)

5.6 Tumours borderline for resection

- Those patients with tumours thought to be borderline for resection may have resectable or ablatable disease and should be referred for discussion with the regional hepatobiliary unit before chemotherapy. (Category of evidence III; strength of recommendation C)
- Resectability may be achieved by portal vein embolisation or two stage hepatectomy to increase hepatic functional reserve and also by combinations of surgery and ablation. (Category of evidence IV; strength of recommendation D)

5.7 Ablative therapy

- The decision to offer ablative therapy to patients with hepatic metastases should be made by the regional hepatobiliary unit.
- Patients who are not candidates for resection should be considered for the CLOCC (chemotherapy + local ablation versus chemotherapy) trial.
- Entry into the CLOCC trial should be considered for patients with nine or less metastases (up to 4 cm) without extrahepatic disease (EORTC 40004).
- Patients who are not suitable for entry to the CLOCC trial may be considered for ablative therapy. (Category of evidence IV; strength of recommendation D)

5.8 Patients not suitable for resection or ablative therapy

- Patients with advanced disease unsuitable for liver resection or ablative therapy should be referred to the clinical or medical oncologist with a special interest in colorectal cancer for further management and supportive care.(Category of evidence II; strength of recommendation B)

5.9 Synchronous metastases

- Normally, colorectal cancer resection and liver resection would not be performed synchronously. However, management of accessible small metastases detected preoperatively should be discussed with the local liver centre for consideration of combined resection.
- Lesions discovered at operation should not be biopsied. (Category of evidence III; strength of recommendation C)
- Excision of small atypical lesions should not be considered without discussion with the regional hepatobiliary unit.
- Patients should be referred for consideration of liver resection after recovery from primary surgery.
- Patients with potentially resectable liver disease and who have undergone radical resection of the primary tumour should be considered for liver resection before consideration of chemotherapy.
- Patients with unfavourable primary pathology such as perforated primary tumour or extensive nodal involvement should be considered for adjuvant chemotherapy prior to liver resection and be restaged at three months.

5.10 Histopathology

- The histopathology report of the resected liver specimen must include specific details which can be used to determine prognosis.
- These should include number, size, and location of metastases, resection margin clearance from tumour, capsular invasion, degree of differentiation, presence of necrosis, vascular and lymphatic invasion, and lymph node status if sampled. (Category of evidence II; strength of recommendation B)

5.11 Follow up after liver resection

- Follow up would normally continue for five years according to local protocol using CT chest and liver and CEA. Follow up should be performed by the liver centre or the referring unit following an agreed protocol. Any abnormality should be referred back to the liver centre for consideration of re-resection or ablation. (Category of evidence III; strength of recommendation C)
- In patients who develop recurrence, it seems appropriate to consider such lesions in the same way as the initial hepatic metastases and offer re-resection or ablation to patients based on operative risk and likely survival. (Category of evidence III; strength of recommendation C)

6.0 BACKGROUND

Colorectal cancer is the commonest gastrointestinal malignancy and the second commonest cause of cancer death, comprising 11% of new cancer diagnoses and 10% of all cancer deaths in the UK. Approximately 32 000 cases are diagnosed each year and 17 000 deaths are attributed to the disease. The liver is often the first site of metastatic disease and may be the only site of spread in as many as 30–40% of patients with advanced disease.[7] Of new cases, 20–25% of patients will have clinically detectable liver metastases at the time of the initial diagnosis and a further 40–50% of patients will eventually develop liver metastases after resection of the primary, most commonly within the first three years of follow up.[8–11] It has been postulated that the principal mode of tumour dissemination is via the portal system and therefore that surgical resection of isolated hepatic metastases from colorectal cancer may be curative in a number of cases.[7]

The natural history of metastatic colorectal cancer is variable. Median survival without treatment is less than eight months from presentation but the prognosis is better for those patients with isolated hepatic metastases.[12] Patients with a limited number of metastases or those with disease confined to one lobe of the liver have a longer duration of survival than those with more advanced disease.[8 10 13] However, even in the group of patients with limited metastatic liver disease, survival at five years is exceptional.[14]

Approximately 20–30% of patients with metastatic colorectal cancer have disease that is confined to the liver and is potentially resectable.[10] Several recent large series on resection for colorectal liver metastases (CRLM) have reported five year survival ranging from 25% to 44%, with operative mortality of 0–6.6%.[8 15–17] Given that approximately 18 000 patients will develop hepatic metastases annually in the UK, approximately 3600 patients may be suitable for hepatic resection although many more patients may benefit from hepatic resection with less restrictive criteria of resectability being employed in many centres.[16] It seems unlikely that a randomised study assessing outcome following resection compared with other treatments modalities will be undertaken in patients with known resectable liver metastases but there has been increased interest in new chemotherapy

regimens[1–4] and other new modalities that allow safe ablation of liver metastases.

7.0 MULTIDISCIPLINARY TEAMS

It is accepted that the management of all patients with colorectal cancer should be the responsibility of colorectal cancer MDTs and that any patient under the care of a clinician who is not a member of such an MDT should be referred immediately to an appropriate team when colorectal cancer is suspected.[18 19] It has been advocated that such colorectal MDTs should identify or establish a specialised hepatobiliary MDT which has the expertise and facilities to provide surgery for patients with liver metastases. Several large studies on resection for colorectal liver metastases (CRLM) have reported lower operative mortality than that reported in previous decades.[8 10 15 17 20] While this is likely to be due to a number of factors, there have been a several recent studies which have demonstrated a volume effect on outcome, particularly for major upper gastrointestinal resections. A recent study has shown a similar effect for both short and long term outcome for patients subjected to major hepatic resection.[21]

Membership of the liver resection or hepatobiliary MDT has been defined in *Improving Outcomes in Upper Gastrointestinal Cancers* but would normally consist of at least two specialist surgeons trained in and maintaining a special interest in liver resection surgery and who can demonstrate a high level of skill and training in this area. The team should also include an oncologist, diagnostic and interventional radiologist with an expertise in hepatobiliary disease, histopathologist, and clinical nurse specialist.

8.0 DETECTION OF HEPATIC AND OTHER METASTASES

Hepatic metastases may be evident at the time of initial presentation or declared at subsequent follow up. It is established that a contrast CT scan of the abdomen has detection rates for hepatic metastases of 68–91% (70% detection for lesions $>$ 1 cm), and has replaced ultrasonography as the preferred imaging modality.[22] However, the sensitivity and specificity of CT liver will vary, depending on the equipment and contrast enhancement methods. MRI can be used as an alternative for assessing the liver. A recent meta-analysis to obtain sensitivity estimates of various imaging modalities for detection of colorectal metastases showed that F-18 fluorodeoxyglucose (FDG) PET had significantly higher sensitivity on a per patient basis but not on a per lesion basis compared with other modalities.[23] Sensitivity estimates for MRI imaging with contrast agent were significantly superior to those for helical CT with 45 g of iodine or less.[23]

A chest CT is ideal to assess the presence of pulmonary metastases but the positive yield of CT scan in patients with a normal chest *x* ray at the time of presentation with potentially resectable liver metastases from colorectal cancer is only 5%.[24] Complete colonic examination by colonoscopy, CT pneumocolon, or barium enema should be carried out, ideally in the preoperative period in patients with colorectal cancer as there is a significant risk of recurrent tumour or of a metachronous lesion.[19] Given that measurement of CEA levels may be useful in the follow up of colorectal cancer patients, it is desirable to establish whether levels are elevated at the time of initial presentation.[25]

Patients who have undergone apparently curative resection of colorectal cancer may be followed up to detect metastatic disease in the expectation that early detection and treatment will result in improved survival. However, uncertainty remains as all the randomised trials are considered to have inadequate numbers.[25] Meta-analysis performed as a Cochrane Review[25] and by others[26] suggests that there may be a survival benefit of follow up for metastatic disease but the heterogeneity of the trials make firm conclusions impossible. Further studies are required. Although the use of ultrasonography, CT, or even MRI to detect recurrence or metastatic disease is very variable,[27–29] interval CT scanning and serial CEA levels appear to be the most promising in this respect.[25 26] Current evidence suggests that an ultrasound examination of the liver is not sufficiently sensitive to exclude the presence of metastases.[11] CEA may be elevated in up to 90% of patients with liver metastases[11 30] and a rise in CEA after an initial fall following surgery may be the first indication of local or distant recurrence in an otherwise asymptomatic patient. However, a rising CEA concentration may be a relatively late phenomenon in patients with liver metastases.

For a patient discovered to have isolated liver metastases, a CT of the chest, abdomen, and pelvis should be performed by the liver surgery unit or using protocols agreed with that unit. The liver surgery centre will also often perform liver specific imaging by local protocol but biopsy of hepatic lesions should not be performed without discussion with the regional hepatobiliary unit. There is evidence that percutaneous biopsy of liver tumours may be associated with extrahepatic dissemination of tumour and result in a reduced prospect of long term survival even when resection of hepatic metastases is undertaken.[31–34] Patients with aggressive primary disease should have careful preoperative investigations. Laparoscopy may identify occult metastatic disease and prevent unnecessary laparotomy in some patients with potentially resectable colorectal liver metastases[31 35–37] although it may be used more selectively in patients with a low risk of tumour.[35] Laparoscopic ultrasound may provide additional information in selected patients.[31 35] FDG-PET has been used both to identify the presence of hepatic colorectal metastases[38] and to improve the staging of patients under consideration of resection of colorectal metastases.[39] It is evident that PET may miss small hepatic lesions and its performance is affected by recent or current administration of chemotherapy. Although the evidence for patient benefit is lacking, it is apparent that it may have a role in the patient at high risk of extrahepatic dissemination of tumour.[40–42]

9.0 LIVER RESECTION FOR COLORECTAL METASTASES

Operative morbidity and mortality following liver resection are related to the development of hepatic failure that is a function of the extent of resection[43–46] and the presence of coexisting liver disease.[47] Other complications that may contribute to or be related to postoperative liver failure include haemorrhage, bile leak, intra-abdominal sepsis, and cardiopulmonary dysfunction.[9 20 47 48] Laparoscopic liver resection may have some advantage in the short term over open surgery but there are no data to indicate the impact of this procedure on long term outcome.[49] Duration of survival is shortened by the presence of inadequate or involved resection margins.[50] Previous data from the Registry of Hepatic Metastases, a multi-institutional database of liver resections, suggested that a margin $>$1 cm was associated with 45% five year survival, but only 23% survived five years if the margin was less.[51] A number of other studies have supported the view that poorer overall survival and disease free five year survival is associated with resection margins less than 1 cm although others have produced evidence to suggest that a lesser margin may be acceptable as long as the tumour pseudocapsule is resected during dissection.[48 52 53]

Studies have shown that long term survival is achieved in patients whose primary colorectal cancer has been managed by radical resection and appropriate local adjuvant treatment.

There is no evidence that the number or location of the liver deposits compromises survival in such patients as long as all macroscopic disease is resected. It has been argued that the limiting factor to the number of lesions that can be resected is whether it is technically possible to remove all tumours.[8] Long term survival may be affected adversely by the presence of more than three metastases but multivariate analysis has provided inconsistent results as to whether the number of resected metastases has a significant effect on long term survival.[8 16 20 51 54]

Resectability of liver tumours requires assessment by a radiologist in conjunction with a liver surgeon experienced in the management of colorectal metastases as there is a need to define the acceptable residual functioning volume. It is accepted that prediction of liver dysfunction following liver resection is difficult to quantify for the individual patient. Previous studies have suggested that that liver volume can be readily calculated by CT volumetry.[43 44] Based on liver transplant and liver resectional experience, acceptable residual functioning volume is thought to consist of approximately one third of the standard liver volume or the equivalent of two liver segments. Such decisions are again best made by the hepatobiliary team.

As for most surgical procedures, the operating surgeon and the anaesthetist are best able to assess the patient's fitness for intervention. Increasing ASA and POSSUM grade have been shown to be of value for several operative procedures.[55] Experience of the managing team is likely to have an effect on outcome and it has been demonstrated that patients who undergo liver resection at low volume hospitals are at a higher risk of postoperative complications and death than those who have the same operation at high volume hospitals.[21]

For those patients not considered fit for operative intervention, radiofrequency ablation has been shown to be a safe and effective treatment for patients unsuitable for liver resection.[56 57] However, its precise role in the management of hepatic colorectal metastases as yet to be defined and no study has addressed its potential superiority over other treatment modalities in the setting of a randomised controlled trial. Therefore, patients should be considered for entry into the NCRN/EORTC CLOCC trial (EORTC 40044-Chemotherapy and local ablation versus chemotherapy (5-FU and oxaliplatin) alone).

10.0 RESECTION OF EXTRAHEPATIC COLORECTAL METASTASES

There is evidence from cohort studies with historical controls that survival can be improved by lung resection for technically suitable metastatic disease.[58] Long term survival has been reported for patients who undergo resection of pulmonary metastases when these have developed after apparently curative resection of hepatic colorectal metastases.[8] Recent data suggest that if lung metastases of colorectal origin are resectable, five year survival following thoracotomy is similar to that observed in patients after resection of colorectal liver metastases.[59 60] It is recognised that these encouraging survival data can be achieved in highly selected patients but that the presence of thoracic lymph node involvement and elevated carcinoembryonic antigen levels before pulmonary resection are associated with reduced survival.[61] Long term survival following resection of adrenal and splenic metastases is recorded.[62 63] Normal contraindications to liver resection include uncontrollable extrahepatic disease. Patients with advanced disease unsuitable for liver resection or ablative therapy should be referred to the clinical or medical oncologist with a special interest in colorectal cancer management.

11.0 CHEMOTHERAPY AND NEOADJUVANT CHEMOTHERAPY

There is evidence from two systematic reviews that chemotherapy for metastatic colorectal cancer can improve survival and should be considered in all patients not suitable for surgery.[64 65] In certain cases, tumours should be considered for downsizing with chemotherapy if they are unable to be resected initially due to location or inadequate hepatic functional reserve. NICE originally recommended that the combination of oxaliplatin, 5-fluorouracil and folinic acid should only be considered for patients with metastases confined to the liver, and whose disease might become resectable after chemotherapy. However, NICE now recommend the use of oxaliplatin based regimens as firstline therapy for all patients with non-resectable disease, and irinotecan based regimens for secondline therapy after failure of firstline treatment.[66] There is no evidence to support ''pretreatment'' with neoadjuvant chemotherapy in patients with resectable disease but the results of the recently closed EORTC study (EPOC) are awaited. Such an approach if employed routinely may compromise the patient's chance of cure. Even with the best combination chemotherapy regimens, 20% of tumours will progress while on chemotherapy and only 50% of tumours can be expected to show a partial response to chemotherapy.[2 3 66]

It has been increasingly evident that tumours which were previously thought to be irresectable can be treated by a combination of advanced techniques with curative intent and long term survival benefit.[67 68] There is evidence that response rates to chemotherapy in initially resectable liver only disease may be a surrogate marker for subsequent liver resection rates with curative intent.[69 70] Concerns regarding compromised hepatic functional reserve following extended hepatic resection have led some clinicians to consider preoperative portal vein embolisation in an attempt to increase the volume of the intended residual liver.[71] Others have suggested a two stage hepatic resection accepting an initial non-curative resection or ablation, but after allowing hypertrophy of the remaining liver, the residual tumour is resected at a subsequent operation.[68 72] Therefore, decisions regarding the feasibility of downsizing to resectability should be taken by the regional hepatobiliary unit. As a consequence of downsizing, all previously identified sites should be treated by surgery and or ablation.[73 74]

12.0 ABLATIVE THERAPY

The decision to offer ablative therapy to patients with hepatic metastases should be made by the regional hepatobiliary unit. The precise role of ablative therapy is yet to be established, and entry into the CLOCC trial should be considered for patients with nine or less metastases (up to 4 cm) without extrahepatic disease (EORTC 40004). Some would consider ablative therapy for patients who do not fulfil the criteria of the CLOCC trial. These might include patients with associated comorbidity that precludes resection and patients who decline surgery although there are significant risks associated with the procedure.[75] Patients with treatable extrahepatic disease may be considered for ablative therapy.[76] Patients whose tumours have been downsized by chemotherapy but are not resectable may be considered for ablative therapy.[57 77]

Patients with advanced disease unsuitable for liver resection or ablative therapy should be referred to the clinical or medical oncologist with a special interest in colorectal cancer for further management and supportive care.

13.0 SYNCHRONOUS METASTASES

Normally, colorectal cancer resection and liver resection would not be performed synchronously but management of

accessible small metastases detected preoperatively may be considered for combined resection. Simultaneous colon and liver resection has been shown to be safe and efficient in the treatment of patients with colorectal cancer and synchronous liver metastases when undertaken in high volume centres with appropriate experience in liver resectional surgery.[78] There is a significant risk of local dissemination of tumour with biopsy of colorectal metastases[79] and recent evidence has suggested a deleterious effect on resectability and long term survival.[33] Excision of small atypical lesions should not be considered without discussion with the regional hepatobiliary unit.

Patients should be referred for consideration of liver resection after recovery from primary surgery and it seems appropriate to allow the patient to recover from colorectal surgery before consideration is given to a further elective operative procedure.

14.0 FOLLOW UP AFTER LIVER RESECTION

Recurrence may occur in up to 60% of patients following liver resection for colorectal metastases with the most common site being in the liver. Approximately 20% of these patients have recurrence only in the liver and therefore may be suitable for re-resection.[80] Of these, 90% are detected within the first two years following liver resection.[81] The reported morbidity and mortality rates and long term survival rates of re-resection are similar to those reported for the original hepatectomy despite the greater technical difficulty of the procedure.[82] Long term survival appears to be similar to that for the initial hepatic resection.[80 82] However, patients with a low tumour load appear to be the best candidates and the presence of extrahepatic disease or incomplete tumour clearance is associated with a poorer outcome.[83] It therefore seems logical to follow up such patients for five years using CT chest and liver and blood CEA levels to identify patients who might benefit from further intervention. It seems appropriate to consider such lesions in the same way as the initial hepatic metastases and to offer re-resection or ablation to patients based on operative risk and likely survival.

15.0 THE PATIENT PERSPECTIVE: IMPACT ON PATIENT AND FAMILY

Most of the published research on colorectal liver metastases focuses on clinical evaluation of treatment. There is some evidence of exploratory qualitative studies identifying the patient perspective in relation to information needs, and also consensus of best practice (incorporating patient perspective) from experts in the field, but research on the organisation and delivery of services to this population is still in its infancy. In patients with colorectal cancer, the greatest need for information appears to be at diagnosis, after discharge from surgery while waiting for oncology review, and on completion of chemotherapy.[84] Healthcare professionals should respect patients' wishes to be involved when making plans about their own management although a systematic review of a large number of controlled studies was able to conclude that interventions aimed at facilitating decision making are under-researched and that there was more need for randomised trials.[85]

Evidence and guidelines with other/heterogenous cancer types, where the interventions and outcomes in relation to communication, information, and the organisation of care delivery may be expected to generalise to this population have therefore been included.[86]

16.0 COMMUNICATION AND INFORMATION

The referring colorectal cancer centre should have agreed guidelines concerning the breaking of bad news[87] and disclosure of diagnosis of colorectal liver metastases to the patient, their carer, and to the patient's general practitioner. There should be written information for patients that includes information about the provision of local specialist cancer services for colorectal liver metastases.[86]

All health professionals working with patients diagnosed with colorectal liver metastases should be competent to communicate with sensitivity, expertise, and clarity. They need to know how best to elicit patients' individual concerns,[88] preferences for information, and involvement in decisions about their treatment and care.[89] They should be competent to discuss treatment options and care choices which enable patients to make informed decisions. These should include the individual's calculated risk/benefits, acknowledged uncertainties, and side effects of any treatment offered.[90]

Patients and their carers should be helped to access and understand appropriate information, including that from voluntary support services and patient self help groups, as well as psychological, social, and spiritual/cultural support.[91 92]

Any locally developed written information should reflect the opinions of representative patients with colorectal liver metastases and their carers.[91 92]

17.0 MULTIDISCIPLINARY TEAM STRATEGIES AND ORGANISATION OF CARE DELIVERY TO IMPROVE THE QUALITY OF LIFE OF PATIENTS WITH COLORECTAL LIVER METASTASES

Patients with cancer often have complex needs that cannot be addressed by a single specialty or discipline. The multidisciplinary team should ensure a consistent and equitable approach to planning and managing care. The clinical nurse specialist or nurse practitioner should be part of this team and be able to provide advice, support, and information.

Following discussion with the regional hepatobiliary unit, the management decision is discussed ideally with the patient in clinic, within seven days of the MDT meeting. However, where previously agreed with the patient, this decision can be divulged over the telephone by a member of the MDT who has previously met the patient and is familiar with the case. Where necessary, or if requested, a further appointment can be made with the surgeon or medical oncologist to discuss the treatment decision. Written confirmation about the treatment decision, including rationale, should be sent to the patient's general practitioner and if desired a copy to the patient.[87]

In addition to the clinic consultation or telephone conversation in which the treatment decision is communicated to the patient, the patient should have ongoing access to the specialist hepatobiliary unit via the hepatobiliary clinical nurse specialist to discuss any further information needs or concerns. A telephone contact number, preferably with access to a 24 hour answer phone, should be available.[87]

Follow up screening after treatment for colorectal liver metastases will be discussed at the hepatobiliary unit, and should be disclosed to patients and their carers in the format as above.[87] If long distances are involved, follow up may be carried out by the local colorectal unit using agreed protocols. Should recurrent disease or further metastatic spread occur, this will be disclosed to the patient and carer in the clinic setting.

An audit of standards should be undertaken on an annual basis and include an audit of patient opinion and satisfaction with organisation of care delivery.

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19.0 APPENDIX 1

PARTICIPATING BODIES

Association of Upper Gastrointestinal Surgeons
British Society of Gastroenteology
British Association of Surgical Oncology
Association of Cancer Physicians
British Oncological Association
British Association for the Study of the Liver
Royal College of Radiologists
Association of Coloproctologists
Royal College of General Practitioners
Colon Cancer Concern
Patient representatives.
Nurse Representatives
Others attending as a result of their known expertise in the field

20.0 APPENDIX 2

THE FACS TRIAL (FOLLOW UP AFTER COLORECTAL SURGERY)

A multicentre, randomised, controlled trial to assess the cost effectiveness of intensive versus minimum scheduled follow up in patients who have undergone curative resection for colorectal cancer with curative intent.

The study aim is to assess the effect on survival of augmenting symptomatic follow up in primary care, plus an optional single CT scan, with two intensive methods of follow up—monitoring of tumour marker in primary care and intensive imaging.

The FACS trial aims to recruit 5000 patients who have undergone resection for colorectal cancer with curative intent. The trial objectives are overall survival, quality of life, cost of NHS services utilised, and NHS cost per life year saved (http://www.facs.soton.ac.uk)