Review Article

Digestive Surgery

Dig Surg 2013;30:337–347
DOI: 10.1159/000351442

Received: May 27, 2012
Accepted after revision: April 10, 2013
Published online: September 17, 2013

Surgery for Colorectal Liver Metastases

S.J. McNally R.W. Parks

Department of Clinical Surgery, University of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK

Key Words
Colorectal cancer · Liver metastases · Hepatic resection

Abstract
Half of all patients with colorectal cancer develop metastatic disease. The liver is the principal site for metastases, and surgical resection is the only modality that offers the potential for long-term cure. Appropriate patient selection for surgery and improvements in perioperative care have resulted in low morbidity and mortality rates, resulting in this being the therapy of choice for suitable patients. Modern management of colorectal liver metastases is multimodal incorporating open and laparoscopic surgery, ablative therapies such as radiofrequency ablation or microwave ablation and (neo)adjuvant chemotherapy. The majority of patients with hepatic metastases should be considered for resectional surgery, if all disease can be resected, as this offers the only opportunity for prolonged survival.

Introduction

Colorectal cancer is the third most common cancer in the world and is increasing in incidence [1]. Half of all patients with colorectal cancer will develop metastatic disease, with the liver being the most common site. Historically the development of hepatic metastases had a poor prognosis with a median survival of approximately 5 months [2, 3]. Newer chemotherapy agents have improved the median survival to over 20 months [4]. However, long-term survival after systemic therapy alone is uncommon, and surgical resection is the only therapeutic modality that offers the potential for long-term cure, with 5-year survival rates of up to 58% [5–8].

Hepatic resection for colorectal liver metastases (CRLM) has developed over the past three decades. Appropriate patient selection and improvements in perioperative care have resulted in low morbidity and mortality rates, meaning that this is the therapy of choice in suitable patients [9, 10].

The indications for resectional surgery have evolved over time, and whilst the presence of multiple bilobar metastases was at one point a contraindication to surgery, this is no longer the case. Strategies for identifying those patients most likely to benefit from resection continue to evolve [11–13]. The current criteria for surgery revolve around the ability to achieve an R0 resection whilst leaving a sufficient residual volume of liver [14–16]. Many factors contribute to a successful outcome, and these include: accurate pre-operative staging; neoadjuvant and adjuvant chemotherapy; operative planning, and the use of combination treatments when appropriate [17].

KARGER

E-Mail karger@karger.com
www.karger.com/dsu

0253–4886/13/0306–0337$38.00/0

Stephen McNally
Department of Clinical Surgery
University of Edinburgh, Royal Infirmary of Edinburgh
51 Little France Crescent, Edinburgh EH16 4SA (UK)
E-Mail Stephen.mcnally@ed.ac.uk

Staging of Colorectal Liver Metastases

Staging consists of a clinical assessment, and radiological imaging. Clinical assessment should determine whether the patient would withstand major resectional surgery, and identify important cardiorespiratory comorbidities. Time should be taken during the initial consultation to assess the understanding patients have of their disease and the goals that they wish to achieve. Liver function tests including prothrombin time and albumin are essential to exclude underlying parenchymal disease, and baseline CEA may be useful for long-term follow-up [18]. There remains debate regarding the best functional measures of liver reserve, which is of particular importance in cirrhotic patients. Approaches including indocyanine green clearance, mebrofenin clearance and lidocaine metabolism (MEGX) have all been used successfully in certain centres, but these are not currently in general use [19–21]. Whilst they provide additional information, they also require additional equipment (indocyanine green clearance) or the use of radioisotopes (mebrofenin) and can be difficult to measure in standard laboratories (MEGX).

Cross-sectional imaging is essential to accurately locate all disease and to plan surgical strategy. The options include CT, CT-PET and MRI. The initial investigation of choice will depend on local expertise, but most centres use CT as the mainstay of investigation, with MRI reserved for selected cases. Modern multislice CT scanners provide high-resolution images which permit multiplanar reconstructions to facilitate operative planning. Most patients who are being staged for colorectal cancer will have a contrast-enhanced abdominal and pelvic CT undertaken during their workup. Arterial and portal venous phases are routinely used to aid identification and characterisation of liver lesions. It will also identify aberrant arterial or venous anatomy, and provides accurate volumetry data on the FLR.

MRI provides high-quality cross-sectional imaging of the liver and is now the imaging modality of choice in several centres [22, 23]. It has excellent discrimination for benign lesions such as fibronodular hyperplasia and haemangiomata. MRI is superior to CT for detection of CRLM [24] and it has an important role in clarification of small lesions and for assessing liver lesions in patients with underlying liver disease [25]. There are a range of contrast agents and MRI sequences which can be performed to optimise the display of mass lesions, and the use of specific hepatobiliary and paramagnetic contrast agents improves lesion detection and discrimination [26].

For any patient who is being considered for operative intervention, exclusion of extrahepatic disease is essential. Previously this was achieved by CT encompassing the entire thorax, abdomen and pelvis. More recently, CT-PET is being used to assess for the presence of extrahepatic disease. FDG is used as a tracer and is sensitive in the identification of distant metastases, modifying the management in up to 20% of cases [27, 28]. As patients with distant non-pulmonary metastases are unsuitable for hepatic resection, this has become an important part of the pre-operative workup of patients with hepatic CRLM. It should be noted, however, that certain colorectal cancers have a low avidity for FDG, and so false negatives can occur, particularly in patients who have had chemotherapy, and a minimum 3-week interval following chemotherapy is recommended before performing PET-CT [29]. If pulmonary metastases are identified, this is only a contraindication for hepatic resection if the lung disease cannot also be resected [30].

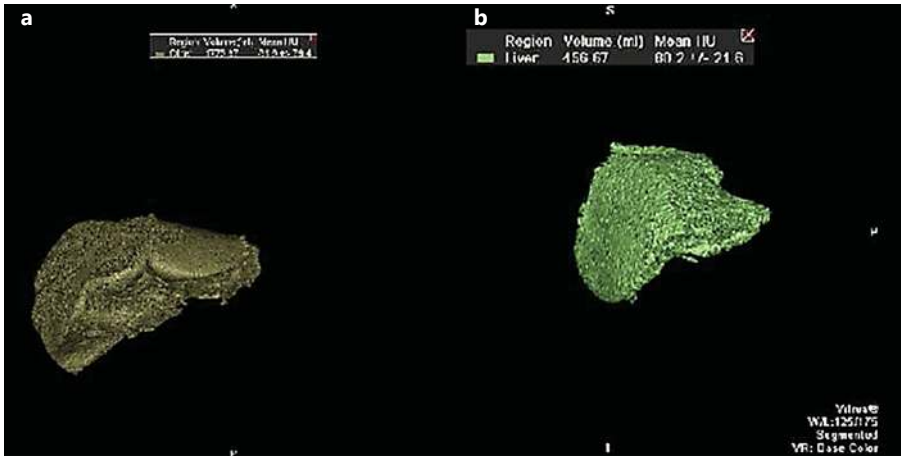
Transabdominal ultrasound has largely been replaced by cross-sectional imaging for pre-operative staging, however in lesions which are difficult to assess it can provide complimentary information, particularly with the use of ultrasound contrast agents. Furthermore, it may be indicated if percutaneous ablative techniques are being utilised.

Role of Pre-Operative Biopsy

In the context of modern imaging techniques, histological confirmation of the diagnosis is not required. In the past, pathological confirmation was required before proceeding to liver resection [31]. However, in addition to the bleeding complications which can result [32], percutaneous biopsy can lead to tumour dissemination along the needle track, and has been shown to be associated with a poorer outcome [33]. With the support of tumour markers where appropriate, a confident pre-operative diagnosis can be made in the majority of cases. Hence the decision to perform a liver biopsy should only be taken following review by a specialist hepatobiliary multidisciplinary team [34].

Operative Planning

Following assessment of the patient and suitable staging, tailored operative planning is required to determine the most appropriate surgical strategy. The intention is to achieve an R0 resection at the end of treatment. Consideration must be given to: the anatomical distribution of



Color version available online

Fig. 1. a, **b** Volumetry for operative planning. CT-based volumetry can assess the FLR volume following extended right hepatectomy. This technique may be used pre- and post-PVE to assess the hypertrophic response to embolisation. The whole liver is seen on the left, and on the right the volume of segments 2 and 3 are shown in green.

the disease; the residual functional volume of liver (future liver remnant, FLR); management of the primary disease (in the setting of synchronous CRLM); the timing and role of (neo)adjuvant chemotherapy, and whether all disease can be resected successfully at one sitting.

Hepatic Anatomy

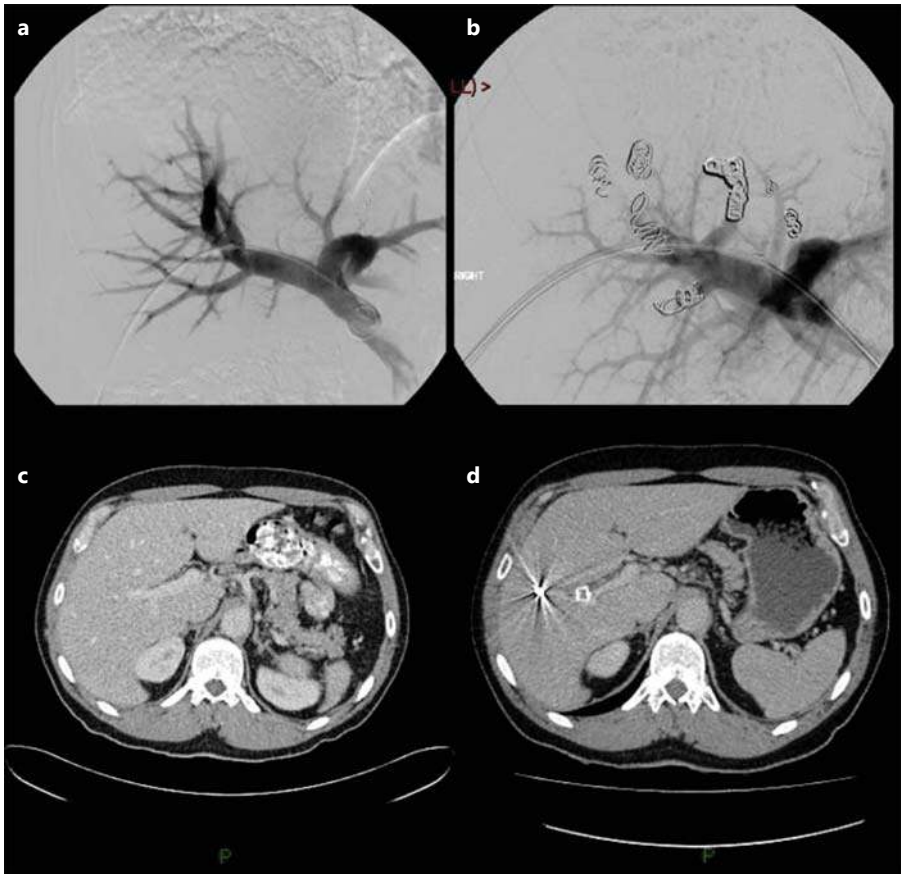
An understanding of the anatomy of the liver is essential for hepatic surgery, and improvements in the knowledge of this anatomy were the key impetus for the development of hepatic surgery. Coinaud's seminal anatomical studies described the segmental anatomy of the liver, making anatomical resection feasible [35]. This formed the basis for the Brisbane terminology to describe hepatic resection, based on the hepatic artery and bile duct divisions [36]. The liver has 8 segments. The right hemi-liver contains segments 5–8, and the left hemi-liver contains segments 2–4. Segment 1 is the posteriorly situated caudate lobe [36]. Minor anatomical hepatic resections are considered as 1–2 segments, and major resections as 3 or more segments. A standard right hepatectomy (segments 5–8) will remove approximately 60% of the liver volume, whilst an extended right hepatectomy (segments 4–8) will remove approximately 75% of liver volume. Maintenance of a suitable volume of FLR is critical to outcome, and a minimum of approximately 25% FLR in two contiguous segments of liver is required to minimise the risk of post-operative hepatic failure (40% in the presence of parenchymal disease, and 30% following chemotherapy) (fig. 1).

Standard anatomically-based segmental resections have traditionally been preferred to atypical resections as an atypical resection was felt to be associated with a higher risk of local recurrence [37, 38]. However, with the increasing need to retain as much functioning liver volume as possible, parenchymal-preserving resections are increasingly performed. Multiple series have demonstrated that atypical resections are not associated with increased local recurrence providing microscopic clearance has been achieved [39–41].

Portal Vein Occlusion

If initial assessment indicates that an extended hepatic resection may achieve cure, but is contraindicated due to a limited FLR, portal vein embolisation (PVE) can be undertaken to induce hypertrophy in the remnant liver. This procedure is premised on the observation that interrupting the flow of blood to one half of the liver increases the flow to the contralateral side, which undergoes compensatory hypertrophy. PVE is usually performed percutaneously under ultrasound guidance to access the portal vein and introduce embolisation coils. The liver is then re-imaged 4 weeks later to assess the degree of hypertrophy, and repeat CT volumetry is undertaken (fig. 2).

Theoretically PVE may induce accelerated growth in any disease present in the liver remnant. This remains a debateable phenomenon [42], and studies addressing this have small sample sizes. In a series of 18 patients undergoing PVE, Kokudo et al. [43] found that not only did tumour volume increase after PVE, but the proliferative index of the tumours appeared greater than seen in control patients. Hence if disease is present in the FLR, consideration should be given to removing this before PVE. Indeed, the portal vein branch may be ligated surgically at the time of the initial hepatic procedure. During either a percutaneous PVE or open portal vein ligation, biopsy of the proposed remnant can be useful to exclude paren-



Color version available online

Fig. 2. Portal vein embolisation. **a**, **b** This patient had a small FLR as measured on volumetry and underwent pre-operative PVE. The portograms show pre- (**a**) and post- (**b**) embolisation appearance of the portal vein branches. In addition to the right portal vein, the segment 4 branches have also been embolised. **c**, **d** demonstrate the CT images pre- and 4 weeks post-embolisation. Clear hypertrophy and the presence of coils within the liver are seen in figure 2d.

chymal disease which may limit the hypertrophic response. Failure of the future remnant to adequately hypertrophy after PVE may indicate patients at high risk of post-operative morbidity and liver failure.

Staged Hepatic Resections

Staged hepatic resections can be performed to allow hypertrophy of residual liver tissue [44]. This approach can be used if it is not possible to resect all hepatic disease during a single procedure, as may occur in patients with multiple bilobar metastases (fig. 3). This can be successfully combined with synchronous resection of the primary tumour during the index procedure [45] or with PVE as required [46]. Staged resections are associated with 5-year survival rates of up to 42% but is only suitable for selected patients [47].

A recent development in marginally resectable patients has been operative portal vein ligation and in situ splitting, followed by hepatic resection 1–2 weeks post-portal vein ligation [48, 49]. This induces rapid growth of the FLR which is greater than that usually seen with PVE. A recent study of 25 patients undergoing this procedure (of whom 14 had colorectal metastases) demonstrated a dramatic increase in the FLR volume even over a short interval (median 9 days) [50]. All patients were scheduled to undergo an extended right hepatectomy, and at the first procedure the right portal vein was ligated and the liver parenchyma split along the falciform ligament, but not resected. Whilst this does expose the patient to two laparotomies in a short period of time, this approach may have a role in permitting R0 resection in cases where the FLR is marginal. This is a technically complex procedure which has as yet only been performed in a few centres, and its place in the armamentarium of hepatic resection for CRLM remains to be determined.

Location of disease is a more important consideration than sheer volume. A 10-cm large tumour in segment 3 is technically easier to resect than a 5-cm tumour in segment 8. Indeed, involvement of the hepatic veins is an important factor in determining the resectability of metastatic disease, and may necessitate an extended resection for what may initially appear to be low-volume disease.

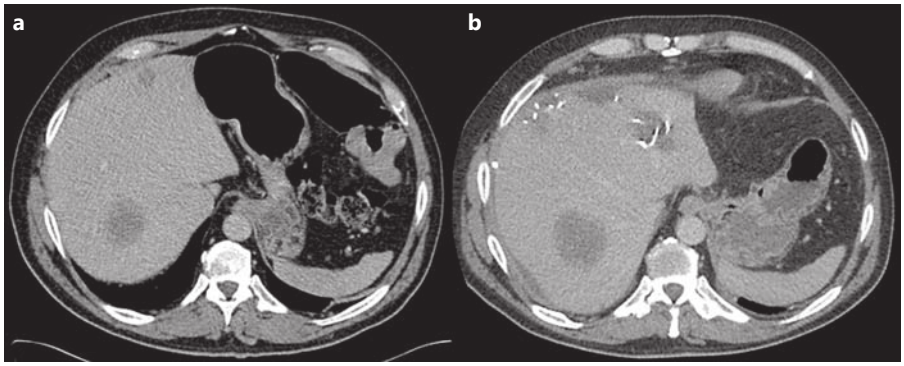


Fig. 3. Staged hepatic resection. **a** Demonstrates a patient with bilobar metastases from a colonic cancer. The residual FLR is small and multiple other metastases are present elsewhere in the liver (not shown). **b** Demonstrates the CT appearance 4 weeks after initial resection. During the initial resection, multiple metastasectomies were performed in the left lobe to ensure that it was clear of tumour, and the right portal vein was ligated intraoperatively. This patient presented with synchronous metastases, and an extended right hemicolectomy was performed at the same time as the initial metastasectomies. The images demonstrate clips at the site of the previous resections, and hypertrophy of the left lobe.

Resection of the hepatic vein confluence and IVC can be undertaken in selected patients with acceptable medium-term outcomes, but this remains a high-risk undertaking [51].

Synchronous Resection

In patients presenting with synchronous CRLM, it is possible to perform synchronous or sequential colonic and hepatic surgery. Theoretically, synchronous resection permits all disease to be dealt with at a single sitting, shortening the hospital stay and attendant costs, with acceptable morbidity in selected patients [52, 53]. However, no trial exists to provide definitive guidance and the decision to perform synchronous resection depends upon the magnitude of both procedures, as there is a synergistic effect on complication rates. The risks are lower with atypical or segmental hepatic resections than with major hemihepatectomy [54]. Similarly, the risks associated with right or extended right hemicolectomy are less than with left-sided colorectal resections. In most centres, synchronous resections are either limited to 4 or less hepatic segments in combination with right-sided colonic resections, or to atypical hepatic resections in combination with left-sided colonic procedures. Some centres report synchronous resection as feasible in 25% of patients [54].

Colon or Liver First Resection?

A 'liver-first' approach is advocated by some groups, whereby the liver resection is performed first, and the colonic surgery is performed only after the patient has recovered from their hepatic procedure [55]. The underlying rationale is to prevent progression of the CRLM which may otherwise occur whilst colonic surgery is undertaken, particularly if the anastomosis is high risk, as anastomotic breakdown may significantly increase the interval until they are sufficiently recovered for liver surgery. In patients who are asymptomatic from their primary cancer, and who will be receiving systemic therapy, this approach does not lead to significant colonic complications and indeed some groups would suggest that resection of an asymptomatic primary lesion is not always required in the age of modern chemotherapy [56].

Chemotherapy

The current mainstay of chemotherapy for metastatic colorectal cancer are regimens based on either oxaliplatin or irinotecan in combination with 5-FU and leucovorin (FOLFOX and FOLFIRI) [57–59]. Current Scottish guidelines suggest that patients with resectable diseases should be considered for perioperative chemotherapy prior to hepatic resection [60], and perioperative treatment does reduce recurrence rates, based on results from the EORTC Intergroup trial [61]. However, although progression-free survival was improved (the primary outcome of the study), there was no effect on overall survival and there was an increase in post-operative complications in those patients receiving chemotherapy. This lack of effect on overall survival is supported by a number of retrospective cohort studies and registry data [62], and a recent systematic review concluded that there was in-

sufficient evidence to support neoadjuvant therapy in patients with resectable disease [63].

Pre-operative chemotherapy has a deleterious effect on hepatic function. Platinum-based therapies are associated with sinusoidal obstruction syndrome, characterised by sinusoidal thrombi, whilst irinotecan-based regimens are associated with an acute steatohepatitis. Both of these responses impair the function of the residual liver and increase post-hepatectomy complication rates [64]. The risk is reduced with shorter pre-operative courses of treatment, and by allowing a window of 4–6 weeks for recovery of liver function between cessation of chemotherapy and subsequent surgical resection. Occasionally a complete radiological response can be seen following chemotherapy. However, the affected area of liver is likely to still contain viable tumour cells [65] and, in most circumstances, resection of the tumour-bearing liver, utilising the pre-treatment imaging, would still be indicated. Disease progression during chemotherapy denotes an aggressive tumour and whilst it is not an absolute contraindication to resection, it may necessitate the use of additional adjuvant therapies in order to achieve satisfactory results [66, 67].

Beyond neoadjuvant treatment, chemotherapy may be used to downsize or downstage the disease, allowing resection to be undertaken [66]. Such downsizing can be achieved with FOLFOX (and to a lesser extent with FOLFIRI), but novel biological agents offer the hope of greater response rates. In the UK, cetuximab is currently licenced specifically for the downsizing of CRLM in patients with K-ras wild-type disease, based on the results of two clinical trials [68–70]. However, the more recent MRC COIN trial [71] failed to confirm an additional effect of cetuximab, and subsequent studies are awaited.

Hepatic artery infusion (HAI) has been used to deliver local chemotherapy to CRLM. It has been used in neoadjuvant, adjuvant and palliative settings and it can be delivered through a surgically-placed catheter introduced to the hepatic artery via the GDA, or through percutaneous techniques. HAI provides a high concentration of chemotherapy in the liver, whilst minimising systemic toxicity. Delivery through the arterial supply improves the tumour specificity, as the metastases preferentially use arterial blood. However it can be associated with biliary toxicity and gastric ulcers [72]. Studies have shown that HAI results in higher response rates than that seen with systemic chemotherapy. However they have failed to consistently demonstrate a survival benefit [73]. Most studies performed on HAI were performed prior to 2,000 and have utilised chemotherapy regimens which would currently be considered suboptimal [74]. There is a need to perform studies using HAI and modern chemotherapy regimens.

Operative Approach

The majority of hepatic resections are currently performed using open surgery. A rooftop or hockey stick incision in the right upper quadrant is used, commonly with a table-mounted retraction system. An initial laparotomy excludes occult disease, and allows intraoperative ultrasound to confirm the pre-operative imaging findings and to confirm the planned resection. Use of intraoperative ultrasound allows the identification of occult disease which may have been missed on previous imaging studies, and also confirms the location of the hepatic veins in relation to the proposed resection. Following mobilisation of the liver from its attachments, parenchymal transection can be performed using a variety of techniques including crush-clamping and ultrasonic aspirator devices such as CUSA. Portal dissection and selective vessel ligation is not required for atypical resections. Portal clamping (Pringle manoeuvre) can be used during transection to minimise blood loss.

Management of Lymph Node Metastases

Whilst the presence of regional lymph node involvement influences survival [75, 76] and portal lymphadenectomy may improve staging accuracy [77, 78], there is no evidence that routine portal lymphadenectomy improves oncological outcomes [79, 80].

Laparoscopic Hepatic Resection

Laparoscopic resections can be performed with satisfactory oncological outcomes [81]. Major anatomical resections are technically demanding but atypical superficial resections or resection of the left lateral segment is increasingly undertaken and is standard practice in certain units [82]. There is a significant learning curve and advanced laparoscopic skills are required [83, 84]. Published series have demonstrated reduced blood loss and conversion rates with the accumulation of experience [85]. The role of laparoscopic major hepatectomy is currently evolving. All forms of major resection can be undertaken laparoscopically [86] and it has the potential to speed post-operative recovery. However, it has not yet achieved the widespread uptake seen in colorectal surgery.

Adjuncts to Surgery

Ablative therapies have gained a role in the management of patients with complex disease [87, 88]. If the full extent of disease is not resectable in a single sitting due to anatomical constraints or a threat to the FLR, then ablation in combination with resection may be utilised. Radiofrequency ablation (RFA) consists of inserting an electrode into the lesion (under ultrasound guidance) and generating an alternating current which passes to a distant ground plate. This results in generation of heat locally within the liver. Current devices provide a 4-cm^3 burn area, meaning that they can be used to target lesions up to 3 cm^3, with a 1-cm margin. Limitations relate to a heat sink effect seen in lesions adjacent to the major veins, and the risk of thermal injury to major biliary structures. In contrast to when it is performed percutaneously, the risk of inadvertent burns to bowel or diaphragm and pleura is reduced when RFA is used intraoperatively. Data from institutional series have shown that it is effective for unresectable disease. However, in the presence of resectable disease, its high local recurrence rate compares unfavourably with surgery [89–91]. This data is obtained from case series, and the poorer outcomes may be explained in part by differences in baseline disease pattern and tumour biology which led to these patients being considered for ablative therapy [92, 93]. Currently, RFA is used as an adjunct to chemotherapy or resection, but it has not yet been able to replace resection [94]. Microwave ablation (MWA) is also utilised to generate thermal ablation. New devices have a greater burn area with a more consistent penumbra when compared to RFA [95, 96]. These treatments are likely to have an evolving role in the future either in combination with resection or in isolation [97].

The first randomised controlled trial of RFA for CRLM has recently reported [98]. This study randomised 119 patients with unresectable hepatic disease to chemotherapy alone or chemotherapy plus RFA. This demonstrated an improvement in progression-free survival of 7 months with the addition of RFA. This was initially intended as a phase III trial but suffered from slow recruitment leading to its re-design as a phase II trial. It was not powered to detect differences in overall survival, and so firm conclusions cannot be drawn. Further trials in this area are needed, but in light of the difficulties in recruitment experienced, the authors question whether an adequately powered trial could be successfully completed.

Specific Considerations

Re-Resection in Face of Recurrent Disease

As the indications for hepatic resection expand, more patients are presenting with recurrent disease. Further resections in this setting should be carefully considered. The principle of resection remains as for primary hepatic surgery, namely that all recurrent disease can be resected and that sufficient liver volume will be preserved following resection. As a result, re-resection can only be offered in a limited proportion of patients. Those individuals with limited tumour load are best suited to repeat procedures [99]. Furthermore, there is a greater need for parenchymal-sparing rather than anatomical resections, as second and third procedures can be considered [100]. If the disease cannot be resected surgically, then these patients may be considered for percutaneous ablation with RFA or MWA, which will result in the greatest preservation of hepatic parenchyma.

Resection in Setting of Pulmonary Metastases

The presence of pulmonary metastases does not preclude hepatic resection, and 5-year survival rates of over 50% can be achieved following pulmonary metastasectomy [101, 102]. If the lung disease can be resected or ablated, then the patient may be considered for hepatic resection [103, 104]. Analogous to synchronous metastases, in the presence of pulmonary and hepatic disease, consideration can be given to either a lung-first or a liver-first resection. Options for dealing with the lung disease may include open or video-assisted resection, or percutaneous RFA [105, 106]. Video-assisted procedures are most suited to smaller, peripheral lesions <15 mm which do not require major lobectomy. Synchronous resection of hepatic and pulmonary metastases is clearly possible, but magnifies the perioperative risk. Repeated resections can be performed if there is late recurrence [107]. The presence of extrahepatic disease is associated with a poorer survival, and careful patient selection is required as the risk of recurrence is high [108, 109]. Nevertheless, if the patient is counselled appropriately, combined liver and lung resection should be considered.

Conclusion

Hepatic resection for colorectal metastases is an important option in the armamentarium of clinicians dealing with colorectal cancer. Long-term survival rates

have continued to improve after liver resection. Such surgery can now be carried out with an acceptable perioperative risk, and the increasing use of parenchymal-sparing resections and the use of ablative therapies such as RFA and MWA mean that this is now a viable option for most patients. All patients with colorectal cancer who develop or present with liver metastases should be considered for hepatic surgery, as this offers the potential for long-term cure in appropriately selected patients.

References

1 Cancer Research UK website: http://info.cancerresearchuk.org/cancerstats/world/colorectal-cancer-world/ (accessed 10/4/12).
2 Bengtsson G, Carlsson G, Hafström L, Jönsson PE: Natural history of patients with untreated liver metastases from colorectal cancer. Am J Surg 1981;141:586–589.
3 Wood CB, Gillis CR, Blumgart LH: A retrospective study of the natural history of patients with liver metastases from colorectal cancer. Clin Oncol 1976;2:285–288.
4 Tournigand C, André T, Achille E, Lledo G, Flesh M, Mery-Mignard D, Quinaux E, Couteau C, Buyse M, Ganem G, Landi B, Colin P, Louvet C, de Gramont A: FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study. J Clin Oncol 2004;22:229–237.
5 Simmonds PC, Primrose JN, Colquitt JL, Garden OJ, Poston GJ, Rees M: Surgical resection of hepatic metastases from colorectal cancer: a systematic review of published studies. Br J Cancer 2006;94:982–999.
6 Choti MA, Sitzmann JV, Tiburi MF, Sumetchotimetha W, Rangsin R, Schulick RD, Lillemoe KD, Yeo CJ, Cameron JL: Trends in long-term survival following liver resection for hepatic colorectal metastases. Ann Surg 2002;235:759–766.
7 Belli G, D'Agostino A, Ciciliano F, Fantini C, Russolillo N, Belli A: Liver resection for hepatic metastases: 15 years of experience. J Hepatobiliary Pancreat Surg 2002;9:607–613.
8 Minagawa M, Makuuchi M, Torzilli G, Takayama T, Kawasaki S, Kosuge T, Yamamoto J, Imamura H: Extension of the frontiers of surgical indications in the treatment of liver metastases from colorectal cancer: long-term results. Ann Surg 2000;231:487–499.
9 Ito K, Govindarajan A, Ito H, Fong Y: Surgical treatment of hepatic colorectal metastasis: evolving role in the setting of improving systemic therapies and ablative treatments in the 21st century. Cancer J 2010;16:103–110.
10 McNally SJ, Revie EJ, Massie LJ, McKeown DW, Parks RW, Garden OJ, Wigmore SJ: Factors in perioperative care that determine blood loss in liver surgery. HPB (Oxford) 2012;14:236–241.
11 Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH: Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1,001 consecutive cases. Ann Surg 1999;230:309–318.
12 Mala T, Bøhler G, Mathisen Ø, Bergan A, Søreide O: Hepatic resection for colorectal metastases: can preoperative scoring predict patient outcome? World J Surg 2002;26:1348–1353.
13 Welsh FK, Tekkis PP, John TG, Rees M: Predictive models in colorectal liver metastases – can we personalize treatment and outcome? Dig Surg 2008;25:406–412.
14 Abdalla EK, Adam R, Bilchik AJ, Jaeck D, Vauthey JN, Mahvi D: Improving resectability of hepatic colorectal metastases: expert consensus statement. Ann Surg Oncol 2006;13:1271–1280.
15 Tsim N, Healey AJ, Frampton AE, Habib NA, Bansi DS, Wasan H, Cleator SJ, Stebbing J, Lowdell CP, Jackson JE, Tait P, Jiao LR: Two-stage resection for bilobar colorectal liver metastases: R0 resection is the key. Ann Surg Oncol 2011;18:1939–1946.
16 Homayounfar K, Bleckmann A, Conradi LC, Sprenger T, Beissbarth T, Lorf T, Niessner M, Sahlmann CO, Meller J, Becker H, Liersch T, Ghadimi BM: Bilobar spreading of colorectal liver metastases does not significantly affect survival after R0 resection in the era of interdisciplinary multimodal treatment. Int J Colorectal Dis 2012;27:1359–1367.
17 Karoui M, Vigano L, Goyer P, Ferrero A, Luciani A, Aglietta M, Delbaldo C, Cirillo S, Capussotti L, Cherqui D: Combined first-stage hepatectomy and colorectal resection in a two-stage hepatectomy strategy for bilobar synchronous liver metastases. Br J Surg 2010;97:1354–1362.
18 Jochmans I, Topal B, D'Hoore A, Aerts R, Vanbeckevoort D, Bielen D, Haustermans K, Van Cutsem E, Penninckx F: Yield of routine imaging after curative colorectal cancer treatment. Acta Chir Belg 2008;108:88–92.
19 Clavien PA, Petrowsky H, DeOliviera ML: Strategies for safer liver surgery and partical liver transplantation. N Engl J Med 2007;356:1545–1559.
20 Bennink RJ, Dinant S, Erdogan D: Preoperative assessment of postoperative remnant liver function using hepatobiliary scintigraphy. J Nucl Med 2004;45:965–971.
21 Lorf T, Schnitzbauer AA, Schaefers SK, Scherer MN, Schiltt HJ, Oellerich M, Becker H, Obed A: Prognostic value of the monoethylglycinexylidide (MEGX) test prior to liver resection. Hepatogastroenterology 2008;55:539–543.
22 Ward J: New MR techniques for the detection of liver metastases. Cancer Imaging 2006;6:33–42.
23 Imam K, Bluemke DA: MR imaging in the evaluation of hepatic metastases. Magn Reson Imaging Clin N Am 2000;8:741–756.
24 Bipat S, van Leeuwen MS, Comans EF, Pijl ME, Bossuyt PM, Zwinderman AH, Stoker J: Colorectal liver metastases: CT, MR imaging, and PET for diagnosis – meta-analysis. Radiology 2005;237:123–131.
25 Tanimoto A, Lee JM, Murakami T, Huppertz A, Kudo M, Grazioli L: Consensus report of the 2nd International Forum for Liver MRI. Eur Radiol 2009;19:S975–S989.
26 Xu LH, Cai SJ, Cai GX, Peng WJ: Imaging diagnosis of colorectal liver metastases. World J Gastroenterol 2011;17:4654–4659.
27 Fong Y, Saldinger PF, Akhurst T, Macapinlac H, Yeung H, Finn RD, Cohen A, Kemeny N, Blumgart LH, Larson SM: Utility of ^{18}F-FDG positron emission tomography scanning on selection of patients for resection of hepatic colorectal metastases. Am J Surg 1999;178:282–287.
28 Wiering B, Krabbe PF, Jager GJ, Oyen WJ, Ruers TJ: The impact of fluor-18-deoxyglucose-positron emission tomography in the management of colorectal liver metastases. Cancer 2005;104:2658–2670.
29 Lubezky N, Metser U, Geva R, Nakache R, Shmueli E, Klausner JM, Even-Sapir E, Figer A, Ben-Haim M: The role and limitations of 18-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) scan and computerized tomography (CT) in restaging patients with hepatic colorectal metastases following neoadjuvant chemotherapy: comparison with operative and pathological findings. J Gastrointest Surg 2007;11:472–478.
30 Neeff H, Hörth W, Makowiec F, Fischer E, Imdahl A, Hopt UT, Passlick B: Outcome after resection of hepatic and pulmonary metastases of colorectal cancer. J Gastrointest Surg 2009;13:1813–1820.
31 Balladur P, Parc R: An unexpected liver secondary. Br J Surg 2001;88:627–628.
32 Grant A, Neuberger J: Guidelines on the use of liver biopsy in clinical practice. Br Soc Gastroenterol Gut 1999;45(suppl 4):IV1–IV11.
33 Jones OM, Rees M, John TG, Bygrave S, Plant G: Biopsy of resectable colorectal liver metastases causes tumour dissemination and adversely affects survival after liver resection. Br J Surg 2005;92:1165–1168.

34 Cresswell AB, Welsh FK, Rees M: A diagnostic paradigm for resectable liver lesions: to biopsy or not to biopsy? HPB (Oxford) 2009;11:533–540.
35 Coinaud C: Le foie; études anatomiques et chirurgicales. Paris, Masson, 1957.
36 Terminology Committee of the IHPBA: Terminology of liver anatomy and resections. HPB Surg 2000;2:333–339.
37 DeMatteo RP, Palese C, Jarnagin WR, Sun RL, Blumgart LH, Fong Y: Anatomic segmental hepatic resection is superior to wedge resection as an oncologic operation for colorectal liver metastases. J Gastrointest Surg 2000;4:178–184.
38 Welsh FK, Tekkis PP, O'Rourke T, John TG, Rees M: Quantification of risk of a positive (R1) resection margin following hepatic resection for metastatic colorectal cancer: an aid to clinical decision-making. Surg Oncol 2008;17:3–13.
39 Zorzi D, Mullen JT, Abdalla EK, Pawlik TM, Andres A, Muratore A, Curley SA, Mentha G, Capussotti L, Vauthey JN: Comparison between hepatic wedge resection and anatomic resection for colorectal liver metastases. J Gastrointest Surg 2006;10:86–94.
40 Guzzetti E, Pulitanò C, Catena M, Arru M, Ratti F, Finazzi R, Aldrighetti L, Ferla G: Impact of type of liver resection on the outcome of colorectal liver metastases: a case-matched analysis. J Surg Oncol 2008;97:503–507.
41 Lalmahomed ZS, Ayez N, van der Pool AE, Verheij J, IJzermans JN, Verhoef C: Anatomical versus nonanatomical resection of colorectal liver metastases: is there a difference in surgical and oncological outcome? World J Surg 2011;35:656–661.
42 Van Gulik TM, van den Esschert JW, de Graaf W, van Lienden KP, Busch OR, Heger M, van Delden OM, Laméris JS, Gouma DJ: Controversies in the use of portal vein embolisation. Dig Surg 2008;25:436–444.
43 Kokudo N, Tada K, Seki M, Ohta H, Azekura K, Ueno M, Ohta K, Yamaguchi T, Matsubara T, Takahashi T, Nakajima T, Muto T, Ikari T, Yanagisawa A, Kato Y: Proliferative activity of intrahepatic colorectal metastases after preoperative hemihepatic portal vein embolization. Hepatology 2001;34:267–272.
44 Adam R, Laurent A, Azoulay D, Castaing D, Bismuth H: Two-stage hepatectomy: a planned strategy to treat irresectable liver tumors. Ann Surg 2000;232:777–785.
45 Karoui M, Vigano L, Goyer P, Ferrero A, Luciani A, Aglietta M, Delbaldo C, Cirillo S, Capussotti L, Cherqui D: Combined first-stage hepatectomy and colorectal resection in a two-stage hepatectomy strategy for bilobar synchronous liver metastases. Br J Surg 2010;97:1354–1362.
46 Jaeck D, Oussoultzoglou E, Rosso E, Greget M, Weber JC, Bachellier P: A two-stage hepatectomy procedure combined with portal vein embolization to achieve curative resection for initially unresectable multiple and bilobar colorectal liver metastases. Ann Surg 2004;240:1037–1049.
47 Wicherts DA, Miller R, de Haas RJ, Bitsakou G, Vibert E, Veilhan LA, Azoulay D, Bismuth H, Castaing D, Adam R: Long-term results of two-stage hepatectomy for irresectable colorectal cancer liver metastases. Ann Surg 2008;248:994–1005.
48 De Santibañes E, Alvarez FA, Ardiles V: How to avoid postoperative liver failure: a novel method. World J Surg 2012;36:125–128.
49 Baumgart J, Lang S, Lang H: A new method for induction of liver hypertrophy prior to right trisectionectomy: a report of three cases. HPB (Oxford) 2011;13(suppl 2):1–145.
50 Schnitzbauer AA, Lang SA, Goessmann H, Nadalin S, Baumgart J, Farkas SA, Fichtner-Feigl S, Lorf T, Goralcyk A, Hörbelt R, Kroemer A, Loss M, Rümmele P, Scherer MN, Padberg W, Königsrainer A, Lang H, Obed A, Schlitt HJ: Right portal vein ligation combined with in situ splitting induces rapid left lateral liver lobe hypertrophy enabling two-staged extended right hepatic resection in small-for-size settings. Ann Surg 2012;255:405–414.
51 Malde DJ, Khan A, Prasad KR, Toogood GJ, Lodge JP: Inferior vena cava resection with hepatectomy: challenging but justified. HPB (Oxford) 2011;13:802–810.
52 De Haas RJ, Adam R, Wicherts DA, Azoulay D, Bismuth H, Vibert E, Salloum C, Perdigao F, Benkabbou A, Castaing D: Comparison of simultaneous or delayed liver surgery for limited synchronous colorectal metastases. Br J Surg 2010;97:1279–1289.
53 Chen J, Li Q, Wang C, Zhu H, Shi Y, Zhao G: Simultaneous vs. staged resection for synchronous colorectal liver metastases: a meta-analysis. Int J Colorectal Dis 2011;26:191–199.
54 De Santibañes E, Fernandez D, Vaccaro C, Quintana GO, Bonadeo F, Pekolj J, Bonofiglio C, Molmenti E: Short-term and long-term outcomes after simultaneous resection of colorectal malignancies and synchronous liver metastases. World J Surg 2010;34:2133–2140.
55 Mentha G, Roth AD, Terraz S, Giostra E, Gervaz P, Andres A, Morel P, Rubbia-Brandt L, Majno PE: 'Liver-first' approach in the treatment of colorectal cancer with synchronous liver metastases. Dig Surg 2008;25:430–435.
56 Damjanov N, Weiss J, Haller DG: Resection of the primary colorectal cancer is not necessary in nonobstructed patients with metastatic disease. Oncologist 2009;14:963–969.
57 Douillard JY, Siena S, Cassidy J, Tabernero J, Burkes R, Barugel M, Humblet Y, Bodoky G, Cunningham D, Jassem J, Rivera F, Kocákova I, Ruff P, Błasińska-Morawiec M, Šmakal M, Canon JL, Rother M, Oliner KS, Wolf M, Gansert J: Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol 2010;28:4697–4705.
58 Bokemeyer C, Bondarenko I, Makhson A, Hartmann JT, Aparicio J, de Braud F, Donea S, Ludwig H, Schuch G, Stroh C, Loos AH, Zubel A, Koralewski P: Fluorouracil, leucovorin, and oxaliplatin with and without cetuximab in the first-line treatment of metastatic colorectal cancer. J Clin Oncol 2009;27:663–671.
59 Saltz LB, Clarke S, Díaz-Rubio E, Scheithauer W, Figer A, Wong R, Koski S, Lichinitser M, Yang TS, Rivera F, Couture F, Sirzén F, Cassidy J: Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study. J Clin Oncol 2008;26:2013–2019.
60 Diagnosis and Management of Colorectal Cancer: A National Clinical Guideline. Scottish Intercollegiate Guideline Network, December 2011. http://www.sign.ac.uk/pdf/sign126.pdf.
61 Nordlinger B, Sorbye H, Glimelius B, Poston GJ, Schlag PM, Rougier P, Bechstein WO, Primrose JN, Walpole ET, Finch-Jones M, Jaeck D, Mirza D, Parks RW, Collette L, Praet M, Bethe U, Van Cutsem E, Scheithauer W, Gruenberger T; EORTC Gastro-Intestinal Tract Cancer Group; Cancer Research UK; Arbeitsgruppe Lebermetastasen und -tumoren in der Chirurgischen Arbeitsgemeinschaft Onkologie (ALM-CAO); Australasian Gastro-Intestinal Trials Group (AGITG); Fédération Francophone de Cancérologie Digestive (FFCD). Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup Trial 40983): a randomised controlled trial. Lancet 2008;371:1007–1016.
62 Adam R, Bhangui P, Poston G, Mirza D, Nuzzo G, Barroso E, Ijzermans J, Hubert C, Ruers T, Capussotti L, Ouellet JF, Laurent C, Cugat E, Colombo PE, Milicevic M: Is perioperative chemotherapy useful for solitary, metachronous, colorectal liver metastases? Ann Surg 2010;252:774–787.
63 Lehmann K, Rickenbacher A, Weber A, Pestalozzi BC, Clavien PA: Chemotherapy before liver resection of colorectal metastases: friend or foe? Ann Surg 2012;255:237–247.
64 Kneuertz PJ, Maithel SK, Staley CA, Kooby DA: Chemotherapy-associated liver injury: impact on surgical management of colorectal cancer liver metastases. Ann Surg Oncol 2011;18:181–190.
65 Benoist S, Brouquet A, Penna C, Julié C, El Hajjam M, Chagnon S, Mitry E, Rougier P, Nordlinger B: Complete response of colorectal liver metastases after chemotherapy: does it mean cure? J Clin Oncol 2006;24:3939–3945.
66 Adam R, Pascal G, Castaing D, Azoulay D, Delvart V, Paule B, Levi F, Bismuth H: Tumor progression while on chemotherapy: a contraindication to liver resection for multiple colorectal metastases? Ann Surg 2004;240:1052–1061.

67 Gallagher DJ, Zheng J, Capanu M, Haviland D, Paty P, Dematteo RP, D'Angelica M, Fong Y, Jarnagin WR, Allen PJ, Kemeny N: Response to neoadjuvant chemotherapy does not predict overall survival for patients with synchronous colorectal hepatic metastases. Ann Surg Oncol 2009;16:1844–1851.
68 Folprecht G, Gruenberger T, Bechstein WO, Raab HR, Lordick F, Hartmann JT, Lang H, Frilling A, Stoehlmacher J, Weitz J, Konopke R, Stroszczynski C, Liersch T, Ockert D, Herrmann T, Goekkurt E, Parisi F, Köhne CH: Tumour response and secondary resectability of colorectal liver metastases following neoadjuvant chemotherapy with cetuximab: the CELIM randomised phase 2 trial. Lancet Oncol 2010;11:38–47.
69 Van Cutsem E, Köhne CH, Láng I, Folprecht G, Nowacki MP, Cascinu S, Shchepotin I, Maurel J, Cunningham D, Tejpar S, Schlichting M, Zubel A, Celik I, Rougier P, Ciardiello F: Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status. J Clin Oncol 2011;29:2011–2019.
70 National Institute for Health and Clinical Evidence: Cetuximab for the first-line treatment of metastatic colorectal cancer – Technology Appraisal TA176. August 2009. http://www.nice.org.uk/TA176.
71 Maughan TS, Adams RA, Smith CG, Meade AM, Seymour MT, Wilson RH, Idziaszczyk S, Harris R, Fisher D, Kenny SL, Kay E, Mitchell JK, Madi A, Jasani B, James MD, Bridgewater J, Kennedy MJ, Claes B, Lambrechts D, Kaplan R, Cheadle JP, MRC COIN Trial Investigators: Addition of cetuximab to oxaliplatin-based first-line combination chemotherapy for treatment of advanced colorectal cancer: results of the randomised phase 3 MRC COIN trial. Lancet 2011;377:2103–2114.
72 Power DG, Healey-Bird BR, Kemeny NE: Regional chemotherapy for liver-limited metastatic colorectal cancer. Clin Colorectal Cancer 2008;7:247–259.
73 Mocellin S, Pilati P, Lise M, Nitti D: Meta-analysis of hepatic arterial infusion for unresectable liver metastases from colorectal cancer: the end of an era? J Clin Oncol 2007;25:5649–5654.
74 Bouchahda M, Levi F, Adam R, Rougier P: Modern insights into hepatic arterial infusion for liver metastases from colorectal cancer. Eur J Cancer 2011;47:2681–2690.
75 Jaeck D, Nakano H, Bachellier P, Inoue K, Weber JC, Oussoultzoglou E, Wolf P, Chenard-Neu MP: Significance of hepatic pedicle lymph node involvement in patients with colorectal liver metastases: a prospective study. Ann Surg Oncol 2002;9:430–438.
76 Adam R, de Haas RJ, Wicherts DA, Aloia TA, Delvart V, Azoulay D, Bismuth H, Castaing D: Is hepatic resection justified after chemotherapy in patients with colorectal liver metastases and lymph node involvement? J Clin Oncol 2008;26:3672–3680.
77 Viana EF, Herman P, Siqueira SC, Taka T, Carvalho P, Coelho FF, Pugliese V, Saad WA, D'Albuquerque LA: Lymphadenectomy in colorectal cancer liver metastases resection: incidence of hilar lymph nodes micrometastasis. J Surg Oncol 2009;100:534–537.
78 Rau C, Blanc B, Ronot M, Dokmak S, Aussilhou B, Faivre S, Vilgrain V, Paradis V, Belghiti J: Neither preoperative computed tomography nor intra-operative examination can predict metastatic lymph node in the hepatic pedicle in patients with colorectal liver metastasis. Ann Surg Oncol 2012;19:163–168.
79 Grobmyer SR, Wang L, Gonen M, Fong Y, Klimstra D, D'Angelica M, DeMatteo RP, Schwartz L, Blumgart LH, Jarnagin WR: Perihepatic lymph node assessment in patients undergoing partial hepatectomy for malignancy. Ann Surg 2006;244:260–264.
80 Gurusamy KS, Imber C, Davidson BR: Management of the hepatic lymph nodes during resection of liver metastases from colorectal cancer: a systematic review. HPB Surg 2008;2008:684150.
81 Abu Hilal M, Di Fabio F, Abu Salameh M, Pearce NW: Oncological efficiency analysis of laparoscopic liver resection for primary and metastatic cancer: a single-center UK experience. Arch Surg 2012;147:42–48.
82 Buell JF, Cherqui D, Geller DA, O'Rourke N, Iannitti D, Dagher I, Koffron AJ, Thomas M, Gayet B, Han HS, Wakabayashi G, Belli G, Kaneko H, Ker CG, Scatton O, Laurent A, Abdalla EK, Chaudhury P, Dutson E, Gamblin C, D'Angelica M, Nagorney D, Testa G, Labow D, Manas D, Poon RT, Nelson H, Martin R, Clary B, Pinson WC, Martinie J, Vauthey JN, Goldstein R, Roayaie S, Barlet D, Espat J, Abecassis M, Rees M, Fong Y, McMasters KM, Broelsch C, Busuttil R, Belghiti J, Strasberg S, Chari RS, World Consensus Conference on Laparoscopic Surgery: The international position on laparoscopic liver surgery: The Louisville Statement, 2008. Ann Surg 2009;250:825–830.
83 Vigano L, Laurent A, Tayar C, Tomatis M, Ponti A, Cherqui D: The learning curve in laparoscopic liver resection: improved feasibility and reproducibility. Ann Surg 2009;250:772–782.
84 Robinson SM, Hui KY, Amer A, Manas DM, White SA: Laparoscopic liver resection: is there a learning curve? Dig Surg 2012;29:62–69.
85 Bryant R, Laurent A, Tayar C, Cherqui D: Laparoscopic liver resection – understanding its role in current practice: the Henri Mondor Hospital experience. Ann Surg 2009;250:103–111.
86 Nguyen KT, Laurent A, Dagher I, Geller DA, Steel J, Thomas MT, Marvin M, Ravindra KV, Mejia A, Lainas P, Franco D, Cherqui D, Buell JF, Gamblin TC: Minimally invasive liver resection for metastatic colorectal cancer: a multi-institutional, international report of safety, feasibility, and early outcomes. Ann Surg 2009;250:842–848.
87 Garcea G, Lloyd TD, Aylott C, Maddern G, Berry DP: The emergent role of focal liver ablation techniques in the treatment of primary and secondary liver tumours. Eur J Cancer 2003;39:2150–2164.
88 Ecre C, Parks RW: Interstitial ablative techniques for hepatic tumours. Br J Surg 2003;90:272–289.
89 Abdalla EK, Vauthey JN, Ellis LM, Ellis V, Pollock R, Broglio KR, Hess K, Curley SA: Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. Ann Surg 2004;239:818–825.
90 Aloia TA, Vauthey JN, Loyer EM, Ribero D, Pawlik TM, Wei SH, Curley SA, Zorzi D, Abdalla EK: Solitary colorectal liver metastasis: resection determines outcome. Arch Surg 2006;141:460–466.
91 Lee KH, Kim HO, Yoo CH, Son BH, Park YL, Cho YK, Kim H, Han WK: Comparison of radiofrequency ablation and resection for hepatic metastasis from colorectal cancer. Korean J Gastroenterol 2012;59:218–223.
92 Gleisner AL, Choti MA, Assumpcao L, Nathan H, Schulick RD, Pawlik TM: Colorectal liver metastases: recurrence and survival following hepatic resection, radiofrequency ablation, and combined resection-radiofrequency ablation. Arch Surg 2008;143:1204–1212.
93 Berber E, Tsinberg M, Tellioglu G, Simpfendorfer CH, Siperstein AE: Resection versus laparoscopic radiofrequency thermal ablation of solitary colorectal liver metastasis. J Gastrointest Surg 2008;12:1967–1972.
94 Stang A, Fischbach R, Teichmann W, Bokemeyer C, Braumann D: A systematic review on the clinical benefit and role of radiofrequency ablation as treatment of colorectal liver metastases. Eur J Cancer 2009;45:1748–1756.
95 Qian GJ, Wang N, Shen Q, Sheng YH, Zhao JQ, Kuang M, Liu GJ, Wu MC: Efficacy of microwave versus radiofrequency ablation for treatment of small hepatocellular carcinoma: experimental and clinical studies. Eur Radiol 2012;22:1983–1990.
96 Fan W, Li X, Zhang L, Jiang H, Zhang J: Comparison of microwave ablation and multipolar radiofrequency ablation in vivo using two internally cooled probes. AJR Am J Roentgenol 2012;198:W46–W50.
97 Jones C, Badger SA, Ellis G: The role of microwave ablation in the management of hepatic colorectal metastases. Surgeon 2011;9:33–37.
98 Ruers T, Punt C, Van Coevorden F, Pierie JP, Borel-Rinkes I, Ledermann JA, Poston G, Bechstein W, Lentz MA, Mauer M, Van Cutsem E, Lutz MP, Nordlinger B, for the EORTC Gastro-Intestinal Tract Cancer Group, Arbeitsgruppe Lebermetastasen und -tumoren in der Chirurgischen Arbeitsgemeinschaft Onkologie (ALM-CAO) and the National Cancer Research Institute Colorectal Clinical Study Group (NCRI CCSG): Radiofrequency ablation combined with systemic treatment versus systemic treatment alone in patients with non-resectable colorectal liver metastases: a randomized EORTC Intergroup phase II study (EORTC 40004). Ann Oncol 2012;23:2619–2626.

99 Petrowsky H, Gonen M, Jarnagin W, Lorenz M, DeMatteo R, Heinrich S, Encke A, Blumgart L, Fong Y: Second liver resections are safe and effective treatment for recurrent hepatic metastases from colorectal cancer: a bi-institutional analysis. Ann Surg 2002;235:863–871.
100 Adam R, Pascal G, Azoulay D, Tanaka K, Castaing D, Bismuth H: Liver resection for colorectal metastases: the third hepatectomy. Ann Surg 2003;238:871–883.
101 Pfannschmidt J, Dienemann H, Hoffmann H: Surgical resection of pulmonary metastases from colorectal cancer: a systematic review of published series. Ann Thorac Surg 2007;84:324–338.
102 Limmer S, Oevermann E, Killaitis C, Kujath P, Hoffmann M, Bruch HP: Sequential surgical resection of hepatic and pulmonary metastases from colorectal cancer. Langenbecks Arch Surg 2010;395:1129–1138.
103 Shah SA, Haddad R, Al-Sukhni W, Kim RD, Greig PD, Grant DR, Taylor BR, Langer B, Gallinger S, Wei AC: Surgical resection of hepatic and pulmonary metastases from colorectal carcinoma. J Am Coll Surg 2006; 202:468–475.
104 Neeff H, Hörth W, Makowiec F, Fischer E, Imdahl A, Hopt UT, Passlick B: Outcome after resection of hepatic and pulmonary metastases of colorectal cancer. J Gastrointest Surg 2009;13:1813–1820.
105 Rotolo N, De Monte L, Imperatori A, Dominioni L: Pulmonary resections of single metastases from colorectal cancer. Surg Oncol 2007;16(suppl 1):S141–S144.
106 Yan TD, King J, Ebrahimi A, Sjarif A, Glenn D, Steinke K, Morris DL: Hepatectomy and lung radiofrequency ablation for hepatic and subsequent pulmonary metastases from colorectal carcinoma. J Surg Oncol 2007;96: 367–373.
107 Riquet M, Foucault C, Cazes A, Mitry E, Dujon A, Le Pimpec Barthes F, Médioni J, Rougier P: Pulmonary resection for metastases of colorectal adenocarcinoma. Ann Thorac Surg 2010;89:375–380.
108 Carpizo DR, Are C, Jarnagin W, Dematteo R, Fong Y, Gönen M, Blumgart L, D'Angelica M: Liver resection for metastatic colorectal cancer in patients with concurrent extrahepatic disease: results in 127 patients treated at a single center. Ann Surg Oncol 2009;16: 2138–2146.
109 Adam R, de Haas RJ, Wicherts DA, Vibert E, Salloum C, Azoulay D, Castaing D: Concomitant extrahepatic disease in patients with colorectal liver metastases: when is there a place for surgery? Ann Surg 2011; 253:349–359.