The detection and management of complications following the treatment of liver metastases

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Abstract

Whilst once considered as incurable systemic disease, treatment options for liver metastases have increased over the last 30 years and safety has improved dramatically, such that for a selected group of patients the hope of cure can now be offered with radical treatment and low morbidity interventions can be offered which prolong survival, even in patients with more widely disseminated disease. Advances have been made in selection and surgical technique for liver resection and several adjuncts to resection now exist in the form of portal vein embolization, thermal ablation and targeted drug or radiotherapy delivery options. A natural consequence of these developments has been the delivery of services within fewer specialist units, with the result that later complications of therapy may present to local hospitals, rather than directly to the specialist centres. This article will describe the current common liver directed therapies and outline the presentation and management of their complications.

Keywords Liver abscess; liver embolization; liver metastases; liver resection; microwave ablation; selective radiotherapy

Introduction

Given its rich blood supply, the liver is a common site for metastatic disease, especially for tumours of the gastrointestinal (GI) tract and those with predominantly haematogenous routes of spread. Colorectal cancer is the fourth most common malignancy in the UK, with an incidence of 42,900 new cases per year (2016—18).[1] Fifty per cent of patients with colorectal cancer will present with or subsequently develop liver metastases over the course of their disease making colorectal metastases the commonest indication for liver resection in the West. Liver resection was formerly associated with a significant mortality rate, with an American multi-centre series from the late 1970s reporting a 13% mortality.[2] The safety of elective liver surgery has however improved significantly over the intervening time period and more recently published series have described post-hepatectomy mortality rates of 0%—4.4% and morbidity of 19.6%—45%, with 5-year survival rates of up to 50%. For this reason, resection is now established as the gold standard treatment for colorectal liver metastases, with an emerging evidence base for disease from other primary sites.

Multi-modality treatment, in the form of preoperative portal/hepatic vein embolization, associating liver partitioning and portal vein ligation procedures (ALPPS), thermal ablations and chemo- or radio-embolization have a role in both radical and palliative treatments and management should be overseen by a specialist liver multidisciplinary team (MDT). Chemotherapy and systemic biological agents have an important role to play, in a neoadjuvant, conversion and adjuvant setting, however they bring their own risks to subsequent liver interventions in the form of chemotherapy associated liver injury (CALI), which is dose dependent and can have a profound effect on surgical and general complications following liver resection. Close collaboration is therefore required between the local and specialist MDTs in terms of the choice and timing of systemic therapies in mitigating the risk of treatment-related complications whilst optimizing outcomes.[3]

Many of the potential complications following liver resection can be predicted and mitigated with appropriate management; however, even the best series report morbidity rates around 20%. With a potentially deleterious effect on long-term outcome in terms of disease-specific and disease-free survival,[4] it is important that both specialist and local teams identify and treat complications quickly and effectively when they occur, so as to minimize the delay to the patient receiving further treatment. Figure 1 provides an overview of the current treatment options for colorectal liver metastases; this article will outline the complications of these treatments, their predisposing factors, presentation and their management.

Liver resection

Bile leak

Bile leakage is a potentially serious complication of liver resection, with a reported incidence of between 4% and 17%, with 4% being the rate usually quoted as part of the consent process and a higher risk described with more complex extended or central resections. Bile leak is defined by the International Study Group for Liver Surgery (ISGLS) as an increased bilirubin concentration in the drain or intra-abdominal fluid of at least three times the serum concentration on or after postoperative day 3 or the need for intervention for biliary collections or biliary peritonitis. Bile leaks are stratified as Grade A — causing no change in the patient's management, Grade B — resulting in intervention, but not requiring re-laparotomy or Grade C — requiring re-laparotomy.[5]

Postoperative bile leak is most commonly caused by a failure to ligate or adequately seal a distal bile duct at a resection margin, but can also be due to an inadvertent bile duct injury or leakage from a bile duct–intestinal anastomosis. Risk factors for bile leak include re-do liver resection; a large surface area of liver

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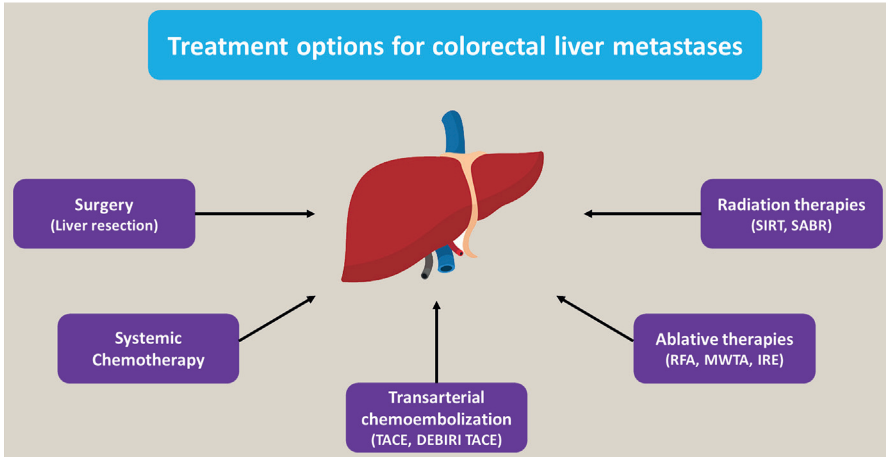

An overview of the current treatment options for colorectal liver metastases. The complications of each of these are discussed in turn in this article.

Figure 1

resection (>57.5 cm); large intraoperative blood loss (>775 ml) and a prolonged operative time (>300 minutes).

Prevention is better than cure, and meticulous biliostasis is key in avoiding postoperative bile leakage. It is vital to ensure that small and large calibre bile ducts are adequately secured with clips, ties or suture ligation. The transected surface of the liver can be "mopped" with clean white gauze to demonstrate small volume bile seepage, which can otherwise be easily missed. The contrast agent, indocyanine green (ICG), has also been used intraoperatively to elicit bile leakage. It is either injected intravenously (where it is metabolized by the liver and excreted in bile), or it can be directly injected into the biliary tree via a transcystic route. It is visualized by illuminating the transected surface of the liver with near-infrared light, which causes ICG to fluoresce — this fluorescence is captured by a special camera attached to the light source and any areas of bile leakage can thus be detected.[6] It is routine practice in our unit to coat the transected liver surface with a combination of fibrin glue and a plant collagen matrix haemostat, and we selectively leave a large diameter silicone drain adjacent to the resection site.

Early bile leaks may present with bile stained drain effluent, but undrained leaks usually result in increasing abdominal pain and a low-grade fever, later progressing to sepsis. Generalized biliary peritonitis will require laparotomy or laparoscopy for lavage and drainage, but localized collections can usually be drained percutaneously.

Most bile leaks will settle spontaneously, however a drain output of >100 ml on the tenth postoperative day is associated with a failure of conservative management.[7]

If conservative treatment fails, an MRI scan with a hepatocyte specific contrast agent such as Primovist and a very delayed post-contrast phase (1 hour) can be useful in identifying the site of a leak (Figure 2) and if in continuity with the main biliary tree an endoscopic sphincterotomy and a temporary stent across the papilla will allow most leaks to settle. Leaks from disconnected areas of parenchyma will not respond to sphincterotomy and stenting and will require re-resection, bilio-enteric reconstruction, or we have had some success with biliary obliteration by the percutaneous injection of alcohol into blind-ended caudate duct leaks.

Infected perihepatic collections

Fluid collections at the site of liver resections are common, and they can sometimes be surprisingly sizable (Figure 3). These are normal postoperative findings that do not require intervention, and are not considered a complication in the absence of infection. The presence of small gas bubbles in these collections on CT is not necessarily indicative of either bile leak or infection in its own right, but as always these findings must be considered alongside the patient as a whole. In the context of sepsis, abnormal liver enzymes and a CT scan showing "rim enhancement" of perihepatic collections, intervention may be required. However, patients admitted to peripheral hospitals unwell following a liver resection should be discussed with the specialist centre wherever possible prior to drainage of any collections. This is because placement of an unnecessary percutaneous drain

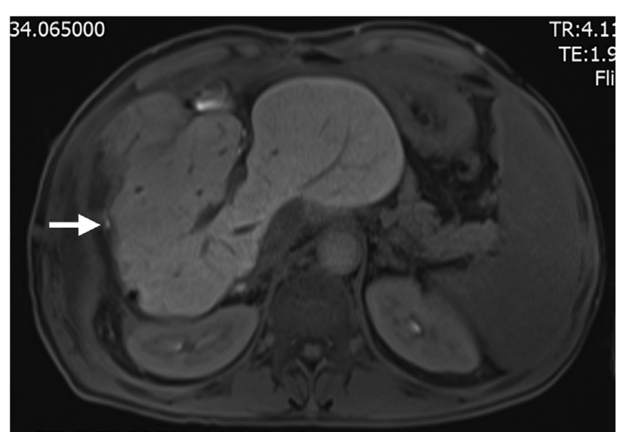

Figure 2 A Primovist MRI scan with an extremely delayed post-contrast phase (1 hour), showing a small volume bile leak following a complex liver resection (arrow).

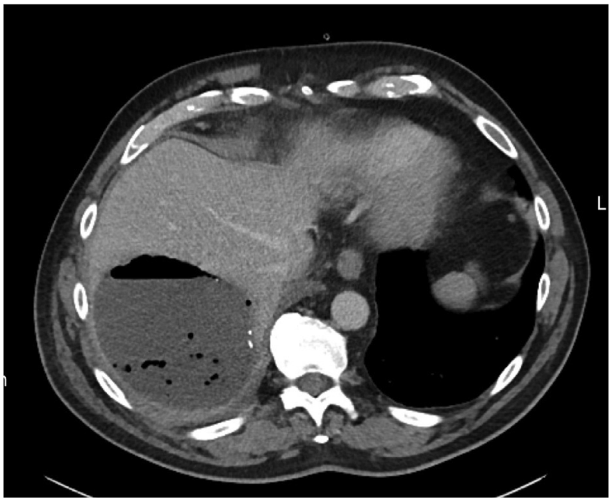

Figure 3 A postoperative CT scan performed as an outpatient on Day 14 to investigate shortness of breath showing a large, but uncomplicated, normal postoperative collection containing gas bubbles at the site of a liver resection. This does not suggest infection, does not require drainage and will resolve spontaneously in time.

may damage the cut edge of the liver surface and result in an iatrogenic bile leak.

Infected collections are unusual (3%–6%), but when they do occur, prompt recognition and drainage is required as untreated sepsis, especially in patients with a small liver remnant, can lead to hepatic insufficiency and renal failure. Local infective complications are associated with extended resections, excessive bleeding and diabetes mellitus. There is no evidence that the routine use of drains reduces the incidence of infected collections and some studies report non-significant suggestions that they may, in fact, increase risk.

Biliary stricture

Biliary stricture as a primary technical failure is unusual, but it is possible to injure the contralateral duct during hemihepatectomy and the risk is increased for more centrally placed tumours and in cases of anomalous biliary tract anatomy. Care should be taken to study the preoperative imaging to minimize such risks and primary injuries will usually be detected and dealt with during the inpatient stay, following the detection of progressively deranged liver enzymes.

Late biliary strictures develop weeks to months following resection, and are usually secondary to ischaemic duct injuries. A good quality MRI is required in the first place to exclude disease recurrence and to document the level and length of the stricture and the volume of the distal remnant. A stent should be placed as early as possible, as these strictures often close down tightly and quickly making subsequent access difficult or impossible and any cholangitis should be treated with appropriate antibiotics. Percutaneous trans-hepatic cholangiogram (PTC) and biliary stenting is often more successful than endoscopic approaches. Definitive treatment options include endobiliary dilatation and/or stenting, a long-term external drain, bilio-enteric reconstruction or further resection and will be tailored by the specialist unit to suit the individual patient.

Haemorrhage

Intraoperative and postoperative bleeding are potentially catastrophic complications of hepatectomy. Hepatectomy in the 1970s was associated with a 13% mortality with major haemorrhage accounting for 34% of the deaths and exsanguinating haemorrhage in the operating room in 18%. Modern liver surgery has become significantly safer in terms of risk of haemorrhage, with on-table deaths an extreme rarity and the risk of major haemorrhage in series from large centres in the region of 1%.[8]

There are two key manoeuvres for the prevention of bleeding during hepatic transection. Low central venous pressure anaesthesia reduces the amount of back bleeding from hepatic veins during transection and should be practised universally unless the patient has cardiovascular disease which precludes its use. Clamping of the portal triad (Pringle manoeuvre) reduces the hepatic inflow by occlusion of the hepatic artery and portal vein and is practised variably – routinely in some units and selectively in others. Inflow occlusion has been shown to significantly reduce blood loss in trials by its proponents and there is a tendency for it to be used routinely by more experienced liver surgeons, though large studies have failed to show difference in blood loss with and without routine Pringle clamping.[9]

Most important, however is a thorough understanding of segmental liver anatomy and meticulous dissection. Attention to intraoperative haemostasis is aided by modern equipment such as the Cavitron Ultrasonic Surgical Aspirator (CUSA®, Integra LifeSciences, USA), argon plasma coagulation, vascular stapling devices and energized dissection instruments such as the Harmonic scalpel® (Ethicon Endo-Surgery, USA), the Ligasure™ (Covidien, USA), the Lotus™ (Bowa Medical, UK) and the Thunderbeat™ (Olympus, Japan). Topical haemostats such as fibrin glue and collagen matrix may have a role to play in securing haemostasis. The use of systemic fibrinolytics, such as tranexamic acid, have been shown to reduce blood loss and transfusion requirements.[10] Pre-existing nutritional deficits and specific disorders of clotting should be addressed preoperatively and a careful medication history should be taken with cessation of anticoagulants and antiplatelet therapies in the perioperative period. Patients at high risk of thromboembolic events should have an IVC filter inserted prior to surgery.

The ISGLS defined post-hepatectomy haemorrhage (PHH) as a fall in haemoglobin level of >3 g/dl following the end of surgery as compared to the postoperative baseline level and/or any postoperative transfusion of red blood cells for a falling haemoglobin and/or a requirement for invasive treatment (re-laparotomy or interventional radiology) to stop bleeding.[11] PHH is diagnosed by evidence of intra-abdominal haemorrhage such as the presence of blood in the abdominal drain or detection of an intra-abdominal haematoma or active haemorrhage by abdominal imaging (CT or ultrasound). It should be remembered that, as with any acute haemorrhage, the initial haemoglobin level may not fall early during the acute episode and a high index of suspicion must be maintained for bleeding as the possible cause in cases of shock, with early imaging if required.

The ISGLS defines three grades of PHH. Grade A PHH can be managed with a minimal transfusion requirement of less than two units of RBCs, and temporary discontinuation of anticoagulant therapy. There is usually no additional postoperative stay. Grade B PHH has a transfusion requirement of more than two units of RBCs, and may in addition require the administration of other blood products such as fresh frozen plasma, platelets or clotting factors. There is no requirement for invasive intervention. Patients with grade B PHH will likely demonstrate signs of hypovolaemia such as hypotension and tachycardia. Patients with grade C haemorrhage have life-threatening bleeding requiring invasive therapy in the form of interventional radiology embolization or re-laparotomy to arrest bleeding. In severe cases, patients may develop multi-organ failure due to hypovolaemic shock and require support in an ITU setting.

Patients typically present with bleeding during their postoperative inpatient stay, but secondary haemorrhage following discharge may occur and radiological evidence of active bleeding or recent bleeding with haemodynamic instability that does not respond to resuscitation are indications for intervention. Interventional radiology and embolization is the mainstay for haemorrhage control, but if this fails, the safest surgical option outside a specialist centre will be temporary packing and transfer. Definitive surgical options include fine suturing of vessels on the transection surface or IVC, suture ligation of feeding vessels or further resection as required.

Liver insufficiency

Postoperative liver insufficiency can be a potentially life-threatening complication following hepatectomy. Factors predisposing to the development of liver failure can be categorized as patient-related (age, sepsis, diabetes mellitus, duration of preoperative chemotherapy), liver-related (poor quality liver remnant due to steatosis or chemotherapy-associated liver injury, or cirrhosis), or surgery-related (a small functional liver remnant (FLR), large volume intraoperative haemorrhage, or prolonged portal inflow occlusion).[12] For healthy patients without previous chemotherapy treatment, a minimum FLR of 25% is considered adequate. Following chemotherapy at least 30% is required and in cirrhotic patients, the FLR must be at least 40%.

Management of hepatic insufficiency is supportive and mortality rates can be high, prevention is therefore important. Strategies to avoid insufficiency focus on preserving volume and quality of the liver remnant and include preoperative portal vein embolization of the contralateral lobe to induce hypertrophy (now often combined with hepatic vein embolization in a method known as liver venous deprivation), the ALPPS Procedure (Associated Liver Partitioning and Portal Vein Ligation – in which the portal vein to the intended specimen is divided and the planned transection line developed in the first stage, with the hepatic artery preserved and the specimen finally resected after hypertrophy of the remnant has occurred), stopping chemotherapy for at least 6 weeks preoperatively, preoperative weight loss, optimization of diabetic control, parenchymal sparing resections and preservation of optimal venous drainage of the remnant.

The International Study Group on Liver Surgery (ISGLS) in 2011 defined post-hepatectomy liver failure as a postoperative reduction in the ability of the liver to maintain its synthetic, excretory and detoxifying functions, characterized by an increased INR and hyperbilirubinaemia on or after the fifth postoperative day.[13] Signs of postoperative liver failure can include confusion or a decreased conscious level, high drain volumes of ascitic fluid, a progressive lactic acidosis and a persistent derangement of liver function tests.

It is normal for liver function tests to become deranged following a resection, with the ALT rising within 24 hours and usually peaking after 48–72 hours before falling, reflecting the acute hepatitic injury. The prothrombin rise and fall usually occurs about 24 hours after the ALT and usually after 48–72 hours, the ALP will start to rise and may remain high for several weeks, depending on the size of the resection, as a marker of liver regeneration. These expected abnormalities should not be a cause for concern.

Management of liver failure is dependent on severity and the ISGLS describe three grades of severity for post-hepatectomy liver failure based upon its impact on clinical management. Grade A post-hepatectomy liver failure requires no change in the patient's clinical management. Patients with grade B post-hepatectomy liver failure require a deviation from the normal postoperative course but no invasive therapy – this may include the administration of diuretics, lactulose, glucagon/insulin therapy and FFP transfusion. Grade C post-hepatectomy liver failure is defined by a requirement for invasive treatment, for example plasma exchange, artificial liver support or surgery.

Liver insufficiency can take a long time to recover and it is not unusual for patients to be discharged before their liver function has fully recovered. During this time, they are at increased risk of sepsis and renal failure and any episodes of infection should be treated aggressively and early. Hyponatraemia and fluid retention may occur, which may require temporary fluid restriction and/or the use of spironolactone.

Atelectasis and chest infection

Postoperative atelectasis and hospital-acquired pneumonia are common following upper abdominal surgery. Prolonged anaesthetic time, surgical trauma, inadequate cough due to surgical site incisional pain and inappropriately long bed rest are major risk factors predisposing to pulmonary atelectasis and infection.

Adequate postoperative analgesia is imperative in promoting deep breathing, enabling sufficient cough to clear pulmonary secretions and promoting early postoperative mobilization. The latter is also important in minimizing the risk of thromboembolic complications. Pain relief should be multi-modal and proactive support from the hospital acute pain team is helpful. Thoracic epidural provides effective postoperative analgesia in patients recovering from major upper abdominal operations. There are, however, issues with thoracic epidural including hypotension and bradycardia, and rare but potentially catastrophic complications such as epidural haematoma or infection leading to permanent sensory or motor neurological deficits. Continuous intramuscular local anaesthetic infiltration with wound catheters provides similar pain control to thoracic epidural analgesia and provides a method of avoiding those rare but serious complications.[14] Incentive spirometry may also play a role in preventing postoperative pulmonary complications, though high quality evidence for this is currently lacking.

Pulmonary infection is most commonly seen between the third and fifth postoperative day. Signs and symptoms may include dyspnoea, a productive cough, cyanosis, tachypnoea and reduced oxygen saturations on pulse oximetry. Consolidation seen on plain chest radiographs and hypoxaemia on arterial blood gas analysis help confirm the diagnosis. Empirical antibiotic therapy should be prescribed in accordance with local guidelines following the collection of sputum samples for culture to guide sensitivities. Chest physiotherapy has an important role and in some, escalation to an HDU or ITU setting for invasive or non-invasive respiratory support may be necessary.

Pleural effusion

Reactive pleural effusions are common following liver resection and are usually right-sided (Figure 4). Operative risk factors for the development of postoperative pleural effusion include: iatrogenic diaphragmatic injury (or intended diaphragmatic excision to ensure radicality); obstruction of thoracic venous or lymphatic outflow; perioperative blood transfusion; surgery on the right lobe of the liver and combined liver with other visceral resection. Patient-related risk factors include: neoadjuvant chemotherapy; older age; asthma; a history of heavy smoking and elevated body mass index.[15] The presence of a pleural effusion is confirmed on chest X-ray. Most pleural effusions will resolve spontaneously without intervention and ultrasound-guided pleurocentesis should be reserved for those patients in whom there is evidence of respiratory compromise or where thoracic empyema is suspected. Reactive effusions will re-accumulate quickly until liver regeneration progresses and unnecessary drainage risks both lung injury and the introduction of infection.

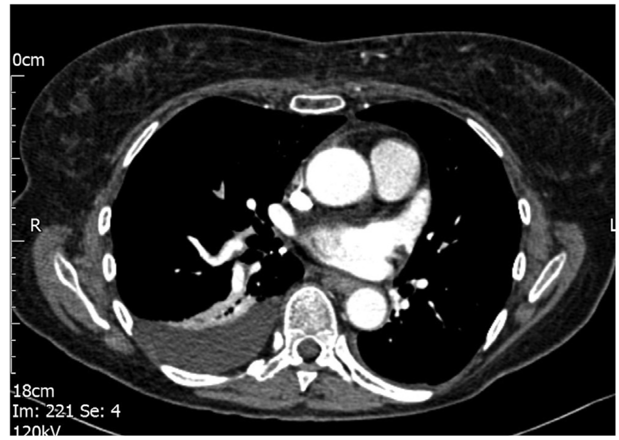

Figure 4 A postoperative CT scan showing a normal right-sided reactive pleural effusion following a right hemi-hepatectomy.

Wound infection

Surgical site infection typically occurs within the first 7 days postoperatively. This can range from mild cellulitis, which will settle with antibiotics, to deeper seated infection leading to wound dehiscence or requiring formal drainage. Subcutaneous haematoma or serous fluid accumulation may play a role in providing a nidus for the development of infection, and it is routine practice in our unit to place a suction drain in the subcutaneous space for 48–72 hours postoperatively to minimize this.

Systemic chemotherapy

Neoadjuvant chemotherapy plays a multifactorial role in the management of colorectal liver metastases. Preoperative chemotherapy can convert initially irresectable disease to a point at which potentially curative surgery could be considered. Preoperative chemotherapy also allows for a 'trial of time', with those liver lesions which progress during chemotherapy suggesting an unfavourable prognosis. Neoadjuvant chemotherapy has a role in the control of micrometastatic disease in patients with high risk features to their primary disease. In addition, perioperative chemotherapy may improve long-term outcome in patients presenting with resectable liver metastases.

In addition to the array of commonly reported chemotherapy side-effects, chemotherapeutic drugs are also known to have a hepatotoxic effect, some to a greater degree than others. Current first-line chemotherapy regimens in the UK include FOLFOX (5-FU, leucovorin and oxaliplatin), FOLFIRI (5-FU, leucovorin and irinotecan), FOLFOXIRI (5-FU, leucovorin, oxaliplatin and irinotecan) and XELOX (also known as CAPOX, capecitabine and oxaliplatin). Both oxaliplatin and irinotecan have specific hepatotoxic effects: oxaliplatin is known to cause sinusoidal obstruction syndrome (which can result in the appearance of a blue liver), whilst irinotecan leads to the development of fatty infiltration and scarring (steatohepatitis). Both cause an impairment of hepatic function, leading to an increased risk of transient liver insufficiency that will impair postoperative liver regeneration.

There is a relationship between the number of cycles of neoadjuvant chemotherapy and postoperative morbidity, with an increase in postoperative complications in those receiving greater than six cycles of chemotherapy prior to resection (54% vs 19%).[3]

Transarterial chemoembolization (TACE)

Transarterial chemoembolization involves catheter-delivered administration of chemotherapeutic agents and embolization material via the hepatic artery. The patient typically requires multiple procedures with at least two treatments to each tumour area and only delivered to one lobe at a time. Though initially used as a second-line palliative therapy in those patients showing progressive disease on systemic chemotherapy, it is now finding use in the neoadjuvant setting as a conversion therapy. The technique can be applied to metastatic lesions (colorectal, breast, neuroendocrine) and primary lesions (HCC and cholangiocarcinoma).

Traditionally TACE involved administration of the chemotherapeutic agent via the relevant hepatic artery branch followed by embolization to cause partial occlusion, thereby reducing blood flow and increasing the effective peri-tumour local concentration of the chemotherapy agent. More recently, drug-eluting beads (such as DEB-IRI beads which are loaded with irinotecan) have been used, which simplify administration through combining the chemotherapeutic and embolizing agent. The overall effect is one of prolonged and more targeted therapy to the relevant lesion, with the microbeads continuing to release drug post-procedure and there being lower collateral exposure to healthy liver tissue.[16]

Postembolization syndrome is common and is characterized by abdominal pain, mild pyrexia, fatigue, nausea and vomiting and a transient derangement of liver function tests and may be related to chemotherapy side effects, tumour necrosis or the effects of embolization. It is common practice for patients to be admitted overnight following treatment to ensure adequate initial analgesia. Later potential complications include arterial thrombosis, gastritis, gastrointestinal haemorrhage, liver abscess and bleeding from the arterial puncture site.

Ablative therapies

Ablation techniques are recognized in having a role in the treatment of inoperable liver metastases. In addition, patients who have small volume resectable disease but are unfit for major surgery should be considered as possible candidates for ablation, as should those who would be left with insufficient functional liver volume following surgical resection. Ablation can be combined with surgical resection for patients with multiple or bilobar liver metastases to reduce the morbidity associated with more major hepatic resection.[17] Ablation techniques can be applied percutaneously in the interventional radiology setting under CT or ultrasound guidance, or intra-operatively using ultrasound to locate the target lesion.

Radiofrequency ablation (RFA)

Radiofrequency ablation (RFA) uses direct current transmission through tissue to generate heat and cause tumour ablation. As the size of the lesion increases, there is an exponential rise in the resistance to current and its efficacy decreases in lesions with a diameter greater than 3 cm. It is less successful if the target lesion is close to a major vessel, as the intended tumour heating effect is reduced by the “heat sink” phenomenon where nearby flowing blood causes a cooling effect, limiting the effectiveness of the ablation. Local recurrence rates are high (10%−31%).

Microwave thermal ablation (MWTA)

Microwave ablation (MWTA) is a newer option in the ablative therapy armamentarium. Electromagnetic waves agitate water molecules to produce friction and heat leading to tissue necrosis. When compared with RFA, MWTA produces higher intra-tumoural temperatures, allows faster ablation times, causes less pain and is suitable for larger lesions (up to 6 cm diameter). There is less of a heat sink effect and it is more suitable for lesions in the vicinity of large vasculature.

Both techniques for thermal ablation carry risks of bleeding (Figure 5) or infection and abscess formation (Figure 6). Bleeding may require control by embolization and abscesses should be drained if of a significant size. It can sometimes be difficult to distinguish abscess from the ablation zone and in cases of doubt, MRI or ultrasound can be helpful. Ablation of lesions close to biliary structures may result in delayed ischaemic strictures, which may require dilatation, stenting or reconstruction, depending on their location and ablation close to blood vessels can lead to thrombosis. Generally, complication rates are lower for microwave ablation, than for RFA and local recurrence rates are also lower.[17]

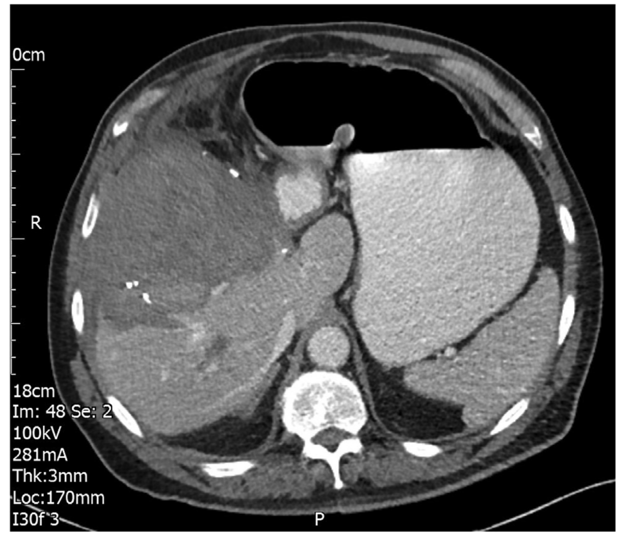

Figure 5 A post-procedure CT scan showing a significant arterial bleed following microwave ablation of a recurrent colorectal liver metastasis. This episode was successfully treated by catheter embolization.

Irreversible electroporation (IRE)

Irreversible electroporation (IRE) is the newest ablative modality, whereby an electrical charge is passed through a tumour between paired needle electrodes, which causes irreversible pores to open up on the tumour cell membrane resulting in cell death. The process is slower than the other ablative techniques, partly due to the time taken for accurate electrode placement and partly due to the speed of delivery of the energy, which is synchronized with cardiac electrical activity. It has the advantage of causing very little collateral damage to surrounding tissues and there is no “heat-sink” effect so it can be used to treat lesions close to

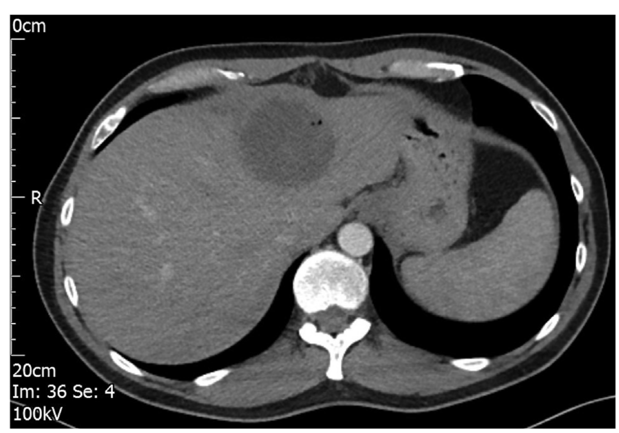

Figure 6 A post-procedure CT scan showing a significant liver abscess at the site of a previous microwave ablation of a colorectal liver metastasis. The abscess caused compression of the left portal vein and was successfully treated by percutaneous drainage.

major structures, however the technique is not haemostatic and so there is a higher risk of bleeding.

Radiation therapies

Selective internal radiation therapy (SIRT)

SIRT is a method of delivering localized radiation therapy using a radioactive isotope such as yttrium-90 (Y-90) bound to microspheres. These are selectively delivered to the tumour via intra-arterial injection in a similar principle to TACE, hence it is sometimes referred to as radioembolization. SIRT allows a higher radiation dose to be delivered to the tumour and means that there is less collateral absorption of radiation by normal liver tissue. Y-90 has a half-life of 2.67 days and 94% of the radiation dose is delivered within 11 days of administration.

SIRT can cause non-specific symptoms of transient abdominal pain, nausea, pyrexia, fatigue and anorexia in around one-third of patients, these are predominantly transient and self-limiting. Inadvertent reflux of Y-90 microspheres into the gastroduodenal vasculature can cause ulcer formation or ischaemic cholecystitis (10.3% in one series).[18]

Radioembolization-induced liver disease is characterized histopathologically by sinusoidal obstruction and clinically by jaundice and ascites, and can occur between 4 and 8 weeks post-procedure. The risk of developing radioembolization-induced liver disease appears to be higher when there is a lower tumour volume relative to normal liver. Reported rates have been 13.6%–20% in small series. In most cases the ascites can be medically managed with diuretics.

Stereotactic ablative radiotherapy (SABR)

SABR, also referred to as stereotactic body radiotherapy (SBRT), is a recent addition to the treatment options for colorectal liver metastases. Traditionally, external beam radiotherapy to the liver was considered only in a palliative setting for symptomatic relief of painful liver metastases, with its use as a therapeutic modality being limited by the low tolerance of the liver to high-dose irradiation.

Using conventional radiotherapy techniques, the radiation dose required to effectively treat metastatic disease carried a high risk of radiation-induced liver disease (RILD) and as such it was not a viable treatment option. However, with technological advances in external beam radiotherapy treatment planning software, as well as improved methods of delivering the radiotherapy using image guidance, it is now possible to create highly focused treatment fields. By delivering radiation therapy that is highly-conformed to the target liver lesions, SABR enables the precise delivery of higher, ablative doses of radiation in fewer fractions, thus minimizing the radiation dose delivered to surrounding healthy liver parenchyma and substantially reducing the risk of RILD. Side effects of this treatment include nausea and vomiting, fatigue, overlying skin erythema, chest wall or upper abdominal pain, transient transaminitis, GI ulcers and thrombocytopenia.[19–21]

Summary

Advances in technology and techniques have allowed an ever-increasing number of patients with liver metastases to benefit from a range of radical or palliative treatments with significant chance of cure or extension of survival. Interventions have however become more complex and are now inevitably delivered in specialist centres. Many of the common complications of the treatment of liver metastases will relate to septic events or haemorrhage and most can be managed either conservatively or by interventional radiology, however early involvement of the specialist centre should be sought when these patients are admitted to local hospitals. ◆

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Practice points

- Liver resection is the gold standard treatment for patients with colorectal liver metastases, provided the patient is fit for surgery and the volume and distribution of disease makes it “resectable”, with or without adjuncts for increasing the size of the future liver remnant.
- Where liver resection is not an option, many other treatments are increasingly available — systemic chemotherapy, transarterial chemoembolization (TACE), ablative therapies and radiation therapies — that aim to improve quality of life as well as prolonging survival.
- Patients with complications following treatment of their liver metastases may present to their local hospital rather than a specialist HPB unit; it is therefore vital that local teams recognize any complications promptly, to enable appropriate treatment to begin in a timely manner.
- Fluid collections at the site of liver resections are quite normal and do not necessarily need to be drained. Patients presenting with postoperative collections should be discussed with their liver centre prior to percutaneous drainage wherever possible.
- Most bile leaks settle spontaneously and with careful monitoring can be managed conservatively — occasionally they may require interventional procedures, but it is rare for a patient to need to return to theatre.
- Postoperative liver insufficiency is potentially life-threatening and management is supportive, so prompt identification and involvement of relevant specialties such as critical care are central to giving the patient the best chance of recovery.

