Imaging of liver metastases (CT scan, MRI, PET scan)

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The early detection of metastatic disease in colorectal cancer either at initial presentation or during follow up has been shown to benefit patients. This is because surgical resection for small volume isolated metastases can be curative and early detection of such disease improves the chances of cure. Even after metastatectomy, continued surveillance is worthwhile since repeat resection for recurrent disease is associated with favourable long-term survival [1–3]. The percentage of patients in whom long term cure is achievable following resection of metastatic disease in lungs or liver has increased in recent years and there is a continuing trend of improving survival and cure rates. Technological advances in imaging have played an important part in contributing to this improvement. This has been achieved through more accurate preoperative imaging leading to rigorous patient selection [4–6].

The relative merits of intensive image based follow up versus a less intensive method have been subject to debate. The evidence base however appears to favour more intensive follow-up. For example, a meta-analysis suggested that more intensive follow up combining CEA monitoring, outpatient clinical assessment and yearly CT scanning improves survival compared with less intensive follow up that does not utilise CT imaging [7]. The meta-analysis showed that intensive follow up was associated with a reduced time to first relapse and significant absolute reduction in mortality rate of 9–13%. Since these trials pre-dated the current wider trend of more aggressive hepatic resections and the use of combined therapies which, in their own right, have improved survival it is likely that the potential survival benefit from intensive follow up may be even greater than identified in the meta-analysis. The American Society of Clinical Oncology has made the following recommendations:

– Annual computed tomography (CT) of the chest and abdomen for 3 years after primary therapy for patients who are at higher risk of recurrence and who could be candidates for curative-intent surgery
– Pelvic CT scan for rectal cancer surveillance, especially for patients with several poor prognostic factors, including those who have not been treated with radiation
– Colonoscopy at 3 years after operative treatment, and, if results are normal, every 5 years thereafter; flexible proctosigmoidoscopy every 6 months for 5 years for rectal cancer patients who have not been treated with pelvic radiation
– History and physical examination every 3 to 6 months for the first 3 years, every 6 months during years 4 and 5, and subsequently at the discretion of the physician
– Carcinoembryonic antigen every 3 months post-operatively for at least 3 years after diagnosis, if the patient is a candidate for surgery or systemic therapy
– Chest x-rays, CBCs, and liver function tests are not recommended, and molecular or cellular markers should not influence the surveillance strategy based on available evidence.

The liver is not only the most frequent site of metastatic disease but the sole site of metastasis in up to 30–40% of colorectal patients. Metastatic disease to the lungs occurs in (15%), followed by ovarian metastases (6–8%) [8], bones (5%) and brain. The spleen, kidneys, pancreas, adrenals, breast, thyroid and skin are rarely involved.

In selecting patients for curative hepatic resection thin collimation CT or MR imaging of the liver with liver specific contrast agents are of critical importance in delineating the distribution of metastases and assessing overall resectability. MR imaging has a further important role to play in characterising co-existing benign lesions.

In preoperative assessment of liver metastases, the following should be taken into account:

– Accurate delineation of anatomical distribution of metastases and segmental sparing in patients undergoing hepatic resection
– Confirmation of absence of widespread multi segmental micro metastatic disease within the liver
– Confirmation of absence of extra hepatic disease
– Discrimination between coexisting benign lesions and metastases

The trend in improved survival following treatment for colorectal hepatic metastases may be attributed largely to improved techniques of anatomic resection [9–11], the availability of intraoperative ultrasonography [12,13], decreased mortality and morbidity in the perioperative period [4], the use of second hepatic resections [14] and the use of chemotherapy [15–18]. The prognostic factors governing survival have been evaluated in a number of series but one of the largest was undertaken by Fong and colleagues based on experience of 1001 patients [19]. These have been recommended as method of assigning a clinical risk score with absence of any of these risk features conferring the highest survival advantage (60% 5 year survival) and four or more risk factors associated with poor (<20% 5 year survival): Clinical Risk Score

- Size >5cm
- Potential resection margin involved
- >1 metastasis within liver
- Poor prognosis primary
- Synchronous primary/liver met <12 months
- Extrahepatic disease

All of these prognostic factors should be assessable by detailed preoperative imaging which should enable rigorous patient selection; furthermore, intraoperative ultrasound has an important role in enabling precise localisation and anatomic resection of lesions with tumour free resection margins.

Extrahepatic disease

It has been shown that patients with solitary unilobar tumours rarely have unrecognised irresectable disease whereas patients with multiple bilobar tumours are at significantly higher risk of occult hepatic and extrahepatic disease [20]; these issues may influence the choice and intensity of preoperative imaging investigations. The main tools for detecting coexisting extrahepatic disease are PET imaging, CT and laparoscopy. Each is complementary and it is important to recognise that each has their limitations and no single technique will identify all instances of extrahepatic disease.

Serial CT examinations of patients after colorectal cancer remains the most frequent follow up imaging modality and careful comparison of serial studies allows the distinction between benign non-malignant lesions in lung and liver. In many cases, the unequivocal demonstration of extrahepatic sites of disease by CT or multifocal irresectable liver disease will rule out hepatic surgery in the first instance. For the patients who appear potentially resectable following CT assessment, preoperative FDG-PET has the greatest potential to alter outcomes by detection of extrahepatic disease not found on conventional imaging [21]. By using FDG-PET imaging to select out patients with extrahepatic disease, unnecessary surgery was prevented in 6/43 patients [21]. The precise anatomic location of intrahepatic metastases was not always possible however using PET scanning. This may result in exclusion of such patients for resection. On the other hand, the demonstration of isolated extrahepatic disease by PET may result in multiple resections (for example lung metastatectomy and liver resection) that may potentially result in cure.

There are however some limitations of PET and CT imaging particularly in their ability to identify small volume peritoneal disease and surface disease on the liver.

In such patients, laparoscopy and intraoperative ultrasound may be the only methods of identifying these types of spread. Finally, there is evidence to suggest that the risk of extrahepatic disease is so low in patients with a clinical risk score of zero that the use of 18FDG-PET in these circumstances is of limited value and has been shown to incorrectly upstage patients undergoing curative resection [22]. The authors suggested that 18FDG-PET should be reserved for those patients with a Fong clinical risk score of 1 or more.

CT detection

Colorectal carcinomas metastasise to the liver by means of the portal venous system however they receive their blood supply from the hepatic artery [23]. CT, performed during peak level of hepatic parenchymal enhancement will identify the vast majority of colorectal metastases and for many institutions is the modality of choice for the surveillance of patients at risk of developing liver metastases. The technique exploits the relative hypovascularity of colorectal neoplasms compared with normal parenchyma and results in accuracy rates of up to 85% (sensitivity 70%, specificity 94%) [24].

MRI detection of liver metastases

MRI assessment

The workhorse of liver imaging is the T1 weighted gradient echo sequence. It allows rapid imaging of the liver in a single breath-hold and can be acquired as a volume in axial or coronal planes enabling precise anatomic localisation of lesions.

The recommended routines include a T1 weighted GRE. T2 weighted sequences will further aid characterisation and T1 in and out of phase imaging are also rapid sequences which exploit the behaviour of fat containing tissues during in and out of phase imaging. The sequence thus provides a useful means of further assessing apparent 'perfusion defects' seen on CT which in some instances may be due to focal fatty infiltration.

The increased sensitivity and specificity afforded by both superparamagnetic iron oxide (SPIO) and Mangafodipir as liver specific agents has led to the more widespread use of MRI in the preoperative assessment of patients with liver metastases. One of the first of such liver specific agents to be evaluated was SPIO. Intravenous infusion of this agent results in uptake by functioning Kupffer cells and darkening of the liver on MR imaging. Thus metastases that do not contain Kupffer cells fail to take up this contrast and are shown up as relatively hyperintense lesions on SPIO enhanced T1 weighted gradient echo images. MRI has shown considerable promise in overcoming the challenge of identifying lesions <1 cm preoperatively and in a study evaluating the clinical impact of preoperative assessment using SPIO compared with CT arterioportography, it was shown that this technique was at least as accurate as spiral CTAP. Mangafodipir trisodium (Mn-DPDP), is taken up by the functioning hepatocytes and excreted by the biliary system. Contrast uptake leads to persistent elevation of T1-weighted signal of normal liver parenchyma within 10 min of injection. Comparison of T1 weighted images before and after administration of this agent shows a 100% increase in the signal to noise ratio of the liver and a 400% increase in conspicuity between the hypointense liver metastasis and surrounding parenchyma [25,26]. When compared with CT the use of liver specific agents increases the sensitivity and accuracy of detection of metastases. Recent findings suggest that Mn-DPDP MRI is more sensitive than spiral contrast enhanced CT in the preoperative prediction of the resectability of hepatic lesions [27].

Conflict of interest statement

None declared.

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