Diagnostic performance of contrast-enhanced US in the detection of liver metastases from colorectal cancer

Lars P. Larsen
Department of Diagnostic Radiology, Aarhus University Hospital, Aarhus, Denmark

Introduction

A characteristic feature of all liver metastases is neoangiogenesis, which guarantees the tumour an adequate flow of blood from the hepatic arterial supply. Liver metastases typically develop new microvasculature internally while larger supplying and draining vessels tend to be found in the tumour’s periphery. These lesions are classified into two types depending on the extent of neoangiogenesis, extend of arterial perfusion and thus on their appearance during contrast-enhanced ultrasonography (US). Hypovascular metastases develop mainly from adenocarcinoma or squamous cell carcinoma and from tumours of the gastrointestinal system, pancreas and ovaries. Hypervascular metastases instead develop from neuroendocrine tumours melanoma malignant and sarcoma, from thyroid and renal cancer, and from about 25% of patients with breast cancer.

During contrast-enhanced US, both hypo- and hypervascular metastases exhibit faster uptake of contrast medium than the surrounding liver tissue and thus appear brighter during the arterial phase (Fig. 1). Hypervascular metastases appear intensely bright while hypovascular metastases exhibit mostly rim enhancement. During the portal venous and late phases, the contrast medium is washed out faster in both types of metastases than in the surrounding tissue, due to the mainly arterial supply in metastases so they appear as dark “enhancement defects”; hypovascular metastases also lose the rim sign.

Accurate investigation for liver metastases in patients with cancer requires an optimized examination:

- The conventional (B-mode) US examination must be performed skillfully and all lesions (typically cysts) identified during this examination must be reexamined after contrast medium administration.
- For best signal detection during contrast-enhanced US, it is important to place the patient correctly so that the liver is close to the front abdominal wall. Since a typical US probe detects contrast medium at a distance of up to 14 cm (penetra-
tion), the possibility of screening the entire liver is increased if patients lie partially on their left sides (Fig. 2).

- The focus of the US probe must be optimal: to image deep parts of the liver, the focus must be changed to the deep area of interest.
- The acoustic pressure also has to be adjusted. For normal CEUS imaging, this is achieved with a low mechanical index (MI) of 0.1-0.2. In obese patients, initial imaging is done with normal low MI but, towards the end of the examination, MI is increased to about 0.3 to improve imaging of deep parts of the liver (e.g. segments 7 and 8).

Fig. 1 a–c. Contrast enhancement of hyper- and hypovascular liver metastases.  

- Hypervascular 
- Hypovascular

Fig. 2. Correct patient positioning for a contrast-enhanced US examination of liver. In this position, the liver is close to the front abdominal wall and penetration of the ultrasound wave through the entire liver is likely.

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Contrast-enhanced US detection of metastases from colorectal cancer

Liver metastasis is a common manifestation of colorectal cancer: 15%-25% of patients already have liver metastases at the time of detection of the primary cancer and another 15%-25% will develop liver metastases after radical surgical excision. Various therapies are available for colorectal metastatic disease, including liver resection, radiofrequency ablation, irradiation and chemotherapy. Correct preoperative staging is crucial for an accurate prognosis and for choosing the most appropriate therapy.

Currently, the search for liver metastases in these patients is done with different imaging techniques, including conventional and contrast-enhanced US, intraoperative and laparoscopic US, CT with arterial portography, multidetector CT, MRI, PET and combined PET-CT. Among these techniques, the most sensitive are intraoperative US and CT with arterial portography. However, for preoperative screening, there is some debate as to the most sensitive technique, as reported rates vary according to the studied patient populations and the diagnostic method used as gold standard.

Therefore, my colleagues and I set out to determine the value of contrast-enhanced US as a preoperative screening method in a normal clinical situation consisting of patients with suspected or known colorectal cancer but without a previous liver examination for metastasis disease [1]. We compared the diagnostic value of contrast-enhanced US to that of conventional US, and used as gold standard the combination of multidetector CT, intraoperative US, cytological analysis and clinical follow-up.

A total of 461 patients were referred for analysis over a 2-year period. Of these, 45 (10%) did not meet inclusion criteria and were excluded, and 51 (11%) missed because of logistical reasons. Therefore, 365 patients entered the study and underwent imaging by conventional and contrast-enhanced US as well as multidetector CT. Of these, 239 also had intraoperative US. The combined gold standard indicated that 54 patients had liver metastases.

Considering the 365 patients who entered the study, liver metastases were diagnosed with conventional US in 37 of the 54 patients with gold standard-diagnosed disease (sensitivity, 69%). This same imaging technique predicted no metastatic disease in 305 of the 365 patients without gold standard-diagnosed disease (specificity, 98%). When contrast-enhanced US was used, the sensitivity increased to 80% (43 of 54 cases identified) while the specificity was similar (304 of 311 cases, 98%). The difference in sensitivity between conventional and contrast-enhanced US was significant ($p=0.031$) and resulted in 6 additional diagnoses of metastatic disease in patients with small lesions. Compared to the gold standard, contrast-enhanced US failed to detect 11 patients with metastatic disease; most of these cases were also misdiagnosed with multidetector CT.

This study found that contrast-enhanced US is superior to conventional US in the detection of liver metastases from colorectal cancer. It detects significantly more patients with liver metastasis and it has a higher sensitivity (69% vs. 80%). The results...
are in accordance to earlier studies [2-4]. A limitation of this study is the fact that intraoperative US was not performed in all patients, mostly due to interference by adhesions in patients who had previously undergone abdominal surgery.

References