The role for contrast-enhanced ultrasonography outside of focal liver lesions

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Introduction

Contrast-enhanced ultrasonography (US) of focal liver lesions using microbubble contrast medium is a well established diagnostic imaging method in Europe, Japan and China, but it is not yet authorized for clinical use in the United States. Hundreds of medical papers have been published regarding research that used Levovist (approximately 850 papers), SonoVue (350 papers) and Definity (100 papers). Guidelines for the use of contrast-enhanced US, with a focus on focal liver lesions, were published in 2004 by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) [1]. A general introduction to the use of contrast-enhanced US in focal liver lesions was recently published by my colleague Berry and myself [2]. Nonetheless, there are many possible uses of contrast-enhanced US outside of focal liver lesions; this paper highlights the most established applications as well as some innovative ones.

Other liver applications of contrast-enhanced US

Contrast-enhanced US can be used to investigate abnormalities of the portal vein. For example, thrombus in the portal vein is found in 5%-10% of patients with end-stage cirrhosis. Although not a contraindication to liver transplant surgery, the presence of portal vein thrombosis must be determined before surgery. Moreover, thrombosis in the portal vein may indicate the presence of a hepatic tumour, such as hepatocellular carcinoma. Portal hypertension, which may cause slow blood flow or counter-current flow (“yo-yo flow”), is another condition that must be investigated prior to liver transplantation. Such slow flow is not detectable with Doppler US or CT but is easily revealed with contrast-enhanced US [3].

In patients with transjugular intrahepatic porta-systemic shunts, contrast-enhanced US is an ideal technique to assess shunt patency, as the passage of microbubbles through the shunt is a clear indication of even small amounts of blood flow.
Assessment of the hepatic artery in liver transplant recipients

A patent, functioning hepatic artery is crucial to the viability of a transplanted liver. Loss of patency of the hepatic artery requires urgent surgery to prevent biliary ischaemia and failure of the transplant. Conventional methods to assess hepatic artery patency include colour Doppler US, angiography and CT angiography. Hepatic artery thrombosis is a common complication of liver transplantation, and is found in 7%-12% adult recipients and in 11%-42% of child recipients, due to their narrower arteries.

At King’s College Hospital, we regularly use US to assess transplanted livers and especially the hepatic artery in these patients. Patients are assessed 3-4 times before discharge. In 96% of patients, colour Doppler US is sufficient to document patency of the artery. Over a 2-year surveillance period, we used US to investigate hepatic artery patency in 231 liver transplant recipients (794 examinations) [4]. Colour Doppler US documented a patent hepatic artery in 759 examinations (200 patients), while the artery was not seen in 35 examinations (31 patients). These patients with suspected thrombosis underwent contrast-enhanced US, which documented a patent hepatic artery in 19 cases. Of the remaining 12 patients, eight underwent arteriography which showed thrombosis in 7 patients and a patent but highly attenuated artery in another. This study suggests that the use of contrast-enhanced US after inconclusive US examinations can reduce the need for invasive arteriography.

Not only thrombosis but also stenosis of the hepatic artery can lead to transplant failure. The incidence of this complication, which is often due to inadequate surgical technique, is approximately 4%-11%. Stenosis typically occurs at the site of arterial anastomosis. It compromises blood supply to the biliary system, and can cause hepatic infarction, sepsis, abscess, bile leak, strictures, and ultimately transplant failure. A characteristic imaging feature of hepatic artery stenosis is the tardus parvus waveform seen on colour Doppler US [5]. With modern techniques of contrast-enhanced US, such as contrast pulse sequencing (CPS), it is possible to visualize the area of stenosis and to document increased velocity through the stricture (Fig. 1).

**Fig. 1 a, b.** Hepatic artery stenosis. a Colour Doppler US image and corresponding tardus parvus waveform on the spectral waveform trace. b Contrast-enhanced US image of stenosed hepatic artery (arrow)
Hepatic artery pseudoaneurysm is a rare complication of liver transplantation that may occur at the anastomotic site or may be intrahepatic (at a biopsy site). In our series of 1327 liver recipients over 10 years, we observed pseudoaneurysm in 1% of cases, and mortality was high (69%). Treatment is by coil embolization but retransplantation is often required. Contrast-enhanced US can be used to assess the pseudoaneurysm and to immediately determine if coil embolization was successful [6].

**Carotid, aorta and peripheral arteries**

While colour Doppler US and angiography are the standard imaging techniques for assessing the large vessels, contrast-enhanced US can provide additional information about an arterial lumen. In the carotid, contrast-enhanced US may show fine details of the internal wall and highlight pathologies such as plaque and stenosis. In the future, this imaging method may become a complementary tool to colour Doppler US.

Contrast-enhanced US may also prove to be the most sensitive imaging method for assessing the outcome of treatment of aortic aneurysms by endovascular aortic repair (EVAR). The continued flow of blood into the aneurysmal sac after placement of a graft or stent is considered a procedural failure, called endoleak. Patients with treated aneurysms require life-long surveillance for early detection of endoleaks. Surveillance imaging is routinely done with CT, but contrast-enhanced US is an attractive alternative for its high sensitivity to small amounts of blood flow and its lack of ionizing radiation.

**Renal diseases**

Applications of contrast-enhanced US in the kidney include the evaluation of renal artery stenosis, pseudotumours, solid tumours and cystic lesions. Pseudotumours, which are variants of normal tissue, include lobar dysmorphism, hypertrophic column of Bertin, foetal lobation and the dromedary (or splenic) hump. These variants can be reassuringly diagnosed with contrast-enhanced US and distinguished from solid tumours on the basis of vascularity.

Cystic renal masses are usually diagnosed on the basis of CT findings according to the Bosniak classification, but diagnosis is difficult for complex cysts. Contrast-enhanced US, with its large images filling the screen in real time, may be a valid alternative for assessing cyst morphology. A recent study [1] found good concordance between CT and contrast-enhanced US in the classification of complex renal cysts and suggested that the latter technique is appropriate for diagnosing this pathology according to the Bosniak classification. Furthermore, contrast-enhanced US (but not CT) can delineate septations within cysts and demonstrate the extent of vascularity in the septae (Fig. 2). Over the coming years, a fully US-based classification of renal cystic masses may be developed.
Gallbladder and spleen

Contrast-enhanced US may provide accessory information regarding gallbladder pathology (Fig. 3). In particular, by revealing vascularity, it can distinguish sludge and cholesterol deposits from vascular tumours and polyps. It can clearly diagnose acute cholecystitis by showing inflammation of the gallbladder wall as a rim of intense contrast enhancement.

Diagnosis of splenic pathology has benefited from the use of US contrast agents. Splenunculus, or accessory spleen, is a common finding in the normal population. Splenunculus may be single or multiple, but always less than a few centimeters in diameter. This normal variant may be mistaken for lymphadenopathy or a mass in the pancreatic tail, but on contrast-enhanced US or CT it will have an imaging appearance similar to normal spleen. Other diagnostic applications of contrast-enhanced US in the spleen regard metastasis, infarct and abscess (Fig. 4).

Other areas of investigation

There are many other areas, particularly in the abdomen, where contrast-enhanced US can be useful. These may include the study of pancreatic, ovarian and prostatic tumours, bowel ischaemia, Crohn’s disease, vesico-ureteral reflux, breast tumours (and associated lymph nodes), and inflammatory joint disease. In Crohn’s disease, contrast-enhanced US shows florid inflammatory changes in a dilated bowel with thickened walls. Finally, in patients with abdominal trauma, contrast-enhanced US may help to identify lacerations and haematoma in liver, kidney and spleen.
Fig. 3 a–c. Gallbladder pathology shown by contrast-enhanced US. a Sludge seen on unenhanced US (left) is not vascularized (right). b Globular “deposits” attached to the gallbladder seen on unenhanced US (left) are vascularized (right) and thus diagnosed as multiple polyps. c Acute cholecystitis is seen as intense enhancement of the gallbladder wall (arrows)
References


Fig. 4 a, b. Splenic pathology revealed by contrast-enhanced US. a Splenic infarct in a patient with bacterial endocarditis: multiple areas of low enhancement are seen. b Splenic abscess in a patient with fever are seen as areas of liquefaction divided by vascularized septae.