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INTERVENTIONAL RADIOLOGY

TECHNICAL NOTE

Agitated saline sonography: a simple technique for intraprocedural feeder identification during transcatheter arterial chemoembolization of hepatocellular carcinoma

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ABSTRACT

Transcatheter arterial chemoembolization (TACE) is the most widely used treatment modality for patients with hepatocellular carcinoma who are not eligible for surgery. Selective tumor embolization is very important, more so in patients with mild to moderate liver cell failure, but determining feeder vessels could be difficult with two-dimensional angiogram alone. Cone beam computed tomography and detection software are available for intraprocedural accurate feeder vessel detection; however, these facilities are not widely available. We have evaluated and successfully applied a very simple technique using only a portable ultrasonography machine to ensure superselective feeder cannulation prior to embolization.

Transcatheter arterial chemoembolization (TACE) is an excellent treatment modality for patients with hepatocellular carcinoma not amenable for surgery or percutaneous ablation therapies (1–4). The success of TACE depends on selectiveness and adequacy of chemoembolic agent delivery within the tumor vascular bed, preserving maximal liver cell function. This becomes more important in patients with mild to moderate liver cell dysfunction (Child Pugh B). Arterial phase computed tomography (CT) is done as part of planning TACE to locate tumor, map feeder vessels, and look for extrahepatic tumor arterial supply (1). Intraprocedural catheter placement is routinely guided by two-dimensional cine and digital subtraction angiography acquisitions; however, confident superselective catheter placement cannot be possible with such guidance alone in certain situations (2–4). This problem has been overcome with the advent of cone beam (C-arm) CT and vessel detection software; however, they are not widely available (2–5). The cases presented here illustrate application of an easily available and simple method that uses a portable ultrasonography (US) machine for distinguishing tumor vessels from normal vessels prior to embolization.

Case 1

A 63-year-old male patient was admitted to our hospital with complaints of right-sided abdominal pain, and significant loss of appetite and weight. He was a known case of cirrhosis, and had been treated conservatively. He had laboratory and imaging features of moderate liver cell failure and was categorized under Child Pugh class B. Triphasic CT showed cirrhosis with two closely related lesions, one 8.2 cm lesion in segments IV A and VIII, and one 4.2 cm lesion in segment IV A and B (Fig. 1a). Arterial feeders could be traced from both left and right hepatic arteries. TACE was planned, and written informed consent was taken. Digital subtraction angiography (AlluraClarity, Philips Healthcare) of the common hepatic artery using a 5F SIM 2 catheter (Cook Inc.) showed tortuous vessels throughout the liver due to cirrhosis; and no definitive tumor blush could be identified (Fig. 1b). A Progreat microcatheter (Terumo Medical Corp.) was used to super-selectively cannulate the suspected feeders. A mixture of 2 mL of patient's blood, 2 mL of saline, and 0.5 mL of air agitated between two Luer Lock syringes (Nipro Medical Corp.) across a three-way stopcock was injected through the microcatheter, and the liver was visualized using a convex US probe (C5-1 Broadband Curved Array, CX50 CompactXtreme Ultrasound System, Philips Healthcare). Hyperechoic blood-saline-bubble mixture flowing through the branches of the cannulated vessel and further into the tissue bed could be seen clearly. Adriamycin 75 mg (DOXOrubicinHCl, Bedford Laboratories) charged Hepaspheres (BioSphere Medical) prepared an hour prior to the pro-

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cedure were mixed with contrast solution for embolization. Injection into a left hepatic branch arising from the proper hepatic artery showed elevated reflection of the segment IV B lesion and also of a rim of adjacent hepatic parenchyma (Fig. 2a, 2b), which was embolized. Injection into a branch of left hepatic artery showed elevated reflection of most of the central parts of the tumor (Fig. 2c, 2d) and was embolized. Injection into the right hepatic artery showed enhanced reflectivity of peripheral parts of the larger tumor and significant amount of adjacent liver parenchyma (Fig. 2e); further selective cannulation into the anterior branch was performed, supply to peripheral parts of the larger tumor without adjacent significant liver parenchymal echo enhancement was confirmed by injection of agitated blood-saline-air mixture (Fig. 2f) and was embolized. CT done the next day showed absent tumor enhancement and filling of tumor vessels, with preserved blood flow to the rest of the liver parenchyma.

Case 2

A 75-year-old male patient with early cirrhosis was referred to the interventional radiology clinic for TACE of the liver lesion. The patient had raised alpha-fetoprotein (3059 ng/mL), and a CT (done elsewhere) detected subtle hypovascular lesion in segment VIII of right lobe of the liver with segmental portal vein thrombosis (Fig. 3a). The patient had mild liver cell dysfunction (Child Pugh class A). CT also showed replaced right hepatic artery. The lesion could be seen on a screening US. TACE was planned and consent was taken. A 4F Cobra catheter (Cook Inc.) was used to cannulate the replaced right hepatic artery and further superselectively cannulate each of the two superiorly directed segmental branches. Angiography (AlluraClarity, Philips Healthcare) did not show a definite tumor blush, and two superiorly directed branches coursing towards the site of the lesion (Fig. 3b). An agitated mixture of 2 mL patient's blood, 2 mL saline, and 0.5 mL air was injected through the catheter into each of the two superior segmental branches while the tumor was insonated continuously with a convex probe (C5-1 Broadband Curved Array, CX50 CompactXtreme Ultrasound System, Philips Healthcare). Injection into the medial branch showed blood-saline-bubble mixture induced increased reflectivity of normal parenchyma away from the lesion (Fig. 3c) and injection of the lateral branch showed elevated reflection of the parenchyma around the tumor and mildly of the tumor (due to hypovascular nature) confirming it to be the feeder vessel (Fig. 3d); the vascular bed of this feeder vessel was embolized with 75 mg Adriamycin (DOXOrubicinHCl, Bedford Laboratories) charged Hepaspheres (BioSphere Medical) prepared an hour before starting the procedure.

Main points

- Selectivity in transcatheter arterial chemoembolization (TACE) is very important to deliver the desired dose of chemotherapeutic agent to the tumor and to preserve function of normal liver tissue, especially in patients with borderline liver dysfunction.
- Finding the feeding vessel can be difficult with 2D angiography when there are too many overlapping vessels; if the tumor is avascular or very small (tumor blush might not be seen), close to diaphragm (cardiac and respiratory motion artifact obscuring tumor blush), or within cirrhotic liver (normal vessels might be tortuous); or when there are non-neoplastic enhancing lesions.
- Incorporating cone beam CT within the interventional suite enables intraprocedural CT scan of the liver while injecting contrast within a particular vessel, thereby allowing confident identification of the feeder; however, this facility is not commonly available.
- Contrast-enhanced US with agitated saline injection through catheter can be applied in nearly all cases to provide similar information, since hepatocellular tumors are almost always visible on US.

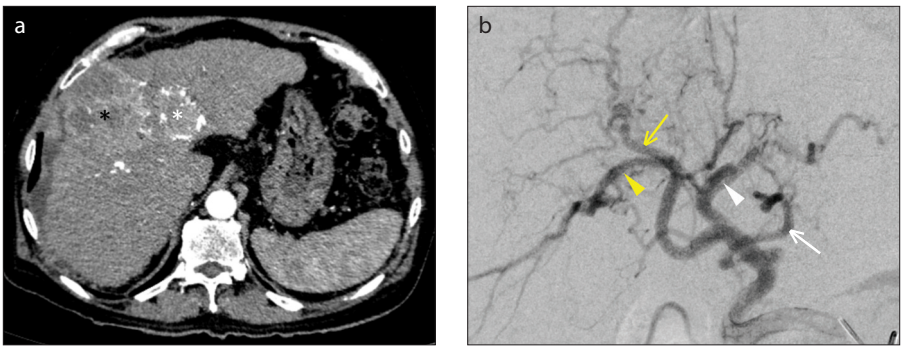

Figure 1. a, b. Axial CT in arterial phase through the liver **(a)** shows cirrhosis, a large centrally placed hepatocellular carcinoma *(black asterisk)* and a smaller carcinoma nodule *(white asterisk)* to the left of it. Digital subtraction angiography of the common hepatic artery **(b)** shows diffusely tortuous hepatic artery branches. Left hepatic arterial branch arising from the proper hepatic artery *(white arrow)*, left hepatic artery *(white arrowhead)*, anterior *(yellow arrow)* and posterior *(yellow arrowhead)* branches of the right hepatic artery are shown.

Discussion

TACE is a widely used treatment modality for hepatocellular carcinoma not amenable for surgery or percutaneous ablative treatments (1–4). Guidance to tumor vessels is usually by two-dimensional angiography, coupled with a prior knowledge of vascular anatomy based on an arterial phase multi-detector CT scan done before the procedure (2, 3). Accurate feeder vessel cannulation for embolization is required so that the intended dose of chemotherapeutic drug reaches the tumor and maximum residual liver parenchymal blood supply is preserved (2, 4). Liver tissue preservation is especially important in patients who already have mild to moderate liver cell dysfunction, where inadvertent necrosis can land the patient in hepatic encephalopathy. However, accurate intubation of tumor feeder is sometimes not possible with two-dimensional angiography when the tumor is hypovascular, in the presence of enhancing nontumor nodules, overlapping vessels, or breathing artifacts, when lesions are small or located near the diaphragm, or background liver is cirrhotic resulting in tortuous vessels and inhomogeneous enhancement throughout the liver (2–4). These problems have been circumvented with the advent of cone beam or C-arm CT, which provides CT sections of the liver intraprocedurally, enabling confident labeling of a particular cannulated vessel as tumor feeder, when the CT is performed while injecting contrast through the catheter (2–5). Such a facility is not available widely (3), and performing an actual CT in between the procedure by shifting the patient to a CT facility is extremely cumbersome and fraught with possibility of puncture site complications and catheter displacements (3).

Contrast-enhanced US with an agitated mixture of saline, blood, and air provides

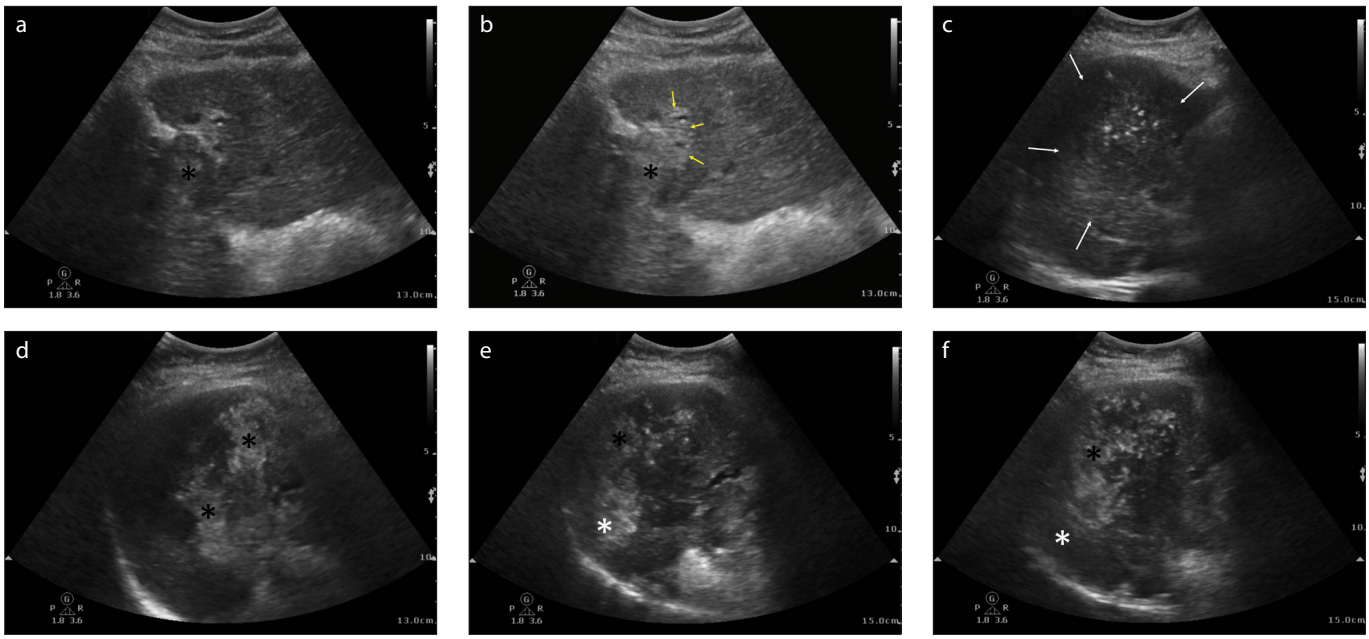

Figure 2. a–f. US images of the smaller lesion before **(a)** and during **(b)** injection of blood-saline-air mixture into the left hepatic arterial branch arising from the proper hepatic artery show increased reflectivity of the entire smaller lesion *(black asterisk)* and of a thin rim of adjacent liver parenchyma *(yellow arrows)*. US images of the larger lesion before **(c)** and during **(d–f)** blood-saline-air mixture injection. Panel **(c)** shows the heterogeneous lesion (*white arrows* along the margin) before injection; panel **(d)** shows increased reflectivity of most of the lesion *(black asterisks)* except for the superolateral peripheral parts during injection into the A4 segmental branch of left hepatic artery; panel **(e)** shows enhanced reflectivity of the superolateral peripheral parts of the lesion *(black asterisk)* and liver parenchyma *(white asterisk)* during injection into the right hepatic artery; panel **(f)** shows isolated echo enhancement of the peripheral parts of the lesion *(black asterisk)* and not of the adjacent liver parenchyma *(white asterisk)* during injection into the anterior branch of right hepatic artery.

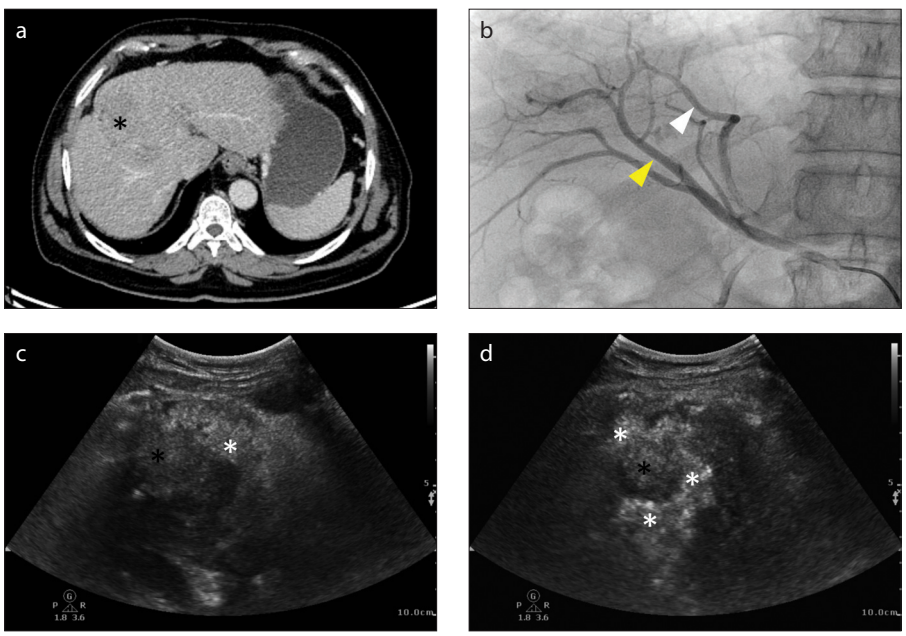

Figure 3. a–d. Contrast-enhanced CT scan of the liver. Axial section **(a)** shows a subtle hypovascular lesion *(asterisk)* in the segment VIII of right lobe. Right hepatic angiography image **(b)** shows two major superiorly directed vessels *(white and yellow arrowheads)* coursing towards the suspected lesion location. US image **(c)** of the right lobe taken during injection of blood-saline-air mixture into the medial of the superiorly directed branches shows echo enhancement of liver parenchyma *(white asterisk)* away from the lesion *(black asterisk)*; and the same section taken during injection into the lateral of the branches **(d)** shows enhanced reflectivity of the parenchyma around the tumor *(white asterisks)* and mildly enhanced reflectivity of the tumor *(black asterisk)*.

similar information and can be applied in nearly all cases since hepatocellular tumors are almost always visible on US (6). Injection of the agitated mixture through the catheter causes bubble-induced increased reflectivity of the vessels and vascular bed that it passes through, because bubbles are more than million times effective at scattering sound waves with to red blood cells and hence enormously augment the blood pool signal (7), seen as bright echoes in two-dimensional US. This technique has popularly been used in echocardiography, especially for the detection of cardiac or extracardiac shunts (7). Addition of blood to saline for agitating with air increases the viscosity, enabling more microbubbles to be trapped in the solution for a longer time (8, 9) and increasing visibility of the bubbles. The echo augmentation of the vascular bed is temporary as the bubbles either flow away to the pulmonary circulation to get excreted or get disrupted by ultrasound waves (10). US contrast is prepared by agitating a mixture of 2 mL saline, 2 mL patient's blood, and 0.5 mL air between two Luer Lock syringes (to prevent accidental spray of blood) across a partially open (lever rotated 30°) three-way stopcock. The agitated mixture has to be used immediately after preparation since bubbles coalesce rapidly to form larger bubbles. This technique is very simple with requirements that are universally available; and it does not induce any additional complications (9). Such successful usage of agitated blood-saline-air mixture for confident intraprocedural feeder vessel identification

in TACE has not been previously described in the literature.

In conclusion, our experience showed that agitated blood-saline-air mixture transcatheter injection enables confident identification of tumor feeder intraprocedurally during TACE with no additional risk.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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