Contrast-Enhanced Intraoperative Ultrasonic Cholangiography for Real-Time Biliary Navigation in Hepatobiliary Surgery

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Recent progress in medical technology, perioperative management, and surgical technique has contributed greatly to the safety of hepatobiliary surgery.[1,2] In particular, imaging techniques, including intraoperative imaging, have played a major role in advancing the success of these operations. Precise assessment of biliary anatomy before and during surgery reduces biliary complications.[3] More than 42% of the population is reported to have anatomical variations of the biliary tree.[4] If a biliary anatomical variation is suspected before surgery, confirmatory intraoperative cholangiography (IOC) is recommended.[5,6]

Using radiography and iodinated contrast medium, IOC was first reported by Mirizzi[7] in 1937 and has been widely used to define the biliary tree in surgery for benign and malignant diseases. However, radiographic IOC has several drawbacks; it exposes patients and medical staff to radiation, it requires a large C-arm machine for fluoroscopy and an attendant to operate it,[8,9] and it requires special techniques to generate 3-dimensional (3D) images. Intraoperative ultrasonography, specifically, contrast-enhanced intraoperative ultrasonic cholangiography (CE-IOUSC), can address these issues.

Intraoperative ultrasonography has become an essential tool for the identification of intrahepatic vessels, tumor location, and definition of surgical margins for safe and effective hepatic surgery.[10-12] Its diagnostic accuracy has been enhanced by the introduction of intravascular ultrasound contrast agents.[13,14] However, it is still limited in visualization of nondilated bile ducts.

Recently, some authors have attempted to perform ultrasonic cholangiography with intrabiliary injection of an ultrasound contrast agent via various routes, including percutaneous transhepatic biliary drainage tube, T tube, and transcystic catheter.[15-20] Their aim was visualization of the biliary tree or evaluation of bile duct anastomosis after surgery. The use of intraoperative ultrasonic cholangiography has not been elucidated. In this study, we demonstrate the usefulness of CE-IOUSC using an ultrasound contrast agent as a tool for real-time intraoperative biliary navigation.

METHODS

From April 2012 to March 2013, twenty-three patients were scheduled to undergo hepatobiliary surgery for the following indications: 16 for hepatocellular carcinoma, 3 for metastatic liver cancer, 2 for intrahepatic cholangiocarcinoma, 1 for hilar cholangiocarcinoma, and 1 for benign bile duct stricture. Four patients underwent right lobectomy, 1 underwent left lobectomy, 3 underwent extended left lobectomy, 7 underwent sectionectomy, 5 underwent segmentectomy, 2 underwent partial hepatectomy, and 1 underwent bile duct resection. All these procedures were open. In all patients, extracorporeal contrast-enhanced ultrasonography, dynamic CT, and MRI with the hepatobiliary contrast agent gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Bayer Schering Pharma) were performed. In patients with intrahepatic biliary dilation, optional magnetic resonance cholangiopancreatography (MRCP) was performed using a 1.5T MR system (Achieva 1.5 Nova Dual; Philips Medical Systems) for evaluation of biliary anatomy. Thick-slab heavily T2-weighted breath-hold images were obtained with a slice thickness of 40 mm. Thin-slab heavily T2-weighted respiratory-triggered images were obtained with a slice thickness of 1 mm.

This study was approved by the Institutional Review Board of Kobe University Hospital. Informed consent was obtained from all patients. A summary of the protocol was submitted (registration ID: UMIN000006259) to the

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Abbreviations and Acronyms

CE-IOUSC = contrast-enhanced intraoperative ultrasonic cholangiography
CHD = common hepatic duct
D = dimensional
IOC = intraoperative cholangiography
LHD = left hepatic duct
MRCP = magnetic resonance cholangiopancreatography
RASD = right anterior sectoral duct
RHD = right hepatic duct
RPSD = right posterior sectoral duct

Clinical Trials Registry managed by the University Hospital Medical Information Network in Japan (http://www.umin.ac.jp/ctr/index-j.htm).

Ultrasound imaging system and contrast agent

Contrast-enhanced intraoperative ultrasonic cholangiography was performed using an Aplio XG ultrasound imaging system (Toshiba Medical Systems Co), with a T-shaped intraoperative linear probe (PLT-705BTH, 7 MHz), a 4D convex probe (PVT-375MV, 3.5 MHz), and a micro-convex probe (PVT-745BTH, 7 MHz). The 4D probe automatically scans multiple sectors to obtain real-time images in 3 orthogonal planes and generates a 3D volume image. The 4D probe was enclosed in a sterile sleeve for intraoperative use. Perfluorobutane microbubbles (Sonazoid; Daiichi-Sankyo Pharmaceutical Co) were used as the contrast agent in this study. A vial of Sonazoid was reconstituted with 2 mL water for intravenous injection. This original Sonazoid solution was diluted 1,000-fold with saline for intrabiliary injection in this study. In preliminary tests on 5 patients, we used 3 different concentrations of Sonazoid to obtain the optimum condition for CE-IOUSC. At the high concentration (1:100), condensed microbubbles in the bile ducts blocked the ultrasound waves and posterior acoustic shadowing interfered with ultrasound imaging. At the low concentration (1:10,000), the contrast between bile ducts enhanced by Sonazoid solution and hyperechoic surrounding tissues decreased. The 1:1,000 dilution of Sonazoid solution enabled us to create a good ultrasound image of both the bile ducts and the surrounding tissues by 2D scanning. Based on these data, we selected the 1:1,000 dilution of Sonazoid for CE-IOUSC.

Contrast-enhanced intraoperative ultrasonic cholangiography procedure and data acquisition

All surgical procedures, CE-IOUSC procedures, and data acquisitions were performed by the same surgeons. After cholecystectomy, a 4F transcystic catheter was inserted into the cystic duct for intrabiliary access. The linear and 4D probes were used to visualize the liver (Fig. 1). The 4D probe was fixed on the liver surface throughout the procedure to avoid the motion effects of the rhythms of the heart beating and respiration. After temporarily clamping the distal common bile duct, a maximum of 10 mL of the suspended microspheres was injected into the biliary tree at a rate of 1 mL/s until it was filled, which was assessed by using the fingers to feel the swelling of the common bile duct, and by visual evaluation. In addition, we checked the swelling of the bile ducts in real time by CE-IOUSC during the procedure to ensure the safety of the intrabiliary injection of Sonazoid. Initially, 3D CE-IOUSC using the 4D probe was performed to delineate the biliary tree. Subsequently, 2D CE-IOUSC of the entire liver was performed using the linear probe. If necessary, 2D CE-IOUSC of the hepatic hilum using the micro-convex probe was also performed.

Figure 1. Photograph of the operative field during contrast-enhanced intraoperative ultrasonic cholangiography using a 4-dimensional probe.

All intraoperative scans were performed in the contrast harmonic imaging mode, which is set at a low mechanical index of 0.1 to 0.25 at 15 frames/s to avoid microbubble disruption. The gain was properly selected at 60% to 90%. The focus was set at the level of hepatic hilum. In 3D CE-IOUSC, the volume of interest was selected with a central focus on the hepatic hilum. For optimum visibility, the sensitivity time control was adjusted to decrease echogenicity of hyperechoic surrounding tissues, such as hepatic hilar plate. Scanning speed was 0.3 to 1.0 volumes/s, with a volume angle of 50 to 75 degrees. All of the imaging data were stored digitally in the ultrasound imaging system.

Three-dimensional contrast-enhanced intraoperative ultrasonic cholangiography image reconstruction

After data acquisition, 3D CE-IOUSC images of the biliary tree were reconstructed using a volume-rendering