Ischemic-type biliary lesions following liver transplantation: Evaluation with Gd-EOB-DTPA-enhanced MR cholangiography

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Purpose

Orthotopic liver transplantation (OLT) has become the treatment of choice for end-stage liver disease, as well as for severe acute liver failure and in the last years the number of transplants is progressively increased.

Despite the enormous improvement in post-OLT survival over the years, complications of the biliary tract, which occur in 5.8% to 24.5% of adult liver transplant recipients, are one of the most important reasons for morbidity, graft loss, and mortality of liver transplant patients.

Anastomotic and non-anastomotic strictures, most of which involve the confluence of right and left hepatic ducts (predominant site for ischemic-type biliary changes) are the most frequent biliary complications. Calculi are typically identified in association with anastomotic (more frequently) or non-anastomotic strictures.

Various authors have already reported encouraging results concerning the use of MR cholangiography (MRC) in the detection of biliary complications in liver transplanted patients, and we have been routinely using this technique as a mean of imaging the biliary tract in transplanted patients.

Primovist® (Gd-EOB-DTPA, Bayer Schering Pharma) is a recent developed liver-specific contrast agent with partial excretion into the biliary tree (~50% of the injected dose) and it is likely to have a great impact on better visualization of biliary system and may potentially increase reliability of the examination or decrease the occurrence of a non diagnostic or equivocal interpretation.

The purpose of our exhibit is to assess the usefulness of contrast-enhanced MR cholangiography (MRC) using Gd-EOB-DTPA for evaluating ischemic-type biliary lesions (ITBLs) in liver transplant recipients.
Methods and Materials

Fifteen liver transplant patients with ischemic changes of the biliary tree underwent MRI at 1.5T-device (Signa Infinity; GE Healthcare, Milwaukee, Wis). The phased-array body coil was used for both excitation and signal reception.

Ten minutes before MR exam, 300 ml of water were used as an oral contrast agent in an attempt to improve the visualization of the duodenum. Scopolamine methylbromide (Buscopan® 20 mg/ml, Boehringer Ingelheim) was intramuscularly administered immediately before starting the examination in order to avoid peristaltic artefacts.

**MR study protocol:**

- T1w sequences (breath-hold FSE or GRE) and T2w sequences (FSE with respiratory-triggered) with and/or without fat suppression at the abdominal level (superior part), 5-6 mm thin-slab, with an interval of 1-2 mm;

- T1w GRE sequence (SPGR) with and/or without fat suppression and breath-hold, both in phase and out of phase, and single-shot breath-hold FSE T2w sequence, only at the liver level, 5 mm thickness;

- cholangio-pancreatographic T2w sequences (respiratory-triggered, 2 mm thin-slab, 3D FRFSE T2w and breath-hold, 10/50 mm thick-slab) in the different spatial orientations (coronal and coronal-oblique planes);

- single manual bolus intravenous injection of Gd-EOB-DTPA (Primovist®, Bayer Schering), at a dose of 0.025 mmol/Kg b/w (2 mL/s followed by 20 mL saline flush);

- after 15, 20, 25, 30 and 40 minutes and, if needed, after 60-90 minutes a coronal 3D fat-suppressed breath-hold gradient-echo T1w LAVA sequence (TR/TE, 3.6 ms/1.6 ms; 2.4 mm thk/-1.8 mm sp; field of view, 35-42 cm; matrix, 224x192; one signal acquired) at the level of the biliary tree (T1w sequence was also obtained after 90 minutes in 5/15 cases).

Maximum intensity projections (MIPs), volume rendering (VR), multiplanar reformatting techniques were applied to the acquired data set of coronal thin-slab T2-weighted and 3D LAVA sequences on an independent workstation (Advantage Windows 4.4; GE Healthcare). MR images were interpreted in conference by two experienced observers who were blinded to patient identification and all clinical, laboratory, and previous imaging findings; differences in interpretation were settled by means of consensus.

Depiction of intra-/extra-hepatic bile ducts, dilation of biliary system, presence of biliary stricture and stone/sludge were evaluated on images by consensus reading of the two observers that utilized a 3-point-scale: 0, absent; 1, visible; 2, excellent. Imaging results were correlated with direct cholangiography and/or follow-up.
Results

MR studies were considered to be diagnostic by the two reviewers in all patients since they well exhibit the biliary anatomy and the ductal anastomosis.

The grading of visualization and depiction of dilation of the intra-hepatic bile ducts was significantly superior on T2-weighted MRC compared with Gd-EOB-DTPA-enhanced T1-weighted MRC; on the contrary, this latter significantly tended to out-perform conventional T2-weighted MRC in delineating strictures involving hepatic bifurcation and extrahepatic donor bile duct (p<0.0001). Sludge/stone formation was correctly identified with both techniques.

Biliary enhancement was recognized within 20 minutes post-Gd-EOB-DTPA injection in 3 subjects [Fig. 1 (A,B,C) on page , Fig. 1 (D,E,F,G) on page ], between 25 and 40 minutes in 8 [Fig. 2 (A,B,C,D) on page , Fig. 2 (E,F,G,H) on page , Fig. 2 (I,L) on page ], and at 90 minutes in 4 cases [Fig. 3 (A,B,C,D) on page , Fig. 3 (E,F,G,H) on page ].
Conclusion

Ischemic-type biliary lesions (ITBLs) are non-anastomotic strictures, mainly involving the hepatic bifurcation, which is a predominant site for ischemic changes after liver transplantation. The appearance of these lesions suggests that microcirculatory problems may play a role in their development. Although the blood supply to the distal common bile duct (recipient) is rich because of collateral flow, that of the more proximal duct (donor) and of the intrahepatic ducts is lower, being derived exclusively from the reconstructed hepatic artery. The strictures often start at the hepatic bifurcation and extend peripherally or may be intrahepatic and involve multiple biliary segments. MRC imaging can also show another typical feature of ITBL that is represented by wall thickening of the donor common bile duct, sometimes associated to the presence of endoluminal debris. In these subjects, interventional measures are frequently only transiently successful and the early detection of these abnormalities is important because the patients are candidates for surgical resection of the bifurcation and reconstruction by means of high hepatico-jejunostomy, which leads to cure or persistent major improvement in most cases. In other cases, surgical treatment is not possible and these patients can undergo a new liver transplantation.

T-tube cholangiography is the examination of choice in patients with suspected ITBLs in the early post-OLT phase during which the T-tube remains in place. However, when it is removed three months after liver transplantation (or if it is not used at all), direct opacification of the biliary system is only possible when invasive procedures such as PTC and ERC are used, which are themselves associated with complications in 3.4% of PTC and 1-7% of ERC procedures.

This situation has changed since the advent of MRC, which allows the same level of imaging to be generated non-invasively and is particularly useful in patients who do not have a T-tube in place.

Primovist® (Gd-EOB-DTPA, Bayer Schering Pharma) is a gadolinium-based contrast agent for T1-weighted MR imaging of the liver, administered by intravenous injection in a concentration of 0.25 M. It is the formulation of the active ingredient gadoxetic acid disodium, a hydrophilic gadolinium chelate of low molecular weight. Due to the ethoxybenzyl (EOB) moiety, about 50% of the administered dose of Primovist® is selectively taken up via the anion transporter present on the cell membrane of normal hepatocytes and subsequently eliminated via the biliary system. It has unique pharmacokinetic properties following bolus injection: about 50% is eliminated via the renal pathway and about 50% is eliminated via the biliary pathway. The high signal intensity of the biliary system after Gd-EOB-DTPA excretion produces excellent contrast when compared with the liver parenchyma and hepatic vessels in the background and has the potential to generate anatomic and functional T1-weighted MRC images by combining
excellent spatial resolution and anatomic depiction with functional evaluation of biliary excretion.

With the bolus injection technique, in the normal subject the optimal time to evaluate bile ducts is 15 to 20 min after injection, which corresponds to the hepatocytic and biliary tract phase on hepatobiliary scintigraphy.

In our study, we performed conventional T2-weighted MRC and gadolinium-EOB-DTPA-enhanced MRC in the evaluation of liver transplant patients with ITBLs. This recently developed technique has provided a combination of anatomic and functional information; in fact, it has allowed to better delineate strictures involving hepatic bifurcation and extrahepatic donor bile duct and has shown different times of contrast agent excretion that is in correlation with different degrees of biliary obstruction.

In conclusion, Gd-EOB-DTPA-enhanced MRC may provide both anatomical and functional information in liver transplant patients with ITBLs.
References


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