Ischemic-type biliary lesions following liver transplantation: evaluation with MR cholangiography and diffusion-weighted MR imaging at 3T

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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 good 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.

Diffusion-weighted MR imaging (DW-MRI) is an MR imaging technique used to show thermally induced molecular diffusion, which is the Brownian motion of the spins in biologic tissues; DWI can be used to differentiate normal and abnormal tissues, and it might help in the characterization of various abnormalities. This technique is widely accepted in neuroradiology for detecting early ischemia in cerebrovascular accidents and characterization of brain tumors and intracranial infections. The use of DWI in other parts of the body is relatively new, but very promising for the detection and differentiation of benign and malignant lesions, imaging for staging in oncological patients before treatment and for follow-up after treatment of liver tumors.

The purpose of our exhibit is to determine the usefulness of MR cholangiography (MRC) and diffusion-weighted MR imaging (DW-MRI) at 3T-device for evaluating ischemic-type-biliary-lesions (ITBLs) in liver transplant recipients.
Methods and Materials

Thirty-two liver transplant patients with ischemic changes of the biliary tree at ERCP/PTC underwent MRI at 3T device (GE-DISCOVERY MR750; GE Healthcare, Milwaukee,Wis). The 8-channel phased-array body coil was used for both excitation and signal reception.

Ten minutes before MRI, a super-paramagnetic suspension (Lumirem® 50 ml, Guerbet) was orally administered to suppress the signal intensity of overlapping fluid-containing organs and in an attempt to improve the visualization of the duodenum. Scopolamine methyl-bromide (Buscopan®20 mg/ml, Boehringer Ingelheim) was intramuscularly administered immediately before starting the examination in order to avoid peristaltic artefacts.

**MR study protocol:**

- 3D/2D breath-hold T1w GRE sequence (SPGR/LAVA flex) with and/or without fat suppression, both in phase and out of phase, at the liver level, 3-5 mm thickness;

- T2w sequences (FSE Propeller with respiratory-triggered and breath-hold single-shot FSE) with and/or without fat suppression at the liver level, 5-6 mm thickness with an interval of 1-2 mm;

- cholangio-pancreatographic T2w sequences (respiratory-triggered, 1-2 mm thin-slab, 3D-FRFSE and breath-hold, 10/50 mm thick-slab, SS-FSE) in the different spatial orientations (coronal and coronal-oblique planes);

- DW sequences (single-shot spin-echo echo-planar imaging) acquired with respiratory gating in the transverse plain, using multiple b-values (0, 150, 500, 1000, 1500 sec/mm²) in all diffusion directions (slice section 5-6 mm, spacing 0.5-1.5 mm, nex 4).

Maximum intensity projections (MIPs), volume rendering (VR), multiplanar reformatting techniques were applied to the acquired data set of coronal thin-slab T2-weighted FRFSE 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.

The observers reviewed all MR images and recorded the presence of biliary and liver parenchyma abnormalities. ADC values of right lobe liver parenchyma in ITBLs group and normal control group (n=30) were respectively calculated by using a dedicated software for fitting the curve obtained from the corresponding ADC for each b-value.
Results

Abnormal findings of bile ducts were observed in all patients; the most common findings were intrahepatic bile duct dilatation (31/32), strictures involving hepatic bifurcation (31/32), extrahepatic biliary wall thickening (30/32) and sludge/stone formation (22/32). On DW-MRI areas of persistent bright signal intensity in the liver parenchyma were observed in 20/32 ITBLs patients. Fitted ADC values of liver parenchyma in ITBLs group were significantly lower than those in normal control group (p<0.05) [Fig. 1 (A,B,C), Fig. 2 (A,B,C), Fig. 3 (A,B)].
Fig. 1: Figure 1 A Ischemic-type biliary lesion in a man with abnormal liver function tests. MR cholangiograms demonstrate a stenosis of the hepatic bifurcation and hepatic ducts with an irregular dilation of the intrahepatic biliary system. Axial T1 and T2-weighted sequences well exhibit the presence of endoluminal casts and circumferential wall thickening at the level of hepatic bifurcation.

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Fig. 2: Figure 1 B On DWI areas of persistent high signal intensity can be observed in the liver parenchyma in all b-value acquisitions.

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Fig. 3: Figure 1 C Multiple ROIs were placed at the level of right hepatic lobe and ADC value ranged between 1 and 1.10x10^-3 mm²/sec.

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**Fig. 4:** Figure 2 A Ischemic-type biliary lesion in a woman with biochemical parameters of cholestasis. MR cholangiograms and axial/coronal T2-weighted images show the classic signs of ITBLs represented by the stricture at the level of hepatic bifurcation, wall thickening of the extrahepatic biliary tree of the graft and the presence of biliary sludge/stones in the dilated intrahepatic biliary system. The correlation with ERCP is excellent.

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**Fig. 5:** Figure 2 B In this case hepatic parenchyma showed only limited areas of persistent high signal intensity in all b-value acquisitions.

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Fig. 6: Figure 2 C ADC value ranged between 1.10 and 1.20x10^-3 mm2/sec.

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**Fig. 7:** Figure 3 A In this liver recipient with chronic pancreatitis and normal liver function tests, no significant abnormality was identified at the level of the biliary tree on MRC. Hepatic parenchyma was substantially homogeneous in all b-value acquisitions.

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**Fig. 8:** Figure 3 B Multiple ROIs were placed in the liver parenchyma and ADC value was higher than that of previous cases, ranging between 1.4 and 1.6x10⁻³ mm²/sec.

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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 these 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 visualization 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.

On the other hand, DWI can non-invasively reflect the structure and function state of living organisms on molecular level. DWI of the liver is a relative new and increasingly used imaging technique in addition to conventional unenhanced and contrast enhanced MRI. The ADC is a quantitative parameter calculated from the DW-MR images, that combines the effects of capillary perfusion and water diffusion in the extracellular extravascular space. DWI seems to be helpful in the characterization of focal liver lesions, but should always be used in conjunction with traditional MRI since there is great overlap between ADC values of benign and malignant lesions. Preliminary reports describe the application of DWI on biliary complications in liver recipients and hypothesize that this technique could be an early and sensitive diagnostic method for ITBL after liver transplantation.

In our study, the accuracy of 3T MRC was high in the non-invasive assessment of ITBL in liver transplant recipients and we identified the typical ischemic changes in nearly all investigated patients.
DWI is a high potential way in studying liver function, and it is sensitive to very small-scale motion of water molecules at a microscopic level. Signal intensity of DWI depends on two main factors, molecular diffusion effect and perfusion role of capillary microcirculation.

The bile duct cells are more vulnerable to reperfusion/reoxygenation injury than hepatocytes, regeneration capacity of cholangiocellular was lower than hepatocyte, and intrahepatic biliary lesion aggravated proportionally with the increase of the ischemia time. When microcirculation disorder caused by ischemia-related injury happened, the tissue oxygen tension would decrease. Consequently, it was assumed that these mechanisms led to anoxia-ischemia of bile duct epithelial cells, thickening and edema of bile duct wall, cholestasis in the hepatocyte and bile duct epithelial cells partly with focal necrosis.

In our present study, the ADC value of the liver parenchyma in ITBL group was significantly lower than normal control group. It may suggest that liver injuries in ITBL group, such as anoxia-ischemia of liver graft, were more serious than normal group. Therefore, the reduction of ADC value of liver might have some value in the diagnosis and differential diagnosis of ITBL. It is assumed that the decreased ADC value of liver could reflect pathology changes. For this reason DWI may be an effective supplement method to detect early ITBL for conventional MRI and MRCP.

In conclusion, in liver transplant recipients with ITBLs MRC in combination with DW-MRI at 3T reveal characteristic features that may allow differentiation from other complications after liver transplantation.
References


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