The Role of Magnetic Resonance Cholangiography for Recipients after Living Donor Liver Transplantation

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ABSTRACT

This is a retrospective study. The purpose of this study was to assess the diagnostic accuracy and utility of post-transplant magnetic resonance cholangiography (MRC) in detecting biliary complications and planning the treatment.

From July 2006 to April 2010, 51 (19%) of these 268 adult living-donor liver transplantation (LDLT) recipients were referred to MRC due to biliary dilatation and abnormalities detected by ultrasound or abnormal liver function. The biliary complications were treated with endoscopic or percutaneous transhepatic approach.

Among those 51 recipients, MRC revealed no definite biliary pathology in 34 patients. In 10 of the 34 MRC-negative cases, additional MR angiography showed vascular stenosis. 15 MRC-positive cases were correctly assessed the site of the obstruction, bile leakage or lithiasis. Under MRC guidance, biliary interventions were completed in 12 of the MRC-positive cases. MRC achieved sensitivity of 100%, specificity of 94.4%, positive predictive value of 88.2%, and negative predictive value of 100%.

MRC is a reliable diagnostic modality in detecting post-transplant biliary complications with 96.1% accuracy. It is an essential diagnostic tool for assessing the necessity for interventional procedure. MR angiography can provide additional information on vascular problems that caused biliary complications. Magnetic resonance imaging (MRI) is thus indispensable before therapeutic biliary or vascular procedure in post-transplant recipients.

Adult living-donor liver transplantation (LDLT) has been developed as an alternative to deceased donor liver transplantation, due to the scarcity of deceased liver donors as well as the increasing number of recipients requiring liver transplants. With improvements made in surgical techniques, immunosuppressive agents, and intensive and anesthesia care, the complications of LDLT have been reduced over the years. The expansion of LDLT, in particular with adult-to-adult right lobe LDLT, resulted in an upsurge of biliary complications with a corresponding rise in mortality among liver transplant recipients. Biliary complications are common after liver transplantation, occurring in 10-30% of liver transplant recipients [1-3]. Despite improved surgical and medical care, biliary complications are still a major source of morbidity, sometimes loss of the graft and in severe cases mortality. With the advancement of magnetic resonance cholangiography (MRC) sequences to dynamic 3D MR imaging, noninvasive visualization of bile ducts became possible [4]. MRC is a noninvasive and very promising diagnostic modality that can detect pathologic biliary tract changes and provide information for planning invasive therapeutic procedures. The purpose of this study was to assess the diagnostic accuracy and utility of post-transplant MRC for detecting biliary complications in LDLT recipients. The value of MR angiography in demonstrating vascular complications and guiding therapeutic interventions is also investigated.

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**MATERIALS AND METHODS**

From July 2006 to April 2010, 51 (19%) of these 268 LDLT recipients (32 men and 19 women; 18-65 yrs, mean age: 48 yrs) were referred to MRC for abnormal liver function or other various anomalies detected with ultrasound and as a routine follow-up. Those patients with biliary anomaly detected by MRC were followed up with ultrasound, percutaneous transhepatic cholangiography (PTC) and/or endoscopic retrograde cholangiography (ERC). Initial management of biliary complications was through endoscopic retrograde biliary drainage (ERBD) and/or percutaneous transhepatic biliary drainage (PTBD). All patients gave informed consent before the MRC and interventional procedures.

**MRC imaging procedure**

MR cholangiography was performed using a 1.5 tesla magnets MRI unit (Gyroscan Intera; Philips, Best, the Netherlands) with a dedicated phase-array torso surface coil. No sedation, antiperistaltic agents or contrast medium was given. The biliary tract was localized with thick-slice (60-mm) rapid acquisition with relaxation enhancement images in coronal–oblique planes. The thick-slice images were then used as guides to evaluate the biliary tract with half-fourier RARE thin-slice (5-mm) images in the coronal–oblique plane, oriented parallel to the longitudinal axis of the extra hepatic bile duct. The thin-slice MR cholangiographic acquisitions were obtained at various angles that allowed optimal visualization of the bile duct. The thin-slice parameters included TR/TE(8000/800) eff., infinite, 88.0; refocusing flip angle, 90°; slice thickness, 5 mm with no gap; field of view, 380×380 mm; number of acquisitions, 1; matrix, 256×205; and acquisition time, 18 sec. Six images were obtained during each 18-sec acquisition. Fat saturation and shim adjust were used in all cases. Post-processing techniques were not used. Both the thick-slice and thin-slice images were obtained while patients held a breath. The patients did not fast before MR cholangiography.

**MR angiography of the hepatic artery, portal vein, and hepatic vein**

Gadolinium-enhanced MR angiography was performed with a body coil and a breath-hold spoiled gradient-echo sequence of 27-34 sec duration. An initial sagittal localizer image was obtained during a breath hold. The purpose of this sequence is two-fold: to guide positioning of the coronal three-dimensional (3D) gadolinium-enhanced sequence and to assess the patient’s breath-holding capability. Gadolinium-enhanced MR angiography was performed with a 3D spoiled gradient-echo technique in the coronal plane. Imaging began approximately 10-15 sec after commencement of the contrast medium injection. With this delay, the first breath-hold sequence can capture the arterial phase of the contrast material bolus; a second breath-hold 3D spoiled gradient-echo sequence was performed immediately thereafter, during the portal venous phase and hepatic venous phase. Additional images were reconstructed with a computer workstation (Windows Advantage; General Electric Medical Systems). Subvolume maximum-intensity projection images and single-voxel-thick reformation images were obtained to assess the celiac, superior mesenteric artery, portal vein, and hepatic vein in a 3-D fashion. The MR angiography was interpreted by one radiologist at the work station, after viewing raw data, reformatted images, projection views, and the axial T1- and T2-weighted sequences.

**Surgical technique**

All biliary reconstructions were performed under a microscope by a single microsurgeon (Lin TS) who also did the hepatic artery reconstruction with a microsurgical technique [5]. Data were collected with a prospective database, and the biliary reconstruction characteristics, complications, and outcomes were analyzed retrospectively.

**Biliary complications**

Biliary complications such as biliary strictures and leaks, were defined as any adverse event relating to biliary reconstructions which occurred immediately after the surgery or during the follow up period and required either percutaneous or surgical interventions. Bile leakage was defined as the presence of bile material in the closed-suction drain that persisted beyond three days after transplantation or as the presence of a biloma within the area of the anastomosis. Biliary strictures were classified into anastomotic stricture and non-anastomotic strictures. A stricture was diagnosed on the basis of magnetic resonance cholangiography, percutaneous transhepatic biliary imaging, or endoscopic retrograde cholangiography. The follow-up period among surviving patients was 14 months to long term follow-up (mean follow-up period of 41 months).

**Image analyses**

The images were interpreted by two independent radiologists (Cheng YF and Huang TL) to determine the diagnosis. They were both blinded to patient identification and all clinical, laboratory, and previous imaging findings; differences in interpretation were settled by means of general agreement. The ERC and PTC images were interpreted in conference by the same two observers, who used the clinical, laboratory, endoscopic, and imaging data during their review.

**Statistical analyses**

The distribution of the qualitative variables was expressed as the relative frequency of the various modalities under observation. MRC findings were compared with the hepatobiliary sonography, ERC, PTC, and clinical
follow-up results and defined as true positives when they correctly detected biliary complications confirmed by the final diagnosis reference standards; false positives when they were not confirmed by ERC, PTC, surgery or clinical, and imaging follow-up; false negatives when complications detected by ERC, PTC, surgery or clinical, and imaging following up were not detected by MRC; true negatives when the absence of complications was confirmed by ERC, PTC, surgery or clinical, and imaging follow-up. To evaluate the diagnostic yield of MRC, we determined the sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the reviewers for the detection of biliary complications, and we also calculated the 95% confidence intervals.

RESULTS

Of the 51 LDLT recipients referred to MRI; 17 with positive MRC included one with lithiasis in the distal common bile duct, 2 bile leakages with biloma and 12 whose MRC revealed biliary tree dilatation with anastomotic strictures that required biliary interventions. Minimal biliary tree dilatation (intrahepatic duct diameter < 3 mm) was found in 2 cases. They were classified as false positive cases in our study. In the remaining 34 recipients, MRC did not show any biliary anomaly.

Accuracy of MRC in detecting the post-transplant biliary complication

Of the 17 initial MRCs revealing biliary pathologic findings, 12 revealed stricture of the biliary anastomosis; lithiasis in one, and bile leakage (with biloma formation) in two cases. No non-anastomotic strictures were noted in our study. Minimal biliary tree dilatation was found in 2 cases so no further biliary intervention was performed. Comparing the findings obtained with direct cholangiography (ERC or PTC) in the 11 patients, MRC was highly accurate for the detection and characterization of post-operative biliary complications. Follow-up of the remaining 34 recipients with MRCs revealing normal biliary tree or no definite biliary stricture showed that none of them had biliary pathology when checked with clinical, biochemical, histopathological, and other image studies. Overall, compared with the final diagnosis in all 51 patients, the global diagnostic accuracy of MRC is 96% (49/51) in detecting all types of biliary complications in LDLT patients. MRC achieved sensitivity of 100%, specificity of 94.4%, positive predictive value of 88.2%, and negative predictive value of 100%.

MRC negative group

In 24 of the 34 MRC negative patients, MRC did not reveal any biliary pathological findings. In the remaining 10 cases, MR angiography (MRA) showed vascular stenosis including portal stenosis (n=8), hepatic venous stenosis (n=1) or hepatic artery stenosis (n=1). 6 of the 8 cases whose MRA revealed severe portal venous stenosis at anastomosis underwent percutaneous transluminal angioplasty with/without portal venous stent placement. Two MRA showed mild portal vein stenosis. One whose MRA showed severe hepatic vein stenosis also underwent successful percutaneous transluminal angioplasty. The remaining one case with MRA showing mild hepatic arterial anastomosis stricture, received conservative treatment instead of invasive intervention or surgery. The following period of this group is 14 months to long term follow-up. In the follow-up period, it showed that none of them had biliary pathology (early or late biliary complications) when checked with clinical, biochemical, histopathological, and other image studies. There were no MRC false negatives in this study. The clinical course and management of 34 MRC negative patients are shown in Fig. 1.

Management of biliary or vascular complications after LDLT under MRI guidance

Management of biliary complications included biloma drainage, PTBD, ERBD and surgically reconstruction. The global biliary complication rate was 5.6% (15/268) in our series. Retrospective analysis of the 15 patients in whom that intervention or surgery was required revealed that in the two patients with biliary leakage, the MRC readers accurately described the presence of a subhepatic fluid collection adjacent to the anastomotic region, but could not demonstrate an active leak. The ultrasound-guided percutaneous drainage revealed a biloma that was presumably the result of a contained leak at the anastomotic site. One with lithiasis in distal CBD shown by the MRC received stone removal by endoscopy. All 12 cases with biliary strictures were correctly assessed as to the site of the obstruction and the MRC reviewers correctly visualized the dilated bile ducts above the stricture. In our series, all of the biliary strictures were at the biliary anastomotic site. 5 biliary strictures were treated with ERBD, 4 biliary strictures with PTBD and one stricture was treated with both ERBD and PTBD. Biliary anastomosis was redone surgically in only one case due to failure of ERBD and PTBD. The remaining one case with biliary stricture combined with severe portal venous stenosis underwent PTBD and PTA with portal venous stent placement successively. No vascular related complications were found to be correlated with the cause of biliary complication. The clinical course and management of 17 patients are shown in Fig. 2.

To analyze the biliary complications detected by MRC, MRC helped decide the location of biliary stricture and cause of biliary stricture besides bile leakage, lithiasis and biliary stricture. In our series, two biliary strictures due to tumor recurrence and compression of bile duct, three with simultaneous hepatic vascular stenosis. All of the biliary strictures in this study are all anastomotic stricture. There
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**Figure 1.** Clinical course and management of 34 MRC-negative LDLT recipients.

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**Figure 2.** Clinical course and management of 17 MRC-positive LDLT recipients.

Figure 2.

Clinical course and management of 17 MRC-positive LDLT recipients.
were two cases that underwent 2-to-2 and 2-in-1 biliary reconstruction with double stricture detected by MRC. ERBD with stent placement was performed smoothly under MRC guidance (Fig. 3a-3d).

**Diagnostic cholangiography vs. Therapeutic biliary intervention**

All of the conventional cholangiograms (ERC and PTC) were performed for “therapeutic” biliary intervention (ERBD or/and PTCD). No unnecessary diagnostic cholangiography was performed in our series.

**DISCUSSION**

The reductions in post LDLT biliary complication was mostly attributed to the improved understanding and experience gained from liver transplantation, and the advances made in surgical techniques, imaging modalities, immunosuppressive agents and postoperative care. However, despite these developments, a significant number of difficulties brought about by biliary complications remained evident, particularly following the usage of reduced size grafts. The early diagnosis and correct management of biliary complications are important elements for ensuring graft and

![Figure 3](image)

**Figure 3.** a. MRC revealed double stricture at the 2-to-2 biliary anastomotic sites. b. ERBD was performed with two plastic stents placement. c. MRC demonstrated anastomotic stricture at the 2-in-1 biliary anastomotic site. d. Two plastic stents placement was require according to the MRC. The ERBD was performed smoothly under MRC guidance eventually.
patient survival after LDLT, and the diagnostic work-up has been repeatedly reviewed in an attempt to reach the most effective strategy [6-7].

Imaging modalities for diagnosis of biliary complications

Diagnostic imaging modalities included hepatobiliary ultrasonography, conventional direct cholangiography, CT cholangiography and magnetic resonance cholangiography. Hepatobiliary ultrasonography is the initial screening tool for detecting biliary tract complications, but it has limited sensitivity, specificity and negative predictive value [8]. Helical CT cholangiography may be useful in patients with a nonobstructive abnormality but the limitation of cholangiographic contrast-enhanced CTC is its hindrance by poor liver function or high-grade biliary obstruction [9-11].

As to endoscopic retrograde cholangiography (ERC), whilst it can provide a precise delineation of the biliary ducts, it is nonetheless invasive. Moreover, apart from radiation exposure, ERC likewise carries the risk of various complications including acute pancreatitis, duodenal perforation and biliary infection [12-15]. ERC has been restricted to patients for whom therapeutic procedures are advocated or whose MRC results are equivocal in our hospital. T-tube cholangiography is another direct cholangiography after LDLT. Due to T-tube related complications and increasing use of partial liver grafts in LDLT, T-tube placement had been abandoned in our hospital since we shifted to biliary microsurgery [16].

Single imaging modality evaluation for biliary complications: MRC

In this study, the global accuracy rate of MRC in detecting post LDLT biliary complications is 96%. MRC studies allowed complete visualization of the extrahepatic bile ducts and biliary anastomoses. MRC is also highly effective in detecting biliary strictures, stones, bile leakage and has made it possible to significantly reduce the number of direct cholangiographies. The therapeutic consequences of MRC findings also need critical consideration. No LDLT recipient was referred to pure “diagnostic” ERC and PTC at our hospital over the past five years. In patients with a duct to jejunum anastomosis, however, MRC provides a whole map for biliary anatomy and it is likely to replace diagnostic PTC and ERC. In view of the considerable risk of infection and bleeding associated with direct cholangiography, in particular after LDLT, this procedure is, at least in asymptomatic patients, no longer reasonable for diagnostic reasons alone.

While biliary complications did occur in those with multiple duct-to-duct anastomoses, managing the complex biliary complications remains difficult. Depending on the MRC findings, further specific invasive secondary therapeutic measures can be employed. MRC aids in pinpointing exactly the obstruction sites exactly and interventional treatment can be well planned and performed smoothly under MRC guidance.

To analyze the biliary complications detected by MRC

MRC demonstrated the location and cause of biliary strictures, including bile leakage, lithiasis. In our series, three types of biliary strictures occurred with simultaneous hepatic vascular stenosis and biliary stricture. All the biliary strictures in this study are all biliary anastomotic strictures. We believe these may be related to biliary microsurgery technique. In additional to lithiasis, bile leakage, MRC is also highly effective in detecting anastomotic/ non-anastomotic strictures and demonstrating the multiple biliary narrowing sites which would be misdiagnosed by ERC.

In our previous report, microsurgery for multiple biliary anastomoses could be performed smoothly because pre-transplant MRC clearly showed the biliary anatomy for surgical planning [17]. Advancement of biliary reconstruction has resulted in increasing use of 2-to-2, 2-to-1 or 2-in-1 duct-to-duct anastomoses in which anastomotic strictures could be misdiagnosed by ERC. In recipients with multiple duct to duct biliary anastomoses, it was complex as multiple biliary strictures occurred. Delicate diagnostic imaging modality and whole biliary mapping can be obtained by MRC. Thus, interventional treatment can be planned for in detail using MRC as guidance. In the two cases with 2-to-2 biliary anastomotic double stricture and 2-in-1 anastomotic stricture, endoscopic biliary stent placement was completed smoothly with MRC guidance. Using MRC guidance, the physician can plan exactly how to place the biliary stent with endoscopic access, so there is no longer a need to operate “blind” while performing ERBD. MRC can be used to plan the percutaneous access through puncturing at right anterior, right posterior or left hepatic duct because MRC reveals the exact obstruction and dilated intrahepatic ducts.

To compare LDLT adult patients who didn’t receive MRC with those undergoing post-transplant MRC, there was no significance of mortality or graft loss between these two groups. We believe post-transplant MRC plays a key role in the management of biliary complication and the results.

The policy of managing the biliary complications

According to our experience and results, the policy for management of post-transplant biliary complications was established in Fig. 4. The initial treatment strategy for biliary anastomotic strictures after LDLT is: (1) In single duct-to-duct anastomosis stricture, ERBD is favored. Using MRC guidance, biliary stents can be placed for drainage. (2) In those with acute cholangitis and sepsis, PTBD is favored due to the high incidence of complications such as acute cholangitis following endoscopic procedures. (3) In multiple duct-to-duct anastomotic strictures, ERBD is favored. With MRC guidance, post-transplant multiple biliary strictures can be managed with endoscopic biliary
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**Additional magnetic resonance angiography in the LDLT patients with suspicious biliary complications**

In addition to MRC study for recipients with suspicious biliary complications, MR angiography of the hepatic artery, hepatic vein and portal vein are three routine MRI additional pulse sequences for liver transplant recipients in our hospital, which do not much increase clinical expense. Doppler ultrasound is the practical image modality for checking vascular flow of hepatic artery, portal vein and hepatic vein. MRA is not the first choice image modality for LDLT recipients with suspicious vascular complications, but it helps us detect the vascular complications in those with suspicious biliary complications to ensure the early management of the liver transplant recipient. In this study, combined biliary and vascular complications occurred in only three adult recipients and the coincidence of MRA findings of vascular stenosis were noted in 10 cases. But there is no strong association between biliary complication and vascular stenosis in this study. Interestingly, based on our unpublished data, there is relatively higher incidence of combined vascular and biliary stenosis in pediatric recipients. More evidence was needed to seek the relationship between biliary and vascular complications.

With the accuracy of MRA, successful percutaneous transluminal angioplasty (PTA) may be necessary in some cases to maintain vessel patency and avoid surgical revision or re-transplantation. PTA for balloon dilatation or stent placement is safer with MRA guidance. We believe that the excellent survival rate of the post-transplant recipients is attributable to prompt MRI detecting biliary/vascular complications and early interventional treatment. Thus, MRI has potential as the single imaging modality in evaluating the vascular and biliary complications in LDLT recipients. Biliary and vascular complications can be managed with non-surgical intervention under MRA and MRC guidance.

**CONCLUSION**

In summary, MRC is a reliable diagnostic modality for depicting post-transplant biliary complications with a 96% accuracy rate. MRC can provide accurate imaging which shows abnormal biliary trees and thus can guide biliary intervention. MRC can accurately show the site of strictures; one of its advantages being the visualization of the bile ducts above and below the stricture or obstruction, which is also mandatory before therapeutic biliary interventions (ERBD and PTBD) in post-transplant recipients. This non-invasive imaging modality, MRA (venography, arteriography, and portography) with 3D reconstruction can replace the traditional conventional catheter angiography, computed tomography, and sonography. MRA with
3D reconstruction would have further essential information for the vascular insults. Thus, MRI has potential to be the single imaging modality in evaluating the vascular and biliary complications in LDLT recipients. Biliary and vascular complications can be managed with non-surgical intervention under MRI guidance.

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