

MR cholangiopancreatography findings of biliary tract complications after liver transplantation

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Background/aim: We aimed to present the magnetic resonance cholangiopancreatography (MRCP) findings of biliary tract complications after liver transplantation.

Materials and methods: Seventy-five patients who underwent MRCP in our department between July 2011 and July 2015 after liver transplantation were retrospectively evaluated. The MRCP images were reevaluated by three radiologists in consensus. Diagnostic confirmation of MRCP findings was obtained with direct cholangiographic examinations or with clinical, radiological, and laboratory findings and concordance between MRCP findings and the final diagnosis was investigated.

Results: Twenty-seven of the 75 patients had normal MRCP findings and at least one type of biliary tract complication was detected on the MR images of 48 patients. These complications included anastomotic stricture, dilatation of the biliary tract, nonanastomotic stricture, biliary leakage, cholangitis, biloma, abscess due to cholangitis, biliary stone-sludge, and donor-to-recipient bile duct disproportion. Thirty of the 75 patients were followed only by clinical and laboratory findings without further imaging. Forty-five patients underwent direct cholangiographic examinations. At the end of the follow-up period, 28 of the 75 patients were considered free of biliary tract complications, and at least one bile duct complication was diagnosed in 47 patients.

Conclusion: With its high sensitivity and specificity, MRCP should be the first choice of method in the diagnosis and follow-up of biliary complications after liver transplantation.

Key words: Liver transplantation, biliary tract complications, magnetic resonance cholangiopancreatography

1. Introduction

Various complications can occur after liver transplantation, and these complications significantly affect the success of the therapy. Bile duct complications are one of the major causes of mortality and morbidity after liver transplantation. Most of the early complications are associated with biliary leakage and occur in the first 3 months. Late complications can develop a few months or a few years after transplantation. Diameter discrepancy between the recipient's and donor's common hepatic ducts is another clinical problem that may arise after transplantation and can sometimes be considered as a complication (1,2).

Magnetic resonance cholangiopancreatography (MRCP) is a noninvasive imaging technique that does not require anesthesia and does not use ionizing radiation. It is a common choice of imaging to diagnose pancreatobiliary diseases, and today in many centers it

is the preferred method before endoscopic retrograde cholangiopancreatography (ERCP). Besides the biliary tract, it also gives information about the liver parenchyma and neighboring soft tissues and organs (3).

Herein we aimed to present the MRCP findings of biliary tract complications after liver transplantation and to emphasize the success of MRCP in demonstrating these complications.

2. Materials and methods

The institutional ethics committee approved this retrospective study protocol and waived the need for informed consent.

2.1. Patient population

Eighty-five consecutive patients who underwent MRCP in our department between July 2011 and July 2015 after liver transplantation were retrospectively evaluated. Medical

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records of these patients including clinical and biochemical data and radiological examinations were investigated from the database of our institution. Ten patients whose medical records were missing, whose follow-up period after MRCP was less than 12 months, or who had insufficient MRCP images due to respiratory, motion, or metallic artifacts were excluded. A total of 75 patients were enrolled. All patients had clinical or biochemical signs of biliary complications (jaundice, nausea, epigastric pain, elevated cholestatic liver enzymes like alkaline phosphatase, etc.) or had abnormal clinical or biochemical findings in which biliary complications had to be ruled out. There were 29 female and 46 male patients with a mean age of 45 ± 13.377 (SD) years. Live donor transplantation was performed for 56 of the 75 patients (74.7%), and the right lobe was transplanted in 53 of these 56 (70.7%) patients. Biliary reconstruction technique was duct-to-duct anastomosis in 48 patients (64%) and hepaticojejunostomy in 27 patients (36%). T-tube insertion was performed in 10 patients during the surgery. Patient characteristics are summarized in Table 1.

The most common indication for transplantation was cirrhosis caused by viral hepatitis, in which hepatitis B virus (HBV) infection was more frequent than hepatitis C virus (HCV) infection. Indications for liver transplantation are listed in Table 2.

Diagnostic confirmation of MRCP findings was obtained with direct cholangiographic examinations including ERCP, percutaneous transhepatic cholangiography (PTC), and/or T-tube cholangiography (TTC) or with clinical, radiological, and laboratory findings in the follow-up

Table 1. Patient characteristics.

| | |
|---|--------------------|
| Age (mean \pm SD) | 45.28 \pm 13.337 |
| Sex (% M/F) | 61.3 / 38.7 |
| Donor (n, %) | |
| Cadaveric | 19 (25.3) |
| Live | 56 (74.7) |
| Transplanted lobe (n, %) | |
| Total | 19 (25.3) |
| Right | 53 (70.7) |
| Left | 3 (4.0) |
| Type of anastomosis (n, %) | |
| Hepaticojejunostomy | 27 (36) |
| Duct-to-duct | 48 (64) |
| T-Tube (n, %) | |
| Present | 10 (13.3) |
| Absent | 65 (86.7) |
| Time interval between transplantation and MRCP (weeks, median, min-max) | 52 (4-730) |

Table 2. Indications for liver transplantation.

| | |
|-----------------------------|-----------|
| HBV-C (n, %) | 25 (33.3) |
| HCV-C (n, %) | 11 (14.7) |
| Cryptogenic-C (n, %) | 7 (9.3) |
| HBV-C, delta (n, %) | 5 (6.7) |
| PSC (n, %) | 4 (5.3) |
| Wilson Disease (n, %) | 4 (5.3) |
| HBV-C, HCC (n, %) | 3 (4.0) |
| Autoimmune hepatitis (n, %) | 3 (4.0) |
| Toxic hepatitis (n, %) | 3 (4.0) |
| HCV-C, HCC (n, %) | 2 (2.7) |
| Primary biliary -C (n, %) | 2 (2.7) |
| Budd-Chiari (n, %) | 2 (2.7) |
| AFH (n, %) | 2 (2.7) |
| Alcohol induced-C (n, %) | 1 (1.3) |
| SSC (hydatid cyst) (n, %) | 1 (1.3) |

-C: Cirrhosis, HCC: hepatocellular carcinoma, PSC: primary sclerosing cholangitis, AFH: acute fulminant hepatitis, SSC: secondary sclerosing cholangitis.

period. Concordance between MRCP findings and the final diagnosis was investigated.

2.2. MRCP technique

MR imaging was performed with a 1.5-T MR system (Optima 450 W, GE Medical Systems) equipped with a phased array torso coil. Single shot fast spin echo T2 weighted coronal and T2 weighted propeller sequence axial images and multisection thin-slab 3D T2 weighted images were acquired using respiratory triggering. Thick-slab coronal oblique sequences were obtained with an average angle of 15–20 degrees. MR imaging pulse sequence parameters are detailed in Table 3.

No patient preparation was required.

2.3. Image analysis

The MRCP examinations were reevaluated by three radiologists in consensus. The diameter and morphology of intra- and extrahepatic bile ducts were assessed. Measurements were made on thick-slab images. Intrahepatic bile ducts were considered dilated if they measured more than 3 mm, and extrahepatic bile ducts were considered dilated if the maximum diameter was over 8 mm. Anastomotic stricture was defined as a focal stricture at the site of anastomosis, and a relatively long segment of stricture distant from anastomosis was considered as a nonanastomotic stricture. Biliary stones or sludge were defined as endoluminal hypointense filling defects located in the dependent portion of the lumen. When

the diameter of the donor's common bile duct was larger than the diameter of the recipient's common bile duct, it was accepted as donor-to-recipient common bile duct disproportion. Collections in relation to the biliary tract and with signal intensity similar to that of the gallbladder were considered as biloma. Irregular enlargements in intrahepatic or extrahepatic bile ducts with wall thickening, microabscesses, and slightly increased signal intensity in the neighboring liver parenchyma on T2-W images were taken into consideration for cholangitis.

2.4. Statistical analysis

The obtained data were loaded and evaluated in a computer environment via SPSS 22.0 (IBM Corp., Armonk, NY, USA). Sensitivity, specificity, positive predictive, and negative predictive values were calculated by comparing MRCP results with direct cholangiographic examinations (ERCP, PTC, TTC). Descriptive statistics were presented as mean \pm standard deviation, frequency distribution, and percentage. The Pearson chi-square test and Fisher exact test were used to evaluate categorical variables. Statistical significance was accepted at $P < 0.05$.

3. Results

During the follow-up period 35 of the 75 patients underwent ERCP, six patients underwent PTC, and four patients underwent TTC. In 30 of the 75 patients (40%) no further cholangiographic imaging was performed and they were followed with clinical findings, abdominal ultrasound, or computed tomography (CT) scanning and laboratory tests for at least 12 months.

The mean time between liver transplantation and MRCP was 52 weeks (range: 4–730 weeks).

MRCP examinations revealed no abnormal findings in 27 of the 75 patients (36%) and at least one bile duct

complication was detected in 48 patients (64%). These complications included anastomotic stricture ($n = 28$; 37.3%), bile duct dilatation ($n = 36$; 48%), nonanastomotic stricture ($n = 4$; 5.3%), biliary leakage ($n = 5$; 6.7%), cholangitis ($n = 17$; 22.7%), biloma ($n = 8$; 10.7%), cholangitic abscess ($n = 6$; 8%), stone-sludge in bile ducts ($n = 6$; 8%), and donor-to-recipient common bile duct disproportion ($n = 5$; 6.7%).

MRCP findings were compared with the findings of ERCP, PTC, and TTC or with the final diagnosis reached on the basis of clinical, radiological, and laboratory data. At the end of the follow-up period, 28 of the 75 patients (37.3%) were considered as free of biliary tract complications, and at least one bile duct complication was detected in 47 patients (62.7%).

In 33 of the 36 patients with intrahepatic bile duct dilatation on MRCP, the diagnosis was confirmed by direct cholangiography. Three of the 36 patients were followed by MRCP and no progression or regression was noted. There were no patients for whom MRCP could not demonstrate bile duct dilatation. The most common complication accompanying intrahepatic bile duct dilatation was anastomotic stricture (79.4%). Intrahepatic bile duct dilatation was seen in 88.9% of the patients with hepaticojejunostomy and 69.4% of the patients with duct-to-duct anastomosis.

The sensitivity, specificity, and positive and negative predictive values of MRCP in detecting anastomotic stricture were determined as 97%, 100%, 100%, and 94%, respectively.

The final diagnosis of anastomotic stricture was detected in 22.2% of the patients with hepaticojejunostomy and 47.9% of patients with duct-to-duct anastomosis. Anastomotic stricture was significantly more common in

Table 3. MR imaging pulse sequence parameters.

| Parameter | T2W SSFSE | T2W propeller | 3D T2W thin-slab | 3D T2W thin-slab | Thick-slab |
|----------------------|------------------|------------------|------------------|------------------|------------------|
| Matrix size | 320 \times 192 | 384 \times 384 | 288 \times 288 | 288 \times 288 | 384 \times 224 |
| Slice thickness (mm) | 7 | 7 | 2 | 1.6 | 40 |
| Spacing (mm) | 0.5 | 1 | 0 | 0 | 0 |
| Echo time (ms) | 80 | 90 | Minimum | Minimum | 900 |
| Echo train length | | 32 | 140 | 140 | 39 |
| FoV (cm) | 42 | 42 | 34 | 32 | 30 |
| Orientation | Coronal | Axial | Oblique axial | Oblique coronal | Oblique coronal |
| Bandwidth (Hz/Px) | 83.33 | 83.33 | 83.33 | 83.33 | 83.33 |

T2W = T2-weighted, SSFSE = single shot fast spin echo, FoV = field of view.

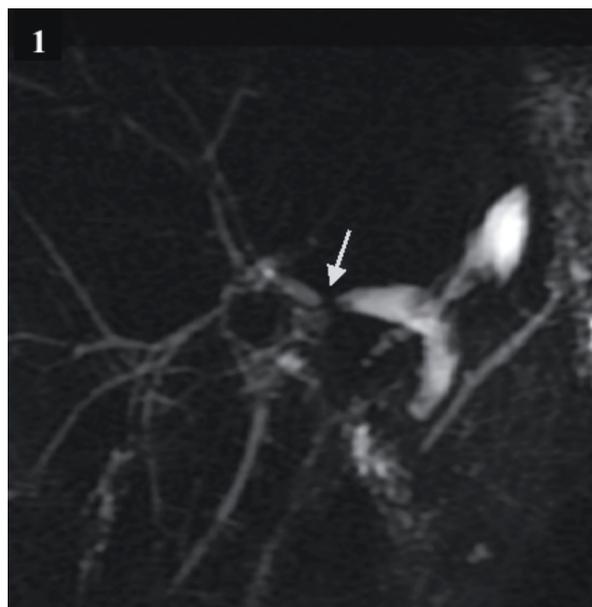


Figure 1. Thick-slab MRCP image of a 56-year-old male patient with duct-to-duct anastomosis shows an anastomotic stricture (arrow), which was confirmed with ERCP. The patient underwent biliary reconstruction.

patients who underwent duct-to-duct anastomosis ($P = 0.028$). In 93.1% of the patients with anastomotic stricture intrahepatic bile duct dilatation was also seen (Figure 1).

In 2 of the 4 patients with nonanastomotic stricture on MRCP images, the diagnosis was confirmed by direct cholangiographic examination. The remaining two patients were followed by MRCP, and there was no clinical indication for a further examination.

In three of the 17 patients with MRCP findings suggesting cholangitis, the diagnosis was ruled out depending on clinical, laboratory, and cholangiographic studies. The sensitivity, specificity, and positive and negative predictive values of MRCP examination in the diagnosis of cholangitis was determined as 100%, 95%, 82%, and 100%, respectively.

In 2 of the 8 patients who had rounded fluid collections regarded as biloma on MRCP images, the presence of biloma was verified by TTC imaging. The remaining six patients were followed by abdominal ultrasonography and CT. Similarly, MRCP revealed cholangitic abscesses in six patients, and the presence of an abscess was confirmed by ERCP in only two of these patients. Abscesses were also demonstrated on CT images in all patients (Figures 2A–2C).

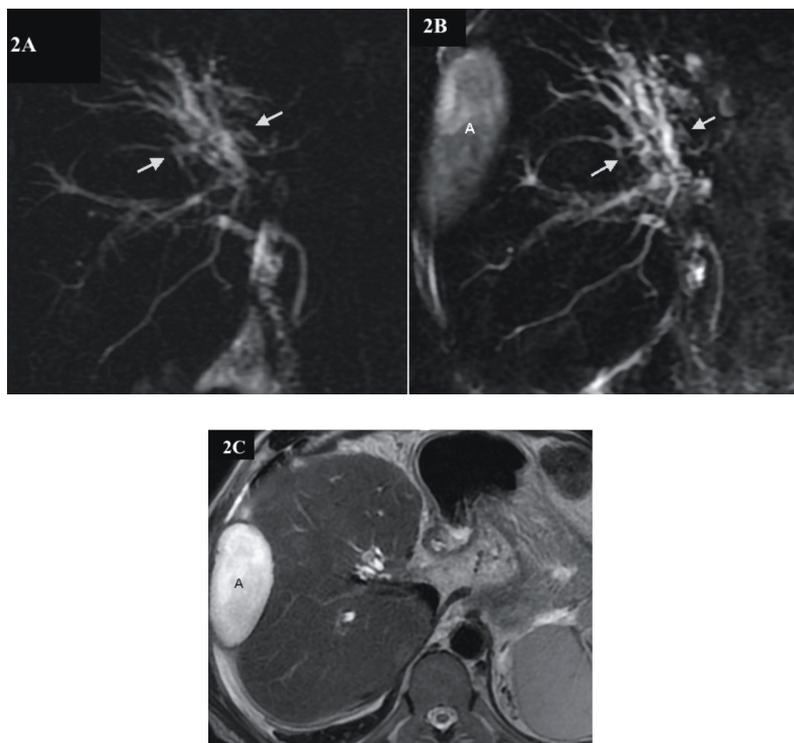


Figure 2. A, B, C) MR images of a 51-year-old man with hepatitis C who underwent cadaveric liver transplantation and hepaticojejunostomy. The patient had clinical and laboratory findings suggesting cholangitis. Thick-slab MRCP image shows dilated intrahepatic bile ducts, which are clustered on the left side of the transplanted liver (arrows on A). On the follow-up MRCP image the irregular biliary duct dilatation is more prominent (arrows on B) with an accompanying abscess formation. The subcapsular hepatic abscess is well demonstrated on the T2 weighted axial image (C). The abscess was drained but the patient deteriorated and ultimately died due to sepsis. A: Abscess.

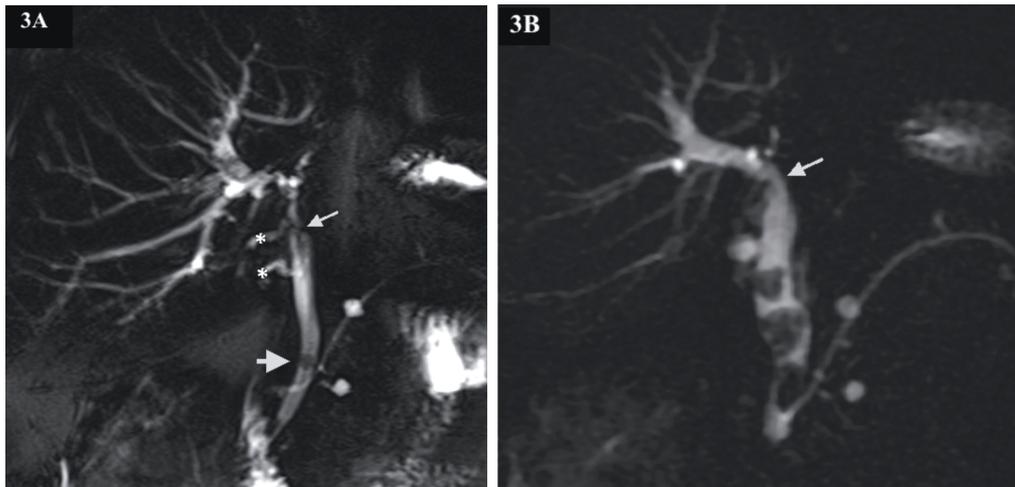


Figure 3. A, B) Thick-slab MRCP images of a 55-year-old male patient with alcoholic cirrhosis who underwent live donor transplantation and duct-to-duct anastomosis. On the initial MRCP image (A) an anastomotic stricture (small arrow) is demonstrated, which was confirmed and dilated with ERCP. Intrahepatic bile duct dilatation and a choledochal stone (large arrow) are also seen. Further MRCP imaging reveals that the anastomotic stricture (arrow on B) and associated intrahepatic biliary duct dilatation have improved but the number and size of the choledochal stones have increased. The biliary stones were extracted with ERCP. Asterisks: Donor's and recipient's cystic ducts.

Bile duct stones or sludge detected on MRCP images were confirmed by cholangiographic imaging techniques in all six patients (Figures 3A and 3B). In the remaining 39 patients who underwent direct cholangiographic studies, no biliary stone or sludge was detected in concordance with MRCP.

Biliary leakage was detected in 5 of the 75 patients and it was confirmed by direct cholangiographic imaging techniques in all patients. MRCP could not show biliary leakage in two patients diagnosed by direct cholangiographic examinations.

The final diagnosis of biliary leakage was seen in 3 of the 10 patients (30%) with T-tube drainage and only in 4 of the 65 patients (6.2%) without T-tube insertion. This relationship was statistically significant ($P = 0.046$).

In 5 of the 75 patients there was discrepancy between the recipient's and donor's common bile duct diameters on MRCP images. Donor-to-recipient common bile duct disproportion was confirmed by reference imaging techniques in 3 of these patients. In 1 of the 5 patients, an anastomotic stricture was detected on ERCP examination. One patient did not undergo further imaging studies.

In 45 of the 75 patients who underwent both MRCP and at least one direct cholangiographic imaging technique (ERCP, PTC and/or TTC), the overall sensitivity of MRCP in detecting biliary tract complications was determined as 98%. Specificity and positive and negative predictive values were 100%, 100%, and 75%, respectively.

4. Discussion

Despite recent advances in surgical techniques, bile duct complications following orthotopic liver transplantation are still important clinical problems that can increase morbidity. Clinical and laboratory findings of bile duct complications are usually nonspecific and imaging is required for diagnosis (2). Direct cholangiographic techniques such as ERCP and PTC are still accepted as the gold standard methods for the diagnosis of bile duct complications. Nevertheless, these are invasive procedures and have relatively high complication rates (4). With the technical advances in MR imaging, faster sequences have allowed reduced acquisition time, reduced artifacts, improved anatomic detail, and improved patient acceptance (5). Various studies have concluded that MRCP is highly sensitive and specific in the diagnosis of biliary tract complications after liver transplantation and our study is consistent with the literature (2,6,7,8).

Anastomotic strictures that are seen as focal and sudden constriction of the lumen at the level of anastomosis with expansion in the proximal bile ducts are the most common biliary complications after liver transplantation. It has been reported that anastomotic strictures may be related to the surgical procedure, and ischemia at the site of anastomosis, postoperative biliary fistula, and/or fibrosis may be associated with the process. Fibrotic changes may cause scarring at the level of the anastomosis leading to retraction and a significant luminal narrowing, which usually involves a short segment (9).

It has been suggested that the incidence of strictures in patients with biliary complications after liver transplantation is over 40%, and anastomotic strictures are seen in more than 30% of the patients (2,10). Our study is consistent with the literature, as the rates of bile duct stenosis and anastomotic strictures were determined as 41.4% and 38.7%, respectively. We also found that anastomotic strictures were more frequent in patients who underwent duct-to-duct anastomosis than in those who underwent hepaticojejunostomy. Although this relationship was statistically significant, we should keep in mind that the numbers of patients in the two groups were not equal and this can be considered as an important limiting factor in this regard. We also found that although intrahepatic bile duct dilatation is usually associated with anastomotic stricture, it was more common in patients with hepaticojejunostomy. We thought that this finding might suggest that biliary drainage is easier when the physiological route is preserved, and mild intrahepatic bile duct dilatation may be associated with hepaticojejunostomy without an anastomotic stricture. Nevertheless, this should be investigated with further studies.

As a cross-sectional form study with high anatomical detail, MRCP is particularly superior to direct cholangiographic examinations in detecting collections such as abscess and biloma, and in depicting the imaging findings of cholangitis. It has been suggested that cholangitis may be less frequent in patients with duct-to-duct anastomosis in which the Oddi sphincter, a natural barrier for colonization, is preserved (11). In our study, hepaticojejunostomy was performed in 43% and duct-to-duct anastomosis was performed in 57% of the patients who had a diagnosis of cholangitis depending on clinical, laboratory, and imaging findings, and the difference was not statistically significant.

The success of MRCP in detecting biliary stone/sludge is quite high with a sensitivity of 90%–95% (12). In the series of Valls et al. (2), the prevalence of isolated biliary stones was 14.2% and MRCP accurately revealed 88.9% of them. In our study, biliary stone/sludge was detected in 8% of the patients with MRCP and they were all confirmed by direct cholangiographic examinations.

Bile leakage is the most common early biliary complication after liver transplantation. More than 70% of the cases occur in the first month following transplantation or after T-tube removal (13). Bile leaks may occur at the level of the anastomosis, at the T-tube insertion site, at the level of cystic duct, or on the liver-cut surface in

partial liver transplantation. The incidence of bile leaks is reported between 5% and 19% in different studies. It has been suggested that the incidence of bile leaks after live donor liver transplantation is slightly higher than that seen after cadaveric total liver transplantation (14–16). The incidence of biliary leakage was 9.3% in our study, and all patients had undergone live donor transplantation. In contrast to direct cholangiographic examinations, bile leakage is indirectly detected by unenhanced MRCP. Collections in relation to the bile ducts can be evaluated in favor of bile leakage, and the sensitivity of MRCP was 71% in our study, which is relatively low. Contrast-enhanced MRCP using hepatobiliary-specific contrast agents can be a problem-solving method in the postoperative assessment of transplantation patients. As hepatobiliary-specific contrast agents are all excreted into the biliary tree, contrast-enhanced MRCP may be useful in the depiction of the biliary tree in complicated patients, and especially in identifying the site of the bile leak (17).

Donor-to-recipient common bile duct disproportion has been suggested as a borderline and a relatively common condition (18.2%) that can be misdiagnosed as an anastomotic stricture (1,2). Nevertheless the incidence of this condition in our study was low (4%). A careful examination should be made and anastomotic stricture should be ruled out before the diagnosis of donor-to-recipient common bile duct disproportion.

There are some limiting factors of our study. The first one is the retrospective nature of the study. The second one is that ERCP, PTC, and TTC were not performed for all patients. Biliary strictures and leaks that we could not detect or strictures that we misdiagnosed as donor-to-recipient bile duct disproportion were correctly diagnosed on cholangiography studies, but as cholangiographic studies were not performed for all patients we could not show exact discordance between the two methods.

The third limiting factor is that the rates we achieved may not reflect the true prevalence of complications, since MRCP was not performed for all liver transplant recipients. The fourth limiting factor is that the numbers of patients were not equal between the two groups in terms of transplantation procedure and anastomosis type and the patient population is heterogeneous. However, our findings are largely consistent with the literature.

We conclude that MRCP can accurately demonstrate biliary complications after liver transplantation and can be used in the diagnosis and follow-up of these conditions. Invasive procedures can be saved for the diagnosis of debatable complications and for treatment.

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