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Added value of gadoxetic acid-enhanced T1-weighted magnetic resonance cholangiography for the diagnosis of post-transplant biliary complications

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Abstract

Objectives—Biliary complications after liver transplantation (LT) are common. This study aimed to ascertain the value of gadoxetic acid-enhanced T1-weighted (T1w) magnetic resonance cholangiography (MRC) to evaluate anastomotic strictures (AS), nonanastomotic strictures (NAS) and biliary casts (BC).

Methods—Sixty liver-transplanted patients with suspicion of biliary complications and T2w-MRCP and T1w-MRC followed by endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC) were analysed. Two readers reviewed the MRCs

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Compliance with ethical standards

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Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of this article.

Statistics and biometry One of the authors has significant statistical expertise.

Ethical approval Institutional Review Board approval was obtained.

Informed consent Written informed consent was waived by the Institutional Review Board.

Study subjects or cohorts overlap No study subjects or cohorts have been previously reported.

Methodology

- retrospective
- case-control study
- performed at one institution

and rated image quality (IQ) and likelihood for AS/NAS/BC on Likert scales. Sensitivity, specificity and predictive values were calculated, ROC curve analysis performed, and inter-reader variability assessed. The subjective added value of T1w-MRC was rated.

Results—IQ was high for all sequences without significant differences (2.83–2.88). In 39 patients ERCP/PTC detected a complication. Sensitivity and specificity for AS were 64–96 using T2w-MRCP, increasing to 79–100 using all sequences. Use of all sequences increased the sensitivity of detecting NAS/BC from 72–92% to 88–100% and 67–89% to 72–94%, respectively. Kappa values were substantial (0.45–0.62). T1w-MRC was found to be helpful in 75–83.3%.

Conclusions—Combining T1w-MRC and T2w-MRCP increased sensitivity and specificity and diagnostic confidence in patients after LT with suspected biliary complications. T1w-MRC is a valuable tool for evaluating post-transplant biliary complications

Keywords

Magnetic resonance cholangiography; Liver transplantation; Gadoteric acid; Biliary complications; Anastomotic stricture

Introduction

Biliary complications after liver transplantation are common and reported in up to 30% of patients [1, 2]. Early postoperative complications include biliary leak due to incomplete or dehiscence biliary anastomoses. Anastomotic strictures (AS) of the bile ducts, as well as non-anastomotic strictures (NAS) involving the intra- and extrahepatic bile ducts are reported to occur 5–8 months and even up to 1 year after transplantation [3–5]. The clinical presentation of patients with a developing stricture is non-specific and may include jaundice, pruritus, right upper quadrant pain and weight loss. Laboratory studies often demonstrate elevated liver enzymes and elevated serum bilirubin. These markers are non-specific and can be seen with other vascular or hepatic complications such as chronic rejection.

One of the first imaging modalities used in the diagnostic workup is abdominal ultrasound, although its sensitivity and specificity to assess biliary complications are low [6]. A recent study demonstrated that biliary dilatation is a poor predictor of biliary strictures, particularly in the early post-transplant phase [7]. For these reasons, surgeons and hepatologists often proceed to endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC), depending on the type of biliary anastomosis. Unfortunately, ERCP/PTC are relatively invasive procedures and carry a significant risk of complications [8, 9].

Magnetic resonance cholangiopancreatography (MRCP) methods use very heavily T2-weighted sequences to visualize fluid-containing structures such as bile ducts. MRCP technology has improved dramatically over the past decade. With these improvements MRCP has demonstrated comparable sensitivity and specificity to ERCP/PTC for the diagnosis of post-transplant biliary complications including end-to-end choledocho-choledochostomies (CC) [10], although the performance of MRCP is lower with bilioenteric anastomosis (BEA) [11].

Early studies have also investigated the use of T1-weighted MR cholangiography (MRC) using gadobenate dimeglumine (MultiHance, Bracco, Milan, Italy) to evaluate possible biliary complications of liver transplantation. This agent has approximately a 3–5% hepatocyte uptake and biliary excretion at approximately 1–2 h [12]. Early studies using gadobenate dimeglumine-enhanced T1w-MRC demonstrated mixed results in the evaluation of post-transplant biliary complications [12].

Gadoxetic acid (Eovist/Primovist, Bayer Healthcare, Berlin, Germany) is a hepatobiliary gadolinium-based contrast agent with approximately 50% hepatocyte uptake and biliary excretion [13, 14]. It has been evaluated extensively for T1w-MRC for a variety of indications [15–17]. Studies have proven its efficiency in cases of earlier post-transplant complications including biliary leakage [18–20]. The functional depiction of bile flow visualized using T1w-MRC adds invaluable physiological information [12]. In recent years, there have been important improvements and optimization of gadoxetic acid-enhanced T1w-imaging methods. Such improvements include the use of high-resolution navigator-based methods and the use of higher flip angles which optimize the SNR and CNR of biliary imaging using T1w-MRC [21].

Therefore, the aim of this study was to evaluate the added value of gadoxetic acid-enhanced T1w-MRC in addition to T2w-MRCP to evaluate patients with suspected post-transplant biliary complications.

Materials and methods

Patients

This retrospective study was approved by the local Institutional Review Board and was Health Insurance Portability and Accountability Act (HIPAA) compliant. Given the retrospective nature of the study, the Institutional Review Board granted a waiver of informed consent to perform this review.

A search of the liver transplant database from our transplant centre was performed for all patients with a suspicion of post-transplant biliary complications. The search was performed for those patients who underwent MRCP and either ERCP (performed by experienced gastroenterologists) or PTC (performed by experienced interventional radiologists) between 1 January 2009 and 31 March 2016. Gadoxetic acid was integrated into our clinical practice late in 2008, which is the reason for these search dates. Figure 1 contains a flowchart for patient inclusion and exclusion criteria. Table 1 gives an overview over the characteristics of patients included in the study.

Magnetic resonance imaging

All patients were studied after a fasting period of at least 4 h. Imaging was performed on one of the following clinical scanners: 3.0T (GE Healthcare Discovery MR750w or MR 750, Waukesha, WI, USA) or a 1.5T MRI scanner (GE Healthcare Optima MR450w or Signa HDxt, Waukesha, WI, USA). Patients were placed in a supine position on the table and an 8- or 32-channel phased-array torso or cardiac coil were used for signal reception. All patients underwent (i) 2D T2w-MRCP imaging with a breath-held sequence, (ii) 3D T2w-MRCP

performed during free breathing with respiratory triggering, and (iii) 3D T1w-MRC using a spoiled gradient recalled echo (SPGR) sequence performed with navigator triggering in axial orientation and with breath-holds in coronal orientation. Imaging parameters are found in Table 2. Imaging parameters were chosen to guarantee a unique image impression for all field strengths and scanner types.

Dynamic phase T1w imaging was performed before and during the injection of 0.05 mmol/kg gadoxetic acid, injected at 2.0 ml/s followed by a 20–30 ml saline flush injected at the same rate. Approximately 20 mins after gadoxetic acid injection, T1w-MRC was performed. If insufficient contrast excretion in the bile ducts was observed after 20 min, additional T1w-MRC images were acquired up to 40 min.

Image analysis

All MR data sets were transferred and evaluated on a standalone picture-archiving and communications system (PACS) workstation. Two radiologists with 11 and 8 years experience of abdominal MRI, respectively, evaluated the images separately. Reader 2 had fellowship training in reading MRCP data sets. Both readers were blinded to each patient's history, laboratory results, clinical presentation, type of anastomosis, underlying pathology and the results of previous imaging tests.

Each radiologist rated the 2DT2w-MRCP, 3DT2w-MRCP and 3D contrast-enhanced T1w-MRC for image quality on a 3-point Likert scale (1=non-diagnostic, 2=adequate image quality, 3=good image quality). For 3D sequences source data and maximum intensity projection (MIP) were available.

Thereafter, the presence of AS, NAS and BC were rated on a 5-point Likert scale (1=definitely absent, 2=probably absent, 3=uncertain, 4=probably present, 5=definitely present). This evaluation was performed three times for the following combinations of images: (i) T2w-MRCP sequences (2D and 3D T2w-MRCP combined), (ii) T1w-MRC sequences, and (iii) the combination of T2w-MRCP and T1w-MRC. Each evaluation was separated by at least 2 weeks to minimize bias, and the T1w-MRC and T2w-MRCP evaluation was performed in random order.

At the conclusion of the combined interpretation, the radiologists were asked whether there was additional value of gadoxetic acid enhanced T1w-MRC rated on a 3-point Likert scale (1=definitely not helpful, 2= somewhat helpful, 3=definitely helpful).

Statistical analysis

To compare the image quality (IQ) for the three different sequence sets a Mann-Whitney U test was used and a p value <0.05 was set to represent a statistically significant difference.

For the final diagnosis of AS, NAS and BC, confidence rankings 1, 2 and 3 were considered negative for the presence of pathology, while scores of 4 and 5 were considered positive for the presence of pathology.

Sensitivities, specificities, negative predictive values (NPVs) and positive predictive values (PPVs) were calculated for each type of pathology (AS, NSA, BC) and for the two types of anastomoses. ERCP/PTC served as the reference standard. Receiver operating characteristic (ROC) curves were created using SPSS software (IBM SPSS 23.0, Chicago, Ill, USA). Areas under the curve (AUCs) were calculated as the indicator of the diagnostic value of each sequence. MedCalc (version 12.3.0.0, MedCalc Software, Ostend, Belgium) was used to test for statistical differences. Inter-observer agreement was calculated for both readers using Cohen's Kappa analysis. A K-value of 0–0.2 indicated slight, 0.21–0.4 fair, 0.41–0.6 moderate, 0.61–0.8 substantial and 0.81–1 almost perfect agreement.

Results

Patient cohort characteristics

As shown in Figure 1, 153 patients with liver transplantation who presented with clinical suspicion for biliary complications were identified. Of these, there were 60 patients who had undergone gadoxetic acid-enhanced MRI and ERCP or PTC within 1 month of the MRI examination. Patient characteristics are shown in Table 1. All patients with CC underwent ERCP, and all patients with BEA underwent PTC within a month after MRI. The cohort included 40 men and 20 women (age range 3–79 years, mean age 50 years). The mean time range between MRI and liver transplantation was 3.4 years, with a maximum of 10 years and a minimum of 2 months.

MR image quality

Image quality (IQ) of the three sequences evaluated did not differ statistically between readers. The IQ of 2D T2w-MRCP was rated on average as 2.80 and 2.83, respectively, while 3D T2w-MRCP reached an average IQ of 2.87/2.88. 3D gadoxetic acid-enhanced T1w-MRC was rated on average at 2.85 by both readers.

Depiction of biliary complications

ERCP and PTC identified AS in 14 of the 60 patients, NAS in 25 patients and BC was reported in 18 of the 60 cases. Seven patients showed AS, 21 patients NAS and four patients BC as single complication. Two patients showed AS in combination with NAS, three AS and BC, nine NAS and BC, and two patients showed AS, NAS and BC. Twenty-one patients had no reported biliary complications with either ERCP or PTC.

Anastomotic strictures—AS were correctly identified in 11 of 14 patients with T2w-MRCP sequences alone and also using the combined T2w-MRCP and T1w-MRC. Reader 2 correctly identified nine of the patients with AS using T2w-MRCP alone.

Eight patients with CC and six patients with BEA had an AS. Reader 1 detected all patients with AS at the CC using T2w MRCP, while Reader 2 only detected six of eight strictures. Using all sequences, both readers identified AS at the CC in seven patients. Both readers were able to detect three of six patients with AS at the BEA with T2w MRCP and four of six patients with the combined T2w-MRCP and T1w-MRC. Sensitivities, specificities, PPV and

NPV for both readers and all sequences are shown in Table 3. ROC curves are provided in Figs. 2. 3 shows a patient with stenosis at the BEA.

Non-anastomotic strictures—NAS were identified in 25 patients. Reader 1 detected 18 of them with T2w-MRCP and T1w-MRC and 22 of them with a combination of the sequences. Reader 2 detected 23 with T2w MRCP, 22 with T1w-MRC and all of them with a combination of the sequences. Sensitivities, specificities, PPV and NPV are shown in Table 3, including for the two different types of anastomosis. ROC curves are shown in Figs. 2. 4 shows an example of a patient with NAS.

Biliary casts—BC were detected in 18/60 patients. Both readers were able to find the most patients with BC with all sequences (13 and 17/ 18 patients), while T2w-MRCP showed this in 12 and 16 patients, respectively, and T1w-MRC in eight and 14 patients. Sensitivities, specificities, PPV and NPV for both readers, all evaluated sequences as well as all anastomosis and BEA versus CC are shown in Table 3. Figure 5 shows a patient with AS and BC, where BC was only seen with the gadoxetic acid-enhanced MRC images.

ROC curve comparison revealed statistically significant differences for Reader 2 when comparing T2-w MRCP to the combined data sets for NAS ($p=.02$) and for BC ($p=.044$).

Interobserver agreement

Kappa values for both readers for the three different biliary complications and different sequence combinations ranged from 0.45 (moderate, T2w-MRCP for AS) to 0.62 (substantial agreement, all sequences).

Additional value of gadoxetic acid-enhanced T1-weighted MRC

Based on a Likert score of 2 (somewhat helpful) or 3 (definitely helpful) Reader 1 found that in 45 of the 60 cases (75%) T1w-MRC provided additional value for diagnosis while Reader 2 found gadoxetic acid-enhanced T1w-MRC valuable in 50 of the 60 cases (83%). The average Likert score was 2.3 for Reader 1 and 2.5 for Reader 2.

Apart from the ten cases with absent biliary excretion, Reader 1 found no additional value (score 1) in five cases where T2w-MRCP already provided clear anatomical depiction without any signs of stenosis or biliary casts. In all other cases, gadoxetic acid-enhanced T1w-MRC improved the diagnostic certainty in 32 patients (score changes from 2 to 1 or 4 to 5 in any of the mentioned complications) or aided in the correct diagnosis in 13 patients (former false negative changed to right positive or vice versa).

Discussion

In this retrospective study we evaluated the diagnostic accuracy of gadoxetic acid-enhanced T1w-MRC and T2w-MRCP for the evaluation of suspected biliary complications in patients with liver transplantation. Our results demonstrated that gadoxetic acid-enhanced T1w-MRC in addition to T2w-MRCP improves both diagnostic certainty and sensitivity and specificity for the detection of anastomotic strictures, non-anastomotic strictures and biliary casts.

Our results are concordant with related studies in patients without a history of liver transplantation. Reiner et al. demonstrated that the addition of gadoxetic acid-enhanced T1w-MRC significantly improved sensitivity and reader confidence in the assessment of biliary obstructions of different origin [22]. In patients with primary sclerosing cholangitis the additional value of gadoxetic acid-enhanced T1w-MRC has also been noted [15, 23], although Frydrychowicz et al. also concluded that gadoxetic acid-enhanced MRC had a complementary role and concluded that T1w-MRC should not replace T2w-MRCP for the evaluation of PSC.

Our experience confirms that of Frydrychowicz et al., namely that gadoxetic acid-enhanced T1w-MRC alone showed lower diagnostic accuracy compared to the combination of T2w-MRCP and T1w-MRC. This is particularly relevant in patients lacking biliary excretion of gadoxetic acid. In patients with biliary obstruction or hepatocyte dysfunction, bilirubin values are elevated and uptake and excretion of gadoxetic acid is reduced. Gadoxetic acid competes with bilirubin for active transport into hepatocytes through organic anion transporting polypeptide 1 (OATP1). Without biliary ductal enhancement, diagnosis of biliary complications must rely on T2w-MRCP alone. As was seen in our study, T1w-MRC is only helpful when biliary excretion of gadolinium is present.

The package insert for gadoxetic acid reports reduced uptake and excretion for bilirubin >3 mg/dl. Tschirch et al. reported a cut-off value for poor visualization of the biliary tree using gadoxetic acid when the total bilirubin levels were $\geq 30 \mu\text{mol/L}$ (3.4 mg/dl) [24]. In our study, ten patients had minimal to no biliary excretion of gadolinium – eight of these had abnormal bilirubin levels of >1.4 mg/dl. However, only three of these eight patients had bilirubin >3 mg/dl. Further, an additional eight of our patients with bilirubin exceeding 1.4 mg/dl had adequate biliary excretion of gadoxetic acid, providing clear depiction of the biliary tree at 20 min. Three of these eight patients had bilirubin levels exceeding 4 mg/dl. Based on these observations, we conclude that proposed guidelines on limiting the use of gadoxetic acid based on bilirubin cutoffs is problematic. In our experience, a more robust strategy is to acquire both T1w-MRC and T2w-MRCP. The lack of biliary excretion of gadoxetic acid provides important diagnostic information, strongly suggesting either hepatocyte dysfunction or central biliary obstruction. Such patients would likely benefit from ERCP/PTC, and potentially liver biopsy, as a study by Wibmer et al. also shows inferior 1-year retransplantation-free survival in patients with impaired biliary excretion [25].

Our study again demonstrated important differences between the performance of MRI in the evaluation of the two types of anastomoses (CC and BEA) used in liver transplantation [11]. Kinner et al. demonstrated low sensitivity and specificity of 50–83% using T2w-MRCP for the detection of anastomotic strictures in patients with BEA. This is concordant with our results where sensitivity and specificity of T2w-MRCP for BEA was 0.43–0.89, compared to 0.71–1 for end-to-end CC. In our current study, we demonstrated that the addition of gadoxetic acid-enhanced T1w-MRC increased the sensitivity and specificity for the evaluation of BEA anastomotic strictures up to 100%.

Kandasamy et al. using gadobenate dimeglumine performed in patients with BEAs reported higher values for T2w-MRCP and biliary excretion in only 61% and concluded that using contrast-enhanced T1w-MRC was not helpful in this setting [26]. The differences from our results can be explained by a higher fraction of biliary excretion of gadoxetic acid (50%) compared to gadobenate dimeglumine (3–5%). Hottat et al. used manganese dipyriddyloxyl-diphosphate (Mangafodipir, GE Healthcare, London, UK) as a hepatobiliary agent and also demonstrated additional value for the visualization of bile ducts. They, like us, concluded that an excreted biliary contrast agent aids in the assessment of the patency of a BEA [27].

It should be noted that some institutions, including ours, use doses that exceed the recommended package dose of gadoxetic acid (0.025 mmol/kg). Studies have shown that higher doses of gadoxetic acid improves the quality of arterial phase dynamic contrast-enhanced MRI [28–30]. Based on these data, the local standard of care at our institution is to administer 0.05 mmol/kg gadoxetic acid.

This study has several limitations. First, patients included in this study underwent clinically indicated MRI and direct biliary imaging (ERCP or PTC), based on abnormal serum markers that suggested biliary complications. This could lead to selection bias, as it ignores those patients without abnormal serum markers. Nevertheless, serum markers such as bilirubin are relatively nonspecific and can be elevated for reasons other than biliary complications, which may explain the relatively large number of patients (35%) without biliary complications.

Second, we focused our study on the use of gadoxetic acid-enhanced T1w-MRC. It is widely known that gadobenate dimeglumine is also excreted into the bile ducts and can be used for T1w-MRC. However, a lower fraction (3–5%) of gadobenate dimeglumine is excreted into the bile and requires a longer delay (approximately 1–2 h). Given the higher excretion of gadoxetic acid (50%) and shorter delay (20 min) to peak biliary excretion, we have found gadoxetic acid to be advantageous for evaluation of biliary complications.

Third, readers were blinded to clinical and laboratory information when analysing the images. In clinical routine, especially in large centres with a working interchange between radiology, internal medicine and transplantation surgery, readers would know at least parts of this important information.

Finally, ERCP and PTC have some limitations as the reference standard. In contrast to T1w-MRC, these techniques are often limited in the depiction of peripheral bile ducts. This is particularly true when centrally located strictures are present and the injected contrast does not advance peripherally to the strictures. In these cases, T1w-MRC and/or T2w-MRCP may be able to detect strictures and casts that cannot be visualized with either ERCP or PTC, leading to false-positive findings. For these reasons, the accuracy of T1w-MRC for the diagnosis of AS, NAS, and BC may be underestimated.

In conclusion, gadoxetic acid-enhanced T1w-MRC is a valuable technique for the assessment of biliary complications in patients after liver transplantation. In addition to an increased diagnostic confidence, T1w-MRC can improve the detection and characterization of strictures and casts when used in addition to T2w-MRCP. Therefore, we have found

gadoteric acid-enhanced T1w-MRC a valuable tool for the evaluation of suspected biliary complications in patients with prior liver transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AS	Anastomotic stricture
BC	Biliary cast
BEA	Bilioenteric anastomosis
CC	Choledocho-choledochostomy
ERCP	Endoscopic retrograde cholangiopancreatography
IQ	Image quality
LT	Liver transplantation
MIP	Maximum intensity projection
MRC	Magnetic resonance cholangiography
MRCP	Magnetic resonance cholangiopancreatography
NAS	Non-anastomotic stricture
PSC	Primary sclerosing cholangitis
PTC	Percutaneous transhepatic cholangiography

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Key Points

- T1w-MRC is a valuable tool for evaluating post-transplant biliary complications
- Adding T1w-MRC to T2w-MRC increases diagnostic confidence for detection of biliary complications
- A combination of T1w-MRC and T2w-MRCP leads to the best results.

Fig. 1.

Flowchart showing patient selection as well as inclusion and exclusion criteria. *MRCP* magnetic resonance cholangiopancreatography, *ERCP* endoscopic retrograde cholangiopancreatography, *PTC* percutaneous transhepatic cholangiography, *MRI* magnetic resonance imaging, *T1w* T1-weighted, *T2w* T2-weighted

Fig. 2.

Receiver operating characteristic (ROC) curves for both readers and all evaluated sequences for all three biliary complications: **(a)** anastomosis stenosis, **(b)** non-anastomotic strictures and **(c)** biliary cast. Reader 1 ratings for T2w-MRCP in *blue*, gadoxetic acid-enhanced T1w-MRC in *green* and all sequences in *black*, and Reader 2 ratings for T2w-MRCP in *purple*, gadoxetic acid-enhanced T1w-MRC in *yellow* and all sequences in *red*. *MRCP* magnetic resonance cholangiopancreatography, *MRC* magnetic resonance cholangiography, *T1w* T1-weighted, *T2w* T2-weighted

Fig. 3.

A 66-year-old male after a second liver transplantation due to recurrent primary sclerosing cholangitis. (a) 2D T2w-MRCP and (b) 3D T2w-MRCP (maximum intensity projection (MIP)) raised a suspicion of bilioenteric anastomotic stenosis with both readers rating it as probably present (score 4). Gadoxetic acid-enhanced T1w-MRC (c) confirmed the suspicion with higher confidence (definite stenosis, score 5) due to a lack of contrast excretion through the stenosis, even with degraded image quality. PTC performed 1 day after MRI confirmed the presence of the stenosis (d). *MRCP* magnetic resonance cholangiopancreatography, *MRC* magnetic resonance cholangiography, *T1w* T1-weighted, *T2w* T2-weighted

Fig. 4.

A 60-year-old male with a liver transplantation for primary sclerosing cholangitis, presenting with elevated liver enzymes. (a) 3D T2w-MRCP (maximum intensity projection (MIP)) suggests a stenosis at the biliary anastomosis (choledocho-jejunostomy, *arrow*) and possible non-anastomotic strictures. Gadoteric acid-enhanced T1w-MRC clearly depicts the excretion of contrast in the small bowel (b) and a beaded appearance of the intrahepatic bile ducts (*arrows* in c). Percutaneous transhepatic cholangiography (PTC, d) confirms the patent bilioenteric anastomosis and the non-anastomotic intrahepatic strictures with irregularities and abrupt interruption of left hepatic bile ducts (*double arrows*). *MRCP* magnetic resonance cholangiopancreatography, *MRC* magnetic resonance cholangiography, *T1w* T1-weighted, *T2w* T2-weighted

Fig. 5.

A 58-year-old female after liver transplantation due to alcoholic liver cirrhosis with elevated liver enzymes. (a) 2D T2w MRCP, (b) 3D T2w MRCP (maximum intensity projection (MIP)) and thin reformatted gadoxetic acid-enhanced T1w MRC show a stenosis at the anastomosis (choledocho-choledochostomy, *solid arrow*). Gadoxetic acid-enhanced T1w MRC also demonstrated the presence of a cast (*dashed arrow* in C) not seen on T2w MRCP. ERCP confirmed the diagnosis of AST (d) and the cast, which was flushed out after anastomotic dilatation. *MRCP* magnetic resonance cholangiopancreatography, *MRC* magnetic resonance cholangiography, *ERCP* endoscopic retrograde cholangiopancreatography, *T1w* T1-weighted, *T2w* T2-weighted

Table 1

Characteristics of the final analysed patient cohort

Patient characteristics	No.
Gender	
Male	40
Female	20
Age	
<18 years	3
18 years	57
Reason for transplantation	
Cirrhosis (hepatitis C or alcohol induced)	28
Primary sclerosing cholangitis	18
Biliary atresia	5
Malignancy or metabolic disorder	5
Primary biliary cirrhosis	4
Type of anastomosis	
Choledocho-choledochostomy	28
Bilio-enteric anastomosis	32
Liver transplant	
First	49
Second	10
Third	1

Table 2

Imaging parameters for the three different sequence types and three different scanners used

	2D T2w-MRCP			3D T2w-MRCP			T1w-MRC		
	Discovery MR750(w) 3T	Optima MR450w 1.5T	Sigma HDxt 1.5T	Discovery MR750(w) 3T	Optima MR450w 1.5T	Sigma HDxt 1.5T	Discovery MR750(w) 3T	Optima MR450w 1.5T	Sigma HDxt 1.5T
Image orientation	Coronal	Coronal	Coronal	Coronal	Coronal	Coronal	Axial	Axial	Coronal
Slice thickness (mm)	4	4	4	1.8	1.8	1.8	1.8	1.8	2
Number of slices	27	36	28	112	144	128	264	248	320
Echo time (ms)	248	252	250	510	700	700	2.1	1.9	1.1
Repetition time (ms)	2,625	3,000	2,800	5,000	3,750	3,750	6.08	4.36	3.0
Bandwidth (kHz)	+/-50	+/-50	+/-50	+/-50	+/-50	+/-50	+A62.5	+/-42	+/-42
Flip angle (deg)	90	90	90	90	90	90	35	40	28
Matrix	320x224	320x192	320x192	288x288	288x288	288x288	320x224	256x192	256x224
Field of view (mm)	320x320 (%100)	300x300 (%100)	350x350 (%100)	320x320 (%100)	350x350 (%100)	370x370 (%100)	320x360 (%80)	360x330 (%90)	310x400 (%80)
Breathing	Breath- hold	Breath- hold	Breath- hold	Resp. triggered	Resp. triggered	Resp. triggered	Breath- hold	Resp. triggered	Breath- hold
Parallel imaging	ARC (R=2)	ARC (R=2)	ARC (R=2)	ASSET (R=2)	ASSET (R=2)	ASSET (R=2)	ARC(R=4)	ARC(R=4)	ARC(R=4)
Scan time (s)	20	20	20	240-100 *	240-100 *	240-100 *	240-360 *	240-360 *	20-24
Fat saturation	No	No	No	No	No	No	Yes	Yes	No

* Respiratory-triggered sequences scan time depending on patients' breathing

Table 3

Sensitivity, specificity, negative (NPVs) and positive predictive values (PPVs) for detection of biliary complications, for both readers for T2w-MRCP, gadoteric acid-enhanced T1 w-MRC and all sequences combined

Complication	Reader 1		Reader 2			
	T2w-MRCP	T1w-MRC	Combined	T2w-MRCP	T1w-MRC	Combined
(A) Anastomotic Stricture (AS, n=14)						
Sensitivity	100% (99.9–100)	75.0% (34.9–96.8)	87.5% (47.3–99.7)	75.0% (34.9–96.8)	87.5% (47.3–99.7)	87.5% (47.3–99.7)
Specificity	95.0% (75.1–99.9)	95.0% (75.1–99.9)	95.0% (75.1–99.9)	95.0% (75.1–99.9)	100% (83.2–100)	100% (83.2–100)
PPV	88.9% (51.8–99.7)	85.7% (42.1–99.6)	87.5% (47.3–99.7)	85.7% (42.1–99.6)	100% (59–100)	100% (59–100)
NPV	100% (99.7–100)	90.5% (69.6–98.8)	95.0% (75.1–99.9)	90.5% (69.6–98.8)	95.2% (76.2–99.9)	95.2% (76.2–99.9)
Non-anastomotic stricture (NAS, n=25)						
Sensitivity	71.4% (29.0–96.3)	57.1% (18.4–90.1)	57.1% (18.4–90.1)	100% (94.6–100)	85.7% (42.1–99.6)	100% (99.9–100)
Specificity	57.1% (34.0–78.2)	81.0% (58.1–94.6)	66.7% (43.0–85.4)	81.0% (58.1–94.6)	100% (83.9–100)	95.2% (76.2–99.9)
PPV	35.7% (12.8–64.9)	50.0% (15.7–84.3)	36.4% (10.9–69.2)	63.6% (30.8–89.1)	100% (77.2–100)	87.5% (47.3–99.7)
NPV	85.7% (57.2–98.2)	85.0% (62.1–96.8)	82.4% (56.6–96.2)	100% (89.1–100)	95.5% (77.2–99.9)	100% (99.7–100)
Cast (BC, n=18)						
Sensitivity	81.8% (48.2–97.7)	54.5% (23.4–83.3)	90.9% (58.7–99.8)	90.9% (58.7–99.8)	90.9% (58.7–99.8)	100% (99.9–100)
Specificity	94.1% (71.3–99.9)	94.1% (71.3–99.9)	88.2% (63.6–98.5)	88.2% (63.6–98.5)	94.1% (71.3–99.9)	94.1% (71.3–99.9)
PPV	90.0% (55.5–99.7)	85.7% (42.1–99.6)	83.3% (51.6–97.9)	83.3% (51.6–97.9)	90.9% (58.7–99.8)	91.7% (61.5–99.8)
NPV	88.9% (65.3–98.6)	76.2% (52.8–91.8)	93.8% (69.8–99.8)	93.8% (69.8–99.8)	94.1% (71.3–99.9)	100% (99.8–100)
(B) Anastomotic Stricture (AS, n=14)						
Sensitivity	50.0% (11.8–88.2)	66.7% (22.3–95.7)	66.7% (22.3–95.7)	50.0% (11.8–88.2)	66.7% (22.3–95.7)	66.7% (22.3–95.7)
Specificity	88.5% (69.8–97.6)	96.2% (80.4–99.9)	96.2% (80.4–99.9)	96.2% (80.4–99.9)	100% (86.8–100)	100% (86.8–100)
PPV	50.0% (11.8–88.2)	80.0% (28.4–99.5)	80.0% (28.4–99.5)	75.0% (19.4–99.4)	100% (39.8–100)	100% (39.8–100)
NPV	88.5% (69.8–97.6)	92.6% (75.7–99.1)	92.6% (75.7–99.1)	89.3% (71.8–97.7)	92.9% (76.5–99.1)	92.9% (76.5–99.1)
Non-anastomotic stricture (NAS, n=25)						
Sensitivity	72.2% (46.5–90.3)	77.8% (52.4–93.6)	100% (81.5–100)	88.9% (65.3–98.6)	88.9% (65.3–98.6)	100% (99.8–100)
Specificity	78.6% (49.2–95.3)	85.7% (57.2–98.2)	85.7% (57.2–98.2)	78.6% (49.2–95.3)	92.9% (66.1–99.8)	92.9% (66.1–99.8)
PPV	81.3% (54.4–96.0)	87.5% (61.7–98.4)	90.0% (68.3–98.8)	84.2% (60.4–96.6)	94.1% (71.3–99.9)	94.7% (74.0–99.9)
NPV	68.8% (41.3–89.0)	75.0% (47.6–92.7)	100% (73.5–100)	84.6% (54.6–98.1)	86.7% (59.5–98.3)	100% (75.3–100)

Complication	Reader 1		Reader 2	
	T2w-MRCP	T1w-MRC	Combined	Combined
Sensitivity	42.9% (9.9–81.6)	28.6% (3.7% – 71.0)	42.9% (9.9–81.6)	85.7% (42.1–99.6)
Specificity	84.0% (63.9–95.5)	96.0% (79.6–99.9)	92.0% (74.0–99.0)	96.0% (79.6–99.9)
PPV	42.9% (99.9–81.6)	66.7% (9.4–99.2)	60.0% (14.7–94.7)	85.7% (42.1–99.6)
NPV	84.0% (63.9–95.5)	82.8% (64.2–94.2)	85.2% (66.3–95.8)	96.0% (79.6–99.9)
(C) Anastomotic Stricture (AS, n=14)				
Sensitivity	78.6% (49.2–95.3)	71.4% (41.9–91.6)	78.6% (49.2–95.3)	78.6% (49.2–95.3)
Specificity	91.3% (79.2–97.6)	95.7% (85.2–99.5)	95.7% (85.2–99.5)	100% (92.3–100)
PPV	73.3% (44.9–92.2)	83.3% (51.6–97.9)	84.6% (54.6–98.1)	100% (71.5–100)
NPV	93.3% (81.7–98.6)	91.7% (80.0–97.7)	93.6% (82.5–98.7)	93.9% (83.1–98.7)
Non-anastomotic stricture (NAS, n=25)				
Sensitivity	72.0% (50.6–87.9)	72.0% (50.6–87.9)	88.0% (68.8–97.5)	100% (86.3–100)
Specificity	65.7% (47.8–80.9)	82.9% (66.4–93.4)	74.3% (56.7–87.5)	94.3% (80.8–99.3)
PPV	60.0% (40.6–77.3)	75.0% (53.3–90.2)	71.0% (52.0–85.8)	92.6% (75.7–99.1)
NPV	76.7% (57.7–90.1)	80.6% (64.0–91.8)	89.7% (72.6–97.8)	100% (89.4–100)
Cast (BC, n=18)				
Sensitivity	66.7% (41.0–86.7)	44.4% (21.5–69.2)	72.2% (46.5–90.3)	94.4% (72.7–99.9)
Specificity	88.1% (74.4–96.0)	95.2% (83.8–99.4)	90.5% (77.4–97.3)	95.2% (83.8–99.4)
PPV	70.6% (44.0–89.7)	80.0% (44.4–97.5)	76.5% (50.1–93.2)	89.5% (66.9–98.7)
NPV	86.0% (72.1–94.7)	80.0% (66.3–90.0)	88.4% (74.9–96.1)	97.6% (87.1–99.9)

(A) Results for patients with a choledochal-choledochostomy (n=28), (B) results for the patients with biliointerteric anastomosis (n=32) and (C) results for all types of anastomosis (n=60). 95% confidence intervals are in parentheses

T1w T1-weighted, T2w T2-weighted, MRCP magnetic resonance cholangiopancreatography, MRC magnetic resonance cholangiography