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Value of Magnetic Resonance Cholangiopancreatography in Assessment of Nonanastomotic Biliary Strictures After Liver Transplantation

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Background. Nonanastomotic biliary strictures (NAS) remain a frequent complication after orthotopic liver transplantation (OLT). The aim of this study was to evaluate whether magnetic resonance cholangiopancreatography (MRCP) could be used to detect NAS and to grade the severity of biliary strictures. **Methods.** In total, 58 patients after OLT from 2 Dutch transplantation centers in whom endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography and MRCP were performed within less than 6 months apart were included in the study. Of these patients, 41 had NAS and 17 were without NAS based on endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography and follow-up. Four radiologists—2 from each center—used an adapted validated classification—termed "Leiden Biliary Stricture Classification" "(LBSC)—to evaluate the MRCP examinations independently. In this classification, NAS severity is assessed in 4 hepatobiliary regions. Interobserver agreement of the severity score for each region was calculated with the κ statistics. **Results.** Optimal cutoff value of the LBSC to detect the presence of NAS with MRCP was calculated at 3 points or greater for all readers. Applying this cutoff sensitivity for each reader was greater than 90%, with a specificity of 50% to 82%, positive predictive value of 86% to 91%, and negative predictive value of 80% to 100%. The MRCP performance was better in evaluation of the intrahepatic than of the extrahepatic bile ducts. The additional value of MRCP for grading severity of NAS was limited. **Conclusions.** The MRCP with the LBSC is a reliable tool to detect or exclude NAS after OLT. Currently, MRCP cannot be used to reliably grade the severity of these strictures.

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Biliary tract complications, such as anastomotic strictures (AS) or nonanastomotic biliary strictures (NAS), remain a frequent complication after orthotopic liver transplantation (OLT).[1] The NAS is considered the most challenging complication because the biliary strictures can be located both in the intrahepatic and extrahepatic bile ducts. Frequently, these strictures can be treated endoscopically or radiologically. Inadequate treatment, however, may lead to cholestasis, cholangitis, and eventually graft failure with the need for retransplantation.[2] Early diagnosis and appropriate treatment of NAS can prevent this in most cases and is therefore important during follow-up.

Direct cholangiography by endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC) is invasive and can be associated with major complications, such as postprocedural cholangitis,

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pancreatitis, perforation, and/or bleeding in 1% to 4% of the cases.[3] Therefore, magnetic resonance cholangiopancreatography (MRCP) is increasingly used as a noninvasive tool to monitor the presence of both AS and NAS after OLT.[4-6] The MRCP is a safe, noninvasive technique to visualize the entire pancreatic and biliary tree without the use of exogenous contrast.[7] However, with regard to NAS specifically, no universal radiologic criteria have been established to describe the presence and severity of the biliary strictures. Rajaram et al[8] previously described a validated ERCP/PTC cholangiographic scoring model for primary sclerosing cholangitis (PSC), a cholestatic disease with biliary strictures resembling NAS. As yet, it is unknown whether MRCP using this model could also be applied post-OLT to detect NAS. The aim of this retrospective study was to evaluate whether MRCP, using a modification of this validated scoring model, can be used as a diagnostic tool to detect or exclude NAS, and whether it can predict the severity of the biliary strictures.

MATERIALS AND METHODS

Between August 2005 and July 2013, a total of 68 liver transplant recipients were referred for MRCP in 2 Dutch liver transplantation centers. The MRCP was not part of the standard protocol after OLT, but was performed on indication. After the exclusion of 3 scans with nondiagnostic quality and 7 incomplete scans, MRCPs of 58 patients could be included in the analysis (center A: n = 32; center B: n = 26). Overall, 41 patients had NAS as diagnosed and confirmed with direct cholangiography, with a maximum interval between direct cholangiography and MRCP of 6 months (center A: n = 21; center B: n = 20). The 17 patients without NAS (center A: n = 11; center B n = 6) were included as "no NAS" group. The presence or absence of NAS was also confirmed by follow-up.

Recipient Surgery

In both centers, OLT with standard technique of "piggyback" side-to-side cavo-caval anastomosis, and end-to-end porto-portal and hepatic artery to hepatic artery anastomosis was performed. A duct-to-duct biliary anastomosis—in center A over a 8–12 Ch stent—was performed if possible. The biliary stent was removed with ERCP in center A at 6 weeks after OLT. Only in a minority of included recipients, that is, 18.8% of patients (n = 6) in center A and 19.2% of patients (n = 5) in center B, a choledochojejunostomy was performed. This was performed because patients were transplanted for PSC (n = 8) or Caroli disease (n = 2). In 1 patient, the indication was not available.

In both cohorts, ultrasound and serum liver biochemistry were performed routinely at least on days 0, 1, and 7, and subsequently at 3, 6, 12 months and yearly after OLT. The ERCP/PTC procedures or MRCP and other imaging studies were performed as indicated. Follow-up protocols were similar for donation after brain death (DBD) and donation after circulatory death (DCD) OLTs.

MRCP Description

The MRCP was performed using a Philips 1.5 T scanner (center A) and a GE 1.5 T scanner (center B). Single-shot fast spin echo sequences with thick (2-dimensional) and thin-slab multislice (3-dimensional) techniques in coronal planes were performed using a phased array body coil. Additional axial MR images were obtained using a single-shot fast spin echo sequence. For 2-dimensional MRCP, thick slabs (40 mm) through the porta hepatis in coronal and coronal oblique planes were planned rotating around a point anterior to the portal vein. The 3-dimensional MRCP was performed with 1.8-mm thick slices, field-of-view 260 mm, matrix size 260 × 260, resulting in a resolution of 1.8 × 1 × 1 mm.

Nonanastomotic Biliary Strictures

In all cases, the diagnosis of NAS was confirmed by invasive cholangiography, that is, ERCP or PTC—which is considered the golden standard—and was confirmed during follow-up. The following definition of NAS was used: NAS was considered as any endoscopically or percutaneously *treated* stricture or irregularity of the intrahepatic or extrahepatic bile ducts occurring at least 1 cm above the anastomosis post-OLT, as previously described.[9] Therefore, only those biliary strictures that were severe enough to cause clinical symptoms or biochemical abnormalities and to require treatment were considered NAS. To enhance the comparability between MRCP and invasive cholangiography, the time interval between both was limited to 6 months in this study. In case of no NAS or the absence of treatment, the bile ducts were considered normal. Therefore, 17 patients could be included in the no NAS group.

Evaluation of Biliary Strictures on MRCP

In each center, MRCPs were evaluated by 2 independent, experienced (>5 years of relevant experience) radiologists with their field of expert in abdominal imaging and MRCP reading. Images were selected and provided by the research coordinator. The participating radiologist retrospectively evaluated the MRCPs for research purpose only, after completion of the study, in 1 setting. Therefore, the radiologists were blinded to indications for MRCP, clinical findings, laboratory results, biopsy findings, or other imaging results or outcome. The presence and localization of biliary strictures was noted and categorized into 4 different hepatobiliary regions (Figure 1): at the anastomosis until 1 cm above the anastomosis (AS, region A), the donor common bile duct and the common hepatic duct until 2 cm above the bifurcation (region B), the hepatic bile ducts (region C) and peripheral bile ducts (region D). Regions C and D were further subdivided as left- and right-sided. A detailed description of this Leiden Biliary Stricture Classification (LBSC), here used for evaluating MRCPs at each hepatobiliary region, is presented in Table 1. The LBSC is a modification of the 'Amsterdam Classification', which is validated for scoring biliary strictures on ERCP/PTC in PSC.[8,10] After modification, the classification system was more appropriate for MRCP interpretation.

Statistical Analysis

Statistical analysis was performed using SPSS version 20.0 for Windows (SPSS Inc. Chicago, IL). For normally distributed variables the Student *t* test was used. Mann-Whitney *U* test, or when appropriate, Kruskall-Wallis test, was performed for non-normally distributed variables. Categorized data were analysed with the χ^2 test and presented in percentages (numbers). Receiver operating characteristic (ROC) curves were constructed to determine the optimal sensitivity and specificity. The level of intraobserver agreement between ERCP/PTC and MRCP and the interobserver agreement

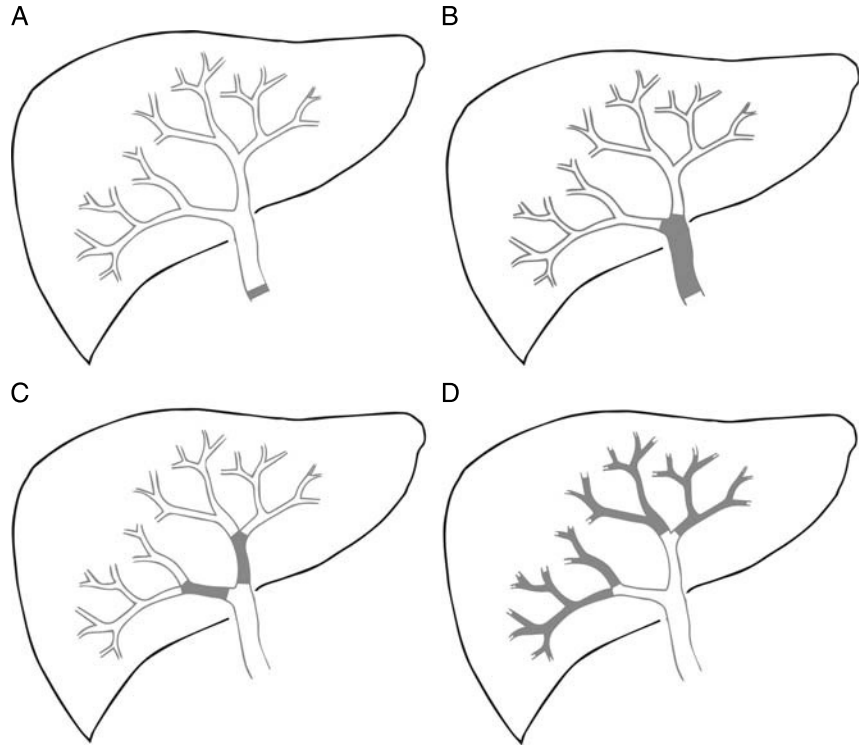

FIGURE 1. The Leiden biliary stricture classification. The presence and localization of biliary strictures is determined and categorized into: the anastomosis until 1 cm above the anastomosis (region A, A), the donor common bile duct and the common hepatic duct until 2 cm above the bifurcation (region B, B), the left and right hepatic bile ducts (region C, C) and the left- and right-sided peripheral bile ducts (region D, D).

between radiologists was calculated with the statistic κ and defined as follows: κ value of 0, no agreement; κ value of 0.01 to 0.40, poor agreement; κ value of 0.41-0.60, fair agreement; κ value of 0.61 to 0.80, good agreement; κ value of 0.81 to 1.00, excellent agreement.

Retrospective studies are approved by the institutional review board by legislation. The study was performed in accordance with the guidelines of the Helsinki and Istanbul declaration.

RESULTS

Within the study period, a total of 210 OLTs were performed in center A and 379 OLTs in center B. The DBD-OLTs accounted for 72.9% of the OLTs in center A and 81.3% of the OLTs in center B. In general, anastomotic strictures were diagnosed in 19.5% of patients and nonanastomotic biliary strictures in 18.6% of patients. The incidence of NAS after DCD-OLT was significantly higher than after DBD-OLT (36.8% vs 11.8%, $P < 0.01$).

In the present study, 41 patients with nonanastomotic biliary strictures and 17 patients without NAS were included. Of the 58 included patients, 42 (72.4%) were men and 16 women (17.8%). Mean age of the patients was 56.0 years (range, 26.6-76.3 years). In 22 patients (37.9%), OLT was performed with a DCD graft. Median follow-up from OLT until the initial MRCP was 7.5 months (range, 0-78 months). The MRCP was performed for several indications. In the majority of NAS patients (61%), patients were already diagnosed and treated before the initial MRCP. In this group, patients were referred for MRCP because sudden changes in clinical presentation (eg, elevations in serum biochemistry or clinical symptoms) had led to the suspicion of progression of the disease or previous unsuccessful treatment (n = 25). In case the presence or absence of biliary strictures had not yet been confirmed, patients were referred for MRCP because clinical presentation led to a suspicion of bile duct abnormalities (n = 26). This was correct in 16 cases, whereas no abnormalities were found in 10 cases. In the remaining cases, patients were referred for other indications, for example, pathology of the pancreas or monitoring recurrence of hepatocellular carcinoma (n = 7).

None of the patients in the no NAS group developed NAS during follow-up until the end of the study (median, 73 months; range, 16-127 months). Because NAS usually presents within the first year after OLT, it is not likely that these patients would develop NAS later on during follow-up.

Patient characteristics of the 2 individual centers are presented in Table 2 and were not statistically different between the centers, with the exception of the simultaneous presence of AS.

In center A, but not in center B, a duct-to-duct biliary anastomosis is preferably performed over an 8 to 12 Ch stent, which is removed after 6 weeks with a routine ERCP. In some patients, elevated serum biochemistry or clinical symptoms may result in the performance of an ERCP earlier than 6 weeks. In patients with biliary strictures, a routine ERCP was performed in 15 patients. Irregular bile ducts or NAS were already described at routine ERCP in 7 of these patients. In the remaining cases, 4 patients had developed strictures at the anastomotic site, but not yet at the nonanastomotic regions, 3 patients had developed bile duct leakages, and only 1 ERCP was considered normal. In 6 cases, routine ERCP was not performed because the biliary stent had already migrated to the small intestines, and there was no

TABLE 1.

LBSC for classifying cholangiographic abnormalities in patients after liver transplantation

Hepatobiliary region	Score	Cholangiographic abnormalities
A	0	No visible abnormalities
Anastomosis + 1 cm above	1	Caliber changes ≤ 50%
	2	Caliber changes 50-75%
	N/A	Choledochojejunostomy
B	0	No visible abnormalities
Donor common bile duct and common hepatic ducts	1	Slight irregularity of duct contour without stenosis
	2	Segmental stenosis
	3	Stenosis of almost the entire length of the duct or multiple strictures
C_{Left}	0	No visible abnormalities
Left hepatic duct until 2 cm proximal from common duct	1	Slight irregularity of duct contour without stenosis
	2	Segmental stenosis
	3	Stenosis of almost the entire length of the duct or multiple strictures
C_{Right}	0	No visible abnormalities
Right hepatic duct until 2 cm proximal from common duct	1	Slight irregularity of duct contour without stenosis
	2	Segmental stenosis
	3	Stenosis of almost the entire length of the duct or multiple strictures
D_{Left}	0	No visible abnormalities
Peripheral	1	One or multiple strictures with normal caliber of bile ducts or minimal dilatation
	2	Multiple strictures with dilatation, sludge and/or decreased aborisation
	3	Severe pruning with only central branches seen
D_{Right}	0	No visible abnormalities
Peripheral	1	One or multiple strictures with normal caliber of bile ducts or minimal dilatation
	2	Multiple strictures with dilatation, sludge and/or decreased aborisation
	3	Severe pruning with only central branches seen

N/A, not applicable.

other indication to perform ERCP (n = 2) or no stent had been placed because a choledochojejunostomy was performed (n = 4).

MRCP and Biliary Strictures

The radiologist classified the quality of MRCPs as "very good" in 68% of the cases, whereas the remaining MRCPs were classified as "moderate" quality. After blinded evaluation using the LBSC, the correct classification of presence and location of biliary strictures was determined by comparing the MRCP results to direct cholangiography. Primarily, the results were obtained in a cohort of center A and afterward validated in a cohort from center B. Overall, the readers correctly assigned ≥1 point(s) at hepatobiliary region A in 83% (50-89%) of patients with an anastomotic stricture, based on direct cholangiography. The results of region A were not included in further analyses because the evaluation of AS was not the purpose of this study. For categories B, C (left and right), and D (left and right) 0 to 3 points each, so a maximum of 15 points in total, could be obtained. The distribution of the reported total LBSC scores was not statistically different between the readers (P = 0.52), indicating a comparable severity of NAS between both centres. Optimal cutoff point for MRCP using the LBSC to predict NAS was calculated using an ROC curve. The area under the ROC curve was excellent (>0.80 for each reader; figures not shown). For each reader, a cutoff of 3 points or greater served as the best predictor for treatment requirement, and this was therefore the most clinically relevant cutoff. The cutoff point was first determined in the cohort of center A and afterward validated in the cohort of center B. Applying this cutoff value, sensitivity, specificity, positive predictive value, and negative predictive value were determined (Table 3).

To determine the overall ability of MRCP using the LBSC to detect NAS, both cohorts were combined using the mean score of both radiologists. When the cutoff point of LBSC of 3 or greater was applied to the radiologists' mean scores, sensitivity was 98%, specificity was 65%, positive predictive value was 87%, and negative predictive value was 92% (Figure 2). The readers reported the presence of casts, biliary stones, purulence, and sludge in the bile ducts in 8 patients (20%) with NAS, which was confirmed in 7 of these cases (88%) on subsequent direct cholangiography. The intraobserver agreement between MRCP and ERCP/PTC, as calculated by the statistic κ, for each reader was 0.15 to 0.22 (region B), 0.22 to 0.53 (region CL), and 0.29 to 0.86 (region CR). The hepatobiliary region D was located beyond the reach of ERCP and therefore presence or absence of casts in this region was difficult to interpret.

Intrahepatic (region C + D) and extrahepatic (region B) bile ducts were evaluated separately. Similar to the calculation of the overall optimal score, the cutoff value for the intrahepatic and extrahepatic bile ducts was determined using an ROC curve. For all readers, the optimal score was set at 3 of the 12 points that could maximally be obtained for the intrahepatic hepatobiliary region, and 1 of 3 points for the extrahepatic hepatobiliary region. Table 3 describes the sensitivity, specificity, positive predictive value, and negative predictive value of intrahepatic and extrahepatic NAS detection for each reader.

Interobserver Agreement on Severity

To evaluate whether MRCP using the LBSC can be used to describe not only presence or absence, but also the severity of NAS, interobserver agreement κ of the severity scores was calculated for each specific hepatobiliary region. Because MRCP appeared not to be distinctive in the stages "no abnormalities" and "slight irregularities" (0 or 1 point), these 2 stages were combined for all hepatobiliary regions. Agreement on severity of NAS was poor for all specific regions, that is, κ in center A 0.31 for hepatobiliary region B, 0.41 and 0.37 for hepatobiliary region C (left and right, respectively), and 0.31 and 0.32 for hepatobiliary region D (left and right, respectively). For center B, the κ for each hepatobiliary region was as follows: 0.22 for hepatobiliary region B, 0.68 and 0.42 for hepatobiliary region C (left and right, respectively), and 0.19 and 0.37 for hepatobiliary region D (left and right, respectively).

In center A, a second or third MRCP was available in 14 patients. The assessment of these MRCPs confirmed that

TABLE 2.

Patients' characteristics

	Center A (n = 32)	Center B (n = 26)	*P*
Age (mean, SD), y	57.6 ± 11.8	54.1 ± 11.6	0.27
Age at MRCP (mean, SD), y	52.5 ± 11.6	50.5 ± 11.6	0.51
Gender			0.20
Male	65.6 (21)	80.8 (21)	
Female	34.4 (11)	19.2 (5)	
Etiology			0.55
ALD	34.4 (11)	23.1 (6)	
Viral	21.9 (7)	15.4 (4)	
PSC	21.9 (7)	34.6 (9)	
AIH	3.1 (1)	0 (0)	
Other	18.8 (6)	26.9 (7)	
Choledochojejunostomy	18.8 (6)	19.2 (5)	0.96
Anastomotic strictures	37.5 (12)	88.5 (23)	<0.01
Indication MRCP			0.10
Suspicion of progression or recurrence (MRCP after diagnosis)	46.9 (15)	38.5 (10)	
Suspicion of bile duct abnormalities (MRCP before diagnosis)	34.4 (11)	57.7 (15)	
Other indication	18.8 (6)	3.8 (1)	
Diagnosis before initial MRCP	71.4 (15)	50.0 (10)	0.16
Interval between OLT and NAS diagnosis (mean, SD), mo	5.0 ± 6.1	7.8 ± 9.6	0.26
Interval between MRCP and ERCP/PTC (mean, SD), mo	0.4 ± 3.0	0.1 ± 1.8	0.69
Interval between OLT and MRCP (median, range), mo	7.9 (0-72)	7.3 (2-78)	0.79
Time between MRCP and diagnosis (median, range), mo	–1.6 (–12.2 to 5.9)	0.2 (–78.0 to 2.5)	0.87

Data are presented as % (n), unless otherwise specified.

ALD, alcoholic liver disease; viral, hepatitis B virus and/or hepatitis C virus; AIH, autoimmune hepatitis.

the severity of strictures is difficult to interpret, and the progression or effect of treatment could not reliably be evaluated.

DISCUSSION

The present study showed that, with the use of the "Leiden Biliary Stricture Classification" (LBSC), 4 independent readers could obtain a sensitivity, positive predictive value, and negative predictive value of MRCP for NAS detection or exclusion of greater than 80% in 2 independent study cohorts. In the LBSC, we combined the modified "Amsterdam Classification," a validated cholangiographic prognostic model for PSC, with a classification into 4 different hepatobiliary regions—and left and right—as shown in Figure 1.[8,10]

Nonanastomotic biliary strictures remain a challenging complication after OLT. The presence of NAS may result in cholestasis and cholestasis-related symptoms (eg, jaundice, pruritus, cholangitis) and, in case of inadequate treatment, graft failure with the need for retransplantation.[11] Whereas currently direct cholangiography is the imaging technique of choice when bile duct abnormalities are suspected, the use of MRCP has become a promising diagnostic tool for this purpose. Several authors have reported similar results in diagnostic accuracy between MRCP and ERCP for the detection of biliary complications after OLT.[5,12,13] However, the

TABLE 3.

Sensitivity, specificity, positive predictive value, negative predictive value for each reader

	Center A		Center B	
	Reader 1	Reader 2	Reader 3	Reader 4
Overall (cutoff ≥ 3)				
Sensitivity	100	91	100	95
Specificity	82	72	50	67
Positive predictive value	91	86	87	91
Negative predictive value	100	80	100	80
Intrahepatic (cutoff ≥ 3)				
Sensitivity	80	75	100	85
Specificity	100	83	50	83
Positive predictive value	100	88	87	94
Negative predictive value	75	67	100	63
Extrahepatic (cutoff ≥ 1)				
Sensitivity	95	100	90	80
Specificity	67	50	50	67
Positive predictive value	83	77	86	89
Negative predictive value	89	100	60	50

Data are expressed as percentage.

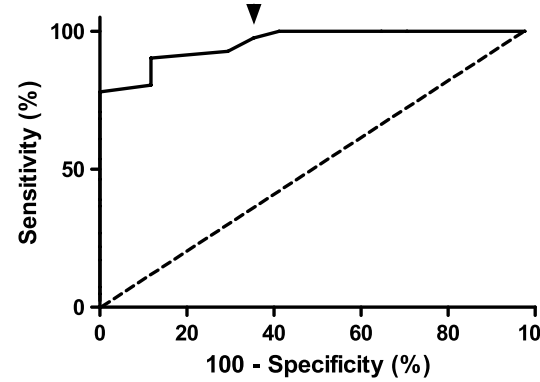

FIGURE 2. The ROC curve of mean MRCP scores for NAS. The arrowhead indicates the position of the cutoff value of 3 points (n = 58).

majority of these studies focussed on the ability of MRCP to detect biliary strictures in general, thereby including the presence of anastomotic strictures in the definition. With regard to NAS specifically, data have only been obtained without a clear classification and in small sample sizes, in which the diagnostic accuracy of MRCP is reported to be lower. Collettini et al[14] described a sensitivity for the detection of NAS of 89% to 100%, which was accompanied by a moderate specificity of 50%. In a study performed by Kinner et al, a sensitivity of 67% to 100% and a specificity of 50% to 88% (depending on the type of biliary anastomosis) for MRCP to detect NAS in patients with a clinical suspicion of biliary strictures were reported. In addition, determination of the exact localization of biliary strictures appeared to be difficult, because Zoepf et al.[4] compared the results to ERCP and reported that MRCP localized NAS correctly in only 22% of cases. The present study confirmed difficulties in determining the exact location of biliary strictures. This may possibly partly be explained by difficulties in distinguishing strictures located at the anastomosis or in the extrahepatic bile ducts. However, the excellent sensitivity and positive and negative predictive values suggest that MRCP using the LBSC can, overall, reliably detect or exclude NAS after OLT on MRCP imaging.

Several studies, including machine preservation techniques, are currently ongoing or being planned with the aim of preventing NAS after OLT.[15] In clinical trials, the use of invasive procedures with a high risk of procedure-related complications and morbidity, such as ERCP or PTC procedures, is less justified and MRCP with the proposed classification may therefore be an alternative.

In accordance with previously described literature, the corresponding specificity in the present study was moderate and varied between 50% and 82%. When the extrahepatic and intrahepatic bile ducts were evaluated separately, specificity improved for the evaluation of intrahepatic bile ducts. These differences in interpretation of intrahepatic and extrahepatic bile ducts are probably the result of better visualization of the intrahepatic ducts as compared with the extrahepatic ducts on MRCP. Moreover, in our experience, sludge and biliary cast formation, which can be present mainly in the common hepatic duct and common bile duct, are difficult to distinguish from NAS on MRCP. This issue is supported by a study from Hoeffel et al,[16] who reported similar observations. This may limit the accuracy of MRCP to exclude or detect the exact location and length of biliary strictures, especially extrahepatic strictures. In addition, because 37.5% of cases in center A and 88.5% cases in center B showed anastomotic strictures on the ERCP, the congestion as a result of these strictures further impaired the interpretation of the extrahepatic bile ducts.

Direct cholangiography has the advantage that the use of contrast can both visualize the bile ducts and determine drainage function. Because bile drainage function cannot be measured with T2-weighted MRCP technique and because distal biliary strictures in a transplanted graft have the tendency to result in less prestenotic dilatation than strictures in a nontransplanted liver graft,[17] the absence of prestenotic dilatation post-OLT may possibly influence the detection rate for strictures with MRCP. This suggests that imaging details of NAS acquired with MRCP can support the decision to perform a more invasive cholangiographic procedure and justify the associated risk of treatment-related complications, but that MRCP cannot fully replace direct cholangiography for diagnostic purposes. Conversely, the absence of NAS on MRCP (LBSC score <3) may be a reason to abstain from or defer invasive cholangiography. In patients with a total LBSC score of 3 points or greater, direct cholangiography may be indicated, or a more intensive follow-up regimen and early intervention in case of symptoms may be appropriate. However, whether this strategy leads to better outcomes and graft survival remains to be established.

In addition to distinguishing the presence of NAS requiring treatment (≥3 points on the LBSC) from minor irregularities (<3 points) that may not be of clinical relevance, it may be of interest to assess the progression over time of these bile duct irregularities to a more severe, clinically relevant stricture. Therefore, we determined whether the severity of strictures can be determined using this classification. Unfortunately, the interobserver agreement for grading biliary strictures severity was poor in this study. This is in accordance with a study performed by Moff et al.[18] In that study, 2 experienced radiologists independently evaluated MRCPs of 36 PSC patients to describe the severity of strictures in PSC using the Amsterdam Classification model. The statistic κ for interobserver agreement for grading the severity of extrahepatic strictures was 0.23, and 0.07 for intrahepatic bile ducts. This implies that other imaging techniques and serum biochemical markers, that is, bilirubin, alkaline phosphatase and γ-glutamyltransferase, remain important in follow-up and the decision whether invasive treatment is indicated.

In the present study, we have not used a T1-weighted contrast-enhanced MR cholangiography using hepatobiliary contrast agents, such as Gd-EOB-DTPA. This is a recently emerged technique that is useful for delineating the anatomy of biliary-enteric anastomoses and detecting biliary complications, for example, biliary strictures, intraductal stones, and bile duct leakages, and it may provide additional functional information in grading biliary obstructions.[19] A future study, using these agents, could show optimising results and be of additional value, although comparative studies between T2-weighted MRCP and T1-weighted contrast-enhanced MR cholangiography which actually have proven this in a large patient group are scarce.[20-22] In addition, Duarte et al[23] described the use of pineapple juice with gadopentetate dimeglumine as a promising contrast-enhancing agent in the evaluation of the biliary tree. An increase in concentration of manganese, that is, a paramagnetic substance present in pineapple juice, increases signal intensity on T1-weighted images. This is especially beneficial because it may improve the visualization of the biliary tree, mainly by suppression of the digestive tube signal. The effect persisted in the entire biliary tree (both intrahepatic and extrahepatic). This may improve the specificity of the LBSC.

A possible limitation is the retrospective study design, because most of the patients included in the analysis had been treated for NAS before the initial MRCP. Yet, the diagnostic accuracy in the present study is probably not influenced by this, because the readers were blinded to clinical data and were not informed whether the biliary strictures had already been diagnosed with invasive cholangiography. The majority of MRCPs were performed for the suspicion of biliary complications. However, it would be interesting to evaluate the use of MRCP with our classification model in patients without a clinical indication on fixed time points after OLT in a

prospective study. The LBSC is universal, and can not only be applied to MRCPs, but also to ERCPs and PTCs.

In conclusion, MRCP using the LBSC is a reliable tool to detect or exclude NAS after OLT. It may also be used to plan the optimal treatment before endoscopic or percutaneous cholangiographic treatment or in the setting of clinical trials—for example, with machine preservation—where non-invasive procedures are desired. The value of MRCP for follow-up for the progression of NAS is limited, because grading severity with MRCP is difficult, and reproducibility for this purpose is low.

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