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Research Article

Magnetic Resonance Cholangiopancreatography as the First Imaging Tool for Diagnosing Anastomotic Biliary Stenosis after Liver Transplantation

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Abstract

Introduction: The diagnostic and therapeutic management of Anastomotic Biliary Stricture (ABS) is controversial. Biliary stenosis after liver transplantation requires endoscopy or surgical therapies. Endoscopic Retrograde Cholangiopancreatography (ERCP) remains a key examination for diagnosing ABS, and therapeutic strategy. However, this is an invasive investigation with potential undesirable effects. This study sought to evaluate the relevance of Magnetic Resonance Cholangiopancreatography (MRCP) as the first imaging tool for diagnosing ABS, and orienting therapeutic choices.

Methods: We retrospectively collected clinical, imaging, and endoscopy data of patients that had undergone liver transplantation between 2010 to 2015, and were suspected of presenting post-surgical ABS. MRCP followed by ERCP were performed when clinical or biological tests were suggestive of ABS. The Predictive Positive Value (PPV) of MRCP for ABS diagnosis was calculated. The related outcomes, including the need for surgery and ERCP imaging results, were analyzed.

Results: Overall, 47 consecutive patients with presumed ABS underwent MRCP, followed by ERCP. Compared to ERCP, the PPV of MRCP in detecting ABS was 95%. Of the 47 patients, 12 needed surgery treatment because the therapeutic endoscopy procedure was not feasible, whereas 35 underwent endoscopic treatment during the ERCP procedure. The MRCP could predict the best therapy choice, but only in case of small stenosis length without dilatation of the intrahepatic bile duct, which guaranteed feasibility of the endoscopy as a therapeutic choice.

Conclusion: MRCP is safe, exhibits excellent PPV for ABS diagnosis, and is likely to constitute a good predictive tool for referring to surgical or endoscopic stenting therapy procedures.

Keywords: Magnetic Resonance Cholangiopancreatography (MRCP); Anastomotic Biliary Stricture (ABS); Liver transplantation; Doppler ultrasonography; Liver biopsy

Introduction

Anastomotic Biliary Strictures (ABS) are the most common cause of biliary stenoses [1,2], following Liver Transplantation (LT), accounting for almost 40% of all biliary complications. Although the incidence of biliary complications after LT has decreased over the last decade, the cumulative risk of biliary stenosis occurring 1, 5, and 10 years after LT is estimated at 6.6%, 10.6%, and 12.3%, respectively [3]. Early diagnosis of ABS is still a challenge, and several attempts have been made to identify the best diagnostic tool, as well as the best-suited therapeutic strategies, in this setting.

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While endoscopic treatment of ABS is a valuable therapeutic procedure, it can only be performed in patients for whom biliary catheterization through ERCP is feasible [4]. Even in these cases, the benefit/risk balance for a complete endoscopy procedure, including long-term therapy, is still a matter of debate, since endoscopy procedures may yield unexpected complications. Whether MRCP is a valuable diagnostic tool for both the diagnosis of ABS and optimal therapy selection has been poorly investigated to date.

The present study sought to evaluate the feasibility and impact of using MRCP as the first diagnostic tool for ABS assessment while considering both therapeutic strategy selections (be it surgical or endoscopic) and the outcome, in an intention-to -treat retrospective analysis.

Materials and Methods

In this study approved by the Institutional Review Board, we retrospectively searched our electronic database and PACS system to retrieve all patients that underwent LT between January 2010 and December 2015 at University Hospital Henri Mondor (Creteil, France), who were later on referred for potential ABS based on clinical and biological criteria and then underwent MRCP followed by ERCP for diagnosis with an intention-to-treat purpose, if feasible.

For the systematic and retrospective review of these patients, the following data were collected: patients' characteristics including age, gender, Model for End-Stage Liver Disease (MELD) score, duration between LT and stenosis development, and clinical and laboratory data (Table 1A). Additionally, the treatment history and related outcomes were collected.

Follow-up protocol

Every 3 months after LT, patients were followed-up by routine clinical evaluation and liver function tests. If a biliary complication was suspected, based on symptoms, liver tests, or Ultrasound (US), MRCP was performed in a first step. Additional diagnostic procedures, such as Doppler ultrasonography and liver biopsy, were subsequently performed to rule out hepatic artery thrombosis and liver graft rejection, respectively. All MRCP procedures were repeated 6 months after ERCP and biliary stent removal, if any.

MRCP technique and image analysis

MRCP imaging was performed on either a 1.5 T MR Unit (AvantoFit, VE11, Siemens, Erlangen, Germany) or 3 T MR Unit (Skyra, VE11, Siemens, Erlangen, Germany) using a body coil (slice thickness 40 mm in the coronal orientation, echo time 800 ms, TR/TE 8000/800 ms, image matrix 300 • 256, FOV 300 • 300 mm). Patients were kept fasting for 4 hours prior to the investigation. No additional preparation was needed.

All image analyses were performed by a radiologist with over 10 years' experience in abdominal MR. On MRCP, ABS was defined as a significant disproportion in the duct caliber between two segments adjacent to the anastomotic site, along with the dilatation of the proximal segment. Difference in caliber between the donor and recipient bile duct was taken into consideration. A cutoff of 6 mm was used to consider Common Bile Duct (CBD) dilatation. This value was adjusted to age in patients older than 60 years (+1 mm for every 10 years). The following measurements were thus obtained: the length of the stenosis, its diameter, its distance from the biliary confluence, as well as the presence or absence of intrahepatic dilatation. The intrahepatic bile ducts were considered dilated if identified beyond the second biliary division. The distance of the stenosis from the biliary convergence was measured from the proximal stenosis end. Additional MRCP findings, including the presence of biloma and intraductal stone or sludge, if any, were recorded.

ERCP

All ERCPs were performed under general anesthesia by experienced therapeutic biliary endoscopists and after routine administration of antibiotic prophylaxis, in the attempt to explore biliary tracts, including the anastomotic site.

During the ERCP examination, the number(s) of sessions, technical details of the procedure, including the need for sphincterotomy or dilatation procedures, as well as stenting were all registered. After successful cannulation of the bile duct, deep biliary cannulation was attempted using a sphincterotome (Olympus ® KD-V211M-0725) that had been pre-loaded with a hydrophilic guidewire (0.025 inch). Cholangiography was carried out, followed by biliary sphincterotomy. If the upper part of the biliary stenosis did not involve the hilum, the patient was considered suitable for biliary stenting with a Fully Covered Self-Expanding Metal Stent (FCSEMS) measuring 60 mm or 80 mm (Boston Scientific Co., Cook Medical). Strictures were sometimes dilated, using 8 mm or 10mm diameter balloon catheters (Hurricane; Boston Scientific Co.), when it was impossible to directly insert the stent, due to anastomotic narrowing. With the help of fluoroscopy, the stent was deployed inside the bile duct, covering the narrowed segment. When access to the Common Bile Duct (CBD) was not feasible or if the complete procedure for biliary tract stenting was proven unsuccessful, the therapy choice was considered a failure, and MRCP images were reviewed to identify potential predictive features in a MRCP-based therapy scenario choice, as "not accurate for endoscopy." Patients with successful endoscopic treatment were enrolled in a survey with a metallic stenting (associated to plastic stenting, in case there was biliary leakage, if necessary). After stent delivery, effective drainage of the radiographic contrast from the intrahepatic side was confirmed, prior to withdrawing the endoscope so as to exclude selective drainage. Given this scenario, the procedure was deemed successful.

The stenoses were characterized by analyzing cholangiography images before and after stent placement. To measure the stenosis length and its distance from the confluence of the right and left intrahepatic bile ducts, images before stenting were taken into account. The edge of the stent was considered as a unit in the image (10 mm). The width of the stenosis was obtained by comparing the edge of the stent with the narrowest part of the ABS.

MRCP and ERCP comparison

The PPV of MRCP in detecting ABS was determined, taking ECRP as the reference standard, whatever treatment strategy was selected after ERCP.

The presence of stenosis, its length, its diameter, and its distance from the bottom of the hepatic biliary confluence, which had been determined on the initial MRCP and ECRP, were compared.

Statistics

Continuous baseline descriptive variables were expressed as means of +Standard Deviation (SD) and were compared using the Student's t-test. Categorical variables were expressed as absolute numbers and proportions. P-values of less than 0.05 were deemed statistically significant. The PPV of MRCP in terms of predicting ABS and informing therapy choices was then estimated in terms of ERCP diagnosed stenosis in the cohort.

Results

Between 2010 and 2015, 468 LTs were performed. Overall, 55 of 468 (11.7%) consecutive patients with potential ABS were screened, of which 47 (85%) underwent both MRCP and ERCP and were thus included in the present study (Table 1).

Only 45 of these 47 stenoses detected on MRCP were confirmed using ERCP, yielding an MRCP PPV of 95%. Two patients without ABS detected on ERCP were not further analyzed. The quantitative analysis was performed on MRCP in all remaining cases. Thus, the measurement of stenosis length, diameter, and distance from biliary convergence was carried out in 45 patients and compared to the ERCP results (Table 1B and C). We defined the measures that were proven congruent if the mismatch between MRCP and ERCP was less than 3 mm. For the diameter, the congruence was 84%, with an ERCP-overestimated size in 93.75%. The length matched in 50%, with a MRCP-overestimated size in 78.12%. The distance from the confluence matched in 26%, with an ERCP-overestimated size in 76.92%.

Overall, 35 of 47 patients underwent endoscopic therapy, using

Table 1A: Characteristics of the population.

Recipient variables, n=47	
Age (years)	54 (9.8) (20;70)
Gender female	5 (10.7%)
Gender male	42 (89.3%)
MELD	20.2 (11.4) (6;40)
Months between liver transplantation and stenosis development	6.8 (10.4) (0;54)

MELD: Model for End-stage Liver Disease.

Table 1B: MRCP parameters in the patients with endoscopy success at baseline.

Covariate	
Stenosis length	10.4 (6.5) (2;27)
Stenosis diameter	0.6 (1) (0;5)
Distance of stenosis by the confluence of IH bile ducts	23.4 (7) (11;37)
Intra-hepatic bile ducts dilatation	0.85
Left intra-hepatic bile duct dilatation	0.824
Right intra-hepatic bile duct dilatation	0.529
Size of proximal CBD in mm	
6	0.059
7	0.118
9	0.147
10	0.265
11	0.088
12	0.118
13	0.029
>14	0.186
Size of left IH bile duct	7.4 (3; 3.1-16)
Size of right IH bile duct	6.1 (2.5; 2.5-12.3)
Size of middle IH bile duct	5 (1.3; 2.8-7.3)
Stone	4(11.4%)

MRCP: Magnetic Resonance Cholangiopancreatography; IH: Intrahepatic; CBD: Common Bile Duct

Table 1C: ERCP parameters in patients with endoscopy success at baseline.

Covariate	
Stenosis length	6.4 (4.4) (2-20)
Stenosis diameter	3.2 (1.2) (1-7)
Distance of stenosis by the confluence of IH bile ducts	26 (8.8) (12-45)
Intra-hepatic bile ducts dilatation	0.31
Dilatation of proximal extra-hepatic CBD	0.405

ERCP: Endoscopic Retrograde Cholangiopancreatography; IH: Intrahepatic; CBD: Common Bile Duct

either metallic or plastic FCSEMS stents, and a combination of both in four cases, whereas 12 patients were referred to surgery because of a too-long CBD, causing an "S" shape duct form (n=5), or due to bile leakage (n=7) that made endoscopy procedures hazardous. These patients were followed-up for a mean duration of 24 months (extremes: 12 to 58 months). At the end of the follow-up period, 92% of patients presented improved liver tests, compared to baseline values. Risk factors for stenosis recurrence and absence of liver function test normalization, according to baseline MRCP, were estimated after the end of the endoscopic treatment (Table 2).

Discussion

Here, we have reported a comparison between MRCP and ERCP with a 1-year continuous follow-up following ABS diagnosis and therapy after LT. We have shown that MRCP is highly sensitive, with an excellent PPV estimated at 95% for ABS diagnosis, taking ERCP as the reference standard for ABS. These rates are in accordance with sensitivity and specificity figures that have already been published in the literature. Indeed, Katzb et al. [5] reported that MRCP correctly diagnosed all anastomotic strictures with a sensitivity of 100%. Beltràn et al. [6] evaluated the diagnostic accuracy of MRCP after T-tube removal in liver transplant recipients with late biliary complications. In their study, the sensitivity was 93% and specificity 97.6%, with a PPV of 96.3% and NPV of 95.2%. The global diagnostic accuracy was 95.6%. More recently, Boraschi et al. [7] have reported their MRCP experience in assessing biliary complications after LT. This research involved 119 patients, including 34 patients with biliary strictures, resulting in similar PPV figures. Of note, in their series, ERCP was not systematically used as reference standard.

Moreover, MRCP evaluation of the stenosis length, diameter of the intrahepatic biliary ducts, and distance from the biliary convergence to ABS were consistent with ERCP-estimated measures. These ABS features are crucial for treatment planning. In our study, MRCP allowed for an accurate prediction of the most adequate therapeutic strategy between endoscopic and surgical therapeutic modalities. However, a trend to a slight overestimation of the stenosis length and underestimation of its distance to biliary convergence were noticed on MRCP examinations, in comparison with ERCP slides. This can be explained by the observation that in ERCP the biliary tree is submitted to direct contrast material injection, thereby increasing the canal pressure. Moreover, MRCP enables evaluating the whole biliary tree, thereby providing information about potential bile dilatation, biloma, endoluminal debris or stones, bile duct irregularity (which could suggest ischemia or recurrent primary sclerosis cholangitis-PSC, in some cases), as well as surrounding structures.

The limitations of MRCP are its low spatial resolution, presence of motion artefacts degrading the images, as well as presence of ascites or collection (including biloma) in the liver hilum that degrades the images. By contrast, and despite potential undesirable effects, ERCP contributes to the diagnosis in all cases while offering a therapeutic approach, depending on the stenosis characteristic features through a single procedure. Moreover, this technique provides the possibility of therapeutic intervention using a balloon, plastic, and metallic stent [8-12]. The endoscopic procedure is significantly linked to the procedure-related morbidity, mortality, and success rate, as compared to surgery. Sutcliffe et al. [13] demonstrated that, after hepaticojejunostomy, normal graft function was observed in 8/44 patients (18%) and improved graft function in 16/44 (36%), with graft function remaining abnormal in 20/44 (45%). This is far behind of the endoscopic treatment results. However, an endoscopy procedure, even if a therapeutic calibration of the biliary tract does not appear necessary, may yield complications, such as infectious cholangitis, hemorrhage, and pancreatitis. This is why MRCP can aid decisions about the best-suited therapy choice. By means of retrospective analysis of the baseline MRCP parameters, in those patients with at least 1-year follow-up after the stent has been removed; the risk factors for recurrence are currently identified as longer stenosis length and larger dilatation of the intrahepatic bile ducts. These results are consistent with the severity of the initial stricture that is reported to be the main predictive factor of ABS recurrence [14]. Of note, the stenosis length and biliary duct diameters can be easily estimated on MRCP.

Our study has several limitations. This is a retrospective study with potential recall bias. In addition, by suggesting no ERCP feasibility in patients with "S" shaped form and long stenosis length, as confirmed by MRCP, the first therapy choice for these patients was surgery. In our series, the duct- to-duct biliary reconstruction was estimated necessary in case of long CBD, particularly when stenoses were associated to the "S" shape of the common bile duct, which might cause a "syphon effect." Based on the surgeons' experience, this stenosis type is considered in our center to render endoscopy

Table 2: Univariate analysis of risk factors for stenosis recurrence and absence of liver function test normalization based on MRCP results at baseline.

Patients with 1-year follow-up following stent removal			
Covariate	**No stenosis recurrence**	**Stenosis recurrence**	p-value
Stenosis length	4 (0.8; 3-5)	8.5 (3; 4-10)	0.05
Stenosis diameter	1.8 (2.4; 0-5)	0.2 (0.5 0-1)	0.296
Distance of stenosis by the confluence of IH bile ducts	23.5 (7.4; 15-33)	24.2 (5.1; 18-30)	0.873
Intra-hepatic bile duct dilatation	0.2 (0.5; 0-1)	1 (0; 1-1)	0.058
Size of left IH bile duct	6.6 (3.5; 3.7-11.5)	9.2 (2.5; 6-12)	0.267
Size of right IH bile duct	5.2 (3.2; 2.5-9.1)	6.3 (2.8, 4.2-10.4)	0.638
Size of middle IH bile duct	4.2 (2.3; 2.8-6.8)	5.4 (1.4; 3.7-7)	0.467
Biological liver tests	**Improvement**	**No improvement**	
Stenosis length	7 (4.2; 4-10)	9 (8.4; 3-27)	0.673
Stenosis diameter	3 (2.8; 1-5)	0.3 (0.8; 0-2)	0.401
Distance of stenosis by the confluence of IH bile ducts	27 (4.2; 24-30)	21.6 (6.7; 14-33)	0.27
IH bile duct dilatation	0.5 (0.7; 0-1)	0.7 (0.5; 0-1)	0.744
Size of left IH bile duct	7.8 (1.6; 6.7-9)	8.6 (3.8; 3.7-12.6)	0.701
Size of right IH bile duct	6.1 (0.6; 5.7-6.5)	6.4 (3.7; 2.5-11.1)	0.834

Values are mean expressed in mm (SD; average)

MRCP: Magnetic Resonance Cholangiopancreatography; IH: Intrahepatic

therapy risky or event not feasible at all. However, further prospective controlled analyses are warranted to confirm our positive results.

Conclusion

ERCP and MRCP are comparable for the diagnosis of Anastomotic Biliary Stenosis after LT. MRCP is an accurate imaging method for the biliary tree assessment in transplanted patients with suspected biliary complications. Due to its accessibility and absent associated morbidity, MRCP offers more advantages as first-line decision tool. Owing to the highly relevant efficiency of MRCP in evaluating the presence of biliary stenosis in this population, a negative MRCP in an adequate clinical context is able to exclude a stenosis. A patient with positive MRCP needs to be further evaluated by means of ERCP for biliary stenosis confirmation, with endoscopy used in an intention-to-treat purpose. In this setting, the biliary stenosis length that is likely to impact endoscopy versus surgery therapy choices should be measured upon ERCP before therapy, since the measures afforded by MRCP still need to be improved.

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