

CLINICAL RESEARCH

## Adult-to-adult right lobe living donor liver transplantation: Comparison of endoscopic retrograde cholangiography with standard T2-weighted magnetic resonance cholangiography for evaluation of donor biliary anatomy

Perdita Wietzke-Braun, Felix Braun, Dieter Müller, Thomas Lorf, Burckhardt Ringe, Giuliano Ramadori

Perdita Wietzke-Braun, Giuliano Ramadori, Abteilung für Gastroenterologie und Endokrinologie, Georg-August-Universität, Göttingen, Germany

Felix Braun, Klinik für Allgemeine Chirurgie und Thoraxchirurgie, Universität Schleswig-Holstein, Campus Kiel, Germany

Dieter Müller, Abteilung für Diagnostische Radiologie, Georg-August-Universität, Göttingen, Germany

Thomas Lorf, Klinik für Allgemeine Chirurgie, Georg-August-Universität, Göttingen, Germany

Burckhardt Ringe, Center for Liver, Pancreas and Biliary Disease, Drexel University College of Medicine, Philadelphia, United States

Correspondence to: Dr. Giuliano Ramadori, Professor, HC Klinik für Gastroenterologie und Endokrinologie, Innere Medizin, Georg-August-Universität, Robert-Koch-Strasse 40, D-37075 Göttingen, Germany. gramado@med.uni-goettingen.de

Telephone: +49-551-396301 Fax: +49-551-396921

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**CONCLUSION:** Pretransplant ERC is safe and superior over standard MRC for detection of biliary variations that occur with a high frequency. However, precise knowledge of biliary variants did not reduce the incidence of postoperative biliary complications.

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**Key words:** Living donor liver transplantation; Donors biliary tree; Endoscopic retrograde cholangiography; Magnetic resonance cholangiography

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### Abstract

**AIM:** To compare the value of endoscopic retrograde cholangiography (ERC) and standard T2-weighted magnetic resonance cholangiography (MRC) in the evaluation process as adult-to-adult right lobe living donor liver transplantation (LDLTx) demands a successful outcome, and exact knowledge of the biliary tree is implicated to avoid biliary complications, postoperatively.

**METHODS:** After starting the LDLTx program, 18 liver transplant candidates were selected for LDLTx by a stepwise evaluation process. ERC and standard T2-weighted MRC were performed to evaluate the biliary system of the donor liver. The anatomical findings of ERC and MRC mapping were compared using the Ohkubo classification.

**RESULTS:** ERC allowed mapping of the whole biliary system in 15/15 (100%) cases, including 14/15 (93.3%) with biliary variants while routine MRC was only accurate in 2/13 (15.4%) cases. MRC was limited in depicting the biliary system proximal of the hepatic bifurcation. Postoperative biliary complications occurred in 2 donors and 8 recipients. Biliary complications were associated with Ohkubo type C, E or G in 6/8 recipients, and 2/3 recipients with biliary leak received a graft with multiple ( $\geq 2$ ) bile ducts.

### INTRODUCTION

Over the past decade, a critical shortage of cadaveric organs for adults in need of liver transplants has developed. The current mortality for patients awaiting liver transplantation (LTx) ranges from 20% to 30%. During this time, the waiting period for LTx and the mortality among patients on waiting lists have increased by a factor of more than 10 while the donor pool has expanded only marginally<sup>[1]</sup>. The use of adult-to-adult right lobe living donor liver transplantation (LDLTx) provides an alternative technique to reduce the waiting list mortality<sup>[2-4]</sup>. Hereby, a transplant candidate gains survival time and quality of life while a proven healthy individual undergoes liver resection for living donation of right or left lobe. The greatest risk in LDLTx is the death of the donor which is estimated to range between 0.1% to 0.5%<sup>[5-7]</sup>. Furthermore, a potentially uneventful outcome of the recipient is a psychological threat for the donor. Thus, healthy donors might undergo an extended invasive diagnostic during evaluation. Also, complications are relatively common in living liver donors<sup>[8]</sup>. Therefore, donor safety has the highest priority when LDLTx is performed<sup>[9]</sup>, and selection

criteria and management of living donors requires continuous refinement<sup>[10]</sup>. Finally, potential advantages in recipients must be faced against any potential risk of morbidity and mortality in the living donor.

Bile duct leaks and stenosis impact morbidity and mortality in the early and late phase after LTx<sup>[11]</sup>. After LDLTx, only few studies focused on anatomical variations of the biliary tree, which is the rule rather than the exception in liver surgery<sup>[12]</sup>. The reported incidences of absent hepatic duct are 26% for the right and 2% for the left side<sup>[12]</sup>. In LDLTx, anatomic variations of intrahepatic bile ducts can complicate both, the donor and the recipient operation<sup>[13]</sup>. Full hepatic lobectomy is required for adult-to-adult LDLTx, and the postoperative risk is greater after right lobe resection<sup>[14]</sup>. Preoperative delineation of the biliary system appears important to achieve a successful outcome<sup>[13]</sup>.

Management of bile duct variations in LDLTx is technically demanding and lacking awareness of biliary variation increases the risk of postoperative complications<sup>[15,16]</sup>. The biliary anatomy is mainly evaluated by endoscopic retrograde cholangiography (ERC), magnetic resonance cholangiography (MRC) or intraoperative cholangiography. The last might cause technical complications or results in oversight of biliary anomalies with consecutive biliary complications<sup>[17]</sup>. Hitherto, about half of the LDLTx programs perform ERC for the evaluation of donor bile-duct anatomy, and about one third of the programs use MRC<sup>[8]</sup>. Therefore, we compared the value of ERC and standard MRC in living donors prior to LTx.

## MATERIALS AND METHODS

### Subjects

Between March 1<sup>st</sup>, 2000 and October 5, 2005, 18 liver transplant candidates were selected for LDLTx by a stepwise evaluation process including identification of potential candidacy, assessment of clinical status and risk factors, assessment of liver function and anatomy, and final measures<sup>[18]</sup>.

Mean age of 18 donors (11 female, 7 male) was  $50.4 \pm 9.7$  years, and  $47 \pm 9.2$  years in 18 recipients (12 male, 6 female). Seven donors had genetic and 11 emotional relation to their recipient. Indications for LTx were hepatitis B or hepatitis C related cirrhosis ( $n = 6$ ), postalcoholic cirrhosis ( $n = 4$ ), hepatic metastasis of neuroendocrine tumor ( $n = 2$ ), primary biliary cirrhosis ( $n = 1$ ), primary sclerosing cholangitis ( $n = 1$ ), cryptogenic cirrhosis ( $n = 1$ ), bile duct cysts ( $n = 1$ ), hepatic metastasis of gastrointestinal stroma tumor ( $n = 1$ ), and echinococcus multilocularis hydatitis with postalcoholic cirrhosis ( $n = 1$ ). Patients with cirrhosis were staged Child A ( $n = 3$ ), B ( $n = 6$ ), and C ( $n = 5$ ) according to the Child-Pugh-Turcotte classification.

### Evaluation of biliary anatomy

Biliary anatomy was evaluated by standard MRC and ERC. Standard MRC technique was provided by a radiologist in daily routine with Half-Fourier Spin-Echo in single shot technique and by Turbo-Spin-Echo with multiplanar

reconstruction in T2-weighted images. Standard ERC was performed by one experienced hepato-gastroenterologist. Patients received midazolam, propofol, and butylscopolaminiumbromide immediately before ERC. Serum amylase and lipase were controlled before and after ERC. Additionally, biliary anatomy was assessed by graft preparation and intraoperative cholangiography.

The biliary anatomy of MRC and ERC films were classified retrospectively according to Ohkubo<sup>[12]</sup> by the specialists in radiology, hepato-gastroenterology, and transplantation surgery at our institution (Table 1).

## RESULTS

### Evaluation of donor biliary anatomy

ERC did not cause procedure-related complications. ERC (MRC) images were completely available in 15 (13) donors for retrospective analysis (Table 1). ERC allowed mapping of the whole biliary system in 15/15 cases (100%), while routine MRC was only accurate in 2/13 cases (15.4%). MRC was limited to depict the biliary anatomy only up to the first hepatic branches (Figure 1, Figure 2, Figure 3). Interestingly, 14/15 (93.3%) donors had biliary variants detected by ERC. Biliary anatomical variants classified according to Ohkubo *et al.*<sup>[12]</sup> are depicted in Table 1. Donor livers were classified type A ( $n = 2$ ), B ( $n = 2$ ), C ( $n = 4$ ), E ( $n = 5$ ), G ( $n = 1$ ), and K ( $n = 1$ ). Right hepatic duct (RHD) was present in 2 (13.3%) and absent in 12 (80.0%) donor livers. Left hepatic duct (LHD) was absent in one donor liver.

The biliary anatomy determined by preoperative ERC was identical to the intraoperative findings (Table 1). Seven of 18 (38.9%) grafts had one, 7/18 (38.9%) two, and 4/18 (22.2%) three bile ducts. In total, 11/18 (61.1%) right lobe grafts presented with two or more bile ducts.

### Biliary complications

Postoperatively, 2/18 donors developed biliary complications (11.1%) including one biliary leak (Ohkubo type E, 2 bile ducts) and one bile duct stenosis (Ohkubo type C, one bile duct). Both complications occurred in livers with absent RHD. The biliary leak was located at the cutting surface and resolved without intervention, but the T-drain was kept for a longer period. Bile duct stenosis was successfully treated by endoscopic stenting. Eight of 18 (44.4%) recipients developed biliary complications (Table 1) including 3 biliary leakages, one bilioma, one bile duct necrosis, and 3 bile duct stenoses. Biliary leakages were associated with Ohkubo type G ( $n = 1$ ) or not classified ( $n = 2$ ). One leakage was related to stent dislocation. This graft had 3 bile ducts reconstructed by hepaticojejunostomy (HJS) with insertion of transhepatic stents. Two leakages were located at the cutting surface. A segment 6 necrosis occurred in one recipient who received an Ohkubo type C graft with one bile duct that was reconstructed by HJS and placement of a transhepatic stent. This patient also developed intrahepatic bilioma. Segmental necrosis might be related to transection of the arterial supply. One recipient developed bile duct necrosis located at the T-tube insertion side. Bile duct stenosis occurred in 3 recipients. One of these patients had received an Ohkubo type E graft including two bile

Table 1 Preoperative MRC, ERC, Ohkubo classification<sup>[12]</sup> and intraoperative findings in donors, biliary reconstruction of the graft and postoperative biliary complications of recipients

Donor			Recipient					
No.	MRC	ERC	Ohkubo classification	Intraoperative findings	Biliary complications	Biliary reconstruction	Stents	Biliary complication
1	NA	NA	NA	3 BD	None	HJS	2 THS	Leak due to dislocated stent
2	Suspicion of early branches to SV and VI from RHD	SV drains into RHD, branch of SV drains into LHD	Type K	3 BD	None	2 D/D	T-drain	None
3	SV drains into LHD	SV and VI drain separately into LHD	Type C	2 BD	None	2 D/D	2 THS	None
4	Suspicion of doubled RHD	2 separate RHD	Type E	2 BD	Leak at cutting surface	2 D/D	2 THS	None
5	No variation	SVI drains separately into CHD	Type G	2 BD	None	2 D/D	2 THS	Leak at cutting surface
6	Early division of CHD	Early division of CHD	Type A	2 BD	None	2 D/D	T-drain	None
7	NA	NA	NA	1 BD	None	1 D/D	T-drain	None
8	No variation	SVII drains into LHD, SIVa drains into RHD	Type E Type K	1 BD	None	1 D/D	T-drain	None
9	No variation	Early division of RHD, SV drains directly into CHD	Type C	1 BD	BD stenosis	HJS	1 THS	SVI necrosis, intrahepatic bilioma
10	SVI drains directly into CHD	SVI and VII drains directly into CHD	Type E	2 BD	None	2 D/D	T-drain	BD stenosis 2 years after LDLTX
11	Doubled RHD	2 separate RHD	Type E	2 BD	None	2 D/D	T-drain	BD necrosis
12	NA	NA	NA	1 BD	None	1 D/D	1 THS	Leak at cutting surface
13	Not evaluable because of artifacts	No variation	Type A	1 BD	None	1 D/D	1 THS	None
14	Suspicion of early division of RHD	Trifurcation of RHD to SV, VI, and VIII	Type B	3 BD	None	3 D/D	1 THS	None
15	Suspicion of early division of RHD	Trifurcation of RHD to SV, VI, and VIII	Type B	3 BD	None	3 D/D	None	None
16	No variation	2 separate RHD	Type E	2 BD	None	HJS	None	BD stenosis 3 mo after LDLTX
17	NA	Early division of RHD	Type C	1 BD	None	HJS	1 THS	BD stenosis 6 mo after LDLTX
18	NA	Early division of RHD	Type C	1 BD	None	1 D/D	T-drain	None

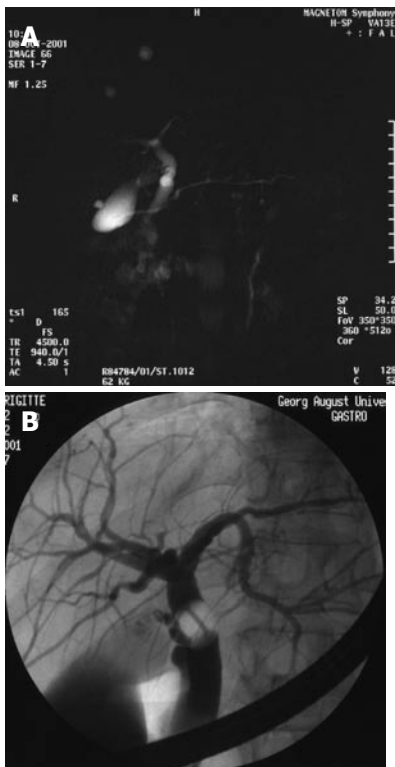
NA: Not available; BD: Bile duct; HJS: Hepaticojejunostomy; THS: Transhepatic stent; S: Segment; RHD: Right hepatic duct; LHD: Left hepatic duct; D/D: Duct-to-duct; CHD: Common hepatic duct; LDLTX: Living donor liver transplantation.



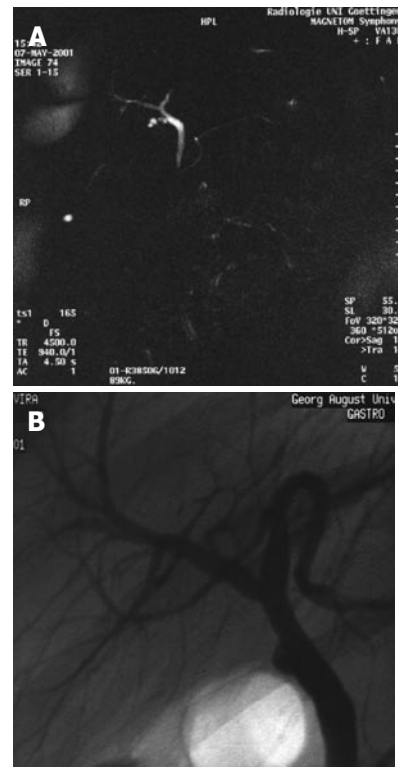
Figure 1 Preoperative MRC and ERC of donor No.11 with RHD. A: MRC, doubled; B: ERC, two separate.

ducts that were reconstructed duct-to-duct with insertion of a T-drain. Bile duct stenosis developed two years after transplantation and was successfully treated by endoscopic stenting. A second recipient also received an Ohkubo type E graft with two bile ducts reconstructed

by hepaticojejunostomy. Bile duct stenosis occurred 3 mo after transplantation and was successfully treated by placement of a Yamakawa prosthesis. A third patient with an Ohkubo type C graft and one bile duct developed bile duct stenosis 6 mo after transplantation that was also



**Figure 2** Preoperative MRC and ERC of donor No. 14 with RHD. **A:** MRC, suspicion of early division; **B:** ERC, trifurcation of RHD to SV, VI, and VIII.



**Figure 3** Preoperative MRC and ERC of donor No. 8. **A:** MRC, no variation; **B:** ERC, SVII drains into LHD, SIVA drains into RHD.

successfully treated by a Yamakawa prosthesis.

In summary, preoperative ERC detected biliary variants in 93.3% of donors. MRC confirmed ERC findings in only 15.4%, and was restricted in depicting the biliary anatomy above the hepatic bifurcation. Biliary complications occurred in 2 donors and 8 recipients. Ohkubo type C, E or G grafts were associated with biliary complications in 6/8 (75%) recipients. Two of 3 recipients with biliary leakage received a graft with multiple ( $\geq 2$ ) bile ducts.

## DISCUSSION

Determination of biliary anatomy in LDLTx can be performed preoperatively by ERC, MRC, contrast-enhanced CT-cholangiography, and intraoperative cholangiography. MRC is less invasive than ERC that can cause pancreatitis as a known complication. In a meta-analysis of 15 prospective trials using endoscopic retrograde cholangio-pancreaticography (ERCP), 14 risk factors of ERCP-associated pancreatitis have been identified involving nine related to the endoscopic technique (e.g. precut sphincterotomy) with a relative risk of 2.2 to 4.09<sup>[19]</sup>. In our series, we used ERC only diagnostically without intervention or pancreatic injection. ERC was well tolerated and none of the patients developed pancreatitis or other procedure related complications. In contrast to standard routine MRC, ERC allowed complete mapping of the biliary system. Preoperative ERC detected variations of biliary anatomy in 93.3% of donors that were confirmed by our intraoperative findings.

The inaccuracy of standard routine MRC in our series might be explained by the imaging slice thickness and artifacts. Recently, new modified MRC techniques such as volumetric mangafodipir trisodium enhanced MRC, heavily T2-weighted thin section MRCP, and gadobenate

dimeglumine enhanced MRC have been developed<sup>[20-24]</sup>. Sensitivity of heavily T2-weighted axial/coronal thin section MRCP for normal biliary anatomy was 89.5% and 71.4% for variants in LDLTx. The accuracy in depicting biliary anatomy was 84.6%<sup>[22]</sup>. In another series, the sensitivity, specificity, positive predictive, and negative predictive value of preoperative heavily T2-weighted radial slab MRC was 92%, 100%, 100%, and 94%<sup>[24]</sup>. Mangafodipir trisodium enhanced 3D MRC in combination with conventional T2-weighted MRC depicted the intrahepatic biliary anatomy correctly in 94% of living liver donors. Especially right duct variants were more accurately depicted with mangafodipir trisodium enhanced 3D MRC compared to conventional T2-weighted MRC<sup>[21]</sup>. Another new technique of mapping the biliary anatomy is multidetector computed topography cholangiography (MDCT-CA) with 1 mm collimation<sup>[16]</sup>. This method depicted anatomical biliary variations up to the fourth level of intrahepatic branches. Superiority of MDCT-CA over conventional MRC is explained by better spatial resolution using 1 mm instead of 4 mm slice thickness. Also, conventional MRC is susceptible for artifacts in T2-weighted images. Therefore, the use T1-weighted images is recommended in combination with Gd-EOB-DTPA or Gd-BOPTA, both biliary excreted contrast-agents<sup>[25,26]</sup>. Also, Gd-BOPTA-MRC can be combined with CE-MRA without injection of a second contrast agent<sup>[16,26]</sup>. Gd-BOPTA-enhanced MRC is superior over T2-weighted MRC sequences in mapping the biliary tree, but spatial resolution remains moderate<sup>[25,26]</sup>. In principal, both imaging modalities can be performed as an all-in-one-protocol for evaluation of liver parenchyma, arterial, venous, and biliary anatomy. However, MDCT-CA harbors potential risks like X-ray exposure and allergic reaction to contrast medium. Both risk factors can be

avoided with Gd-BOPTA T1-weighted MRC<sup>[26]</sup>. However, the role of the above-mentioned procedures needs to be defined for evaluation of biliary anatomy in living liver donors in the near future. At present these new techniques have not been compared to preoperative ERC yet.

In our series, biliary complications occurred in 2/18 (11.1%) donors. In larger series, incidence of biliary complications ranged from 4% to 13%<sup>[27-31]</sup>. Incidence of biliary leaks at the cutting surface is approximately 5% in living donors<sup>[32-36]</sup> and was 5.6% (1/18 donors) in our series. Notable, donors with absent RHD (Ohkubo type C and G) grafts are at risk to develop biliary leakage or obstruction<sup>[12]</sup>. Both biliary complications in our donors occurred in livers with absent RHD (Ohkubo type C and E). In recipients, biliary complications are the Achilles' heel of all segmental LTx<sup>[9]</sup>. Incidence of biliary complications in LDLTx recipients is 15%-40%<sup>[8,9,15]</sup>. In our series, 8/16 (44.4%) recipients had complications despite exact preoperative determination of biliary variants by ERC. Nevertheless, anatomic variations of the biliary tract are common but may not contraindicate donation<sup>[13,37]</sup>. The risks of biliary complications increase with the number of bile duct openings in the graft<sup>[38]</sup>. Rogiers *et al*<sup>[9]</sup> focused on two complex biliary variations: (1) Ramus posteriomediales (RPM) drains into the common hepatic duct (CHD), ramus lateralis (RL) merges with segment (S) II, and drain together into the left hepatic duct (LHD), and (2) RPM drains into CHD; S I, S II, S III, and S IV drain separately or together into RL. These two biliary variations cease splitting of the liver in selected cases. Recently, a case was published in which an anatomic biliary variation was seen as a contraindication for right lobe LDLTx<sup>[38]</sup>.

In conclusion, biliary anatomy in living liver donors is highly variable, but does not exclude from donation. ERC is superior to the standard MRC technique for detailed preoperative mapping of intra- and extrahepatic bile ducts, but does not reduce the incidence of postoperative biliary complications.

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