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The role of MR cholangiography in the detection of biliary complications after orthotopic liver transplantation

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Summary

Background: To assess the usefulness of magnetic resonance cholangiography (MRC) in the diagnostics of biliary complications after liver transplantation.

Material/Methods: In 40 patients (17 men, 23 women) 51 MRC examinations were performed, from 1 to 58 months (mean-12) after liver transplantation. Studies were performed with 1.5 T unit. The imaging protocol consisted of tree hydrographic TSE sequences: 2D, 3D and single-slice technique. The results were compared with ERCP (n=10), percutaneous cholangiography (n=4), T-tube cholangiography (n=1), T-tube cholangiography and percutaneous cholangiography (n=1), T-tube cholangiography and ERCP (n=1), fistulography (n=2) and histopathology (n=3). In remaining patients other imaging studies (US, CT), laboratory liver functions tests and clinical status were evaluated.

Results: In 46 cases (90%) abnormalities of biliary tract were depicted. Following biliary complications were diagnosed: dilatation of biliary tree (n=29), biliary strictures located beside anastomosis site (n=19), anastomotic biliary strictures (n=17), intrahepatic strictures (n=7), biliary obstruction (n=2), biliary stones/sludge (n=14), bile leak (n=12). In 5 cases (10%) MRC was normal. In 50 cases (98%) there was concordance between MRC results and the standard of reference, 1 remaining case (2%) of bile duct ischemia was not confirmed by other studies.

Conclusions: MRC is a noninvasive modality, providing accurate assessment of biliary complications in patients after liver transplantation.

Key words: Liver transplantation • magnetic resonance • bile ducts • biliary strictures • cholelithiasis

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Background

Orthotopic liver transplantation was performed for the first time in 1963 by Tomas Starzl and has since been used more and more often, establishing its position as a method of treatment for various hepatic disorders, mainly chronic parenchymal liver diseases, several biliary tracts' dysfunctions, congenial metabolic disorders and tumors [1].

Despite obvious progress in surgical techniques and use of increasingly effective immunosuppressive drugs and methods of organ storage, the complications after the transplantations are still a major problem. The most frequent and most serious of them is acute graft rejection (according to some publications it is up to 64% of cases) [2]. Complications concerning the biliary tracts are the second most frequent cause of dysfunction of the transplanted liver [3] and constitute from 19% [3] to 34% [4] of cases with

mortality up to 5% [5]. Due to non-specific clinical and biochemical symptoms correct diagnosis is often difficult to state. Therefore, the radiological methods are necessary for fast and accurate diagnosis resulting in longer survival time of the transplanted organ.

The aim of this study was to evaluate the utility of magnetic resonance cholangiography (MRC) in diagnostics of biliary complications in the transplanted liver.

Materials and methods

From June 1999 to October 2005 51 MRC examinations were performed in 40 patients after liver transplantations (17 men, 23 women aged 19-62, mean age 44). The period from liver transplantation until the examination varied from 1 -58 months (mean: 12 months). All patients were referred to the MR due to confirmed clinical symptoms or improper biochemical test results suggesting pathology of biliary tracts. 26 patients underwent end-to-end biliary anastomosis, 14- biliary-intestinal anastomosis.

Indications for liver transplantation in the examined group included: postinflammatory cirrhosis after HCV and HBV infection (n=13), postalcoholic cirrhosis (n=8), sclerosing cholangitis (n=6), primary biliary cirrhosis (n=4), acute hepatic failure (n=2), hepatocellular carcinoma (n=2), postinflammatory biliary cirrhosis (n=1), toxic hepatic failure in mushroom poisoning (n=1), hemochromatosis (n=1), Wilson's disease, cystic disease of liver (n=1).

Patients were not prepared for the MR examinations in advance. All MR studies were performed with 1.5 T ACS NT Gyroscan (Philips), using the body coil and three hydrographic sequences (MRCP): 2D, 3D and SS (single slice). The parameters of hydrographic sequences were shown in Table 1. The MRCP sequence performed with the single slice technique was repeated 5-6 times with various inclinations of the studied slice. Due to long duration of the exam, the 3D sequence required respiratory gating in order to reduce motion artifacts. In 2D and 3D hydrographic sequences the reconstructions were performed with the use of maximum intensity projection (MIP), producing 18 images rotated every 20 degrees. Source images were also evaluated in each case, especially when biliary stones were suspected.

Moreover, the protocol of examination included the T2 TSE, T2 STIR, T1 GRE sequences performed in order to study the hepatic parenchyma and possible coexistence of other complications.

All MRC images were evaluated prospectively for the presence of strictures in biliary tracts, their dilatation or loss of signal within the biliary tree, as well as bile leak from the biliary tracts.

Based on the collected data, biliary complications were classified as follows: biliary strictures located beside anastomosis site, anastomotic biliary strictures, intrahepatic strictures, biliary obstruction, widening of biliary tracts, biliary stones/sludge and bile leak outside the tracts.

All patients referred to magnetic resonance examination underwent US of liver and biliary tracts prior to the MRC. Additionally, in 17 patients the verification of MRC examinations was carried out based on the results of roentgen cholangiography: endoscopic retrograde cholangiopancreatography (ERCP) in 10 cases, percutaneous transhepatic cholangiography (PTC) in 4 cases, T-tube cholangiography in 1 case, T-tube and percutaneous cholangiography in 1 case, T-tube cholangiography and ERCP in 1 case. In 3 cases the final diagnosis was based on histopathologic examination; in 2 cases the studied material consisted of liver removed during retransplantation, in one case it was taken during biopsy of liver. In 2 patients with confirmed presence of fluid collections US was repeated with a following fistulography that proved the presence of biloma. In 3 patients the total result of imaging examinations (US+MRC+CT) and laboratory tests allowed us to state the final diagnosis. In other 25 patients whose MRC was unequivocal and agreed with US image other imaging examinations were not performed and the diagnosis was based on laboratory exams and clinical observations.

The sensitivity and specificity of MRC examination in detection of complications in biliary tracts of transplanted liver were calculated.

Results

In all 51 cases quality of MRC studies were assessed as good what enabled diagnostic evaluation of intra- and extrahepatic biliary tracts. In 46 cases (90%) the image of biliary tracts was abnormal, while in the remaining 5 cases (10%) the MRC showed no abnormality. In 45 of 46 cases in which MR cholangiography showed abnormal image of biliary tracts the result agreed with final diagnosis (sensitivity 97.8%). The one case of false positive diagnosis concerned a patient with generalized obstruction of intra- and extrahepatic biliary tracts, in whom the ischemia resulting from thrombosis of hepatic artery was suspected. The diagnosis was not confirmed by other imaging

Table 1. Selected parameters of the used sequences.

Sequence	TR/TE	Flip	TF	NSA	Time	Slice thickness (mm)	Artifact reduction	Matrix
3D MRC	1800/650	90	128	2	~4min	1.8	Respiratory gating	256
2D MRC	8000/260	90	128	1	21 s	4	Apnea	256
SS MRC	8000/1200	90	256	1	8 s	40	Apnea	256

TR – time of repetition; TE – time of echo; flip – flip angle; TF – turbo factor; NSA – number of signal average.

techniques (Doppler's US, CT). In the study material there were no falsely negative recognitions (specificity 100%).

The following biliary complications were found: dilatation of biliary tree (n=29), biliary strictures located beside anastomosis site (n=19), anastomotic biliary strictures (n=17), intrahepatic strictures (n=7), biliary obstruction (n=2), biliary stones/sludge (n=14), bile leak (n=12) (table 2). In 43 examinations (84%) more than one complication was stated.

Dilatation of biliary tree:

The pathology found most often was the dilatation of biliary tree (29 patients-57%). MR cholangiography enabled differentiation between obstructive and non-obstructive dilatation of biliary tree. In our material only one case showed no mechanic obstruction in the biliary tree that would cause its dilatation. In the remaining 28 cases the causes of dilatation included: occlusion at the level of hepatic hilus (n=2), strictures in biliary tracts (n=18), stricture with biliary stones (n=7) or biliary stones itself (n=1). In 20 cases extrahepatic strictures were found- 9 of them at anastomosis site, 9 outside the site and 2- at the anastomosis site and outside of it at the same time. Stricture that occurred exclusively in intrahepatic biliary tracts was stated in 1 case, while in 4 cases the strictures affected both: the intra- and extrahepatic tracts.

Strictures:

Segmental strictures were diagnosed in 33 patients. In 18 single strictures were shown, in 15 they were multiple.

We revealed 19 extrahepatic strictures beside the anastomosis, in 3 cases there were additional strictures in the intrahepatic tracts. In 4 cases marked strictures located in the hepatic hilum led to separation of biliary tracts of the right and left lobe (fig. 1). In 2 patients with accompanying intra- and extrahepatic strictures the histopathologic examination (biopsy, reOLTx) revealed recurrence of cholangitis sclerosans in the transplanted liver. In the third case ischemic lesions were suspected due to thrombosis of hepatic artery but additional examinations (CT, Doppler US) did not confirm the initial diagnosis.

Seventeen of the 36 extrahepatic strictures were located at the site of anastomosis. In 10 cases they were accompanied by extrahepatic strictures outside anastomosis and/or intrahepatic strictures. In one case significant discrepancy in the size of common bile duct of the host and donor (fig. 2).

Table 2. Results of MRC examinations.

Biliary complications	N	Percent
Dilatation of biliary tree	29	56,9%
Extrahepatic strictures of biliary ducts outside the anastomosis	19	37,3%
Extrahepatic strictures of biliary ducts in the anastomosis	17	33,3%
Stones and/or sludge	14	27,5%
Bile leak / biloma	12	23,5%
Intrahepatic strictures of biliary ducts	7	13,7%
Occlusion	2	3,9%
Normal view of biliary ducts	5	9,8%

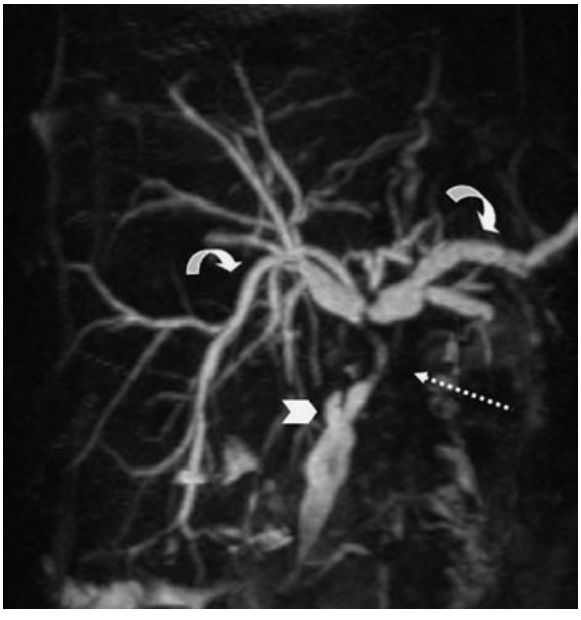

Figure 1. MIP image generated from 3D MRC sequence. Narrowing of biliary ducts situated at hepatic hilium (straight arrow). Separation of right and left hepatic ducts, with dilatation of intrahepatic biliary tract (curved arrow). Stump of cystic duct.

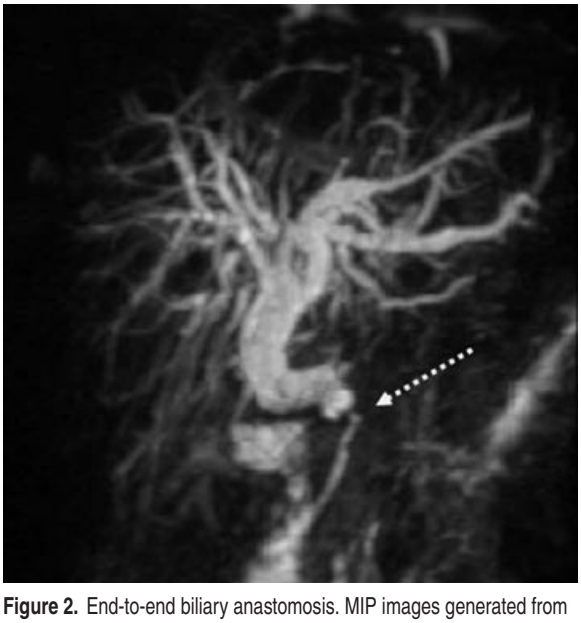

Figure 2. End-to-end biliary anastomosis. MIP images generated from 3D MRC sequence. Discrepancy between the diameter of common bile ducts of the donor and the host. There is stenosis at anastomosis site (arrow), which causes marked dilatation of biliary tract above anastomosis.

Figure 3. Debris in common bile duct distal to end-to-end biliary anastomosis, without significant dilatation of proximal bile ducts. MIP image from 3D MRC.

Most strictures were accompanied by dilatation of biliary tracts with the exeption of 7 cases – one concerned moderate stricture at the anastomosis site and 6 extrahepatic strictures above the anastomosis.

Coexistence of strictures and stones (or sludge) was observed in 8 cases.

Stones and /or sludge:

The presence of stones and/or sludge was stated in 14 of the examinations. In 8 patients the stones coexisted with strictures of biliary ducts: in 5 patients the stones or sludge were located above the stricture in the anastomosis (fig. 3), in 2 patients- above the stricture located outside the anastomosis, while in 1 patient the stones coexisted with numerous intra- and extrahepatic strictures. In 3 other cases only the dilatation of biliary tracts was found above the obstruction site (fig. 4) and in 2 patients no accompanying symptoms were visualized. In one case the MRC image (small signal loss from 3 to 7 mm) was equivocal and required differentiation between stones and pneumobilia, but the ERCP examination confirmed the presence of stones.

Bile leak:

In the analyzed material bile leak was described in 12 examinations (23%) of 8 patients. In 4 of them the MRC was repeated twice in a short period of time (app. 1 month). In one patient there was necrosis of extrahepatic biliary tracts of the donor with separation of right and left lobe ducts and presence of fistula, what was confirmed by PTC examination (fig. 5). In 2 cases the leak resulted from leakage in the place of end-to-end anastomosis, while in one case it was caused by leakage at the site of end-to-end anastomosis. In 2 patients the confirmation was based on fistulography, by aspiring the bile from punctured fluid aggregation. Two other patients underwent the ERCP and one- the Kehr's drainage cholangiography. Other cases of suspected small leaks were controlled with US and clinical observation.

Discussion

Complications from the biliary tracts are the second most frequent cause of dysfunction of the transplanted liver. Early biliary complication that occurs within 3 months after the transplantation, found most often, is the bile leak. Usually it is in form of patch along the Kehr's drain in the end-to-end anastomosis, which, if small, does not require treatment. Leaks inside the anastomosis are less frequent but they are more dangerous for the patient as they can

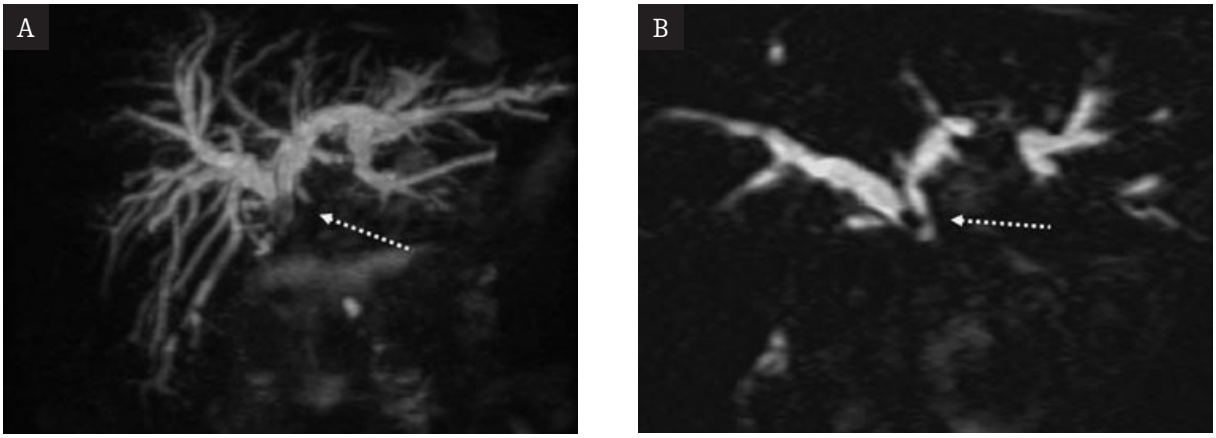

Figure 4. A. In MIP images from 3D MRC sequence at the confluence of right and left hepatic ducts, oval area of signal void is visible, consistent with the stone. **B**. The same stone in source image. Marked dilatation of intrahepatic biliary tract.

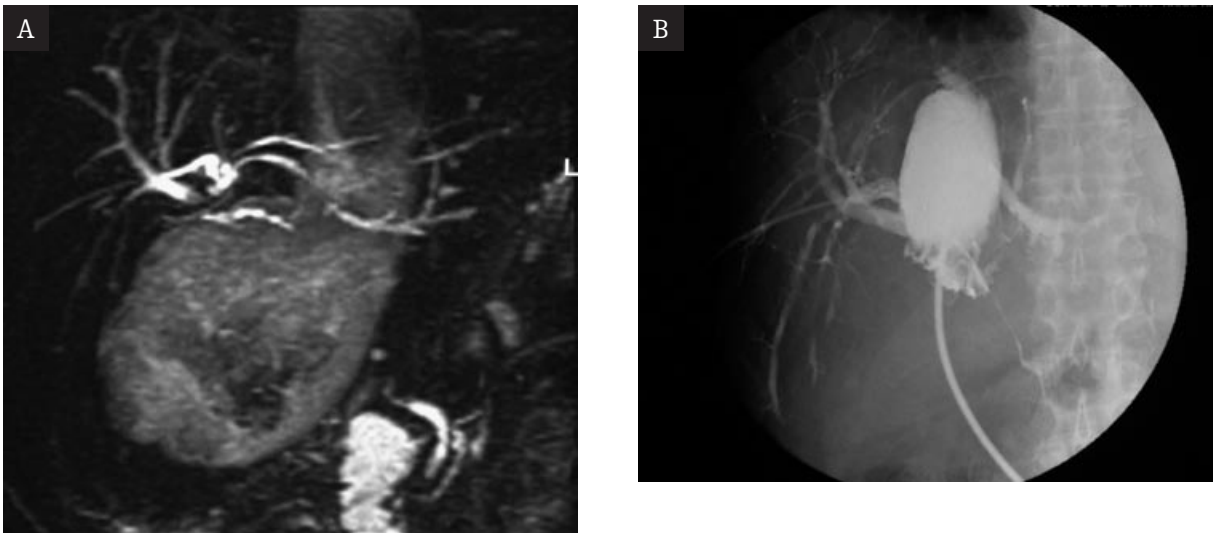

Figure 5. **A**. Large fluid collection (biloma) in hepatic hilum and in subhepatic area; moderate dilatation of biliary ducts of both liver lobes with its separation. **B**. Percutaneous cholangiography in the same patient. CBD and duodenum are not visible.

lead to death in some cases [5]. The treatment is based on placing a stent that covers the site of leak. In our material the bile leak was observed in 8 patients (in 12 examinations-23.5%) and was connected with leakage of anastomosis or necrosis in biliary ducts and formation of bilomas.

Late complications such as strictures in biliary ducts, stones and dysfunctions of Oddie's sphincter occur from 3 months to a few years after the liver transplantation.

Extrahepatic strictures which are most often found in the end-to-end anastomosis and result from scar formation can be treated with balloon plastics, if necessary – completed with stent implantation. In our material we found 17 strictures at the site of anastomosis (33%), including 3 in the biliary-intestinal anastomosis and the rest in the end-to-end anastomosis. In 11 cases they were accompanied by dilatation of biliary ducts. In 6 patients the stricture was widened and in 3 patients a stent was applied.

Ischemic lesions resulting from thrombosis in the hepatic artery are believed to be the cause of multifocal intra- and extrahepatic strictures. Balloon plasty is hardly effective in such cases [6]. Recurrence of scerosing cholangitis is a rare cause of multifocal strictures in the transplanted liver.

Changes in the bile composition after the transplantation (which results from the intake of cyclosporin) can lead to increase in quantity of biliary sludge and formation of stones [7], although there are authors who claim that the occurrence of biliary stones in the transplanted liver is similar as in another group of patients [8, 9]. Based on our data we can conclude that strictures in biliary ducts stimulate the formation of stones – they coexisted with stones in 8 of 13 cases (62%).

Dysfunction of Oddie's sphincter is a very rare complication, which is associated with dilatation of biliary ducts in donor and host and results from disordered vascularization and innervation of Vater's papilla [10]. There was no such case among the patients we studied.

Early recognition of the aforementioned complications is extremely important as it enables fast application of proper treatment and increases the chance for longer life of the organ and the patient.

The diagnostic algorithm depends on the type of biliary anastomosis. The most common end-to-end anastomosis is better for the patient due to maintenance of bile passage through the Vater's papilla, what prevents from infection of biliary ducts by bacteria from alimentary tract. In this group of patients the Kehr's drain is left inside for 6 months allowing the performance of cholangiography if biliary complications are suspected. In our material there were 26 patients with this kind of anastomosis and 14 with biliary-intestinal anastomosis in the Roux-en-Y loop. The latter is performed less frequently, mainly in patients with scerosing cholangitis and it is believed to prevent from recurrence of the disease in the donor's organ. In biliary-intestinal anastomosis the Kehr's drain is not inserted which is why in those patients, as well as in patients with end-to-end anastomosis with previously removed drain, noninvasive imaging examinations such as US, MR or less frequently CT, are performed. As for the invasive methods-the PTC and ERCP (in end-to-end anastomosis patients) are also performed.

US is an inexpensive, widely accessible examination, very useful in imaging vascular complications in the transplanted liver. However, the method is hardly reliable in diagnostics of early biliary complications, reaching the sensitivity of 54% (including 86% for dilatation of biliary ducts and 31% for biliary stones) [11]. In comparison- according to literature, the MRC sensitivity in recognition of dilatation of biliary ducts and strictures inside and outside the anastomosis amounts to 100% [12], and of biliary stones-90-95% [13]. In our material all cases of dilatations and strictures in biliary ducts were identified by means of MRC (sensitivity 100%).

In one case of a patient with leakage in end-to-end anastomosis and bile leak the suspicion of small stones required

differentiation from air bubbles. Reverse cholangiopancreatography confirmed presence of stones in common bile duct. The MR cholangiography (MRC) uses strongly T2-weighted images (TE>250ms) in which the static and slowly translocating fluids (e.g. bile) show high signal intensity, unlike the remaining tissues characterized by low signal. It enables thorough evaluation of biliary tracts, also in cases of massive stricture or occlusion. Owing to visualization of biliary ducts above and below the possible obstruction, the MR cholangiography combines the advantages of PTC and ERCP.

The results of our study and reports from other authors also suggest that the magnetic resonance cholangiography allows differentiation of character of bile ducts dilatation (obstructive and non-obstructive). Undoubtedly, the disadvantage of hydrographic technique is lack of possibility to distinguish the bile collections and aggregations of fluid of a different kind, as they have similar high signal intensity in this examination (comparable T2 times), what was also confirmed in our material. Therefore, the MR cholangiography enhanced with hepatropic contrast medium excreted with bile, has an unquestionable advantage (e.g. Mangofodipir trisodium). The technique uses T1-weighted sequences with saturation of fat tissue signal what allows to obtain high quality images of biliary ducts even in case of the surrounding fluid or oedema of soft tissues. It also enables visualization of passage of contrasted bile towards the duodenum, as well as its leakage (fistula). We did not use the technique in diagnostics of patients with transplanted liver.

Another group of MRC disadvantages includes overestimation of the degree of stricture and hindered evaluation of the anastomosis site for different width of common biliary tract in host and donor [14]. In the analyzed material we found one case of discrepancy between the diameter of common bile tract in host and donor with associated stricture at the anastomosis site.

With the introduction and popularization of multirow CT units, there are attempts to use the method to investigate the biliary ducts [15]. The authors are acquainted with only one preliminary report on the application of CT cholangiography in diagnostics of transplanted liver [16]. The evaluation of its applicability requires further studies on a larger group of patients.

Invasive methods such as PTC or ERCP characterized by highest spatial resolution allow obtaining biliary ducts' image of very good quality but the possibility of complications (PTC-3.4%, ECPW-5%) limits their application to cases in which the diagnosis after noninvasive examinations is uncertain or cases requiring therapeutic procedure [17]. Moreover, in patients with biliary-intestinal anastomosis the ERCP examination is often difficult or impossible to perform.

The disadvantage of this study is a limited number of patients (n=20) in whom it was possible to obtain histopathologic correlation or verification based on the result of roentgen cholangiography, which continues to be considered as a gold standard in imaging of biliary ducts. In half of patients the final diagnosis was based on total score of result of MRC and other imaging, such as US and CT, as well as laboratory investigations and clinical observation. In several patients, such method of verification resulted from the agreement of results from MRC and clinical observation, imaging and laboratory examinations on one hand, while on the other hand it was justified by opinion of the research team that there was no necessity for the patients to undergo additional invasive examinations. It also indicates the increasing role of MRC and growing confidence of surgeons towards the method. At the Clinic of General, Transplantation and Liver Surgery of Medical University in Warsaw the MR cholangiography has become a method used almost routinely in diagnostics of patients with transplanted liver, in whom the clinical symptoms or results of biochemical examinations suggest pathology in biliary ducts.

Conclusions

The MR cholangiography is a noninvasive method useful in diagnosing patients after liver transplantation, characterized by high effectiveness in recognition of complications in biliary ducts. Diagnostic difficulties can occur in differentiation of biloma and fluid collections of different character.

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