DOI: 10.15825/1995-1191-2024-3-72-90

POST-LIVER TRANSPLANT BILIARY COMPLICATIONS

K.O. Semash
National Children's Medical Center, Tashkent, Republic of Uzbekistan

Biliary complications (BCs) are the most frequent complications following liver transplantation (LT). They are a major source of morbidity after LT. The incidence of BCs after LT is reported to range from 5% to 45%. The main post-LT biliary complications are strictures, biliary fistulas and bilomas, cholelithiasis, sphincter of Oddi dysfunction, hemobilia, and mucocele. Risk factors for biliary complications are diverse. In this article we seek to review the main types of biliary complications and modern approaches to their diagnosis and treatment.

Keywords: liver transplantation, biliary complications.

INTRODUCTION

Since the first experiences with liver transplantation (LT) in 1963 by Thomas Starzl, this procedure has become the standard treatment for end-stage liver disease [1]. Despite organ shortage, the number of orthotopic liver transplants (OLT) has continued to increase. According to the American Liver Foundation, 9,234 liver transplants were performed in 2021 in the United States alone, and over 35,000 worldwide [2–3]. In the Republic of Uzbekistan, more than 40 LT have been performed to date [4].

However, with the increasing number of transplants, this patient cohort continues to experience the problem of postoperative biliary complications (BCs). BCs are the most common complications following LT. They are a major source of post-LT morbidity and their frequency, according to various sources, ranges from 5% to 45% [4–6]. As surgical techniques continue to improve, the rate of BCs following LT has been decreasing, but they still remain a major source of morbidity and mortality in liver recipients. BCs are the Achilles' heel of LT, and represent pressing problems all over the world [5, 6].

BCs following LT include strictures, jaundice, cholelithiasis, and sphincter of Oddi dysfunction. Type of biliary reconstructions, bile duct ischemia, reperfusion injury, hepatic artery thrombosis, cytomegalovirus infection, and primary sclerosing cholangitis are some of the risk factors that influence the rate of BCs [7–8]. This review examines the main types of BCs, risk factors for these complications, and modern approaches to their diagnosis and treatment.

DIAGNOSIS OF BILIARY COMPLICATIONS AFTER LIVER TRANSPLANTATION

The presentation of BCs varies considerably. Some complications such as bile leaks may occur immediately in the post-operative period, while others may take weeks to develop. The clinical presentation can vary from asymptomatic patient with moderate liver enzyme elevations to a septic patient. Whenever a biliary complication is suspected, work-up usually begins with laboratory evaluation and an abdominal doppler ultrasound. Abdominal ultrasounds are relatively inexpensive, and are easy to perform (Fig. 1). Abdominal Doppler ultrasound of liver vessels allows differential diagnosis between biliary and vascular complications [9]. The positive predictive value of abdominal ultrasound is very high, especially in the presence of dilated bile ducts. In the absence of dilated bile ducts, the sensitivity of the ultrasound for detecting biliary obstruction ranges from 38% to 68% according to various sources [10].

Depending on which diagnostic technique makes the most sense to use, either magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP) may be performed if ultrasound is unable to detect signs of bile duct dilatation despite a clinical suspicion.

It is preferable to perform ERCP in patients with biliobiliary anastomoses of bile ducts, as this allows for

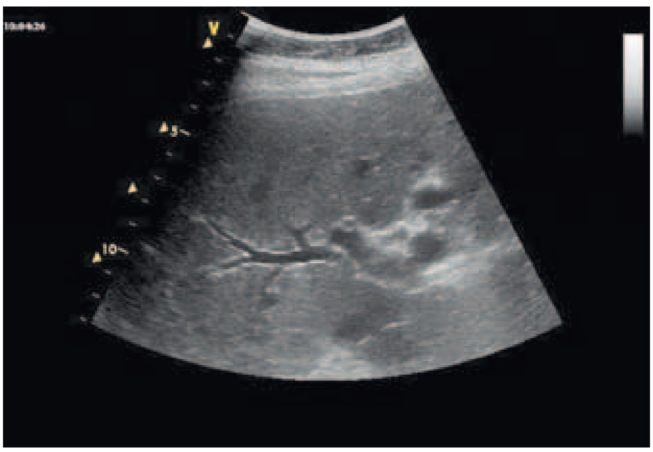

Fig. 1. Ultrasound imaging of intrahepatic bile duct dilation [5]

Corresponding author: Konstantin Semash. Address: 294, Parkentskaya str., Yashnobod district, Tashkent, 100171, Uzbekistan.
Phone: +998 (94)-090-89-05. E-mail: mail@doctorsemash.com

therapeutic manipulation to be performed, such since papillosphincterotomy or stenting of bile ducts, removal of mechanical obstruction of bile ducts (lithoextraction), etc. Percutaneous transhepatic biliary drainage with cholangiography, or percutaneous transhepatic cholangiography (PTC), is used in rare cases where none of the aforementioned techniques may be used.

ERCP is technically very difficult to perform in biliodigestive anastomosis, so magnetic resonance (MR) cholangiography is preferable in such patients for diagnosis. However, in recent years, with the development of medical technologies, enteroscopes have become available and allow for endoscopic biliary examinations even in biliodigestive anastomosis [11, 12]. However, it may not be possible to use this strategy in all patients due to unfavorable surgical anatomy, adhesions, limited maneuverability of the endoscope, and the limited number of small caliber instruments that can be used through these endoscopes. In addition, these procedures require high skill and experience, and the learning curve is complex and therefore only available at specialized centers.

Another specialized method that has now been tested is gastrostomy by surgical or percutaneous means using endoscopic ultrasound followed by ERCP through the gastrostomy port [13].

MR cholangiography has excellent sensitivity (93% to 100%) in detecting biliary strictures. Based on MRCP data, it can also offer a road map for the endoscopist in planning the necessary intervention. Another advantage of MRCP is that this technique is noninvasive and does not create additional risks for the patient, unlike ERCP [14].

BILE LEAKAGE AFTER LIVER TRANSPLANTATION

Bile leaks (biliary fistula), along with bile duct strictures, are the most frequent post-OLT complications. Biliary fistulas, according to world reports [4–8, 15–18], occur in 2% to 35% of liver recipients. They can be classified in two categories [15–18]:

– Early (presenting within 4 weeks of OLT);
– Late (presenting from 5 weeks of OLT and beyond).

Etiology. Early bile leaks after LT usually occur due to anastomotic leakage, ischemia-reperfusion injury, infection, or after T-tube removal. Also, they can be caused either by coagulative necrosis (when bile ducts are damaged by an electrocoagulator or bipolar forceps) [14, 19].

Presentation. Bile leak should be suspected in any patient presenting with abdominal pain, fever, or having any peritonitis after LT, especially after T-tube removal. Bile leaks not related to T-tube removal typically present within the first 30 days after LT. Some patients, especially those on corticosteroids, may be asymptomatic, with no signs of pain or fever. In such cases, any unexplained elevations in serum bilirubin, fluctuation in liver transaminases, or the presence of free fluid accumulation in the abdominal cavity on ultrasound should raise suspicion for a bile leak [20].

Treatment of biliary leaks (biliary fistula). If a biliary fistula is suspected, it should be drained. Further tactics depend on the cause of the biliary leak. Thus, if bile leakage is associated with T-tube removal, ERCP and papillosphincterotomy are performed to increase bile flow resistance, a stent is placed in the defect zone. Additionally, complex antibacterial, analgesic, infusion and detoxification therapy is performed [15, 16]. Girotra et al. state that in the presence of end biliary anastomosis, most patients with biliary anastomosis can be treated endoscopically with papillosphincterotomy and bile duct stenting. The stent can remain in the bile duct for up to three months. After stent placement, the symptoms disappear quickly, but the actual healing of the leak may take up to 6–10 weeks [21].

Kochhar et al. report that in those cases where bile flow is associated with ductal ischemia – coagulative necrosis in the anastomosis area – the above-described technique cannot achieve such a good therapeutic effect. In such cases, the abdominal cavity is drained, a tube under the control of fistulography is installed in the defect area. Against the background of complex conservative therapy, such biliary fistulas close on their own. In rare cases, surgical intervention may become necessary to perform biliary reconstruction [20].

There is another method of treatment for BCs by nasobiliary drainage. For example, Thuluvath reports about successful closure of bile leaks using nasobiliary drainage [16]. Nevertheless, many authors consider that installation of an internal biliary stent provides better decompression from bile ducts into duodenum [15].

Biloma. Bile rupture and spilling of bile within the liver and abdominal cavity may result in the formation of a biloma (a cluster of bile surrounded by a pseudocapsule). Small bilomas, especially ones that communicate with the biliary tree, may resolve on their own. Bilomas are usually treated conservatively (antibiotic therapy). At the same time, biloma drainage options are available. In rare cases, open surgery to remove the biloma is required [15].

BILE DUCT STRICTURES

Biliary strictures (narrowings) are the second most common complication after LT. According to reports [4, 10, 13, 14, 18], the incidence ranges from 5% to 15% after deceased-donor LT, and 28–32% after living donor LT. Strictures are commonly seen as late complications, occurring approximately 5–8 months after transplantation, although there are cases of early postoperative strictures [10]. Post-LT biliary strictures are usually classified as anastomotic or non-anastomotic.

Anastomotic strictures (AS)

Strictures at the site of biliary anastomosis are the most frequent after OLT and can occur both in choledochojejunostomy and in choledochocholedochostomy [4, 18].

Causes of anastomotic strictures. The causes of AS are believed to include the following: inadequate mucosa-to-mucosa anastomosis, surgical technique, local tissue ischemia, and the fibrotic nature of the healing process [22]. Early bile leak after LT is also considered to be a risk factor for developing AS [15, 23]. In addition, vascular complications often lead to AS [9, 27]. In patients with T-tube, strictures at the choledochocholedochostomy anastomosis are often not typically evident until after removal of the T-tube [20]. A slight and transient narrowing of the biliary lumen occurs frequently in biliary anastomosis shortly after the LT due to postoperative edema. However, it is uncertain how many of these cases progress to clinically significant strictures [14]. In pediatric practice, the main risk factors for the development of strictures in liver fragment transplantation are impaired arterial blood flow, presence of an end-to-end biliobiliary anastomosis, and donor-side factors such as coagulation injury.

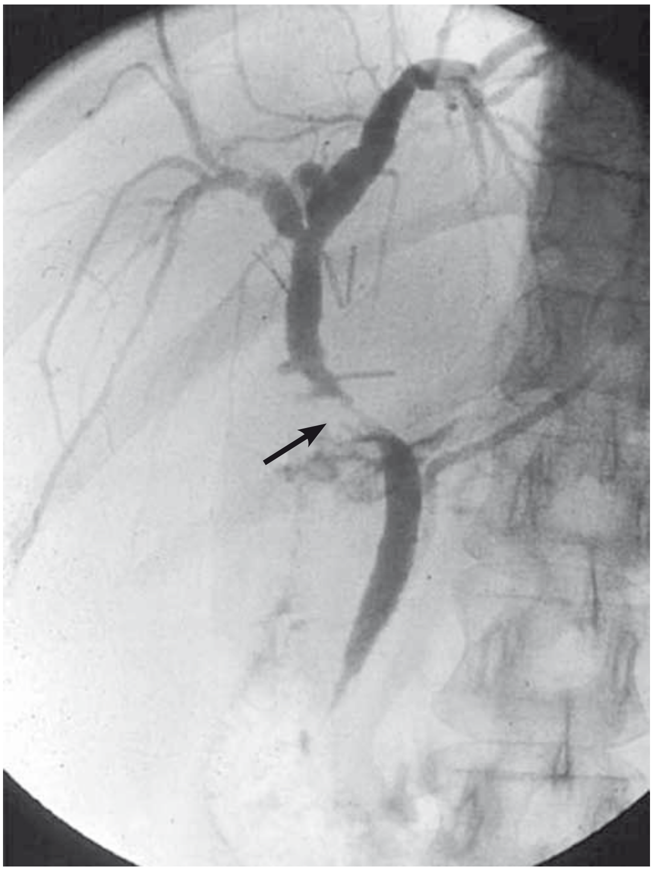

Fig. 2. Endoscopic retrograde cholangiopancreatography. Orange arrow indicates the anastomotic biliary stricture site [18]

Clinical presentation in anastomotic strictures. AS should be suspected in any liver transplant recipient who presents with jaundice, fever, abdominal pain, or even in patients with asymptomatic biochemical cholestasis. Bile duct dilatation can be observed with various imaging methods (ultrasound, MR cholangiography), however, it often does not develop immediately, so the absence of duct dilation is not a prerequisite for diagnosing strictures. When performing biopsy in such patients, histological findings may be suggestive of pericholangitis or bile duct proliferation [20].

Treatment of anastomotic strictures. Treatment varies depending on the type of biliary reconstruction performed on the patient during LT.

For example, in choledochojejunostomy biliobiliary anastomosis, it is advisable to perform ERCP followed by papillosphincterotomy and stenting of the common bile duct in the narrowing area (Fig. 2). Although outcomes vary markedly, studies have demonstrated good response to endoscopic therapy in over 75% of the patients [24, 25]. Endoscopic treatment is thus regarded as the treatment of choice for AS, especially in the choledochocholedochostomy group of patients. There are described techniques when the primary stent is replaced every three months with a larger diameter stent for a year, then the stent is removed permanently [20].

Sharma et al. report that when clinical AS occurs in the early postoperative period, the cause of jaundice and bile duct dilation may not be a true AS but postoperative edema, in such cases it is reasonable to perform ERCP and balloon dilation at the narrowing site; as a rule, this manipulation is enough to resolve obstructive jaundice [10].

It is also reported that SpyGlass technology has recently been actively used during ERCP for the treatment of strictures after LT. The Spyglass peroral cholangioscopy system is designed to be used by one operator rather than two operators as in the classical ERCP procedure. The system consists of two components: the SpyGlass fiber-optic probe (reusable) and the Spyscope access and delivery catheter, which is a single-use system. The instrument is inserted into the bile ducts through the duodenoscope's 4.2 mm diameter working channel. It has two main channels: a working channel for using forceps for biopsy or insertion of a 0.035-diameter guidewire, and a separate channel for the SpyGlass optical probe. The endoscopist operates the duodenoscope, optics, guidewire and probe simultaneously. This new technique not only allowed strictures to be clearly visualized and treated, but also simultaneously facilitated fairly easy and rapid cannulation, preventing the need for repeated ERCP/percutaneous access or surgery [28–30].

The rendezvous technique is employed when endoscopic bile duct cannulation is not feasible. This technique combines endoscopic technique with percutaneous transhepatic cholangiography (PTC) to facilitate bile duct cannulation in cases where previous endoscopic attempts have failed. This integrated method increases the likelihood of success of biliary cannulation and facilitates the diagnosis and treatment of biliary diseases [65].

Intraductal magnetic compression is one of the newest techniques for treating biliary strictures endoscopically. Magnets are placed on the distal side of the stricture using an endoscope and on the proximal side using percutaneous access (Fig. 3). Then the magnets gradually move closer together and thus the stricture is resolved [31, 32]. Jang et al. reported that the overall clinical success rate of magnetic compression anastomosis for biliobiliary strictures was 87.5% of patients, and the recurrence rate was 7.1%. The clinical success rate of this method varies depending on the etiology of the stricture [33].

Ultrasound- and fluoroscopy-guided percutaneous transhepatic biliary drainage is performed in patients with biliodigestive anastomosis. Further, the drainage catheter (cholangiojejunostomy) during the year is replaced by similar ones with a larger diameter (bougienage).

In pediatric practice, percutaneous transhepatic bilioplasty is also used – it is a minimally invasive method, whose outcome is similar to that of surgical revision. For instance, several papers describing this technique have been published at the Shumakov National Medical Research Center of Transplantology and Artificial Organs [34–36]. A puncture needle was inserted into the dilated bile duct (primarily the second segment of the liver) under ultrasound guidance. A guidewire was used to try to pass the biliodigestive stricture, and if the stricture was successfully passed through the guidewire, an external-internal drainage catheter of 8.5 Fr diameter was installed, which, within over the next year, they were gradually replaced with drainage catheters of a larger diameter in order to bougienage the stricture (Fig. 4) [34]. In their results, the authors report that almost all patients in whom external-internal drainage catheter could be placed achieved a sustained response to this treatment modality after completion of the bougie course.

Although it has traditionally been considered that ERCP is virtually impossible to perform in patients

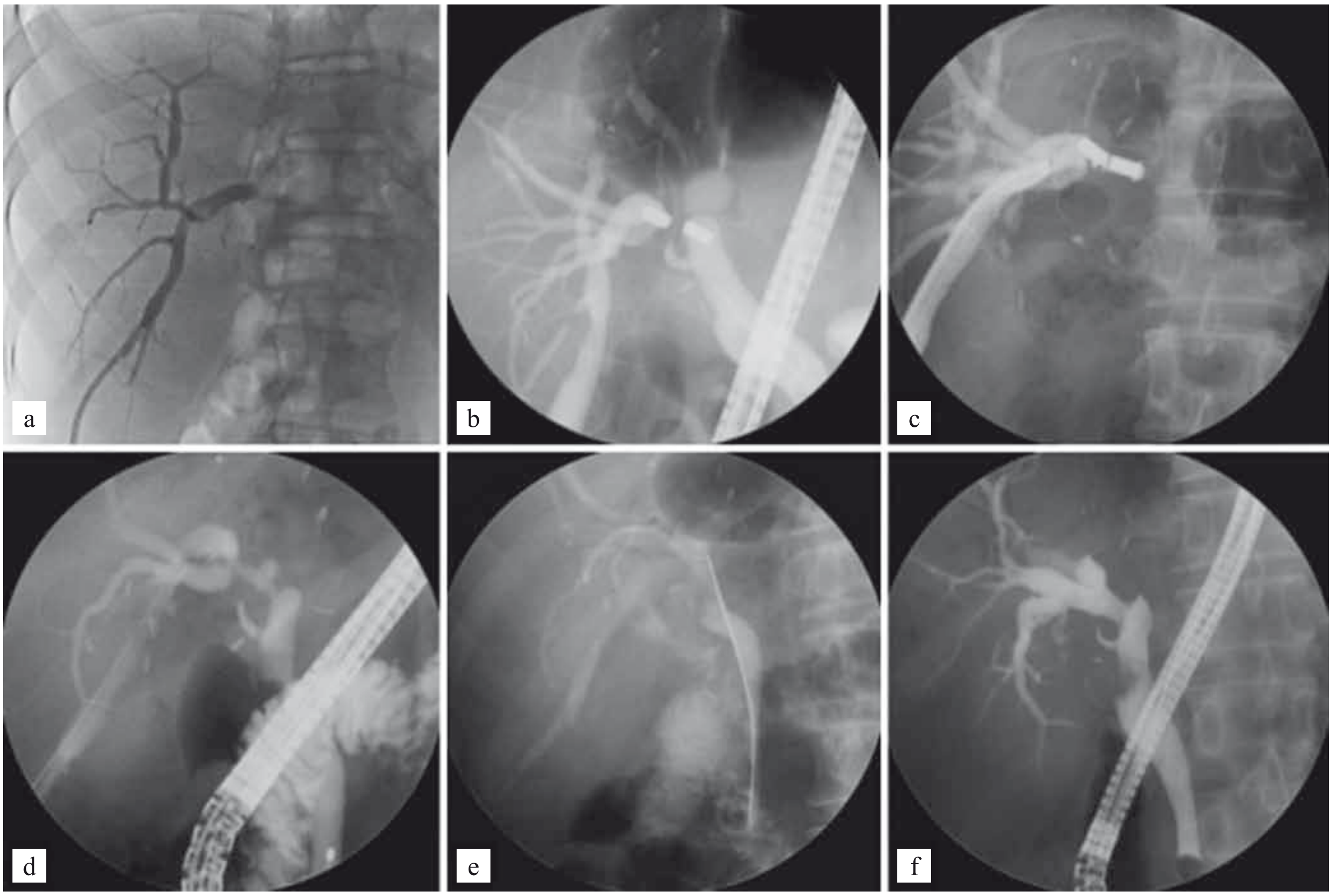

Fig. 3. Intraductal magnetic compression for stricture after liver transplantation from a living donor: a, dilated bile duct was cannulated by percutaneous transhepatic access; b, one magnet was placed via percutaneous access and the second magnet was placed by endoscopic retrograde cholangiopancreatography through the common bile duct. Magnet apposition was successful, and the percutaneous catheter was left in place to decompress the biliary tree; c, the magnets were removed by percutaneous transhepatic cholangioscopy; d, cholangiogram demonstrates recanalized biliary after removal of the magnets; e, a retrievable, fully covered, self-expandable metallic stent was placed for 6 months (replaced every 3 months); f, endoscopic picture after stent removal demonstrates a good effect from the procedure performed [33]

with biliodigestive anastomosis, many attempts have been made in the last decade to develop this surgical option in this patient cohort. For example, Arain et al. used elongated pediatric endoscopes to provide greater maneuverability during enteroscopy [37]. Japanese surgeon Tsujino describes balloon plasty and stenting of anastomotic biliary strictures in patients after LT using enteroscopy [38]. Also, a method is described when a percutaneous gastrostomy is formed using endoscopic ultrasound, and ERCP enteroscopy is performed through the formed access via a gastrostomy port. The authors explain the advantages of this technique by the possibility to work with standard duodenoscopes. In addition, as advantages, the authors note the convenience of maneuvering the endoscope during the procedure. The disadvantages of the procedure include additional surgical trauma [13].

AS, which are diagnosed earlier, are considered to be better amenable to therapy than strictures detected at a later date after LT. In cases where strictures cannot be treated with the above methods, surgical treatment – repeated biliary reconstruction – is performed [39].

Non-anastomotic strictures (NAS)

Non anastomotic strictures (NAS), also known as ischemic type strictures, are well known and have been described since the beginning of LT. They are frequently hilar in location, but can also be diffusely intrahepatic. Unlike AS, NAS symptoms tend to be longer and multiple on presentation. NAS incidence ranges from 5–15% with mean time to presentation of 3.3–5.9 months post-LT [40, 41].

Etiology. A few theories have been proposed for the development of NAS. Blood supply to the supraduodenal bile duct is predominantly from vessels which are resected during LT. The remaining blood supply to the donor bile duct then comes from the hepatic artery and its branches, which are tenuous and highly susceptible to

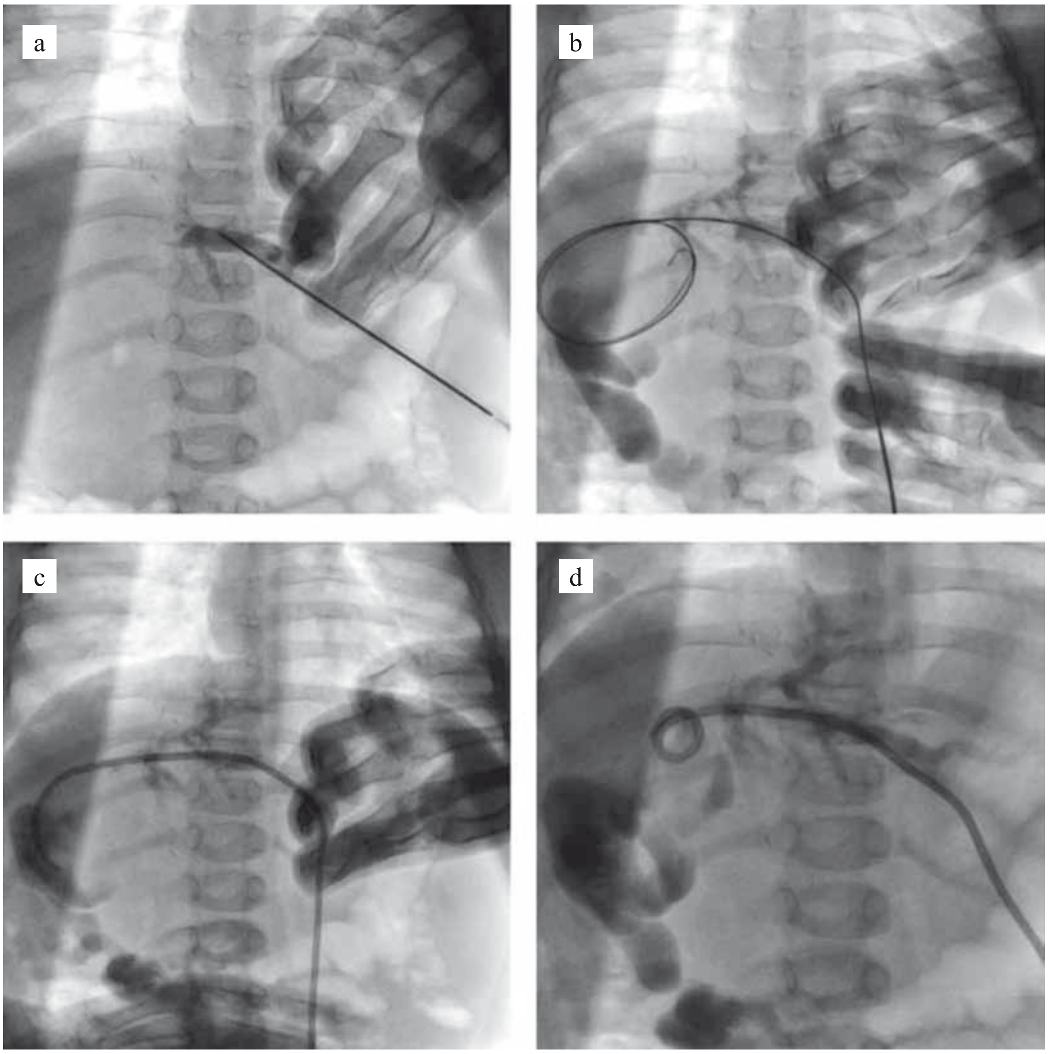

Fig. 4. Stages of placement of external-internal drainage catheter: a, contrast is injected through the Chiba needle into the dilated duct; b, guidewire is passed through the stricture into the efferent loop of the intestine; c, Dawson–Mueller drainage catheter through a guidewire is passed through the stricture; d, distal loop of the drainage catheter is placed in the intestine behind the stricture [36]

ischemic injury. In patients with NAS, up to 50% have demonstrable hepatic artery thrombosis. Prolonged cold ischemia time has also been shown to be responsible for the development of NAS. Besides ischemia, an immunological cause has also been proposed. This is mainly due to the observation of an increased incidence of NAS in cases with ABO-incompatible grafts, in patients with autoimmune hepatitis or primary sclerosing cholangitis. Thus, the causes of NAS are multifactorial and debatable [10, 42, 43].

Management. The presentation of NAS is similar to that of AS. NAS are more difficult to manage than AS, and treatment is often more "aggressive". In cases with early, revascularization should be attempted (in the presence of ischemia or hepatic artery occlusion), because prolonged ductal ischemia may lead to graft abscessation, resulting in the need for retransplantation [44].

In balloon dilation/stenting of strictures, treatment success depends largely on the number and location of strictures. Extrahepatic strictures generally respond better to therapy. If radiological and endoscopic therapies fail, open biliary reconstruction may become necessary. Success rates are higher if surgery is done within two years of LT and if the liver biopsy does not show any significant fibrosis [16, 38].

Retransplantation may also be considered in patients with treatment failure, or in the presence of secondary biliary cirrhosis, recurrent cholangitis, or progressive cholestasis [16, 38, 39, 44–46].

SPHINCTER OF ODDI DYSFUNCTION (SOD)

One of the common phenomena after LT is a mild increase in the size of donor and recipient common bile ducts. In certain cases, significant dilatation of both recipient and donor bile duct in association with biochemical abnormalities occurs in the absence of cholangiographic evidence of obstruction. In these cases, SOD is suspected. The incidence of SOD is reported to be up to 7% [17, 39, 47].

Etiology. The pathogenesis of SOD is attributed to denervation of the sphincter during OLT. This leads to an increase in basal pressure, thus causing increased pressures in the choledochal duct. Two types of SOD have been proposed: stenosis and dyskinesia. Any process that leads to chronic inflammation can lead to sphincter stenosis. Dyskinesia, on the other hand, is usually seen as a result of functional disturbance of the sphincter [22, 48, 49].

Management. There have been virtually no clinical trials that demonstrate the best treatment option for SOD. In recent years, endoscopic therapy (ERCP) with papillosphincterotomy with or without stenting has been the most acceptable treatment option for SOD [20, 21, 38, 47, 50].

BILIARY STONES, SLUDGE, AND CASTS AFTER LIVER TRANSPLANTATION

Bile duct obstruction by stones or sludge can occur at any stage following the OLT. Sludge is described as a thick collection of mucous, calcium bicarbonate and cholesterol crystals, which, when left untreated, can go on to form biliary stones. Sludge and casts usually occur within the first year of transplant, while stones tend to occur later on. Also, the so-called biliary cast is a complete encrustation of the bile duct by sludge or stones with the formation of a biliary cast [20, 21, 51]. Biliary cast disease is described in 3.3–12.3% of cases in patients after liver transplantation [21, 25].

Etiology. Theoretically, anything that increases the viscosity of bile or reduces flow can predispose to the formation of sludge, and stones. Bile duct mucosal damage due to obstruction, ischemia, or infection is thought to play a role in the development of cholelithiasis [21]. Of patients presenting with biliary stones and sludge after LT, most will have an underlying stricture. Among other things, immunosuppressants such as cyclosporine may play a role in bile lithogenicity by inhibiting bile secretion and promoting biliary stasis [20, 21].

Presentation. Patients commonly present with abdominal pain, cholestatic liver tests, and, possibly obstructive jaundice.

Management. According to reports, cholangiography is the only reliable imaging method for sludge, while ultrasonography and computed tomography (CT) scans are of limited value. If sludge alone is present, then it would be reasonable to first attempt medical treatment with ursodeoxycholic acid. ERCP with sphincterotomy, lithotripsy and stone extraction are successful in the presence of end-to-end choledochoduodenostomy.

According to Girotra et al., ERCP with sphincterotomy has high rates of success in removing gallstones and sludge in 90–100% of cases [21]. However, removal of biliary casts can be challenging and may require several procedures including sphincterotomy, extraction of casts with a balloon and/or basket, stent placement and lithotripsy, or may ultimately require PTC [61, 81]. In various studies, endoscopy has shown successful removal of biliary casts in 25–60% of patients [41, 52]. In fact, in cases of severe biliary necrosis and presence of casts, repeated endobiliary interventions using baskets and balloon dilatation are often necessary, and stent placement is usually not recommended in early stages because of the risk of occlusion by small residual stones and sludge [53].

In contrast, bile duct stones are usually easily removed with ERCP. Sometimes, proximal stones may present a problem, and in such cases, direct cholangioscopy can be performed to remove stones. In addition, if the filling defect is located proximal to an existing anastomotic stricture, treatment of the stricture becomes the first step toward clearing the duct. Lithotripsy can be combined with stone removal procedure [21]. Direct cholangioscopy can be performed using ultrathin pediatric endoscopes that can be inserted directly into the bile ducts to study the ductal anatomy and remove stones and casts from bile ducts [37]. In addition, enteroscopy can be used to perform ERCP in patients with biliodigestive anastomosis to remove gallstones or casts [38].

However, in many patients with choledocholithiasis, the clinical course may be completely asymptomatic, which is often due to the fact that the graft is denervated. Patients often do not experience pain and fevers due to steroids and immunosuppressants after LT. Sometimes cholelithiasis can form in the background of strictures due to bile stasis and this occurs proximal to the stricture. In such cases, endoscopic treatment becomes difficult [21].

MUCOCELE

In rare cases, the donor's cystic duct can be included in the suture line of biliary anastomosis. As a result, a blind sac lined with mucous membrane is formed. Due to mucin accumulation, this sac may increase in size and cause bile flow obstruction. Endoscopy is often ineffective in these cases. Percutaneous drainage or surgical treatment are effective treatment options. Differential diagnosis of mucocele includes any type of fluid accumulation, such as bilomas, abscesses, hemorrhages, and aneurysms [46, 54].

HEMOBILIA

Hemobilia is a rare complication following liver transplantation. As a rule, it develops after biopsy of the graft or after percutaneous hepatic manipulations on the graft. However, cases of spontaneous hemobilia and hemobilia against the background of bile duct pseudoaneurysm rupture have been reported [9, 46, 55]. Treatment of hemobilia requires both hemostasis and treatment of obstructive jaundice, which is caused by blood clots. In some cases, bleeding spontaneously stops with supportive therapy and correction of coagulopathy. Embolization of bleeding vessels using interventional techniques is necessary if bleeding is permanently prolonged or there is a large blood loss. Removal of clots from the biliary tree to resolve the obstruction is usually performed endoscopically [56].

Shinjo et al. described an effective technique for resolving hemobilia by performing ERCP with thrombus extraction and nasobiliary placement. They consider this therapy to be the first choice. Nasobiliary drainage provides the possibility of biliary tract lavage, which prevents cholangitis and indicates the presence of recurrent bleeding. In most cases, a combination of endoscopic treatment (stenting) and hemostatic therapy gives good outcomes [57, 58].

KINKING OF THE COMMON BILE DUCT

Excessive length of the donor's common bile duct can lead to its kinking. Bile flow may be impaired as a result of this. The reported incidence is 1.6% among all OLTs. ERCP with placement of a long plastic stent usually resolves cholestasis. Biliary reconstruction is required in rare cases [59].

FOREIGN BODIES

Suture material or remnants of perforated tube can be sources of obstructive jaundice or stone formation. ERCP and PTC are effective methods for diagnosing and treating bile duct foreign bodies. Biliary reconstruction is required in very rare cases [46, 60].

RISK FACTORS FOR BILIARY COMPLICATIONS AND METHODS OF THEIR PREVENTION

Risk factors. There are many risk factors of BCs. The type of biliary reconstructions, bile duct ischemia, reperfusion injury, hepatic artery thrombosis, cytomegalovirus infection, surgical technique, variant biliary anatomy, biliary stasis, and primary sclerosing cholangitis (PSC) are some of the risk factors that influence the rate of these complications (Fig. 5) [7, 8, 26, 63]. Moreover, a recent systematic review of 45 articles (14,411 patients) showed that BCs develop more frequently in patients with MELD >25, PSC or malignancy [63, 100].

Living-donor liver transplant can be a risk factor for BCs. According to reports, various transplant centers compared the outcomes of living-donor and deceased-donor transplantations. In almost all studies, BCs developed more often in patients who received liver from living donors. The same applies to a comparison of the outcomes of related liver transplantation and split liver transplantation in both adults and children (see Table 1).

Type of biliary anastomosis is one of the main factors determining the risk of BCs after orthotopic LT. The two most common forms of biliary tract reconstruction are choledochocholedochostomy (anastomosis of the common bile duct of the transplant to the common bile duct of the recipient) and choledochojejunostomy (anastomosis of the bile duct to a part of the jejunum; such anastomosis is most often performed with a part of the jejunum taken out according to the Roux technique) [61]. The choice of the type of biliary reconstruction may be influenced by many factors, including an underlying disease of the recipient, diameter of the bile ducts of the donor and recipient, number of biliary ducts on the graft (for living donor transplantation), history of bile duct surgery, retransplantation, other intraoperative circumstances, as well as the preferences of the operating surgeon. There are no clear guidelines regarding the optimal type of biliary reconstruction, and many surgeons have their own opinion on this matter [20].

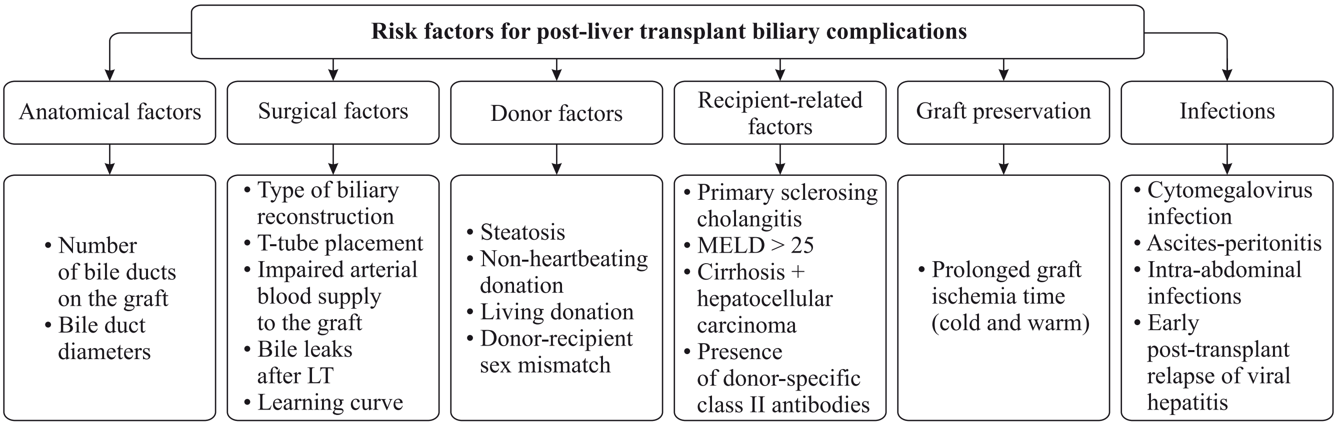

Fig. 5. Risk factors for biliary complications following liver transplantation

Table 1

Comparison of the number of biliary complications after split liver transplantation from living and from deceased donors

Study	Transplant type	Patient count	Age	MELD PELD	Biliary complications	
					Stricture	Bile leaks
Barbas et al. [84]	Living RL donor	48	54.7 ± 9.4	17.8 ± 8.7	3 (6.3%)	4 (8.3%)
	Deceased liver	128	56.7 ± 9.3	21.8 ± 10.3	4 (3.1%)	2 (1.6%)
Reichman et al. [85]	Living RL donor	145	54.2 ± 7.5	14.4 ± 3.8	26 (17.9%)	15 (13.3%)
	Deceased liver	145	53.9 ± 7.7	14 ± 6.8	16 (11%)	5 (3.4%)
Lei et al. [86]	Living RL donor	31	44.4 ± 9.7	9.3 ± 6.1	1 (3.2%)	1 (3.2%)
	Deceased liver	52	44 ± 8.2	9.1 ± 5.8	0	1 (1.9%)
Li et al. [87]	Living RL donor	128	43 ± 8.6	19.5 ± 10.7	12 (9.4%)	3 (2.3%)
	Deceased liver	221	44.5 ± 9.7	18.2 ± 9.6	3 (1.4%)	6 (2.7%)
Chok et al. [88]	Living RL donor	54	51 ± 12	40 ± 1.3	2 (3.7%)	0
	Deceased liver	40	51 ± 10.8	39 ± 1.3	1 (2.5%)	0
Liu et al. [89]	Living RL donor	124	47.5 ± 8.3	21 ± 6.5	31 (25%)	5 (4%)
	Deceased liver	56	48 ± 9.8	19 ± 10.8	3 (5.4%)	2 (3.6%)
Wan et al. [90]	Living RL donor	40	48.6 ± 9.7	–	7 (17.5%)	1 (2.5%)
	Deceased liver	80	49.5 ± 8.9	–	5 (6.25%)	1 (1.3%)
Hu et al. [91]	Living RL donor	389	48.1 ± 8.7	–	BL + AS – 81 (20.8%)	
	Deceased liver	6471	50.1 ± 9.4	–	BL + AS – 721 (11.1%)	
Kim et al. [92]	Living RL donor	21	53.1 ± 10.3	13.1 ± 5.4	2 (9.5%)	2 (9.5%)
	Deceased liver	29	51.3 ± 9.2	24.9 ± 11.6	0	0
E. Kim et al. [93]	Living RL donor	109	52 ± 8.5	12.5 ± 8.3	BL + AS – 10 (9.1%)	
	Deceased liver	76	53.2 ± 11	24.9 ± 11.7	BL + AS – 5 (6.5%)	
Jiang et al. [94]	Living RL donor	70	40.3 ± 8.2	23.9 ± 11.1	5 (7.1%)	4 (5.7%)
	Deceased liver	191	44.1 ± 9.3	21.7 ± 9.9	7 (3.6%)	8 (4.2%)
Latypov [95]	Living RL donor	22	17.9 ± 12.5	11.9 ± 8.5	0	5 (23%)
	Split DRL	22	21.9 ± 17.5	15.6 ± 10.2	2 (9.2%)	2 (9.2%)
	Living LLQ donor	22	1	1	0	4 (18.4%)
	Split DRL	22	1	1	0	4 (18.4%)
Dalzell et al. [96]	Living LLQ donor	508	1	1	1 (0.2%)	0
	Split DRL	403	1	1	2 (0.5%)	0
Yoon [97]	Living LLQ donor	56	1.4 (0.9–2.8)	–	BL + AS – 3 (4.3%)	
	Split LLQ	63	1.0 (0.8–7.8)	–	BL + AS – 721 16 (28.6%)	
Diamond et al. [98]	Deceased liver	1183	6.6	11.6	38 (3.2%)	44 (3.7%)
	Split LLQ	261	3.2	16.7	6 (2.2%)	41 (15.7%)
	Reduced liver	388	3.2	18.2	20 (5.1%)	46 (12%)
	Living LLQ donor	360	2.6	16.6	15 (5.2%)	53 (14.7%)

Note: MELD, model for end-stage liver disease; BL, bile leak; AS, anastomotic stricture; RL, right lobe; DRL, dilated right lobe; LLQ, left lateral quadrant.

In orthotopic cadaveric LT, biliobiliary anastomosis is the most common modality of biliary reconstruction. This technique is preferred because it is technically easier to perform and the sphincter of Oddi function is preserved in this type of reconstruction. Also, amidst bile duct complications after this type of reconstruction, it is possible to resolve the complication endoscopically with retrograde cholangiography (ERCP). In addition, preservation of the sphincter of Oddi theoretically reduces the risk of ascending cholangitis because it serves as a barrier against reflux of intestinal contents into the biliary tree [11].

Roux-en-Y hepaticojejunostomy is another type of biliary reconstruction. Usually, this type of biliary reconstruction is used in patients with a history of biliary diseases, such as primary sclerosing cholangitis, with previous surgical biliary interventions, in size discrepancy between the donor and recipient ducts. This type of anastomosis is also often used in related LT, in split LT or in pediatric LT [75, 76]. Compared to choledocho-choledochostomy, biliodigestive anastomosis requires more time to perform and does not provide adequate opportunity for endoscopic evaluation of the biliary system after LT [20]. Potential complications of biliodigestive reconstructions include intestinal perforation, bile duct stricture, anastomotic leak and bleeding at the site of interintestinal anastomosis [10].

Also, the technique of both biliobiliary and biliodigestive anastomosis may influence the incidence of complications. Many studies on living-donor LT have focused on the question of which suture to use: continuous or interrupted? Even if the outcomes are partially contradictory, it can be summarized that the incidence of biliary leakage increases with single sutures, whereas the incidence of stenosis increases with continuous sutures [68–69]. However, there are no randomized studies on this issue. In a retrospective study of 100 patients after LT, Castaldo et al. showed the outcomes of BCs with choledocho-choledochostomy. With an almost identical incidence of about 8% leak, anastomosis strictures were almost twice as common with continuous suturing (9.8% *vs.* 5.1%), but this was not statistically significant [70]. Kasahara et al. reported an increased incidence of strictures in choledocho-choledochostomy by using continuous suture, while the incidence of strictures in choledochojejunostomy was decreased [71]. However, the opposite outcome was observed by another working group [72] (Table 2).

The frequency of BCs is also influenced by donor biliary anatomy. Voskanyan et al. presented their own classification of biliobiliary and biliodigestive reconstructions used in transplantation of the right liver lobe from a living donor. Based on this classification, the authors calculated the risks of BCs when performing a certain type of anastomosis. A statistically significant risk of biliary bleeding was noted in ductoplasty (merging of two or more bile ducts into one mouth) and applying biliobiliary anastomosis after such plasty. The authors also noted that the patients with a history of bile leakage were at a higher risk of developing AS [27].

A similar outcome is demonstrated by Baker et al. [62]. A multicenter study was conducted, where the results and the number of BCs following related LT were analyzed. The researchers note that the rate of BCs is influenced especially by donor biliary anatomy. Thus, according to data from this study, in patients with complex variable anatomy of bile ducts, the rate of BCs can reach 76%, despite various surgical techniques (Fig. 6).

Routine placement of T-tubes in the formation of biliobiliary anastomosis is a risk of cholangitis and bile leakage after their removal. In a retrospective study by Olivier Scatton, which included analysis of 180 patients, it was demonstrated that the incidence of biliary fistula and risk of cholangitis was 10% in the T-tube group and

Table 2

Comparison of the incidence of bile leaks and anastomotic biliary stricture depending on the suturing technique in living related liver transplantation

Author	Total cases (n)	Suture	Cases (n)	Biliary effusion	Stricture
Kasahara et al. [71]	321	Interrupted	25	8%	36%
		Twisted	148	4.7%	25%
Soejuma et al. [72]	182	Interrupted	63		10% (BB); 31.8% (BD)
		Twisted	37		45.9% (BB); 0 (BD)
Hwang et al. [68]	282	Interrupted	259	5%	16.8% (BB); 15.8% (BD)
		Twisted	23	13%	21.7% (BB)
Tashiro et al. [72]	80	Interrupted	30	15%	6.7% 20%
Mita et al. [73]	231	Interrupted	50 48		9.5%
Marubashi et al. [69]	83	Interrupted	118 44	1.2%	7.2%

Note: BB, biliobiliary anastomosis; BD, biliodigestive anastomosis.

2.2% in the group without a T-tube. Also, the cumulative 3-year patient survival rate was higher in the group without a T-tube (80.1% *vs.* 72.8%), which the authors attributed to the higher complication rate among T-tube patients [82].

At the same time, German surgeon S. Weis and co-authors conducted a prospective randomized study of BCs following LT after bile duct anastomosis with or without T tubes. They found out that According to the results of the study, there was a significant increase in the complication rate in the group without a T-tube. So, the authors concluded that the usage of T-tubes is safe and an excellent tool for the quality control of biliary anastomosis [83].

According to a meta-analysis of 1027 patients, those without a T-tube had a lower incidence of cholangitis and peritonitis with an overall lower biliary complication rate. Interestingly, this meta-analysis found no significant differences between the groups of patients with and without T-tube insertion in terms of other complications such as biliary leak, hepatic artery thrombosis, and retransplantations. Mortality due to BCs did not differ in the same way [83]. On the contrary, a larger meta-analysis from 2021, which included a population of 2399 patients, showed that the use of T-tubes increased the incidence of strictures, biliary leak, and cholangitis in cadaveric liver recipients. The authors conclude that studies published in the last decade have not provided sufficient evidence to support the routine use of T-tubes in adult recipients [83].

Surgical risk factors for BCs also include vascular complications after LT [9]. The main contributor to the development of BCs is complications related to the liver transplant artery due to bile duct ischemia (Fig. 7).

Some authors have noted that a patient's baseline MELD is a risk factor for biliary strictures [23, 26, 64]. However, there are studies that refute this statement [65].

According to Egawa et al. [66], BCs are more common in female recipients. These data are inconsistent with the work by Voskanyan et al. where the researchers did not obtain statistically significant differences in the number of BCs in men and women, so the gender difference cannot be considered an unambiguous risk factor [26].

Donor-recipient gender mismatch has been reported as a risk factor for various complications, including biliary. A higher complication rate is noted in a pair where the donor is female and the recipient is male [26, 67].

New data suggest that immunosuppression regimens may influence the development of various BCs. For example, sirolimus administration has a higher risk of developing bile duct strictures, and cyclosporine may influence enhanced gallstone formation [21, 51].

Early recurrence of viral hepatitis after transplantation also increases inflammation and, consequently, the risk of strictures [21].

Methods of preventing biliary complications. Many transplant centers use perforated tubes of bile ducts when performing hepaticojejunostomy. It allows to estimate the quality of bile secreted by the transplant, and also such drainage is used to control strictures and bile leakage in the postoperative period [66, 77, 78].

Ando et al. performed frame drain of bile ducts at biliodigestive anastomoses in pediatric cohort recipients and reported only one stricture and one biliary leak out of 49 patients [78].

Monakhov A.R. and co-authors describe their experience of using frame drains in pediatric practice. They describe the experience of left lateral sector transplantation in 149 patients, where frame drainage was installed in 82 patients, and frame drainage was not used in 67 patients. It has been reported that BCs in the group without frame drain was 20%, which was higher than that in the group with external frame drain 8.5% [79].

However, the data on the use of frame drains are contradictory. For example, Japanese surgeon Egawa, analyzing 400 patients after LT, reports increased number of bile leaks when using frame drainage during biliodigestive anastomosis (16.6% *vs.* 10%), while the number of strictures decreased (8.2% *vs.* 9.6%) [66].

To reduce the frequency of biliary leaks in the pediatric cohort of patients, Gautier et al. suggest using peritonization of the left lateral sector of the upper lip of the biliodigestive anastomosis with the round ligament [80, 81]. A lower bile leak rate in patients who underwent

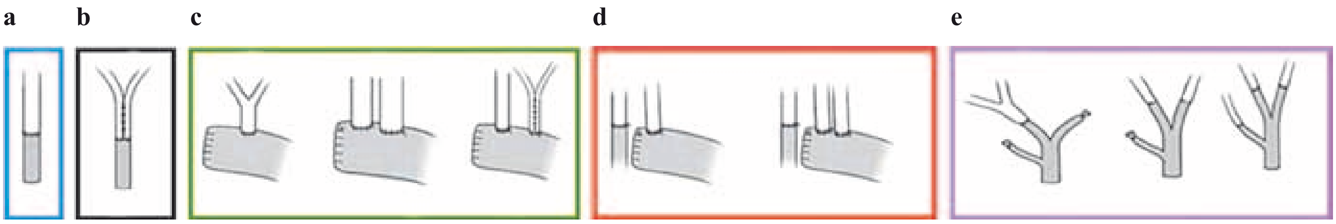

Fig. 6. Surgical techniques for biliary reconstruction for anatomic variant of bile ducts: a, choledocho-choledochostomy; b, choledocho-choledochostomy with ductoplasty; c, variants of biliodigestive anastomosis, including ductoplasty; d, a combination of choledocho-choledochostomy and biliodigestive anastomosis; e, variants of choledocho-choledochostomy for complex biliary anatomy of donor liver [62]

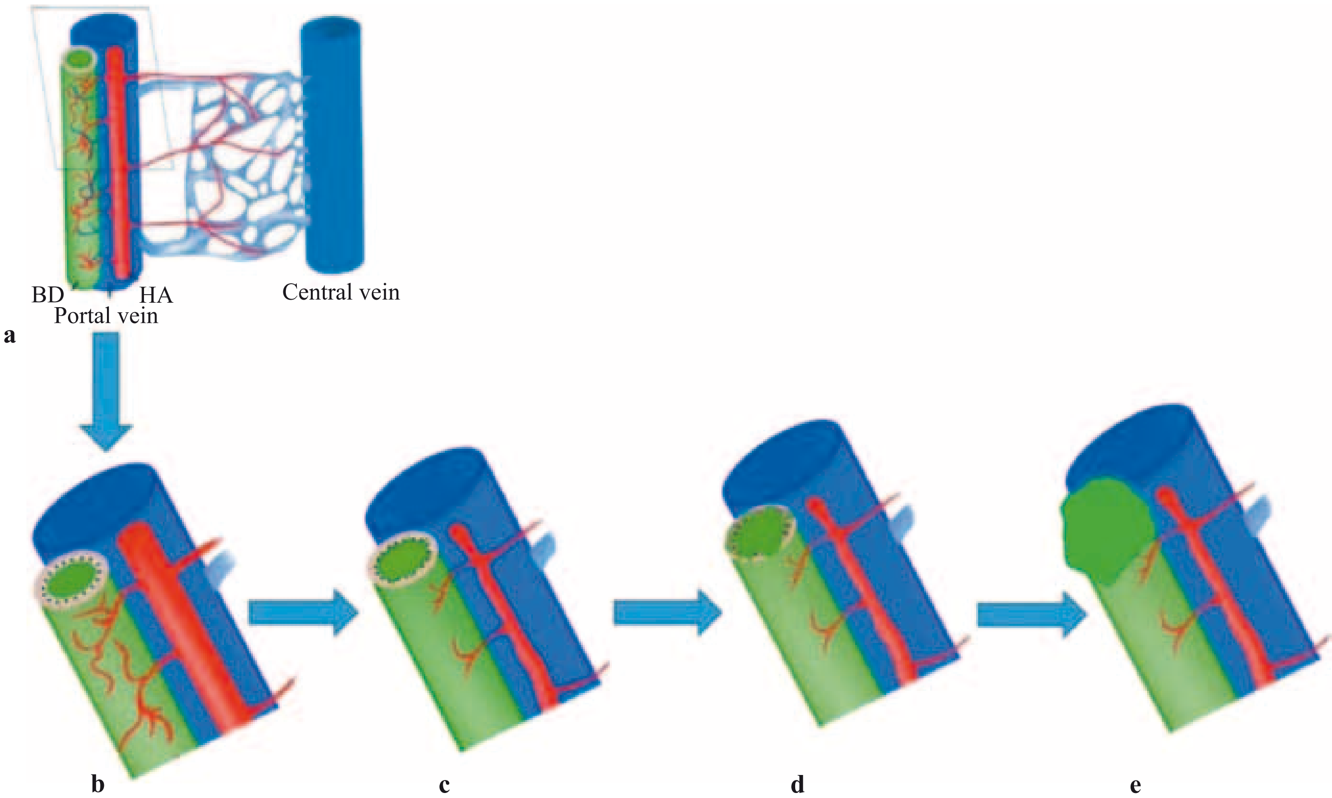

Fig. 7. Schematic influence of ischemia on formation of post-liver transplant biliary complications: a, the bile ducts (BD) are supplied by the hepatic artery (HA), which forms an arterial network around the bile ducts – the peribiliary plexus. The peribiliary plexus drains into the hepatic sinusoids via the periportal plexus The arterial collateral network ruptures after transplantation, leaving the bile ducts at greater risk of ischemia; b, the arterial collateral network is compromised after transplantation due to reperfusion syndrome or arterial stenosis/thrombosis, so the bile ducts are at greater risk of ischemic injury; c, ischemic bile duct injury resulting in epithelial damage due to stenosis, HA thrombosis; d, persistent ischemia progresses and leads to bile duct necrosis; e, formation of a biliary fistula. Ischemia can also lead to formation of bile duct strictures and cholangiogenic abscesses [46]

peritonization of the biliary anastomosis with the round ligament of the left lateral sector graft has been reported (7.6% *vs.* 13.7%).

If CMV infection is detected both before and after LT, it is recommended to prescribe specific antiviral therapy since CMV infection is a proven factor in the development of BCs [63, 98].

CONCLUSION

Biliary complications, known as the Achilles' heel of LT, occur in a quarter of liver recipients. The incidence has increased in recent years due to the increasing number of liver transplant operations worldwide. Living donor LT has a higher rate of BCs and involves more complex scenarios. Endoscopic treatment is the key therapy for most BCs in patients with biliobiliary anastomosis. Ultrasound- and fluoroscopic-guided percutaneous techniques are alternative options for access to bile ducts when endoscopic resolution is ineffective. Treatment of BCs in patients with biliodigestive anastomosis is more complicated due to limitations in endoscopic technology and more often requires invasive, including reconstructive, surgical interventions.

There are a number of directions that need to be developed for more effective treatment and prevention of BCs. It is necessary to pay attention to minimally invasive techniques (including ERCP), especially in the treatment of anastomotic biliary strictures. More functional duodenoscopes are already being developed to enable treatment of complications in the presence of biliodigestive anastomosis. This development has the potential to reduce the risk of relaparotomy in this group of patients. Also, further study of risk factors and their influence on the development of BCs, as well as development of strategies to reduce risk factors will help to prevent BCs, which, in turn, may reduce liver recipient morbidity. Reducing ischemia-reperfusion injury to the graft may also potentially reduce the risk of biliary complications. The development of machine perfusion in the context of cadaveric LT could potentially solve this problem, but further research in this area is required.

The authors declare no conflict of interest.

REFERENCES

1. *Gautier SV, Moysyuk YG, Poptsov VN, Kornilov MN, Tsirulnikova OM, Yaroshenko EB et al*. One hundred deceased donor liver transplantations at a single center. *Russian Journal of Transplantology and Artificial Organs*. 2012; 14 (1): 6–14. (In Russ.). https://doi.org/10.15825/1995-1191-2012-1-6-14.
2. *Schladt DP, Israni AK*. OPTN/SRTR 2021 Annual Data Report: Introduction. *Am J Transplant*. 2023; 23 (2 Suppl 1): S12–S20. https://doi.org/10.1016/j.ajt.2023.02.003.
3. *Terrault NA, Francoz C, Berenguer M, Charlton M, Heimbach J*. Liver Transplantation 2023: Status Report, Current and Future Challenges. *Clin Gastroenterol Hepatol*. 2023; 21 (8): 2150–2166. https://doi.org/10.1016/j.cgh.2023.04.005.
4. *Semash K, Dzhanbekov T, Akbarov M, Mirolimov M, Usmonov A, Razzokov N et al.* Implementation of a living donor liver transplantation program in the Republic of Uzbekistan: a report of the first 40 cases. *Clin Transplant Res*. 2024 Jun 30; 38 (2): 116–127. doi: 10.4285/ctr.24.0013. Epub 2024 Jun 24.
5. *Hampe T, Dogan A, Encke J, Mehrabi A, Schemmer P, Schmidt J et al.* Biliary complications after liver transplantation. *Clin Transplant*. 2006; 20 Suppl 17: 93–96. doi: 10.1111/j.1399-0012.2006.00607.x.
6. *Doskhanov MO, Skakbayev AS, Baimakhanov ZhB, Baimakhanov BB, Kaniyev ShA, Serikuly E et al*. Biliary complications after liver transplantation. *Annaly khirurgicheskoy gepatologii = Annals of HPB Surgery*. 2019; 24 (4): 80–90. (In Russ.). https://doi.org/10.16931/1995-5464.2019480-90.
7. *Davidson BR, Rai R, Kurzawinski TR, Selves L, Farouk M, Dooley JS et al.* Prospective randomized trial of end-to-end versus side-to-side biliary reconstruction after orthotopic liver transplantation. *Br J Surg*. 1999; 86 (4): 447–452. doi: 10.1046/j.1365-2168.1999.01073.x.
8. *Pascher A, Neuhaus P.* Biliary complications after deceased-donor orthotopic liver transplantation. *J Hepatobiliary Pancreat Surg*. 2006; 13 (6): 487–496. doi: 10.1007/s00534-005-1083-z.
9. *Semash KO, Dzhanbekov TA, Akbarov MM*. Vascular complications after liver transplantation: contemporary approaches to detection and treatment. A literature review. *Russian Journal of Transplantology and Artificial Organs*. 2023; 25 (4): 46–72. (In Russ.). https://doi.org/10.15825/1995-1191-2023-4-46-72.
10. *Sharma S, Gurakar A, Jabbour N.* Biliary strictures following liver transplantation: past, present and preventive strategies. *Liver Transpl*. 2008; 14 (6): 759–769. doi: 10.1002/lt.21509.
11. *Lennon AM, Kapoor S, Khashab M, Corless E, Amateau S, Dunbar K et al.* Spiral assisted ERCP is equivalent to single balloon assisted ERCP in patients with Roux-en-Y anatomy. *Dig Dis Sci*. 2012; 57 (5): 1391–1398. doi: 10.1007/s10620-011-2000-8.
12. *Saleem A, Levy MJ, Petersen BT, Que FG, Baron TH.* Laparoscopic assisted ERCP in Roux-en-Y gastric bypass (RYGB) surgery patients. *J Gastrointest Surg*. 2012; 16 (1): 203–208. doi: 10.1007/s11605-011-1760-y.
13. *Attam R, Leslie D, Freeman M, Ikramuddin S, Andrade R.* EUS-assisted, fluoroscopically guided gastrostomy tube placement in patients with Roux-en-Y gastric bypass: a novel technique for access to the gastric remnant. *Gastrointest Endosc*. 2011; 74 (3): 677–682. doi: 10.1016/j.gie.2011.05.018.
14. *Khot R, Morgan MA, Nair RT, Ludwig DR, Arif-Tiwari H, Bhati CS, Itani M.* Radiologic findings of biliary complications post liver transplantation. *Abdom Radiol (NY)*. 2023 Jan; 48 (1): 166–185. https://doi.org/10.1007/s00261-022-03714-y.
15. *Londoño MC, Balderramo D, Cárdenas A.* Management of biliary complications after orthotopic liver transplantation: the role of endoscopy. *World J Gastroenterol*. 2008; 14 (4): 493–497. doi: 10.3748/wjg.14.493.
16. *Thuluvath PJ, Pfau PR, Kimmey MB, Ginsberg GG.* Biliary complications after liver transplantation: the role of endoscopy. *Endoscopy*. 2005; 37 (9): 857–863. doi: 10.1055/s-2005-870192.
17. *Stratta RJ, Wood RP, Langnas AN, Hollins RR, Bruder KJ, Donovan JP et al.* Diagnosis and treatment of biliary tract complications after orthotopic liver transplantation. *Surgery*. 1989; 106 (4): 675–684.
18. *Gunawansa N, McCall JL, Holden A, Plank L, Munn SR.* Biliary complications following orthotopic liver transplantation: a 10-year audit. *HPB (Oxford)*. 2011 Jun; 13 (6): 391–399. doi: 10.1111/j.1477-2574.2011.00300.x.
19. *Scanga AE, Kowdley KV*. Management of biliary complications following orthotopic liver transplantation. *Curr Gastroenterol Rep*. 2007; 9 (1): 31–38. doi: 10.1007/s11894-008-0018-7.
20. *Kochhar G, Parungao JM, Hanouneh IA, Parsi MA.* Biliary complications following liver transplantation. *World J Gastroenterol*. 2013; 19 (19): 2841–2846. doi: 10.3748/wjg.v19.i19.2841.
21. *Girotra M, Soota K, Klair JS, Dang SM, Aduli F.* Endoscopic management of post-liver transplant biliary complications. *World J Gastrointest Endosc*. 2015; 7 (5): 446–459. doi: 10.4253/wjge.v7.i5.446.
22. *Verdonk RC, Buis CI, Porte RJ, van der Jagt EJ, Limburg AJ, van den Berg AP et al.* Anastomotic biliary strictures after liver transplantation: causes and consequences. *Liver Transpl*. 2006; 12 (5): 726–735. doi: 10.1002/lt.20714.
23. *Chang JH, Lee I, Choi MG, Han SW.* Current diagnosis and treatment of benign biliary strictures after living donor liver transplantation. *World J Gastroenterol*. 2016; 22 (4): 1593–1606. doi: 10.3748/wjg.v22.i4.1593.
24. *Semash KO, Dzhanbekov TA, Gaybullaev TZ*. Single-center experience of intraoperative ligation of the splenic artery for prevention of splenic artery steal syndrome in patients after living donor liver transplant. *Transplantologiya. The Russian Journal of Transplantation.* 2024; 16 (2): 230–243. https://doi.org/10.23873/2074-0506-2024-16-2-230-243.
25. *Park JS, Kim MH, Lee SK, Seo DW, Lee SS, Han J et al.* Efficacy of endoscopic and percutaneous treatments for biliary complications after cadaveric and living donor

liver transplantation. *Gastrointest Endosc*. 2003; 57 (1): 78–85. doi: 10.1067/mge.2003.11.

26. *Voskanyan SE, Popov MV, Artemiev AI, Sushkov AI, Kolyshev IYu, Rudakov VS et al*. Bilary anastomotic strictures after right lobe living donor liver transplantation: a single-center experience. *Pirogov Russian Journal of Surgery*. 2021; (2): 5–13. (In Russ., In Engl.). https://doi.org/10.17116/hirurgia20210215.
27. *Voskanyan SE, Popov MV, Mal'tseva AP, Artem'ev AI, Kolyshev IY, Zabezhinskii DA et al*. Biliary reconstruction during right lobe living donor liver transplantation: state of the problem, options and classification. *Annaly khirurgicheskoy gepatologii = Annals of HPB Surgery*. 2020; 25 (4): 33–48. (In Russ.). https://doi.org/10.16931/1995-5464.2020433-48.
28. *Chen YK*. Preclinical characterization of the Spyglass peroral cholangiopancreatoscopy system for direct access, visualization, and biopsy. *Gastrointest Endosc*. 2007; 65 (2): 303–311. doi: 10.1016/j.gie.2006.07.048.
29. *Gürakar A, Wright H, Camci C, Jaboour N*. The application of SpyScope® technology in evaluation of pre and post liver transplant biliary problems. *Turk J Gastroenterol*. 2010; 21 (4): 428–432. doi: 10.4318/tjg.2010.0131.
30. *Wright H, Sharma S, Gurakar A, Sebastian A, Kohli V, Jabbour N*. Management of biliary stricture guided by the Spyglass Direct Visualization System in a liver transplant recipient: an innovative approach. *Gastrointest Endosc*. 2008; 67 (7): 1201–1203. doi: 10.1016/j.gie.2007.10.055.
31. *Graziadei IW, Schwaighofer H, Koch R, Nachbaur K, Koenigsrainer A, Margreiter R, Vogel W*. Long-term outcome of endoscopic treatment of biliary strictures after liver transplantation. *Liver Transpl*. 2006; 12 (5): 718–725. doi: 10.1002/lt.20644.
32. *Moy BT, Birk JW*. A Review on the Management of Biliary Complications after Orthotopic Liver Transplantation. *J Clin Transl Hepatol*. 2019; 7 (1): 61–71. doi: 10.14218/JCTH.2018.00028.
33. *Jang SI, Cho JH, Lee DK*. Magnetic Compression Anastomosis for the Treatment of Post-Transplant Biliary Stricture. *Clin Endosc*. 2020; 53 (3): 266–275. doi: 10.5946/ce.2020.095.
34. *Monakhov AR, Mironkov BL, Voskanov MA, Meshcheryakov SV, Azoev ET, Semash KO et al*. Treatment of biliodigestive anastomotic strictures after transplantation of left lateral segment of the liver. *Russian Journal of Transplantology and Artificial Organs*. 2020; 22 (3): 18–25. https://doi.org/10.15825/1995-1191-2020-3-18-25.
35. *Monakhov A, Mironkov B, Tsiroulnikova O, Voskanov M, Dzhanbekov T, Semash K et al*. Interventional Radiology in Complication Management after Pediatric Liver Transplantation. *Transplantation*. 2018; 102 (Suppl 7): S150. doi: 10.1097/01.tp.0000542777.01469.8e.
36. *Gautier SV, Voskanov MA, Monakhov AR, Semash KO*. The role of endovascular and endobiliary methods in the treatment of post-liver transplant complications. *Russian Journal of Transplantology and Artificial Organs*. 2020; 22 (4): 140–148. https://doi.org/10.15825/1995-1191-2020-4-140-148.
37. *Arain MA, Attam R, Freeman ML*. Advances in endoscopic management of biliary tract complications after liver transplantation. *Liver Transpl*. 2013; 19 (5): 482–498. doi: 10.1002/lt.23624.
38. *Tsujino T, Isayama H, Sugawara Y, Sasaki T, Kogure H, Nakai Y et al*. Endoscopic management of biliary complications after adult living donor liver transplantation. *Am J Gastroenterol*. 2006; 101 (10): 2230–2236. doi: 10.1111/j.1572-0241.2006.00797.x.
39. *Fasullo M, Shah T, Zhou H, Siddiqui MS*. Post-Transplant Biliary Strictures: An Updated Review. *Semin Liver Dis*. 2022; 42 (2): 225–232. doi: 10.1055/s-0042-1744144.
40. *Rerknimitr R, Sherman S, Fogel EL, Kalayci C, Lumeng L, Chalasani N et al*. Biliary tract complications after orthotopic liver transplantation with choledochocholedochostomy anastomosis: endoscopic findings and results of therapy. *Gastrointest Endosc*. 2002; 55 (2): 224–231. doi: 10.1067/mge.2002.120813.
41. *Pfau PR, Kochman ML, Lewis JD, Long WB, Lucey MR, Olthoff K et al*. Endoscopic management of postoperative biliary complications in orthotopic liver transplantation. *Gastrointest Endosc*. 2000; 52 (1): 55–63. doi: 10.1067/mge.2000.106687.
42. *Moench C, Moench K, Lohse AW, Thies J, Otto G*. Prevention of ischemic-type biliary lesions by arterial back-table pressure perfusion. *Liver Transpl*. 2003; 9 (3): 285–289. doi: 10.1053/jlts.2003.50015.
43. *Pan B, Liu W, Ou YJ, Zhang YQ, Jiang D, Li YC et al*. Gastroduodenal artery disconnection during liver transplantation decreases non-anastomotic stricture incidence. *Hepatobiliary Pancreat Dis Int*. 2023; 22 (1): 28–33. doi: 10.1016/j.hbpd.2022.09.013.
44. *Thuluvath PJ, Atassi T, Lee J*. An endoscopic approach to biliary complications following orthotopic liver transplantation. *Liver Int*. 2003; 23 (3): 156–162. doi: 10.1034/j.1600-0676.2003.00823.x.
45. *Gambaccini D, Ruggiero L, Marciano E*. Cholangioscopy in Recurrent Cholangitis after Liver Transplantation: Selective Guidewire Cannulation of Non-anastomotic Biliary Stricture. *J Gastrointestin Liver Dis*. 2022; 31 (4): 381. Published 2022 Dec 16. doi: 10.15403/jgld-4552.
46. *Boeva I, Karagyozov PI, Tishkov I*. Post-liver transplant biliary complications: Current knowledge and therapeutic advances. *World J Hepatol*. 2021; 13 (1): 66–79. doi: 10.4254/wjh.v13.i1.66.
47. *Suo L, Liang X, Zhang W, Ma T, Gao Z*. Risk Factors Related to Early Biliary Complications After Liver Transplantation: a Single-Center Analysis. *Transplant Proc*. 2023; 55 (1): 164–169. doi: 10.1016/j.transproceed.2022.12.007.
48. *Kim ES, Lee BJ, Won JY, Choi JY, Lee DK*. Percutaneous transhepatic biliary drainage may serve as a successful rescue procedure in failed cases of endoscopic therapy for a post-living donor liver transplantation biliary stricture. *Gastrointest Endosc*. 2009; 69 (1): 38–46. doi: 10.1016/j.gie.2008.03.1113.

49. *Parsi MA, Stevens T, Dumot JA, Zuccaro G Jr.* Endoscopic therapy of recurrent acute pancreatitis. *Cleve Clin J Med*. 2009; 76 (4): 225–233. doi: 10.3949/ccjm.76a.08017.
50. *Nasr JY, Slivka A.* Endoscopic approach to the post liver transplant patient. *Gastrointest Endosc Clin N Am*. 2013; 23 (2): 473–481. doi: 10.1016/j.giec.2012.12.014.
51. *Kinner S, Dechêne A, Paul A, Umutlu L, Ladd SC, de Dechêne EM et al.* Detection of biliary stenoses in patients after liver transplantation: is there a different diagnostic accuracy of MRCP depending on the type of biliary anastomosis? *Eur J Radiol*. 2011; 80 (2): e20–e28. doi: 10.1016/j.ejrad.2010.06.003.
52. *Shah JN, Haigh WG, Lee SP, Lucey MR, Brensinger CM, Kochman ML et al.* Biliary casts after orthotopic liver transplantation: clinical factors, treatment, biochemical analysis. *Am J Gastroenterol*. 2003; 98 (8): 1861–1867. doi: 10.1111/j.1572-0241.2003.07617.x.
53. *Buxbaum JL, Biggins SW, Bagatelos KC, Ostroff JW.* Predictors of endoscopic treatment outcomes in the management of biliary problems after liver transplantation at a high-volume academic center. *Gastrointest Endosc*. 2011; 73 (1): 37–44. doi: 10.1016/j.gie.2010.09.007.
54. *Chatterjee S, Das D, Hudson M, Bassendine MF, Scott J, Oppong KE et al.* Mucocele of the cystic duct remnant after orthotopic liver transplant: a problem revisited. *Exp Clin Transplant*. 2011; 9 (3): 214–216.
55. *Park TY, Lee SK, Nam K, Oh D, Song TJ, Park DH et al.* Spontaneous hemobilia after liver transplantation: Frequency, risk factors, and outcome of endoscopic management. *J Gastroenterol Hepatol*. 2017; 32 (3): 583–588. doi: 10.1111/jgh.13497.
56. *Parsi MA*. Hemobilia: endoscopic, fluoroscopic, and cholangioscopic diagnosis. *Hepatology*. 2010; 52 (6): 2237–2238. doi: 10.1002/hep.23948.
57. *Shinjo K, Matsubayashi H, Matsui T, Kawata N, Uemura S, Yamamoto Y, Ono H*. Biliary hemostasis using an endoscopic plastic stent placement for uncontrolled hemobilia caused by transpapillary forceps biopsy (with video). *Clin J Gastroenterol*. 2016; 9 (2): 86–88. doi: 10.1007/s12328-016-0637-8.
58. *Goenka MK, Harwani Y, Rai V, Goenka U.* Fully covered self-expandable metal biliary stent for hemobilia caused by portal biliopathy. *Gastrointest Endosc*. 2014; 80 (6): 1175. doi: 10.1016/j.gie.2014.03.029.
59. *Torres V, Martinez N, Lee G, Almeda J, Gross G, Patel S, Rosenkranz L*. How do we manage post-OLT redundant bile duct? *World J Gastroenterol*. 2013; 19 (16): 2501–2506. doi: 10.3748/wjg.v19.i16.2501.
60. *Choi JH, Lee SK.* Percutaneous transhepatic cholangioscopy: does its role still exist? *Clin Endosc*. 2013; 46 (5): 529–536. doi: 10.5946/ce.2013.46.5.529.
61. *Heidenhain C, Rosch R, Neumann UP.* Hepatobiliäre Anastomosentechniken [Hepatobiliary anastomosis techniques]. *Chirurg*. 2011; 82 (1): 7–10, 12–13. doi: 10.1007/s00104-010-1902-x.
62. *Baker TB, Zimmerman MA, Goodrich NP, Samstein B, Pomfret EA, Pomposelli JJ et al.* Biliary reconstructive techniques and associated anatomic variants in adult living donor liver transplantations: The adult-to-adult living donor liver transplantation cohort study experience. *Liver Transpl*. 2017; 23 (12): 1519–1530. doi: 10.1002/lt.24872.
63. *Magro B, Tacelli M, Mazzola A, Conti F, Celsa C*. Biliary complications after liver transplantation: current perspectives and future strategies. *Hepatobiliary Surg Nutr*. 2019; 10 (1): 76–92. doi: 10.21037/hbsn.2019.09.01.
64. *Dumortier J, Chambon-Augoyard C, Guillaud O, Pioche M, Rivory J, Valette PJ et al.* Anastomotic bilio-biliary stricture after adult liver transplantation: A retrospective study over 20 years in a single center. *Clin Res Hepatol Gastroenterol*. 2020 Sep; 44 (4): 564–571. https://doi.org/10.1016/j.clinre.2019.08.008.
65. *Melcher ML, Pomposelli JJ, Verbesey JE, McTaggart RA, Freise CE, Ascher NL et al.* Comparison of biliary complications in adult living-donor liver transplants performed at two busy transplant centers. *Clin Transplant*. 2010; 24 (5): 137–144. https://doi.org/10.1111/j.1399-0012.2009.01189.x.
66. *Egawa H, Inomata Y, Uemoto S, Asonuma K, Kiuchi T, Fujita S et al.* Biliary anastomotic complications in 400 living related liver transplantations. *World J Surg*. 2001; 25 (10): 1300–1307. doi: 10.1007/s00268-001-0114-4.
67. *Germani G, Ferrarese A, Adam R, Karam V, Belli L, O'Grady J et al.* Influence of Donor and Recipient Gender on Liver Transplantation Outcomes in Europe: A Eltr Study. *J Hepatol*. 2016; 64 (2): 537–538. https://doi.org/10.1016/s0168-8278(16)00956-9.
68. *Hwang S, Lee SG, Sung KB, Park KM, Kim KH, Ahn CS et al.* Long-term incidence, risk factors, and management of biliary complications after adult living donor liver transplantation. *Liver Transpl*. 2006; 12 (5): 831–838. doi: 10.1002/lt.20693.
69. *Marubashi S, Dono K, Nagano H, Kobayashi S, Takeda Y, Umeshita K et al.* Biliary reconstruction in living donor liver transplantation: technical invention and risk factor analysis for anastomotic stricture. *Transplantation*. 2009; 88 (9): 1123–1130. doi: 10.1097/TP.0b013e3181ba184a.
70. *Castaldo ET, Pinson CW, Feurer ID, Wright JK, Gorden DL, Kelly BS, Chari RS*. Continuous versus interrupted suture for end-to-end biliary anastomosis during liver transplantation gives equal results. *Liver Transpl*. 2007; 13 (2): 234–238. doi: 10.1002/lt.20986.
71. *Kasahara M, Egawa H, Takada Y, Oike F, Sakamoto S, Kiuchi T et al.* Biliary reconstruction in right lobe living-donor liver transplantation: Comparison of different techniques in 321 recipients. *Ann Surg*. 2006; 243 (4): 559–566. doi: 10.1097/01.sla.0000206419.65678.2e.
72. *Soejima Y, Taketomi A, Yoshizumi T, Uchiyama H, Harada N, Ijichi H et al.* Biliary strictures in living donor liver transplantation: incidence, management, and technical evolution. *Liver Transpl*. 2006; 12 (6): 979–986. doi: 10.1002/lt.20740.
73. *Tashiro H, Itamoto T, Sasaki T, Ohdan H, Fudaba Y, Amano H et al.* Biliary complications after duct-to-duct biliary reconstruction in living-donor liver transplantation: causes and treatment. *World J Surg*. 2007; 31 (11): 2222–2229. doi: 10.1007/s00268-007-9217-x.

74. *Mita A, Hashikura Y, Masuda Y, Ohno Y, Urata K, Nakazawa Y et al.* Nonsurgical policy for treatment of bilioenteric anastomotic stricture after living donor liver transplantation. *Transpl Int*. 2008; 21 (4): 320–327. doi: 10.1111/j.1432-2277.2007.00609.x.
75. *Gautier SV, Monakhov AR, Tsiroulnikova OM, Latypov RA, Dzhanbekov TA, Mescheryakov SV et al.* Split liver transplantation: a single center experience. *Almanac Of Clinical Medicine*. 2020; 48 (3): 162–170. doi: 10.18786/2072-0505-2020-48-031.
76. *Gautier SV, Tsiroulnikova OM, Moysyuk YG, Akhaladze DG, Tsiroulnikova IE, Silina OV et al*. Liver transplantation in children: six-year experience analysis. *Russian Journal of Transplantology and Artificial Organs*. 2014; 16 (3): 54–62. (In Russ.). https://doi.org/10.15825/1995-1191-2014-3-54-62.
77. *Sanada Y, Katano T, Hirata Y, Yamada N, Okada N, Ihara Y, Mizuta K*. Biliary Complications Following Pediatric Living Donor Liver Transplantation: Risk Factors, Treatments, and Prognosis. *Transplantation*. 2019; 103 (9): 1863–1870. doi: 10.1097/TP.0000000000002572.
78. *Ando H, Kaneko K, Ono Y, Tainaka T, Kawai Y.* Biliary reconstruction with wide-interval interrupted suture to prevent biliary complications in pediatric living-donor liver transplantation. *J Hepatobiliary Pancreat Sci*. 2011; 18 (1): 26–31. doi: 10.1007/s00534-010-0301-5.
79. *Monakhov AR, Dzhanbekov TA, Meshcheryakov SV, Semash KO, Khizroev KhM, Voskanov MA*. Karkasnoe drenirovanie zhelchnykh protokov pri biliarnoy rekonstruktsii pri transplantatsii levogo lateral'nogo sektora pecheni. *Russian Journal of Transplantology and Artificial Organs*. 2020; 22 (S): 74.
80. *Gautier SV, Monakhov AR, Tsirul'nikova OM, Dzhanbekov TA, Meshcheryakov SV, Semash KO*. Retrospektivnyy analiz primeneniya modifikatsii biliarnoy rekonstruktsii pri transplantatsii levogo lateral'nogo sektora pecheni. *Russian Journal of Transplantology and Artificial Organs*. 2017; 19 (S): 92–93.
81. *Gautier S, Monakhov A, Tsiroulnikova O, Dzhanbekov T, Meshcheryakov S, Semash K et al.* Retrospective Analysis of Using the Modified in Pediatric Recipients of Left Lateral Segment Liver Graft. *Transplantation*. 2018; 102 (Suppl 7): S153. doi: 10.1097/01.tp.0000542783.78359.bf.
82. *Scatton O, Meunier B, Cherqui D, Boillot O, Sauvanet A, Boudjema K et al.* Randomized trial of choledochocholedochostomy with or without a T tube in orthotopic liver transplantation. *Ann Surg*. 2001; 233 (3): 432–437. doi: 10.1097/00000658-200103000-00019.
83. *Weiss S, Schmidt SC, Ulrich F, Pascher A, Schumacher G, Stockmann M et al.* Biliary reconstruction using a side-to-side choledochocholedochostomy with or without T-tube in deceased donor liver transplantation: a prospective randomized trial. *Ann Surg*. 2009; 250 (5): 766–771. doi: 10.1097/SLA.0b013e3181bd920a.
84. *Barbas AS, Goldaracena N, Dib MJ, Al-Adra DP, Aravinthan AD, Lilly LB et al*. Early Intervention With Live Donor Liver Transplantation Reduces Resource Utilization in NASH: The Toronto Experience. *Transplant Direct*. 2017 May 10; 3 (6): e158. doi: 10.1097/TXD.0000000000000674.
85. *Reichman TW, Katchman H, Tanaka T, Greig PD, McGilvray ID, Cattral MS et al*. Living donor versus deceased donor liver transplantation: a surgeon-matched comparison of recipient morbidity and outcomes. *Transpl Int*. 2013 Aug; 26 (8): 780–787. doi: 10.1111/tri.12127.
86. *Lei J, Yan L, Wang W.* Comparison of the outcomes of patients who underwent deceased-donor or living-donor liver transplantation after successful downstaging therapy. *Eur J Gastroenterol Hepatol*. 2013 Nov; 25 (11): 1340–1346. doi: 10.1097/MEG.0b013e3283622743.
87. *Li C, Mi K, Wen Tf, Yan Ln, Li B, Yang Jy et al*. Outcomes of Patients with Benign Liver Diseases Undergoing Living Donor versus Deceased Donor Liver Transplantation. *PLoS One*. 2011; 6 (11): e27366. https://doi.org/10.1371/journal.pone.0027366.
88. *Chok KS, Fung JY, Chan AC, Dai WC, Sharr WW, Cheung TT et al*. Comparable Short- and Long-term Outcomes in Living Donor and Deceased Donor Liver Transplantations for Patients With Model for End-stage Liver Disease Scores ≥35 in a Hepatitis-B Endemic Area. *Ann Surg*. 2017 Jan; 265 (1): 173–177. doi: 10.1097/SLA.0000000000001671.
89. *Liu CL, Fan ST, Lo CM, Wei WI, Chan SC, Yong BH, Wong J.* Operative outcomes of adult-to-adult right lobe live donor liver transplantation: a comparative study with cadaveric whole-graft liver transplantation in a single center. *Ann Surg*. 2006 Mar; 243 (3): 404–410. doi: 10.1097/01.sla.0000201544.36473.a2.
90. *Wan P, Zhang JJ, Li QG, Xu N, Zhang M, Chen XS et al*. Living-donor or deceased-donor liver transplantation for hepatic carcinoma: a case-matched comparison. *World J Gastroenterol*. 2014 Apr 21; 20 (15): 4393–4400. doi: 10.3748/wjg.v20.i15.4393.
91. *Hu Z, Qian Z, Wu J, Zhou J, Zhang M, Zhou L, Zheng S.* Clinical outcomes and risk factors of hepatocellular carcinoma treated by liver transplantation: A multi-centre comparison of living donor and deceased donor transplantation. *Clin Res Hepatol Gastroenterol*. 2016 Jun; 40 (3): 315–326. doi: 10.1016/j.clinre.2015.08.003.
92. *Kim DS, Yu YD, Jung SW, Yang KS, Seo YS, Um SH, Suh SO.* Balanced approach can help initial outcomes: analysis of initial 50 cases of a new liver transplantation program in East Asia. *Ann Surg Treat Res*. 2014 Jul; 87 (1): 22–27. doi: 10.4174/astr.2014.87.1.22. Epub 2014 Jun 24.
93. *Kim EJ, Lim S, Chu CW, Ryu JH, Yang K, Park YM et al*. Clinical Impacts of Donor Types of Living vs. Deceased Donors: Predictors of One-Year Mortality in Patients with Liver Transplantation. *J Korean Med Sci*. 2017 Aug; 32 (8): 1258–1262. doi: 10.3346/jkms.2017.32.8.1258.
94. *Jiang L, Yan L, Tan Y, Li B, Wen T, Yang J, Zhao J.* Adult-to-adult right-lobe living donor liver transplantation in recipients with hepatitis B virus-related benign liver disease and high model end-stage liver disease scores. *Surg Today*. 2013 Sep; 43 (9): 1039–1048. doi:

10.1007/s00595-013-0539-z. Epub 2013 Mar 7. PMID: 23467980.

95. *Latypov RA.* Split-transplantatsiya pecheni. [Dissertation]. M., 2019; 215.
96. *Dalzell C, Vargas PA, Soltys K, Dipaola F, Mazariegos G, Oberholzer J, Goldaracena N.* Living Donor Liver Transplantation vs. Split Liver Transplantation Using Left Lateral Segment Grafts in Pediatric Recipients: An Analysis of the UNOS Database. *Transpl Int*. 2022 Mar 22; 36: 10437. doi: 10.3389/ti.2022.10437.
97. *Yoon KC, Song S, Lee S, Kim OK, Hong SK, Yi NJ et al*. Outcomes of Split Liver Transplantation vs Living Donor Liver Transplantation in Pediatric Patients: A 5-Year Follow-Up Study in Korea. *Ann Transplant*. 2022 May 3; 27: e935682. doi: 10.12659/AOT.935682.
98. *Diamond IR, Fecteau A, Millis JM, Losanoff JE, Ng V, Anand R, Song C; SPLIT Research Group*. Impact of graft type on outcome in pediatric liver transplantation: a report From Studies of Pediatric Liver Transplantation (SPLIT). *Ann Surg*. 2007 Aug; 246 (2): 301–310. doi: 10.1097/SLA.0b013e3180caa415.
99. *Liu JY, Zhang JR, Sun LY, Zhu ZJ, Wei L, Qu W et al*. Impact of cytomegalovirus infection on biliary disease after liver transplantation – maybe an essential factor. *World J Clin Cases*. 2021 Dec 16; 9 (35): 10792–10804. doi: 10.12998/wjcc.v9.i35.10792.
100. *Nemes B, Gámán G, Doros A.* Biliary complications after liver transplantation. *Expert Rev Gastroenterol Hepatol*. 2015 Apr; 9 (4): 447–466. doi: 10.1586/17474124.2015.967761.

The article was submitted to the journal on 29.01.2024