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Review article

Post-Orthotopic Liver Transplant Cholangiopathy Assessment and Surveillance with Endoscopic Ultrasonography: The Way Forward

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Abstract

Post-orthotropic liver transplant (POLT) cholangiopathies are a group of biliary complications that develop after liver transplantation. These conditions can lead to significant morbidity and mortality if not detected and treated early. Traditionally, magnetic resonance cholangiopancreatography and computed tomography scan have been used to identify biliary complications after OLT. Hence, the current study aimed to evaluate the accuracy of endoscopic ultrasonography (EUS) in assessing and monitoring POLT cholangiopathies by performing a comprehensive review of the literature. Relevant articles published until February 2023 were searched from various databases including PubMed, Embase, and Cochrane Library. The search terms used were "endoscopic ultrasound," "post-orthotopic liver transplantation," "primary sclerosing cholangitis," and "cholangiopathy." Relevant articles were selected and included in this review. EUS has emerged as a state-of-the-art method for the assessment and surveillance of POLT cholangiopathies, with high success rates in diagnosing and treating biliary complications. In patients with primary sclerosing cholangitis, EUS can help in the early detection of primary tumors and biliary strictures and can be a guide in therapeutic interventions such as endoscopic retrograde cholangiopancreatography and biliary drainage. In conclusion, EUS has a superior diagnostic accuracy than other imaging modalities such as magnetic resonance cholangiopancreatography and computed tomography scan in detecting biliary complications after OLT.

Keywords: ***Endoscopic Ultrasound, Orthotropic Liver Transplantation, Cholangiopathies.***

Introduction

Liver transplantation is a life-saving procedure for patients presenting with end-stage liver disease. However, up to 30% of liver transplant recipients can develop post-orthotopic liver transplant (POLT) cholangiopathies, including biliary strictures and bile duct ischemia, thereby significantly affecting patient outcomes [1]. According to the UK National Health Service in 2020–2021, 1,435 liver transplants were conducted in the UK [2].

POLT cholangiopathies are a group of biliary complications that develop after liver transplantation [3]. These complications can lead to significant morbidity and mortality if not detected and treated early [4]. Post-liver transplantation biliary complications can be classified into several categories, including anastomotic and nonanastomotic strictures, leaks, and stones [5]. Anastomotic strictures are the most frequently observed types of biliary complication, and they occur at the bile duct anastomosis site [6]. Nonanastomotic strictures can occur anywhere along the biliary tree, and they are often caused by ischemia, infection, or immune-mediated injury [7]. Bile leaks can develop at the site of anastomosis or biliary injury during the transplant procedure [8]. Stones can form in the biliary tree due to stasis or infection [9].

POLT biliary complications are commonly diagnosed based on clinical evaluation, laboratory test, imaging study, and endoscopic procedure findings [10]. Traditionally, endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard for diagnosing and managing these complications [11]. ERCP facilitates the direct visualization of the biliary tree, and it can be used to obtain tissue samples for histopathological evaluation [12]. However, ERCP has some limitations. That is, it requires patient sedation. Moreover, it can cause procedural complications and has limited visualization of the surrounding structures [13].

EUS has become an alternative diagnostic and therapeutic modality for POLT cholangiopathies. It can be applied for high-resolution imaging of the biliary tree and surrounding structures, with the additional benefit of preventing ERCP-related complications [14]. Further, it can be used to obtain fine-needle aspiration (FNA) samples for cytological and histopathological evaluation [15]. EUS has several potential advantages over ERCP. For example, ERCP has a high safety profile and can visualize the surrounding structures. In addition, patients who undergo this procedure do not require sedation [16]. Despite the potential benefits of EUS, its role in the assessment and surveillance of POLT cholangiopathies is still debated [17].

Several studies have investigated the diagnostic accuracy of EUS in detecting POLT biliary complications. According to a meta-analysis of 13 studies, the pooled sensitivity and specificity of EUS for detecting biliary strictures after liver transplantation were 88% and 96%, respectively [18]. Another study revealed that EUS was more sensitive than magnetic resonance cholangiopancreatography (MRCP) for identifying biliary strictures after liver transplantation (97% vs. 62%) [19].

In addition to its diagnostic capabilities, EUS has also been considered a therapeutic modality for managing POLT biliary complications. A retrospective study was conducted on 29 patients with POLT biliary strictures. Results found that EUS-guided biliary drainage was successful in 86% of patients, with a median stent patency of 155 days [20]. Another study assessed 15 patients with POLT biliary leaks. Results showed that EUS-guided transmural drainage was successful in all cases, with a median follow-up of 18 months [21].

Some experts have recommended EUS as the first-line diagnostic tool for POLT biliary complications. Meanwhile, others have suggested that EUS should be reserved for cases where ERCP is unsuccessful or not feasible [22].

Endoscopic ultrasonography (EUS) has emerged as a state-of-the-art diagnostic tool for the assessment and surveillance of post-orthotopic liver transplantation (OLT) cholangiopathies [23]. EUS combines high-frequency ultrasound imaging with endoscopy to provide a detailed visualization of the biliary tree and surrounding structures. Several studies have revealed that EUS is superior to other imaging modalities, such as MRCP and ERCP, in detecting and characterizing biliary complications after OLT [24]. In terms of advantages, EUS can visualize the biliary tree from both the intra- and extrahepatic segments, thereby allowing for a comprehensive assessment of biliary anatomy and pathology. EUS can detect subtle abnormalities in the bile ducts, such as small leaks and strictures, which may be missed by other imaging modalities. Moreover, EUS can be used to obtain tissue samples for histological analysis, which can help in diagnosing biliary malignancies and other rare conditions [16].

EUS is used as not only a diagnostic tool but also a therapeutic modality for managing POLT biliary complications [25]. Previous studies have shown that EUS-guided biliary drainage can be effective in treating biliary strictures and leaks, with high success rates and prolonged stent patency [26]. Despite its advantages, the use of EUS in the assessment and surveillance of POLT cholangiopathies is still debated. Some experts have recommended EUS as the first-line diagnostic modality. Meanwhile, others believed that EUS should be considered only for cases in which ERCP is not successful or feasible [27].

The current study aimed to evaluate current data on the use of EUS in the assessment and surveillance of POLT cholangiopathies. In particular, these studies have important implications on clinical practice and may help guide the development of future guidelines for managing POLT cholangiopathies.

Methodology

Literature search strategy

A comprehensive literature search on electronic databases, including PubMed, MEDLINE, and EMBASE, was conducted. The search was performed from the inception of each database to the latest available date during the search (February 2023). The following search terms were used: “endoscopic ultrasound,” “EUS,” “post-orthotopic liver transplantation,” “post-OLT,” “cholangiopathy,” “biliary complication,” “diagnosis,” and “surveillance.” The Boolean operators (AND, OR) were used to combine search terms and limit the search results.

Study selection

The published studies, literature, trials and cases have been of the relevant topics have been screened. The inclusion criteria were as follows: (1) studies evaluating the use of EUS in the assessment and surveillance of POLT cholangiopathies, (2) those reporting the diagnostic yield or accuracy of EUS for detecting POLT biliary complications, and (3) those showing the safety and feasibility of EUS-guided interventions for POLT biliary complications. Studies not published in English and abstracts from conference proceedings were excluded.

Results

EUS is an increasingly useful tool for diagnosing and managing cholangiopathies. It can provide a detailed image of the biliary system, thereby allowing for an accurate assessment of the extent and severity of the disease. Further, it can be used to obtain tissue samples for histological analysis, thereby helping in the diagnosis and differentiation of different cholangiopathies [16].

Cholangiopathies is managed based on the specific etiology and severity of the disease. The treatment options range from supportive care, such as pain management and nutritional support, to targeted therapies for specific underlying causes. In some cases, endoscopic or surgical interventions may be required to relieve biliary obstruction or address other complications. EUS can be essential in guiding these interventions, thereby allowing for the accurate localization of lesions and the visualization of surrounding structures [28].

Classification of cholangiopathies and their assessment and management with EUS

Cholangiopathies are a group of liver diseases characterized by the damage or dysfunction of the biliary tree, which includes the bile ducts and associated structures. These disorders can be classified based on their various underlying etiologies, including autoimmune, infectious, genetic, and drug-induced causes [28].

Table 1: General presentation of the overall complications of POLT.

Type of complications	Prevalence of OLT in adult patients	Risk factors	Time of onset from OLT
Vascular complications	9%		
Hepatic artery complications	3%–10%	Rejection End-to-end anastomosis ABO blood group incompatibility	Weeks to months
Hepatic artery thrombosis	2%–10%	Prolonged cold ischemia time of graft pediatric transplantation Rejection Poor surgical technique	Within the first 3 months
Hepatic artery stenosis		Clamp injury Angioplasty Liver biopsy	
Pseudoaneurysm	Rare	Focal infection	Variables

	1%–13%	Technical issues during surgery	
Portal vein complications	1%–2%	Excessive vessel length	
Thrombosis	1%	Discrepancy between donor and recipient calibers	Variables Variables
Stenosis		Hypercoagulability state	
	Rare	Previous history of thrombosis	
	< 1%		
		Size discrepancy between donor and recipient vessels	
IVC and hepatic vein complications Thrombosis and stenosis		Suprahepatic caval kinking from liver rotation	Variables
		Surgical technique	
		Hypercoagulability state	
		Compression from graft edema or adjacent fluid collection	
		Chronic thrombus	
		Neointimal hyperplasia	
		Re-transplantation	
		Pediatric OLT	
		LDLT (hepatic vein stenosis)	
		Piggyback anastomosis	
			Early from OLT 1–3 months
		T-tube displacement or removal (T-tube leak)	
Hemorrhage		Technical failure during surgery (anastomotic leak)	
Biliary complications	Up to 3%	HAT (nonanastomotic leak)	
Bile leak	11%–30%	Ischemic-related injury, immunologically related injury,	
	4%–5%	cytotoxic injury induced by bile salts (nonanastomotic leak in patients without HAT)	Within 1 year
		Roux-en-Y choledochojejunostomy	
Biliary obstruction: anastomotic strictures	Up to 17.6%	Anastomotic leakage	Within 6 months (NAS)
		Technical factors HAT (NAS)	
		Microangiopathic injury (prolonged warm or cold	After 6 months (ITBL)
Biliary obstruction: NAS and ITBL	5%–10%	ischemia times) (ITBL)	
		Immunogenic injury	
		(AB0 incompatibility between donor and recipient,	
		chronic ductopenic rejection, and primitives sclerosing	Within 1 year (casts
	5.70%	cholangitis) (ITBL)	and sludge)
		Cytotoxic injury caused by bile salts (ITBL)	After 1 year (stones)
Stones, casts, and sludge		Anastomotic and non-anastomotic biliary strictures	
		Presence of T-tube or stent Hepaticojejunostomy ischemia	
		Infection	
Primary hepatic complications			
Acute cellular rejection		Alteration in bile composition	Early from OLT
		Immunosuppression	
Chronic ductopenic rejection		Transplantation for cholestatic disease	
		Preservation injury	
Malignancies		Re-transplantation for chronic rejection	6 weeks to 6 months
HCC recurrence	Common		
PTLD		Transplantation for cholestatic disease	
Other causes of graft	Up to 17%	CMV infection	
dysfunction Collections,		Immunosuppression	
hematoma, abscess	-	Variables	Variables

Complications

Alagille syndrome (ALGS) is a rare autosomal dominant disorder affecting multiple organs, including the liver, heart, eyes, and kidneys [29]. ALGS is primarily caused by mutations in the JAG1 or NOTCH2 genes, which are involved in the Notch signalling pathway [30]. This pathway plays an important role in cell differentiation and proliferation. Further, JAG1 or NOTCH2 gene mutations lead to an abnormal development of various organs, including the liver. ALGS is characterized by a paucity of intrahepatic bile ducts, resulting in cholestasis and liver damage [29]. Patients with ALGS commonly present with jaundice, pruritus, and hepatomegaly. Moreover, they may develop complications such as portal hypertension, cirrhosis, and liver failure. ALGS diagnosis is based on clinical features and genetic testing and liver biopsy results. EUS can be important in diagnosing and managing ALGS, particularly in assessing the number and size of intrahepatic bile ducts [31]. Further, it can evaluate portal hypertension and the presence of varices before OLT and after liver transplantation if ALGS recurrence is suspected. ALGS treatment is primarily supportive, with a focus on managing cholestasis and preventing complications. Ursodeoxycholic acid (UDCA) is frequently used to improve bile flow and decrease liver damage. In severe cases, liver transplantation may be required [29].

Caroli syndrome is a rare inherited disorder characterized by the segmental dilatation of the intrahepatic bile ducts, leading to recurrent episodes of cholangitis and biliary sepsis. The disease can be classified into simple and complex [32]. Simple Caroli syndrome affects the bile ducts only, and it is often asymptomatic. Meanwhile, complex Caroli syndrome is associated with liver fibrosis, portal hypertension, and hepatic failure [29,32]. It can be diagnosed via imaging studies such as ultrasonography, computed tomography scan, and magnetic resonance imaging, which can identify characteristic features such as cystic dilatation of the bile ducts and

intrahepatic. OLT may be required for severe hepatic dysfunction or intractable cholangitis in complex Caroli syndrome.

EUS can be used in managing Caroli syndrome to assess the extent of bile duct dilatation and the presence of biliary stones or sludge. Moreover, EUS-guided cholangiography can be performed to obtain samples for cytological and microbiological analysis and to place biliary stents for Caroli-related biliary obstruction [29]. Caroli syndrome is managed based on disease severity and the presence of complications. In simple Caroli syndrome, surveillance with regular imaging studies and cholangitis management are typically recommended [32].

Cystic fibrosis (CF) is a genetic disorder affecting the respiratory, digestive, and reproductive systems. It is caused by mutations in the CFTR gene, which encodes a protein that regulates the transport of ions and water in and out of the cells. CFTR gene mutations lead to the production of a defective protein, which results in thick and sticky mucus production in the affected organs [33]. CF diagnosis is based on clinical symptoms and genetic and sweat chloride test results. CF management includes a multidisciplinary approach that aims to prevent and manage complications. In the respiratory system, the management includes airway clearance, inhaled medications, and antibiotics. In the digestive system, the management includes pancreatic enzyme replacement therapy, nutritional support, and monitoring for the development of cystic fibrosis-related diabetes. Lung transplantation may be considered in severe CF cases [34]. In recent years, the development of novel therapies, such as CFTR modulators, has significantly improved the outlook of patients with CF. These therapies target the underlying genetic defect, improve lung function, and reduce exacerbations in CF [35]. In the USA and Europe, numerous patients receive liver transplant for CF with an extremely good overall outcome. However, the recurrent rate is guarding. EUS can assess the pancreas in patients with CF, as pancreatic insufficiency is a common complication of the disease. EUS can detect early changes in the pancreas, such as hyperechoic foci, which can precede the development of cystic fibrosis-related diabetes [36].

Polycystic liver disease (PLD) is a rare, genetic disorder causing the development of multiple cysts in the liver parenchyma. PLD can occur as a primary disease, known as autosomal dominant polycystic liver disease, or as a manifestation of autosomal dominant polycystic kidney disease (ADPKD) [37]. Autosomal dominant polycystic liver disease is caused by mutations in the PRKCSH or SEC63 genes. Meanwhile, ADPKD is caused by mutations in the PKD1 or PKD2 genes [38]. PLD is often asymptomatic and is commonly diagnosed incidentally on imaging studies. However, as the cysts grow in size and number, they can cause symptoms such as abdominal pain, distension, and early satiety [39]. EUS can diagnose PLD and assess the size, number, and location of the liver cysts. In addition, it can be applied to guide cyst aspiration and sclerotherapy, which can provide symptomatic relief in some patients [40]. The management of PLD is primarily supportive, with a focus on managing symptoms and preventing complications. Surgical interventions, such as hepatic resection and liver transplantation, may be considered in severe cases [41]. UDCA is effective in reducing liver volume in PLD [42].

Autoimmune cholangitis (AIC) is an autoimmune-mediated cholangiopathy characterized by progressive destruction of bile ducts, leading to cholestasis, liver fibrosis, and cirrhosis [43]. AIC is associated with the presence of autoantibodies, such as antinuclear and smooth muscle antibodies. Further, it may overlap with other autoimmune disorders, such as autoimmune hepatitis and primary biliary cholangitis (PBC). AIC is diagnosed based on the combined use of clinical, biochemical, radiological, and histological criteria. EUS can assess the extent and severity of bile duct damage in AIC. EUS-guided liver biopsy can provide a larger sample size than percutaneous biopsy, which can be helpful in cases of focal bile duct involvement [44]. AIC treatment involves the use of immunosuppressive agents, such as corticosteroids and azathioprine, which can improve liver function and delay disease progression [45]. Moreover, UDCA can be an adjunctive therapy in AIC. In cases of advanced-stage liver disease, liver transplantation may be required [46].

Biliary atresia (BA) is a rare, life-threatening disease of unknown etiology that affects neonates and infants [47]. It is characterized by the absence or obstruction of the extrahepatic bile ducts, resulting in cholestasis and liver damage [48]. The clinical presentation of BA includes jaundice, acholic stools, and hepatomegaly, which typically appear within the first 2-4 weeks of life [49]. Early diagnosis and prompt surgical intervention are important to successfully manage BA [47]. EUS can be essential in diagnosing and managing BA, particularly in evaluating the patency of the biliary tree and the presence of associated anomalies [50]. Moreover, EUS-guided liver biopsy can provide useful diagnostic information and assess disease severity [51]. The treatment of BA involves Kasai portoenterostomy, which involves the removal of the damaged bile ducts and the creation of a new bile duct using a loop of intestine [47]. Early Kasai surgery is associated with better outcomes, including improved bile flow, a low incidence of cirrhosis, and a higher survival [52]. In cases where Kasai surgery is not successful, liver transplantation may be required [47].

Idiopathic childhood/adulthood ductopenia is a rare, chronic liver disease characterized by the progressive loss of intrahepatic bile ducts, resulting in cholestasis and liver failure [53]. The disease etiology is unknown. Currently, there are no effective medical therapies available. Liver transplantation is the only curative treatment option for end-stage disease [54]. EUS can be important in diagnosing and managing idiopathic childhood/adulthood ductopenia. It can also assess the extent of intrahepatic ductal loss and evaluate the presence of associated anomalies, such as portal hypertension [50]. Moreover, EUS-guided liver biopsy can provide useful diagnostic information and assess disease severity [51].

Liver transplantation is the mainstay of treatment for end-stage idiopathic childhood/adulthood ductopenia, and EUS can evaluate potential transplant candidates and monitor disease progression after transplantation [54].

IgG4-associated cholangitis is a rare, autoimmune-mediated disease affecting the bile ducts, resulting in inflammation, fibrosis, and strictures [55]. EUS can be an essential tool in diagnosing and managing IgG4-associated cholangitis, particularly in evaluating the extent of biliary involvement, identifying associated masses or lymphadenopathy, and guiding tissue sampling for histological diagnosis [16]. This condition is typically treated with corticosteroids, which can commonly induce remission [55]. However, some patients may require long-term maintenance therapy to prevent relapse. If corticosteroids are ineffective or contraindicated, other immunosuppressive agents or biliary stenting may be considered [56].

Primary biliary cholangitis (PBS) is a chronic autoimmune cholestatic liver disease primarily affecting middle-aged women [57]. PBC diagnosis is based on clinical, laboratory, and histologic findings, including the presence of antimitochondrial antibodies and histologic evidence of nonsuppurative cholangitis and destruction of interlobular bile ducts [46]. EUS can evaluate the severity of PBC-related liver disease, including the extent of bile duct involvement, and the presence of associated complications, such as portal hypertension and varices [58]. Moreover, EUS-guided liver biopsy can provide valuable diagnostic information, particularly in cases where traditional percutaneous biopsy may be challenging or unsafe [59]. PBC management primarily involves UDCA therapy, which improves liver function and survival and delay disease progression

[60]. Liver transplantation may be required in cases of end-stage liver disease or refractory symptoms [57].

Primary sclerosing cholangitis (PSC) is a common indication for OLT [46]. However, PSC recurrence after OLT remains a significant challenge, with incidence rates ranging from 5% to 30% [1]. ERCP is the gold standard for diagnosing and managing PSC recurrence. However, it is an invasive procedure with possible complications [32]. EUS is important in evaluating PSC recurrence after OLT [27]. It can visualize the bile duct wall and surrounding structures with high resolution, thereby detecting subtle changes in the biliary system [45]. Moreover, EUS-guided FNA can obtain tissue samples for histopathological analysis, thereby leading to PSC recurrence diagnosis [16]. In a study of 27 patients with suspected PSC recurrence after OLT, the sensitivity and specificity of EUS for detecting biliary abnormalities were 86% and 100%, respectively, with a positive predictive value of 100% and a negative predictive value of 90% [61]. Further, the diagnostic yield of EUS-FNA for evaluating suspected PSC recurrence after OLT was 80% [27].

Cholangiocarcinoma is a malignant tumor arising from the epithelial cells of the bile ducts. EUS can be useful in assessing cholangiocarcinoma, particularly the extent of the tumor, the involvement of nearby structures, and the presence of metastases [62]. Cholangiocarcinoma is managed based on disease stage and the patient's overall health status. Surgery is preferred for respectable tumors. EUS can help in preoperative staging, the selection of patients who require surgery, and the assessment of patients suspected of recurrence after OLT. For unrespectable tumors, palliative therapy, including chemotherapy and/or radiation therapy, can be considered.

ABCB4 deficiency is a rare genetic disorder affecting the hepatobiliary system, leading to cholestasis and liver injury [63]. It is caused by mutations in the ABCB4 gene, which encodes the multidrug-resistant protein 3, a phospholipid transporter that plays an important role in bile formation. The clinical presentation of ABCB4 deficiency varies, and it can range from mild to severe cholestasis, with or without liver disease. EUS can be used to assess the biliary system in patients with ABCB4 deficiency, including those with gallstones, biliary sludge, and strictures [42]. Further, EUS-guided sampling of the biliary tree can be performed for diagnostic purposes [42]. However, the role of EUS in managing ABCB4 deficiency is not well-established. ABCB4 deficiency is treated with ursodeoxycholic acid, which can improve liver biochemistry and delay liver disease progression. Liver transplantation may be required in cases of end-stage liver disease or intractable pruritus [63].

AIDS cholangiopathy is a spectrum of biliary tract disorders in individuals with HIV/AIDS [64]. It is a relatively rare complication of HIV infection. Nevertheless, it can lead to significant morbidity and mortality [65]. The exact pathogenesis of AIDS cholangiopathy is not well understood. However, it is related to HIV-related immune dysfunction, opportunistic infections, and/or the adverse effects of antiretroviral therapy [64]. The clinical characteristics of AIDS cholangiopathy can vary, which include abdominal pain, jaundice, pruritus, and fever [66]. AIDS cholangiopathy is diagnosed based on clinical, laboratory, and radiological findings. Traditionally, ERCP has been considered the gold standard for diagnosing AIDS cholangiopathy. However, EUS can also be important in diagnosing and managing this condition [67]. This procedure can be important in evaluating the biliary tree for strictures, dilatations, and intraluminal filling defects. Moreover, it can help in diagnosing complications such as cholecystitis, pancreatitis, and abscess formation. EUS-guided biliary drainage can be used to manage biliary obstruction in patients with AIDS cholangiopathy who are not responsive to conventional therapies [65-67]. AIDS cholangiopathy is typically managed by treating the underlying HIV infection and any associated opportunistic infections. Antiretroviral therapy is the cornerstone of HIV treatment, and it improves cholangiopathy in some cases [65]. In addition, endoscopic interventions such as biliary stenting and balloon dilation can be used to manage biliary obstruction and improve symptoms [66].

Amyloidosis is a group of disorders characterized by the extracellular deposition of misfolded proteins, known as amyloid fibrils, in various organs and tissues [68]. It can affect multiple organs, including the liver, resulting in hepatomegaly, elevated liver enzyme levels, and, in some cases, liver dysfunction and failure. Only a few patients require liver transplantation due to advanced-stage liver cirrhosis. The use of EUS-guided liver biopsy can increase the diagnostic yield after OLD and reduce the risk of complications associated with percutaneous liver biopsy, particularly in patients with coagulopathy or ascites [69]. Amyloidosis is managed based on the underlying cause and the extent of organ involvement [68]. The treatment options may include supportive care, chemotherapy, stem cell transplantation, or liver transplantation in cases of severe liver involvement.

Choledocholithiasis refers to the presence of gallstones in the common bile duct, which connects the liver and the small intestine. The condition can result in serious complications such as cholangitis, pancreatitis, and liver abscess. Choledocholithiasis is commonly diagnosed via imaging studies such as abdominal ultrasonography, computed tomography scan, and MRCP [71]. However, ERCP remains the gold standard for diagnosing and treating choledocholithiasis. In addition to ERCP, other minimally invasive techniques such as endoscopic ultrasound-guided biliary drainage (EUS-BD) and percutaneous transhepatic biliary drainage (PTBD) can manage choledocholithiasis, particularly in patients with contraindications to ERCP or failed ERCP [16]. Choledocholithiasis should also be managed by treating underlying risk factors such as obesity, diabetes, and dyslipidemia. In addition, prophylactic antibiotic therapy should be considered in high-risk patients to prevent infectious complications.

Eosinophilic or mast cell cholangitis is a rare type of cholangitis characterized by eosinophil or mast cell infiltration in the bile ducts, leading to biliary obstruction and subsequent cholestasis [72]. Eosinophilic or mast cell cholangitis can be challenging to diagnosis due to its rarity and the lack of specific clinical features. EUS can be a useful tool in diagnosing eosinophilic or mast cell cholangitis as it can identify bile duct wall thickening, dilation, and other features indicative of cholangitis [73]. Eosinophilic or mast cell cholangitis is commonly treated with combined corticosteroids and immunomodulatory agents to reduce inflammation and prevent disease recurrence. However, the optimal management strategy for this condition is still uncertain due to limited data availability [72].

Graft-versus-host disease (GVHD) is a condition that occurs in patients with hematopoietic stem cell transplantation [74]. GVHD involving the liver is a major complication and can be characterized by elevated liver enzyme levels, jaundice, and hepatomegaly. EUS is important in assessing POLT GVHD, including the evaluation of bile ducts, liver parenchyma, and portal vein patency [75]. GVHD involving the liver is managed with immunosuppressive therapy, which may be augmented with photopheresis or other modalities. Data on the role of EUS in assessing GVHD involving the liver are limited. However, de la Serna et al. described the use of EUS in diagnosing GVHD in a patient with hematopoietic stem cell transplantation. EUS was used to evaluate the bile ducts, and it revealed thickened walls and narrowed lumen, consistent with GVHD involvement [76]. The patient then received immunosuppressive therapy and showed improvement in liver enzyme levels. GVHD treatment involving the liver typically involves systemic immunosuppression, including corticosteroids and other immunosuppressive agents such as tacrolimus and

mycophenolate mofetil. The treatment response varies based on the severity of liver dysfunction and the extent of involvement [77].

The common complications of biliary interventions are managed with cholecystectomy, hepatic surgery, and ERCP [78]. The incidence of **iatrogenic biliary strictures** in all ERCP procedures is approximately 0.2%–2%, with higher rates observed in specific patient populations and in more complex procedures [79]. EUS-BD is effective in managing iatrogenic biliary strictures that are refractory to other treatments [78]. It involves visualizing the bile ducts and evaluating the site, length, and severity of the stricture. Further, EUS-guided sampling techniques can obtain tissue samples for diagnosis and staging [80]. EUS-guided biliary dilation and stenting are effective in treating iatrogenic biliary strictures, and their technical success rate is high [78].

Portal hypertensive biliopathy (PHB) is a group of biliary abnormalities caused by portal hypertension. PHB may include bile duct wall abnormalities, cholecystitis, gallstones, and biliary strictures. It can lead to complications such as cholangitis, cholestasis, and hepatic decompensation [81]. PHB is commonly diagnosed using imaging techniques such as MRCP and ERCP. However, EUS has emerged as a promising tool for evaluating PHB, particularly in cases where MRCP or ERCP may be inconclusive [82]. EUS can be used as not only a diagnostic tool but also a therapeutic intervention for PHB. EUS-BD is a minimally invasive alternative to PTBD and surgical bypass in patients with PHB-related biliary strictures [16]. EUS-BD and PTBD were similar in terms of technical success rates and adverse event rates. However, EUS-BD has lower reintervention rates.

Recurrent pyogenic cholangitis (RPC) is a rare but serious bacterial infection affecting the biliary system, leading to recurrent episodes of cholangitis, biliary strictures, and biliary stones [83]. It is most commonly observed in Southeast Asia and is strongly associated with parasitic infestation and biliary stones. RPC is typically diagnosed using imaging modalities such as ultrasonography, computed tomography scan, and MRCP [84]. EUS has become important in the assessment and management of recurrent POLT RPC [85]. EUS can accurately visualize the biliary tree and adjacent structures, which can help in RPC diagnosis and the identification of biliary strictures or stones. In addition, EUS-guided biliary drainage procedures can be performed for managing RPC, which can alleviate biliary obstruction and prevent further episodes of cholangitis.

Sarcoidosis is a chronic inflammatory disease affecting various body organs, including the lungs, lymph nodes, skin, and eyes. The etiology of sarcoidosis is still unknown, and it is diagnosed based on clinical presentation and imaging study and biopsy findings [69]. EUS has become essential in assessing sarcoidosis. Further, it can be used to evaluate mediastinal lymph nodes and lung lesions and to obtain tissue samples for pathological examination. EUS-EUS-FNA was performed on 54 patients with suspected sarcoidosis, and the diagnostic yield was 81%. Further, EUS-FNA had a high concordance rate with conventional transbronchial needle aspiration in diagnosing sarcoidosis [16]. In addition to its diagnostic role, EUS can monitor disease activity and treatment response. Bhutani et al. showed that EUS-guided needle-based confocal laser endomicroscopy can provide real-time visualization of granulomas and can be used to monitor treatment response in patients with sarcoidosis. Notably, needle-based confocal laser endomicroscopy had a high sensitivity and specificity in detecting granulomas. Hence, it a useful tool in managing sarcoidosis [86]. Sarcoidosis is managed with corticosteroids, immunosuppressive agents, and biologics based on disease severity and organ involvement. Baughman et al. (2018) revealed that infliximab, a tumor necrosis factor-alpha inhibitor, was effective in treating refractory sarcoidosis. Therefore, infliximab can be a treatment option for patients with sarcoidosis who do not respond to conventional therapy [87].

Sickle cell disease (SCD) is a hemoglobinopathy that can lead to various complications, including liver involvement. Cholelithiasis, or gallstone formation, is a common complication of SCD that can lead to cholangiopathy and subsequent liver damage [88]. Stankovic et al. (2017) showed that 24% of patients with SCD who underwent magnetic resonance cholangiopancreatography develop cholangiopathy. Thus, patients with SCD who have a history of cholelithiasis or elevated liver enzyme levels may require routine screening for cholangiopathy [89]. SCD can also lead to different liver complications, in addition to cholelithiasis, which include hepatic sequestration crisis and sickle cell intrahepatic cholestasis [88], which is a rare but severe complication of SCD characterized by cholestasis, jaundice, and liver dysfunction. SCD is commonly managed with supportive care and exchange transfusions, which can decrease hemoglobin S levels, improve liver function, increase the production of fetal hemoglobin, and reduce the rate of pain crises and hospitalizations [89]. Moreover, blood transfusions can improve oxygen delivery and prevent or treat complications such as stroke in SCD [88].

In terms of vascular/ischemic complications, **hepatic artery stenosis (HAS)** can occur after liver transplantation and can lead to graft dysf/unction or loss (Chu et al., 2017) [90]. HAS is a relatively common complication, with an incidence of up to 15% in liver transplant recipients [91]. The early diagnosis and prompt management of HAS can prevent further graft damage. HAS is usually diagnosed via imaging studies, such as Doppler ultrasonography and computed tomography angiography [90]. EUS can facilitate the detailed visualization of the hepatic artery and surrounding structures and can help guide endovascular interventions, such as angioplasty and stent placement, for assessing and managing vascular/ischemic complications after liver transplantation, including HAS [92]. The EUS-guided placement of a covered self-expandable metallic stent was successful in treating HAS in three of four liver transplant recipients. Therefore, EUS-guided stent placement may be a safe and effective alternative to traditional endovascular techniques in some patients with HAS [93].

Discussion

EUS has an important role in the assessment and surveillance of POLT cholangiopathies. In particular, the procedure is useful in diagnosing biliary tract diseases such as choledocholithiasis, primary biliary cirrhosis, PSC, and IgG4-associated cholangitis [80]. In addition, it has high accuracy rates in detecting biliary strictures, which can be indicative of cholangiocarcinoma [94]. It can provide detailed information about the biliary system, including bile duct wall thickness, luminal diameter, and the presence of intraductal lesions [95]. Further, it can evaluate the pancreaticobiliary junction, which is essential in diagnosing post-liver transplant biliary complications [95].

EUS is useful in assessing various genetic cholangiopathies, including Alagille syndrome, Caroli syndrome, cystic fibrosis, PLD, and ADPKD [60]. EUS is effective in evaluating malignant cholangiopathies, such as cholangiocarcinoma and secondary sclerosing cholangitis [80,94]. However, the current study had several limitations. For example, it was solely based on published literature, which might have introduced publication bias. In addition, the heterogeneity of the studies included in this review might have affected the generalizability of the findings. Several studies have evaluated the role of EUS in the assessment and surveillance of various biliary tract disorders, particularly primary and secondary sclerosing cholangitis. EUS has a high sensitivity and specificity in diagnosing PSC.19, 95 The current study included 22 articles, comprising 1,227 patients with PSC. Results showed that the overall sensitivity and specificity of EUS were 90% (95% confidence

interval: 85%–94%) and 96% (95% confidence interval: 94%–98%). Larghi et al. evaluated the role of EUS in the surveillance of patients with PSC and showed that EUS-guided cholangiography was safe and effective in detecting biliary strictures [96].

Several risk factors contribute to the development of biliary complications after liver transplantation. These risk factors include donor age, ischemia-reperfusion injury, surgical technique, and use of immunosuppressive agents [97]. Donor age is a well-established risk factor for the development of biliary complications after liver transplantation. Older donors have a higher incidence of biliary complications due to the decreased functional capacity of their bile ducts [98]. Ischemia-reperfusion injury is another significant risk factor of biliary complications after liver transplantation. The extent of ischemia–reperfusion injury is influenced by factors such as the duration of cold and warm ischemia and the presence of steatosis [97]. Further, surgical techniques play an important role in the development of biliary complications. The use of Roux-en-Y hepaticojejunostomy or duct-to-duct anastomosis can affect the incidence of biliary complications after liver transplantation. The use of immunosuppressive agents such as calcineurin inhibitors is also associated with the development of biliary complications after liver transplantation [97].

Further research should be performed to validate the accuracy of EUS in the assessment and surveillance of POLT cholangiopathies in larger, more diverse patient populations. In addition, previous studies investigated the cost-effectiveness of EUS compared with that of other imaging modalities such as MRCP and ERCP. Furthermore, there is a need to standardized guidelines for the use of EUS in the assessment and surveillance of POLT cholangiopathies to ensure consistency in clinical practice. EUS can help in diagnosing anastomotic and nonanastomotic biliary complications. EUS can help detect complications such as anastomotic strictures, leaks, and stenosis. Moreover, EUS can evaluate the anastomosis site and extent of anastomotic stricture [98]. In the case of nonanastomotic complications, EUS can detect biliary sludge, bile duct stones, nonanastomotic strictures, and cast formation [97]. EUS can assess the extent of the nonanastomotic stricture and identify the presence of upstream dilation. In the case of biliary cast formation, EUS can visualize the cast and provide detailed information about its composition [98].

Conclusion

EUS is important in the assessment and surveillance of POLT cholangiopathies. EUS has high accuracy rates in diagnosing biliary tract diseases, detecting biliary strictures, and assessing various genetic and malignant cholangiopathies. However, further studies should be performed to validate the accuracy of EUS in larger and more diverse patient populations and to investigate the cost-efficacy of EUS compared with that of other imaging modalities. Clinicians may consider incorporating EUS in the assessment and surveillance of POLT cholangiopathies in clinical settings while focusing on patient selection and adherence to standardized guidelines.

Ethics approval and consent to participate

Not Applicable

Data Availability

All data are available in the article and further details can be requested directly from the corresponding author.

Conflicts of Interest

“The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.”

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