



Case Report

An Emerging Problem: Multidisciplinary Treatment of Liver Transplant-Associated Biliary Complications in Patients with Roux-En-Y Gastric Bypass.

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Abstract

Introduction: There is an increasing number of patients with a history of both liver transplantation (LT) and Roux-en-Y gastric bypass (RYGB). Biliary tract complications are the most prevalent LT-associated complication, with endoscopic retrograde cholangiopancreatography (ERCP) as the preferred therapeutic approach. However, surgically altered anatomy after RYGB renders ERCP technically challenging. This overview attempts to address, through real-life practical cases, the various available approaches for the management of biliary tract complications in LT patients with RYGB.

Methods: Descriptive single Center overview of endoscopic treatment modalities of biliary tract complications in LT recipients with a history of RYGB. Different techniques are discussed and illustrated with clinical cases.

Results: Balloon enteroscopy-assisted-ERCP (BE-ERCP), endoscopic ultrasound (EUS)-directed trans gastric endoscopic retrograde cholangiopancreatography (EDGE), percutaneous trans hepatic biliary drainage (PTBD), or a combination of these procedures can be used according to the clinical indication or the surgical reconstruction of the bile duct (biliary duct end-to-end anastomosis vs hepaticojejunostomy) in conjunction with RYGB. Case 1 was treated with PTBD, followed by BE-ERCP; case 2 was treated with BE-ERCP, followed by EDGE; case 3 was treated with PTBD, followed by EDGE; and case 4 was treated with BE-ERCP.

Conclusion: Both BE-ERCP, EDGE and PTBD in different combinations are promising endoscopic therapeutic approaches for treating LT-associated biliary tract complications in RYGB patients. Since the number of these patients with combined LT and RYGB is expected to increase, more studies focusing on this specific population are warranted to comprehensively assess the efficacy and safety profiles of these interventions.

Introduction

Obesity is the most prevalent metabolic disease worldwide and already affects nearly one-sixth of adults worldwide [1]. Metabolic associated steatotic liver disease (MASLD), which is strongly linked to obesity, has emerged as an important cause of chronic liver disease and is expected to become the leading indication for liver transplantation (LT) in developed countries within the coming decade [2,3]. Bariatric surgery, which is widely considered to be the most effective therapy for weight-control and reducing obesity-related comorbidities, may also improve accessibility to LT, as well as both short- and long-term LT outcomes [4-6]. Thereafter, the number of patients with a history of liver transplantation and bariatric surgery, either performed prior to, concurrently or after LT, is already substantial and anticipated to expand in forthcoming years [7].

Despite notable improvements in terms of survival rates, biliary tract complications remain frequent after orthotopic LT, significantly impacting graft viability, patient morbidity, and even mortality [8,9]. The prevalence of these complications ranges between 5 and 30% and varies depending on factors such as graft origin (deceased or living donor) and the type of biliary anastomosis, often co-occurring with vascular complications, prolonged ischemia, and reperfusion injury [10-12]. Endoscopic retrograde cholangiopancreatography (ERCP) is the preferred approach for the management of LT-associated biliary complications [13]. However, surgically altered anatomy renders ERCP a significant technical challenge due to the long intestinal limbs to get to the target site and the complexities associated with biliary cannulation from a distal approach with a forward viewing endoscope [14].

Double- or single-balloon enteroscopy assisted-ERCP (BE-ERCP), endoscopic ultrasound (EUS)-directed trans gastric endoscopic retrograde cholangiopancreatography (EDGE) and laparoscopy-assisted ERCP represent different endoscopic approaches of the biliopancreatic systems in patients with Roux-en-Y gastric bypass (RYGB) with acceptable safety profiles and success rates, compared to percutaneous trans hepatic biliary drainage (PTBD) [15]. Nonetheless, there exists a lack of information regarding the application of these different techniques in the specific context of patients who have undergone both bariatric RYGB surgery and LT. Moreover, to treat LT-associated biliary pathology, the type of biliary reconstruction (conventional biliary anastomosis vs hepaticojejunostomy) plays an important role in the setting of RYGB surgery.

We describe and illustrate different endoscopic procedures of the biliary system in the emerging group of patients with both LT and RYGB either with an end-to-end biliary anastomosis with an intact papilla or with an hepaticojejunostomy onto the biliopancreatic limb (Figure 1). The study was approved by the local Ethics Committee (No. 2021/07AVR/162).

Case Descriptions

Case 1

A 56-year-old female patient with a history of several previous surgical interventions including cholecystectomy, abdominoplasty, and gastric sleeve resection with a subsequent RYGB performed six years prior, underwent LT with an end-to-end ductal biliary anastomosis for acute liver failure following paracetamol overdose. Six months later an anastomotic biliary stricture was treated using PTBD with balloon dilatations and finally the placement of a fully covered metal stent in the common bile duct.

Following this initial intervention, the patient remained asymptomatic for twelve years, wherein fracture and distal migration of the metallic stent prompted its removal and replacement by two uncovered metallic stents through PTBD. Subsequently, four years thereafter, fracture in both metallic stents required multiple PTBD procedures with internal/external drainage. Ultimately, the internal/external drain was replaced by two plastic 7 Fr stents through BE-ERCP using the single-balloon enteroscope, which were electively replaced every 3 to 4 months. At this point, liver allograft secondary sclerosing cholangitis was diagnosed, with clinically significant portal hypertension and progressively worsening liver function. Finally, twenty years after the first LT, she underwent a second LT with a ductal end-to-end biliary anastomosis with partial removal of the indwelling biliary metal stents. After two more plastic stent replacements using BE-ERCP all plastic stents were removed leaving a fractured indwelling metal stent in situ with an acceptable result (Figure 2). This case illustrates the deleterious outcome when uncovered metal stents are used to treat benign biliary strictures. Also BE-ERCP allows to internalize the internal/external PTBD drain and to perform multiple plastic stent exchange procedures in the setting of RYGB.

Case 2

A 33-year-old female patient, with a history of RYGB surgery performed 2 years prior, resulting in significant subsequent weight loss, underwent urgent LT due to acute liver failure of uncertain etiology, with autoimmune or rapid weight loss-associated liver injury as primary hypothesis. The surgery was conducted without complications, and an end-to-end ductal biliary anastomosis was created. Three months later she developed progressive cholestasis, with magnetic resonance cholangiopancreatography (MRCP) suggestive for biliary cast syndrome due to ischemic cholangiopathy.

BE-ERCP confirmed an anastomotic biliary stricture with upstream dilatation of intrahepatic bile ducts, accompanied by biliary cast syndrome (Figure 3). Biliary sphincterotomy was performed, along with a dilatation of the anastomotic stricture to 7 mm and partial extraction of intrahepatic biliary casts. Given

the imperative need for multiple ERCP procedures with peroral cholangioscopy an EUS-guided fully-covered lumen-apposing metal stent (LAMS) was placed for the creation of a gastro-gastrostomy between the gastric pouch and the excluded stomach (EDGE procedure). Subsequently, two ERCP procedures using a conventional side-viewing duodenoscope were performed through the LAMS in order to dilate the anastomotic stricture and to further remove biliary casts using cholangioscopy (Figure 3). This endoscopic treatment is currently ongoing in an attempt to save the transplanted liver. This case illustrates the practical aspect of the EDGE procedure in RYGB patients allowing multiple and more complex (cholangioscopy) ERCP procedures.

Case 3

A 46-year-old male patient, with a history of RYGB surgery performed more than 10 years prior, underwent LT with an end-to-end biliary duct anastomosis because of decompensated alcoholic liver cirrhosis complicated with refractory hepatorenal syndrome. Six months later he underwent PTBD with liver biopsy and additional dilatation of an anastomotic biliary stricture, leaving an external/internal drain in situ (Figure 4). Acknowledging the anticipated need for progressive stenting through multiple therapeutic interventions, it was decided after multidisciplinary discussion that an EDGE procedure was warranted. Therefore, an EUS-guided LAMS was placed between the gastric pouch and the excluded stomach, followed by conventional ERCP carried out two weeks later with biliary sphincterotomy and replacement of the percutaneous internal/external drain by 2 plastic 10 Fr biliary stents (Figure 4). Further endoscopic progressive stenting of the biliary anastomosis is ongoing. This case illustrates the quick and efficient biliary drainage through PTBD allowing more time to prepare the patient for the EDGE procedure and the subsequent progressive stenting of the biliary anastomotic stricture.

Case 4

A 36-year-old female patient, with a history of RYGB surgery performed 4 years ago, resulting in substantial weight loss of nearly 100 kg, underwent urgent LT because of acute liver failure following paracetamol overdose. She underwent a second LT due to iatrogenic injury of the hepatic artery during surgery for an anastomotic biliary stricture. The redo LT was successfully executed, entailing the creation of a hepaticojejunal anastomosis onto the biliopancreatic limb of the RYGB reconstruction (Figure 1). Three months later she presented with a stricture at the level of the hepaticojejunostomy. Subsequent BE-ERCP using single-balloon enteroscopy confirmed the anastomotic stricture of the hepaticojejunostomy as well as a hilar biliary stricture of the left hepatic duct (Figure 5). Successful dilatation of the hepaticojejunostomy stricture with additional placement of a 7 Fr plastic stent in the right hepatic duct were performed. Three months

later, a second BE-ERCP demonstrated significant improvement of both strictures, with additional balloon dilatation of both the hepaticojejunostomy and the left hepatic duct stricture, and removal of the biliary stent. This case illustrates the additional difficulty of a LT hepaticojejunostomy on the RYGB biliopancreatic limb, excluding the biliary access through the EDGE procedure. Here PTBD and BE-ERCP can be used, whether or not in combination.

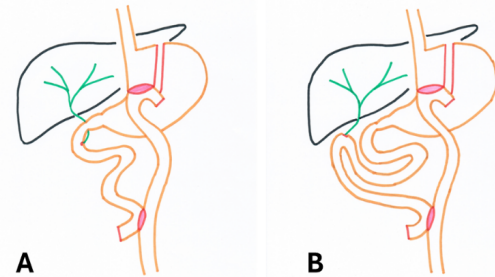


Figure 1: Combination of Roux-en-Y gastric bypass (RYGB) and liver transplantation (LT) with a biliary anastomosis draining through Vater's papilla (A) or through an hepaticojejunostomy onto the biliopancreatic limb (B).

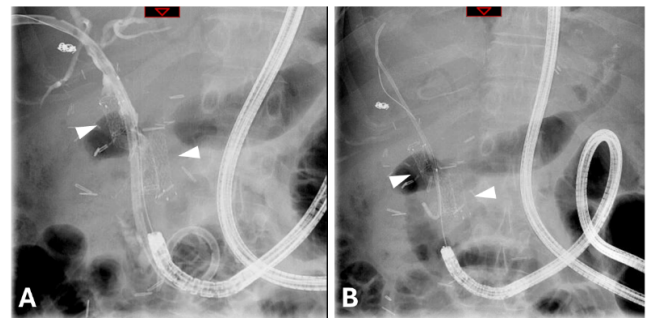


Figure 2: Balloon-assisted enteroscopy-assisted endoscopic retrograde cholangiopancreatography (BE-ERCP) using a single-balloon enteroscope in a liver transplant (LT) patient with a Roux-en-Y gastric bypass (RYGB) surgical reconstruction. Retrograde cholangiography is performed through the papilla over the percutaneous internal-external drain, with multiple fractured and deformed uncovered metallic stents (white arrows) in the common bile duct after LT (A). After the removal of the percutaneous transhepatic biliary drain (PTBD), a 7 Fr plastic stent is placed from within the duodenum into the intrahepatic bile ducts (B).

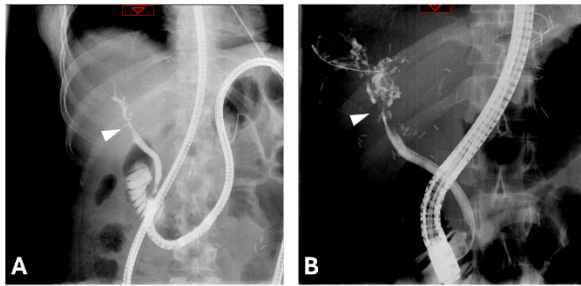


Figure 3: Balloon-assisted enteroscopy-assisted endoscopic retrograde cholangiopancreatography (BE-ERCP) using a single-balloon enteroscope in a liver transplant (LT) patient with a RYGB surgical reconstruction showing a biliary anastomotic stricture (white arrow) with dilated intrahepatic bile ducts and biliary casts (A). A more detailed image of the same BE-ERCP procedure (B).

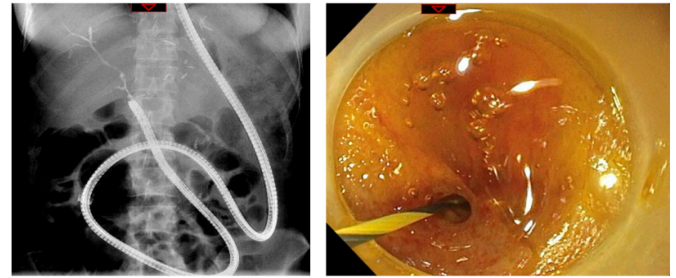


Figure 5: Balloon-assisted enteroscopy-assisted endoscopic retrograde cholangiopancreatography (BE-ERCP) using a single-balloon enteroscope in a liver transplant (LT) patient with a RYGB surgical reconstruction and a hepaticojejunostomy onto the biliopancreatic limb (A). Endoscopic image of the guidewire catheterization of the hepaticojejunostomy (B).

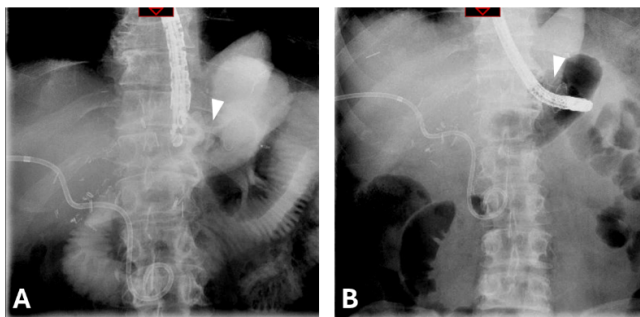


Figure 4: Placement of a lumen apposing metal stent (white arrow) to create a gastro-gastrostomy in the setting of Roux-en-Y gastric bypass (RYGB) in a liver transplant (LT) patient with a percutaneous transhepatic biliary drain (PTBD) (A). Introduction of a conventional duodenoscope through the lumen apposing metal stent (white arrow) to perform endoscopic retrograde cholangiopancreatography (ERCP) and replacement of the PTBD by multiple plastic biliary stents (B).

Discussion

LT is the definitive treatment for acute liver failure, hepatocellular carcinoma, and end-stage liver disease [3]. The increasing medical and surgical expertise in the execution of this procedure has led to a significant improvement in survival rates across European countries, with fewer complications over time [8,9]. However, biliary tract complications remain common and are expected to increase even more, mainly attributable to the increasing use of extended criteria for marginal grafts [16,17]. On the other hand, as the prevalence of obesity rises among the population, the number of patients undergoing bariatric surgery such as RYGB also increases, particularly in the LT setting where weight can impact the selection process and is strongly related to short- and long-term outcomes [18,19]. Thus, addressing the management of LT-associated biliary tract complications in this specific population, where they are expected to be frequent and prompt tailored management, has become highly relevant.

This overview attempts to address, through real-life practical cases, the various available approaches for the management of biliary tract complications in patients who have undergone both LT and RYGB. The available options are diverse and include BE-

ERCP, EDGE procedure, LA-ERCP, PTBD and redo surgery [15]. To date, clear guidelines or evidence-based recommendations have yet to be established for determining the optimal management strategy in this context of combined LT and RYGB. Nevertheless, several factors could potentially impact the decision regarding the most suitable approach for each patient and multidisciplinary discussion involving hepatology, endoscopy, radiology and surgery is warranted in most cases.

Balloon enteroscopy-assisted ERCP (BE-ERCP)

The first and most important hurdle to overcome is to reach Vater's papilla or the hepaticojejunostomy in patients with RYGB surgically altered anatomy. BE-ERCP has been described as a safe and effective procedure for treating complications of the hepaticojejunostomy following Roux-en-Y living-donor LT (20). However, due to the long-limb reconstruction technique in RYGB, the path to the target site (Vater's papilla or hepaticojejunostomy) is significantly longer and requires correct identification of the biliopancreatic limb at the foot of the Roux-en-Y anastomosis. A recent multicenter study evaluated BE-ERCP in patients with surgically altered anatomy, excluding liver transplant recipients, and found that Roux-en-Y reconstruction was independently associated with procedural failure, mainly because of insertion failure [21].

The second notable challenge encountered in these patients involves the cannulation of Vater's papilla or the hepaticojejunostomy using a long forward-viewing enteroscope without elevator to steer the cannulation catheter. This can be difficult as the papilla appears as an inverted image and is frequently positioned tangentially due to the distal approach from within the small bowel. Factors such as a native papilla and the absence of a tip cap are associated with an increased risk of cannulation failure [22]. In cases of failed biliary cannulation, alternative approaches based on PTBD or EUS-guided rendez-vous techniques can be considered, being technically challenging, prompting another therapeutic approach [23-26].

Finally, after getting to the target site and achieving successful bile duct cannulation, subsequent procedures, such as stricture dilatation, stone extraction and stent placement, may also be challenging. Due to the long and small caliber working channel of the enteroscope compared to a conventional duodenoscope, specifically adapted devices are necessary to perform ERCP with an enteroscope. Moreover, cholangioscopy has become a useful endoscopic tool for both diagnostic and therapeutical ERCP procedures in LT recipients [27,28]. However, currently no cholangioscopy system is compatible with the enteroscope.

EUS-directed trans gastric endoscopic retrograde cholangio-pancreatography (EDGE)

EDGE entails the creation of a fistula tract between the RYGB gastric pouch or proximal jejunum and the excluded stomach utilizing a fully covered LAMS placed under the guidance of EUS. The main advantage of this procedure is that it allows repetitive ERCP procedures to be performed with a conventional side-viewing duodenoscope and standard devices, including cholangioscopy. EDGE can be performed in a single- or two-stage procedure, depending on the clinical indication, and the experience of the endoscopist, with a mandatory final stage for LAMS removal that is usually performed three-to-four weeks after the final ERCP procedure [29].

Within the last decade, EDGE has emerged as a new and viable approach for treating biliopancreatic pathology in patients with RYGB anatomy. Although being a highly technical procedure usually only performed in experienced centres, EDGE is considered a relatively safe procedure with an excellent technical success rate [30]. Compared to BE-ERCP, reported technical success rates of EDGE are higher, but with also significantly higher adverse event rates, because of the trans parietal approach with the risk of misdeployment or migration of the stent [31-33]. This has been associated to stent diameter and timing of the ERCP, with a lower likelihood observed with stents >15mm and when employing a two-stage strategy [34].

Another notable advantage of EDGE in this particular population, as opposed to alternative approaches such as BE-ERCP or LA-ERCP, is its capacity to facilitate multiple ERCP sessions, if necessary. The most common treatment protocol for biliary anastomotic stricture typically involves sphincterotomy in addition to balloon dilatation and placement of multiple plastic stents, in view of progressive stenting, with the objective of achieving stricture resolution and mitigating long-term recurrence [35]. Between three and four ERCP procedures are frequently required to achieve stricture resolution [35,36]. Thus, EDGE emerges as a good option for addressing post-LT biliary complications that may require multiple ERCP sessions.

Percutaneous transhepatic biliary drainage (PTBD)

Despite the gradual displacement of interventional radiology and surgery by endoscopic treatment in many clinical scenarios, PTBD remains a common approach for managing biliary tract complications following LT in patients with surgically modified anatomy across numerous centers, mainly because its widespread availability and extensive experience in these patients [12]. PTBD

has been described as a relatively safe and efficient method for addressing biliary tract complications [37]. Nonetheless, it typically serves as a secondary option when endoscopic interventions prove unsuccessful, primarily because of the patient's discomfort, the elevated risk of complications and the potential risk of damaging the donor liver [38]. Conversely, the combined utilization of endoscopic and PTBD techniques is emerging as a popular trend, particularly in patients with multiple intrahepatic biliary strictures, where the rendez-vous technique has demonstrated being useful [39]. PTBD also allows rapid biliary drainage when clinically indicated.

Other procedures

Apart from the procedures described, laparoscopy-assisted ERCP (LA-ERCP) and redo surgery are also available to treat biliary pathology in RYGB patients [15]. However, both techniques are surgical invasive procedures not allowing multiple interventions. They are considered less suitable for the treatment of LT-associated biliary complications in RYGB patients.

Conclusion

The management of LT-associated biliary tract complications in patients with RYGB anatomy poses a significant challenge and prompts a multidisciplinary discussion for deciding the optimal strategy. Next to PTBD, both BE-ERCP and EDGE have emerged as promising endoscopic therapeutic methods for this indication, owing to their established safety and efficacy in various other clinical contexts. With the expected rise in patient numbers with both LT and RYGB, more studies focusing on this specific population are warranted to comprehensively assess the position, efficacy and safety profiles of (combinations of) these therapeutic procedures.

Declaration

Generative AI and AI-assisted technologies in the writing process. The authors did not use generative AI and AI-assisted technologies in the writing process of the manuscript.

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Author contributions: Nuñez-Pizarro JL performed the endoscopic procedures and wrote the first draft of the manuscript. Dahlqvist G ensured clinical follow-up of the patients described and revised and approved the manuscript. Goffette P performed the interventional radiological procedures and revised and approved the manuscript. Bonaccorsi Riani E, Coubeau L and Ciccarelli O operated on the patients and revised and approved the manuscript. Moreels TG performed the endoscopic procedures, created the figures, wrote and finalized the manuscript.

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