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Endoscopic treatment of biliary complications after liver transplantation

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ABSTRACT

Background: biliary complications are an important cause of morbidity and mortality after liver transplantation. Endoscopic retrograde cholangiopancreatography (ERCP) is a therapeutic option, which is less invasive than surgical management.

Materials and methods: the endoscopic management with ERCP of patients with biliary complications after liver transplantation in the Complejo Hospitalario Universitario de A Coruña between 2012 and 2018 was reviewed.

Results: there were 232 liver transplant recipients and biliary complications occurred in 70 (30.1 %) patients. Anastomotic strictures, most of them choledocho-choledochal, constituted the most frequent complication in 43 (61.4 %) patients. Biliary leak occurred in 16 (22.9 %) patients, non-anastomotic strictures in six (8.6 %) and choledocholithiasis in five (7.1 %). ERCP was performed in 39/43 patients with anastomotic strictures, achieving clinical success in 36 (92.3 %). All patients with a biliary leak were treated with CPRE, with a clinical resolution in 10/16 (62.5 %). ERCP was successful in 3/5 patients (60 %) with bile duct stones. In non-anastomotic strictures, ERCP was not effective in any case. Regarding complications, five (7.7 %) patients presented mild-moderate bleeding after biliary sphincterotomy.

Conclusion: in our study, ERCP is useful in most biliary anastomotic strictures, early biliary leaks

and choledocholithiasis after liver transplantation. The rate of ERCP complications in these patients was low and none were lethal.

Keywords: Liver transplantation. Biliary complications. Endoscopic retrograde cholangiopancreatography.

INTRODUCTION

Biliary complications constitute an important source of morbidity and mortality after liver transplantation. According to previously published studies, the incidence ranges between 10 and 30 %. The most common complications after transplantation are anastomotic strictures, non-anastomotic strictures, biliary leaks and choledocholithiasis. Surgical technique is considered as a risk factor for biliary complications. Thus, Roux-en-Y hepaticojejunostomy and t-tube anastomosis have a higher risk of developing complications than choledocho-coledochostomy. Hepatic artery thrombosis, arterial stenosis and surgical technique complications are also considered as risk factors for biliary problems (1-5).

Currently, endoscopic retrograde cholangiopancreatography (ERCP) is a therapeutic alternative, with a low morbidity and mortality in high-expertise centers (6-9). Several studies have shown that ERCP can be a successful therapeutic option for anastomotic strictures (10-12), biliary leaks, particularly early leaks (13), and choledocholithiasis. However, resolution rates with an endoscopic approach are lower, around 50 % for non-anastomotic strictures, mostly related to vascular problems. The aim of this study was to analyze the role of ERCP for the treatment of biliary complications after liver transplantation in our center.

MATERIALS AND METHODS

This was an observational retrospective study, using a database of biliary complications in 232 liver transplant recipients, between 2012 and 2018 in the Complejo Hospitalario Universitario de A Coruña (Spain). Treatment with ERCP was analyzed. All ERCPs were performed by experienced endoscopists. As a rule, sphincterotomy was performed after cannulation to facilitate the treatment of strictures, leaks and cholecocholitis. Stent use to dilate the stenosis and treat leaks depended on the choice of the endoscopist. Patients who received plastic stents were reevaluated after three months.

The factors analyzed included: demographic factors, type of biliary complications, endoscopic management, time between transplantation and ERCP, number of ERCP, number of stents, time that the stent had been placed and the resolution of each complications. Biliary complications were considered to be resolved when there was no recurrence during the first year after ERCP. Statistical analysis was performed with SPSS®.

RESULTS

All biliary complications in 232 recipients who received a liver transplant between January 2012 and December 2018 at Complejo Hospitalario Universitario de A Coruña were reviewed. Table 1 shows the epidemiological characteristics of the patients. Seventy patients presented biliary complications (30.1 %). Anastomotic strictures were present in 43 (61.4 %), biliary leak in 16 (22.9 %), non-anastomotic strictures in six (8.6 %) and choledocholithiasis in five (7.1 %). ERCP was performed in 55 of 70 patients with biliary complications.

ERCP was the selected therapeutic approach in 39 (90.7 %) patients with anastomotic strictures, five (83.3 %) patients with non-anastomotic strictures, six patients (37.5 %) with biliary leaks and five (100 %) patients with choledocholithiasis. Radiological-endoscopic *rendez-vous* was performed to gain access to the bile duct in 16 patients with anastomotic strictures (41 %), one patient with non-anastomotic strictures (20 %), one patient with biliary leak (16.7 %), and one patient with choledocholithiasis (25 %).

The mean time between liver transplantation and ERCP was 5.6 months in anastomotic strictures, 15.5 months in non-anastomotic strictures, 3.2 months in biliary leaks and 8.8 months in choledocholithiasis. The mean number of ERCP performed was 2.2 in anastomotic strictures, 2 in non-anastomotic strictures, 1.7 in fistulas and 1.6 in choledocholithiasis.

The mean number of stents per patient was 1.4 in patients with anatomotic strictures, 1 in non-anastomotic strictures, 1.3 in patients with biliary leaks and 1 in patients with choledocholithiasis. Stents were maintained for 85.1 days in anastomotic strictures, 70 days in non-anastomotic strictures, 29.6 in biliary leaks and 13.7 in choledocholithiasis.

Table 2 describes the types of stents used. Balloon dilation was performed in one patient with anastomotic strictures (2.6 %), one patient with non-anastomotic stricture (20 %) and three patients with a biliary leak (50 %). No patients with choledocholithiasis needed a balloon dilation.

The resolution rate with ERCP was 36/39 (92.3 %) in anastomotic strictures. Two failures were due

to the inability to locate the guide wire proximally. The procedure was not able to resolve the stricture and surgical biliary reconstruction was required in the remaining cases. ERCP was unsuccessful in patients with non-anastomotic strictures, who needed surgical repair of biliary anastomosis or liver retransplantation. ERCP was successful in 4/6 (66.67 %) patients with biliary leaks. The remaining two patients required surgery.

In patients with choledocholithiasis, the resolution rate was 80 % (4/5 patients). The only failure was due to the inability of papilla cannulation. The mean time without recurrence was 41 months in anastomotic strictures, 25 months in bile leaks and 50 months in gallstones. Regarding complications, there were five cases of bleeding after sphincterotomy (9.09 %), in patients with anastomotic stenosis, with no serious consequences.

DISCUSSION

Despite a significant improvement in graft survival, biliary complications after liver transplantation are still an important cause of morbidity and mortality (1,2). The rate of biliary complications in our center (30.1 %) was similar to previously reported data (3,4). The approach to these complications should be multidisciplinary with hepatologists, endoscopists, interventional radiologists and surgeons. Although ERCP management is usually the choice in most cases, as reported in the literature (6-8), the results are influenced by the availability of ERCP and experience in each center.

ERCP success rate depends on the type of biliary complication. ERCP was successful in 92.3 % of cases with anastomotic stenosis, which is similar to that reported previously, ranging between 65-100 %. Moreover, our results are among the highest rates (7,9), probably due to the early diagnosis of biliary complications and a short time between liver transplantation and ERCP (two months).

Biliary stents have more favorable results in early anastomotic strictures, especially in the first six months after transplantation. A follow-up strategy according to the type of stent could not be established. Our data are comparable to those reported in literature, which reported similar resolution rates (between 65 and 100 %) and recurrence rates (between 20 and 30 % per year) for both plastic and metal stents (12-14). Metal stents have the advantage of needing fewer procedures when used to treat benign biliary strictures (16).

In our center, ERCP was not successful in any cases of non-anastomotic strictures. It is well known

that this type of biliary stricture is more difficult to treat with endoscopy (14,15). Clinical success in biliary leaks is comparable to that reported in the literature, greater than 60 %. ERCP is more effective in early (related to complications in the surgical technique) than in late leaks (related to withdrawal of T-tube). In these cases, conservative treatment is preferred and ERCP is a second line strategy (13).

With regard to choledocholithiasis after liver transplantation, the success was comparable to the efficacy of ERCP in other pathologies. Although the number of patients in our center was low (17,18), our ERCP complication rate (9.09 %) was similar to that reported in other centers (19). All complications were bleeding after biliary sphincterotomy and there were no cases of pancreatitis or perforation.

In conclusion, most biliary anastomosis strictures, early biliary leaks and choledocholithiasis after liver transplantation can be successfully treated by ERCP.

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Accepted Article

Table 1. Patient characteristics

<i>Recipient age, years</i>	57.6 ± 7
<i>Gender</i>	
Male, n (%)	57 (81.4 %)
<i>Reason for transplant, n (%)</i>	
- Hepatocellular carcinoma	29 (41.4 %)
- Alcoholic cirrhosis	17 (24.3 %)
- Hepatitis C cirrhosis	7 (10 %)
- Autoimmune (AIH, PBC, PSC)	6 (8.6 %)
- Hepatitis C + alcoholic cirrhosis	5 (7.1 %)
- Other	6 (8.6 %)
<i>Child-Pugh n (%)</i>	
- A	26 (37.1 %)
- B	22 (31.4 %)
- C	22 (31.4 %)
<i>Donor age, years</i>	62.4 ± 14.5
<i>Donor after cardiac death n (%)</i>	10 (14.3 %)
<i>Anastomosis used</i>	
- Choledocho-choledochostomy	67 (95.7 %)
- Roux-en-Y	3 (4.3 %)
<i>T-tube, n (%)</i>	68 (97.1 %)
<i>Hepatic artery thrombosis, n (%)</i>	6 (8.6 %)
<i>Cold ischemic time, min</i>	367 ± 101
<i>Warm ischemic time, min</i>	30 ± 7.9

Table 2. Characteristics of the stents

	<i>Anastomotic strictures</i>		<i>Non-anastomotic strictures</i>		<i>Leaks</i>		<i>Bile duct stones</i>	
	Patients, n		Patients, n		Patients, n		Patients, n	
Stent	1 stent	> 1 stent	1 stent	> 1 stent	1 stent	> 1 stent	1 stent	> 1 stent
Plastic*	21	4		2	6			
Metal (SEMSs)	7	1					5	
Plastic + metal		3						
Metal + plastic		1						

*Plastic stent: 10 F x 5 cm, 7 F x 7cm, 8.5 F x 7 cm, 10 F x 7 cm, 7F x 10 cm, 10 F x 10 cm.