CIRUGÍA ESPAÑOLA

www.elsevier.es/cirugia

Original article

# Role of surgery in the management of biliary complications after liver transplantation

*Laura Lladó,[a,*] Joan Fabregat,[a] Emilio Ramos,[a] Carme Baliellas,[b] Jaume Torras,[a] David Julià,[a] Ana Berrozpe,[b] Rosa Jorba,[a] and Antoni Rafecas[a]*

[a]*Departamento de Cirugía, Unidad Trasplante Hepático, Hospital Universitario de Bellvitge, Barcelona, Spain*
[b]*Hepatología, Unidad Trasplante Hepático, Hospital Universitario de Bellvitge, Barcelona, Spain*

ARTICLE INFORMATION

*Article history:*
Received December 29, 2009
Accepted March 12, 2010

*Keywords:*
Biliary complications
Endoscopy
Hepaticojejunostomy
Liver transplantation
Radiology

A B S T R A C T

Management of biliary tract complications (BTC) after liver transplantation (LT) has progressed in recent years.

The aims of this study were, to analyse the incidence and management in our institution of BTC after 1000 LT; and to study the management of patients with anastomotic strictures (AS).

*Results:* The incidence of BTC was 23%. There were 76 cases of bile leak, 106 cases of anastomotic strictures, 46 non-anastomotic strictures, 42 choledocolithiasis and 19 other complications.

Among 106 cases of anastomotic strictures, radiological treatment, either PTC or ERCP, was initially indicated in 62. The AS of 38 patients (33%) were resolved with surgical treatment, 18 of them after a previous attempt at radiological treatment. Patients who were treated initially by radiologically required more procedures. Morbidity and mortality related to BTC were slightly higher in the group of patients treated by radiology (morbidity: surgical: 4 (18%) vs radiological: 20 (32%); *P*=.2 and mortality: surgical: 0% vs radiological: 8 (11%); *P*=.23).

Among 46 patients with non-anastomotic strictures, 29 were resolved with retransplantation (63%).

*Conclusions:* Surgery has a significant role in the management of BTC, and is the treatment of choice in some cases of anastomotic strictures. Retransplantation may be the preferred option in patients with non-anastomotic strictures.



## Papel de la cirugía en el manejo de las complicaciones biliares tras el trasplante hepático

*Palabras clave:*
Complicaciones biliares

R E S U M E N

El manejo de las complicaciones biliares (CB) postrasplante hepático ha evolucionado en los últimos años.

*Corresponding author.
E-mail address: 31513llg@comb.cat (L. Lladó).

Endoscopia
Hepaticoyeyunostomía
Trasplante hepático
Radiología

Los objetivos de este estudio fueron analizar la incidencia y el manejo de las CB en nuestro centro en 1.000 trasplantes hepáticos; y estudiar específicamente el manejo de las estenosis anastomóticas (EA).

*Resultados:* La incidencia de CB fue del 23%. Se dieron 76 casos de fístula biliar, 106 casos de estenosis anastomóticas, 46 casos de estenosis no-anastomóticas, 42 coledocolitiasis y 19 otras complicaciones.

De los 106 casos de estenosis anastomóticas, se indicó tratamiento radiológico (CPRE o CTPH) en 62 casos. En 38 casos (33%), la estenosis anastomótica se resolvió mediante tratamiento quirúrgico, en 18 tras previo tratamiento radiológico. La morbilidad y mortalidad relacionada con el tratamiento radiológico de las CB fue discretamente superior (morbilidad: Quir: 4 [18%] vs. Radiol: 20 (32%); p = 0,2 y mortalidad: Quir: 0% vs. Radiol: 8 [11%]; p = 0,23).

De los 46 pacientes con estenosis no anastomóticas, 29 (63%) fueron tratados mediante retrasplante.

*Conclusión:* El tratamiento quirúrgico tiene un papel relevante en el manejo de las CB postrasplante hepático, y es el tratamiento de elección en algunos casos de estenosis anastomóticas. El retrasplante, sin manipulación previa, es el tratamiento de elección en los pacientes con estenosis no anastomóticas.



Despite the significant advances in surgical and preservation techniques, and the perioperative management of patients, biliary complications (BC) are still an important cause of morbidity and graft loss after liver transplantation (LT).[1,2] The incidence in recent series remains around 20%.[1-3]

Anastomotic and non-anastomotic strictures are the most frequent CB at this time. While in the early stages of LT development most strictures were treated with surgerym,[4] the advances in endoscopic and radiological technologies have led to a tendency to manage BC without surgery. In many centres, non-surgical methods have become the standard of care for most BC.[5-8] Surgery is usually reserved for those patients with whom endoscopic and/or percutaneous treatments have not been successful. However, there are no randomized studies comparing both approaches, and there is no definitive consensus regarding the therapeutic management of BC.

The objectives of this work were: first, to analyze the incidence and management of BC in our centre after 1000 LT, and second, to study the evolution of patients with anastomotic strictures (AS), considering the type of treatment given.

## Patients and methods

Between 1984 and 2007, 1000 LT were performed in our hospital. Follow-up was discontinued in January 2008. Therefore, all the patients studied had a minimum follow-up of 1 year.

The clinical information about the characteristics of the donors and patients was acquired from our prospective database. All the cases of BC were retrospectively reviewed with regard to the detailed data of the type of BC and how it was managed.

It should be pointed out that nearly all the LT were performed with cadaver donors. There were only 3 cases of non-heart beating donors, 31 cases of domino transplants, and no cases of living donors.

### *Surgical technique for biliary anastomosis*

The technique of choice in our centre is end-to-end hepatic hepaticostomy. Routine intraoperative cholangiography is performed by cystic duct cannulation. Intraoperative cholangiography allows us to rule out leakage, as well as the subsequent radiological correlation during the patient's recovery. The anastomoses are performed with absorbable sutures, using individual stitches or continuous suture, at the surgeon's discretion depending on the calibre of the bile duct. In cases of extrahepatic bile duct disease, when the recipient's bile duct is not long enough, or when there is a big discrepancy between the calibres of the bile ducts of the donor and the recipient, hepaticojejunostomy (HJ) is indicated. As a matter of routine, closed aspiration drainage is used posterior to the hepatic hilum.

These criteria were followed to perform 837 end-to-end anastomoses, 91 hepaticojejunostomies, 42 side-to-side hepatic hepaticostomies (technique used temporarily in 1998 and 1999), and 30 end-to-side hepatic hepaticostomies.

A Kehr's tube was used in 97 cases (9%), but its routine use was stopped in 1993.

### *Radiological clinical follow-up*

Obviously, after 23 years' evolution the follow-up has changed, but it has always followed the same principles.

Generally, daily analyses are carried out during the first week post LT, every 48 h during the second week, and subsequently on a monthly basis until the sixth month.

If required by clinical criteria, any necessary analyses are added. Ultrasound scans are performed to assess blood vessel structures, the bile duct and liver parenchyma at the least 24 h after LT, during the first week, and after one, three and six months. Subsequently, this procedure is then performed every 6 months, depending on the patient's evolution. Since 1998, the routine follow-up has included a magnetic resonance cholangiogram, which is carried out in the first month after LT. If the ultrasound scan leads to the clinical suspicion of BC, the study is completed with cholangiography (in the beginning with ERPC or PTC, and with MRC since 1998).

The diagnosis and management of all patients suspected of BC are discussed by the multidisciplinary LT committee. The results of the MRC are correlated with the patient's clinical evolution and analyses to confirm the diagnosis and consider the treatment. Likewise, comparing these results with those of basal MRC or intraoperative cholangiography makes it possible to confirm the diagnosis.

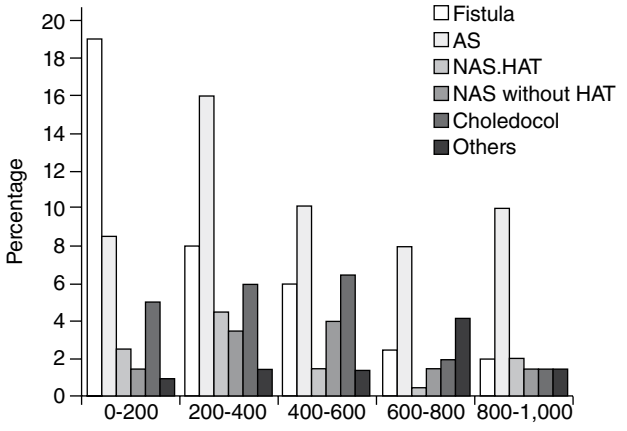


**Figure 1 – Evolution in the incidence of the different types of BC. Groups/200LT. AS indicates anastomotic stricture; Choledocol., choledocolithiasis; HAT, hepatic arterial thrombosis; NAS, non-anastomotic stricture.**

In accordance with the clinical radiology findings, the BC were classified as[9]: biliary fistula (discharge of bile by drainage placed in the hepatic hilum, or the appearance of a biloma), anastomotic stricture (AS: defined as a focal stricture at the level of the anastomosis), non-anastomotic stricture (NAS: long hilar stricture and/or intrahepatic strictures with/without signs of biliary necrosis and/or biloma with/without associated arterial thrombosis), choledocolithiasis, and other complications (biliary cast, Oddi sphincter dysfunction, etc.).

## Results

A total of 289 BC were diagnosed in 227 LT. Therefore, 23% of the patients had one or more BC. The incidence of BC fell from 29% for the first 200 LT to 16% in the last 200 LT. This reduction is mainly due to a significant decrease in the frequency of biliary fistulas, while the incidence of AS and NAS has remained fairly stable over time (Figure 1). There were 76 cases of biliary fistulas, 106 cases of AS, 46 cases of NAS (22 with hepatic artery thrombosis-HAT- and 24 without thrombosis), 42 choledocolithiases, and 19 other complications.

The characteristics of the patients and donors are shown in Table 1.

Overall, having a BC had no influence on survival (P=.25) (Figure 2A). However, depending on the type of BC, and in particular in the case of NAS, differences were seen in long-term survival (P=.03) (Figure 2B).

The management and evolution of each type of BC is described individually below.

1) *Biliary fistula* (Figure 3): most of the cases were resolved spontaneously, maintaining drainage, or using ultrasound-guided percutaneous drainage. In 8 patients with a biliary fistula associated with peritonitis, surgical treatment was indicated for drainage; in 17 cases temporary catheterization of the bile duct was performed by means of radiological drainage (ERPC or PTC). Of the 51 patients initially managed

**Table 1 – Characteristics of the patients**

| | Fistula (n=76) | AS (n=106) | NAS (HAT) (n=22) | NAS (no HAT) (n=24) | Choledocol. (n=42) |
|---|---|---|---|---|---|
| Mean age, years | 52±13 | 53±11 | 45±14 | 55±9 | 55±9 |
| Sex (M/F), n | 50/26 | 83/23 | 18/4 | 14/10 | 34/8 |
| Indication,[a] n | 19/23/16/10/8 | 25/30/28/13/10 | 6/6/5/1/4 | 7/7/4/6/0 | 14/10/11/7 |
| Donor age, years | 40±18 | 50±17 | 45±18 | 55 ±10 | 45±16 |
| Isquemia time, min | 500±180 | 478±168 | 544±171 | 408±87 | 495±184 |
| Surgery time, min | 450±115 | 431±118 | 475±162 | 408±87 | 417±99 |
| Anastomosis,[b] n | 53/7/16 | 91/8/6 | 18/2/2 | 21/2/1 | 36/3/3 |
| Kehr tube, n (%) | 22 (29) | 6 (6) | 1 (4) | 0 | 2 (5) |
| Month of diagnosis | 0.4±0.8 | 17±24 | 20±34 | 17±37 | 43±42 |

AS indicates anastomotic stricture; Choledocol., choledocolithiasis; F, female; HAT, hepatic arterial thrombosis; M, male; NAS, non-anastomotic stricture.
[a]Viral, HCCA, alcohol, retransplant, others.
[b]Hepatico-hepaticostomy/hepaticojejunostomy/others.

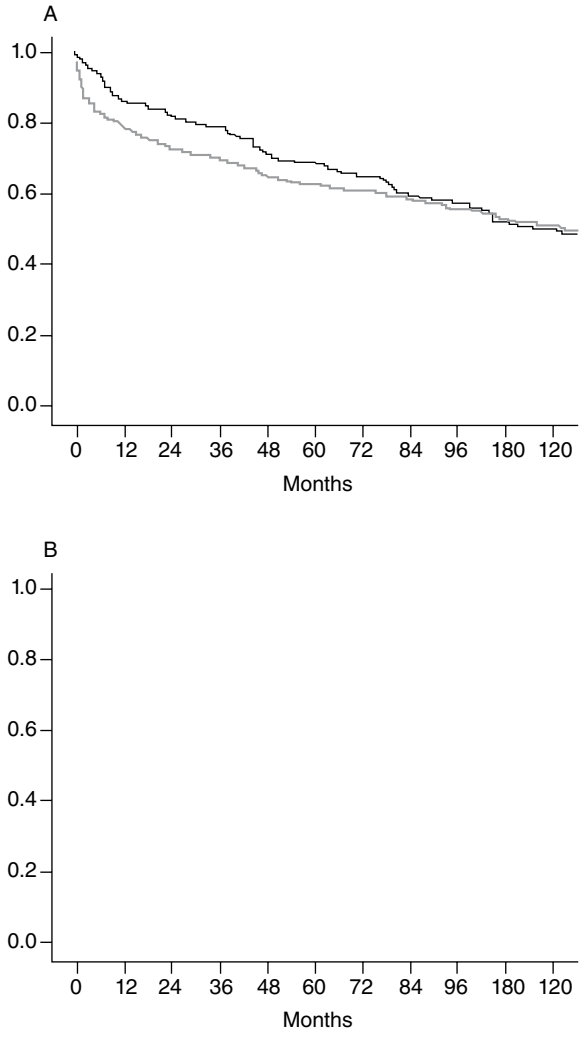


**Figure 2 – A) Actuarial survival comparing patients with/without BC. - - - - - - Patients with BC (n=227); ——patients without BC (n=773). B) Actuarial survival comparing patients according to the type of BC. — — — Fistula (n=76); — — anastomotic stricture (n=106); —— non-anastomotic stricture with HAT (n=22); - - - - - without HAT (n=24); ····· choledocolithiasis (n=42); ····· others (n=19).**

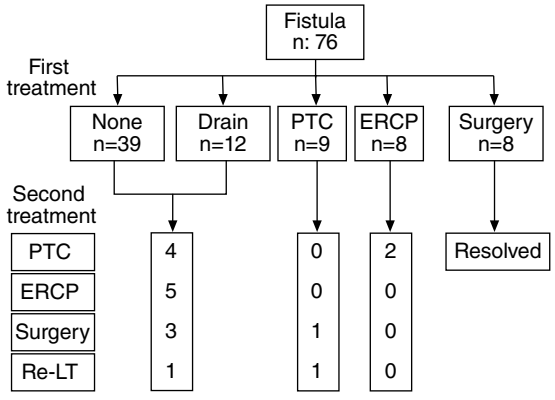


**Figure 3 – Treatment of biliary fistulas.**

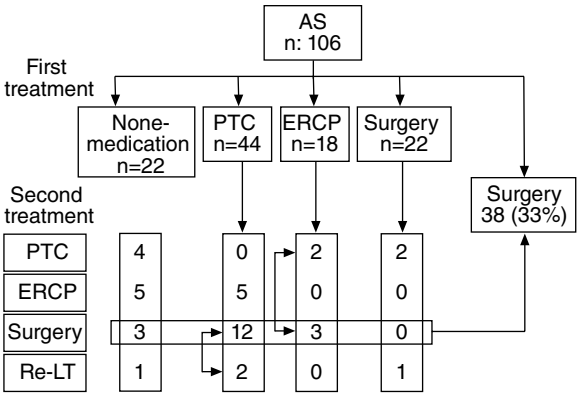


**Figure 4 – Treatment of anastomotic strictures (AS).**

with conservative treatment, 13 (20%) required further treatment due to this failing. On the other hand, of the 76 patients with biliary fistulas, 18 (25%) were diagnosed with AS during the follow-up (the management of the AS is described below). In most of the patients the biliary fistulas were resolved after 1.3±1.6 procedures (median: 1), with a complication rate of 9%. Finally, 7 patients (9%) died of causes related to the biliary fistula.

2) *Anastomotic stricture (AS)* (Figure 4): initially, 22 asymptomatic patients were treated with medication (ursodeoxycholic acid), as a chance diagnosis was made during routine radiological tests, but they had no symptoms or alterations in their analyses. However, 13 of these patients (60%) required some kind of treatment during their evolution. Nine were treated with radiology (ERCP or PTC), in 3 cases hepaticojejunostomy was carried out, and 1 required retransplantation.

   Of the 84 patients with symptomatic AS, 62 were treated with radiology (ERCP or PTC). Of this group, 7 required some other kind of radiological procedure at a later time, while 15 needed surgical treatment after radiology was not successful. In the end, 2 patients were retransplanted. After the initial diagnosis, 22 patients were operated on straight away, with no previous radiological treatment. Therefore, overall, the AS of 38 patients (33%) was resolved by means of surgical treatment, in 18 of these after a previous attempt at radiological treatment.

   The resolution of AS required a mean of 2.5±1.7 procedures (range: 1-7; median: 2).

   Despite the groups probably not being comparable, no differences were observed between patients treated initially by means of radiology or surgery with regard to the type of anastomoses performed, the use of Kher tubes, or the moment of diagnosis (early or late) (Table 2). The patients who were initially given radiological treatment required more procedures, and were thus admitted to hospital more often, compared to those who were initially treated by means of surgery. The morbidity and mortality related to BC were slightly higher in the group treated initially with radiology (Table 2).

3) *Non-anastomotic stricture (NAS):* the patients with NAS were analyzed separately, depending on whether the NAS was associated or not with thrombosis of the hepatic artery. Of the 22 patients with NAS with arterial thrombosis,

**Table 2 – Characteristics and evolution of the AS depending on the initial treatment**

| | Surgery (n=22) | Radiological (n=62) | P |
|---|---|---|---|
| Early/late, n | 9/13 | 18/44 | .30 |
| Anastomosis, n | 18/0/4 | 51/4/7 | .59 |
| Kehr tube, n | 2 | 1 | .46 |
| Procedures | 1.7±1.4 | 2,9±1,5 | .003 |
| Admissions | 1.5±1.3 | 2.8±1.4 | .002 |
| Complications (%) | 4 (18) | 20 (32) | .2 |
| Associated mortality, % | 0 | 8 (11) | .23 |

Early: before 6 months after transplant; late: over 6 months after transplant; anastomosis: hepatico-hepaticostomy/hepaticojejunostomy/others.
AS indicates anastomotic stricture.

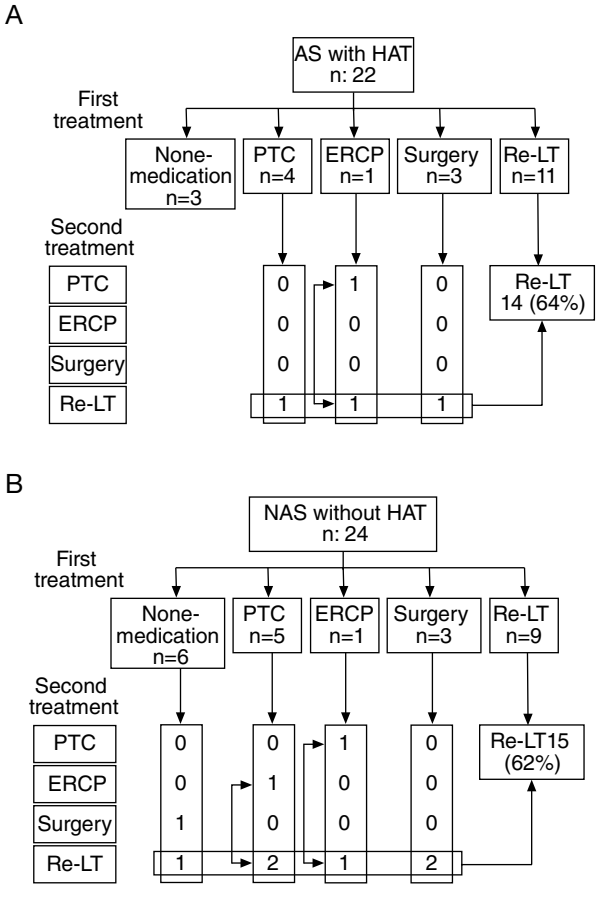


**Figure 5 – A) Treatment of non-anastomotic strictures (NAS) with hepatic arterial thrombosis (HAT). B) Treatment of non-anastomotic strictures (NAS) without hepatic arterial thrombosis (HAT). AS indicates anastomotic strictures.**

3 received no treatment; one was asymptomatic, and 2 were considered unsuitable for retransplantation due to their comorbidities. Four were diagnosed early (less than 30 days). Eight patients received radiological or surgical treatment due to localized NAS; 3 of these went on to develop more diffuse strictures and in the end underwent retransplantation. In most cases, retransplantation was indicated as the initial measure, without other previous treatment. Therefore, in the end, 14 patients (64%) with NAS with arterial thrombosis underwent retransplantation. Four of the 14 retransplant patients were diagnosed during the first month after their transplant. Two patients (9%) died of causes related to the BC (these were the 2 patients who did not undergo retransplantation).

Four of the 24 patients with NAS without arterial thrombosis were diagnosed early (before 30 days after the transplant). Of the 24 patients with NAS without arterial thrombosis, 6 were not treated initially, but one underwent retransplantation and another was treated by means of a hepaticojejunostomy because of a localized NAS (Figure 5B). Nine patients were initially given radiological or surgical treatment; one was asymptomatic at the time of diagnosis and is still alive after 24 months of follow-up. However, 6 patients finally required a retransplant. In most cases, retransplantation was recommended as the initial treatment, with no other previous procedure. Therefore, in the end, 15 patients (62%) with NAS without arterial thrombosis underwent retransplantation. Two of the 4 patients with NAS without early arterial thrombosis died after retransplantation.

4) Six patients (25%) died of causes related to the BC (2 after retransplants, 1 of sepsis after PTC, and 3 due to cholangitis related to untreated BC).
5) *Choledocolithiasis* (Figure 6): Most of the cases of choledocolithiasis were resolved with ERCP, except 8 who were treated with PTC. A small group of 6 patients who remained asymptomatic were only given treatment with medication (ursodeoxycholic acid). 4 cases were treated with hepaticojejunostomy, 3 initially and 1 after radiological treatment failed.

A mean of 2 procedures were necessary to resolve the cases of choledocolithiasis, with few complications (0.5±0.7; range 0-2). Only 2 patients (4.8%) died of causes related to the BC (biliary sepsis).

## Discussion

BC is considered the Achilles' heel of LT.[8-10] Although there tended to be a decrease in their incidence during the 80s, current series still show an incidence of 20%-25%.

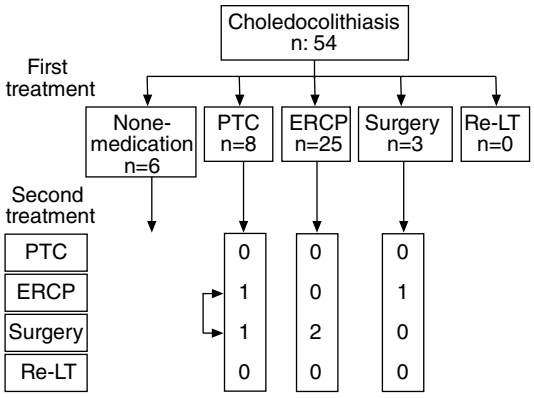


**Figure 6 – Treatment of choledocolithiasis (n=49).**

Our centre started to perform LT in 1984, and by February 2007 1000 had been carried out. This study assesses the incidence of BC and their management in this broad series of patients. As in previous series, incidence remains around 20%. There has been a small decrease in the incidence of BC, particularly thanks to the reduced number of biliary fistulas. Technical factors are known to have the most influence on biliary fistulas (surgical technique, anastomotic tension, etc.); advances in the technique and increased experience have made it possible to have a current incidence of biliary fistula of 2% (4 cases in the last 200 LT). Kehr tubes stopped being used in our centre in 1993, with no influence in the incidence of biliary fistulas or anastomotic strictures. Recent randomized studies have shown that their use on a routine basis provides no benefits.[11,12]

From our experience, the incidence of AS and NAS have remained stable over the years. AS are mainly due to technical factors, but as with NAS, immunological and ischemic factors also have an influence.[13-15] Recently, factors related to bile cytotoxicity have been proposed as being involved in the pathogenesis of NAS.[16] The strategies used over the years to standardize surgical techniques, maintain the correct vascularization of the ends of the bile duct, standardize extraction and perfusion techniques, and reduce ischemia times as much as possible have not improved our results. Refinements in organ preservation techniques may play a role in the pathogenesis of AS and NAS,[17,18] but further clinical trials are necessary to confirm its actual influence.

### *Management of biliary complications*

Once it was observed that the incidence of BC has remained stable, the main aim of our study was to assess their management. There is no controversy related to the management of biliary fistulas and choledocolithiasis.

1) *Biliary fistulas:* biliary fistulas are the most common complication in the immediate post-op period. Their diagnosis is usually based on the bilious appearance of the fluid from the drain that we routinely leave during LT. Their management consists of keeping the surgical drain in place until the resolution of the fistula, or the placement of a percutaneous drain. From our experience, very few patients require surgery for a poorly drained biloma, and in some initial cases it is associated with ERCP. It is worth pointing out that 25% of the patients with a biliary fistula which closed spontaneously had an AS during their evolution, probably secondary to the scarring process produced in the resolution of the fistula.
2) *Choledocolithiasis:* regarding choledocolithiliasis, the diagnosis is usually made later. It is usually resolved with ERPC,[19,20] but it is common for more than one procedure to be required. The role played by ursodeoxycholic acid in the prevention of the development of choledocolithiasis or relapse after LT has not been proven in randomized studies.
3) *Anastomotic stricture:* no consensus has been reached in the literature about the management of AS. Recent advances in endoscopic techniques and interventional radiology have led to the non-surgical management of AS in many centres.[5,19,21,22] However, the way endoscopic and radiological techniques or surgical treatment is applied highly divers among medical centres. As Davidson et al[23] suggest, the initial results of non-surgical treatment, as well as the availability of each treatment modality and the experience with them, could have influenced their application and results in each hospital. On the other hand, there are no prospective randomized studies comparing the results of surgical and endoscopic or radiological treatment in the management of AS after LT. Overall, non-surgical management has 2 theoretical drawbacks: first, the possible related morbidity; second, the possibility of failure and/or relapse which has been described as being as high as 20%-30%.[7,22,24,25] The only prospective observational study published to date[21] studied the results of a standardized endoscopic therapy for treating AS. After analyzing all the complications related to ERPC, Holt et al[21] concluded that although endoscopic treatment is safe and well-tolerated, there is an accumulated risk which is relevant after 3-4 procedures. In fact, they emphasize the importance of offering surgical treatment as an alternative, despite the efficacy of non-surgical treatment.

Our experience is similar. The patients treated with non-surgical procedures (ERPC or PTC) required a mean of 2.9 procedures, with an accumulated morbidity of 30% and a failure rate of 30%. However, the patients given surgical treatment from the outset had no related mortality and morbidity was low. However, it is important to remember that this is not a randomized study, and the 2 groups of patients are probably not comparable. In our hospital, surgery is indicated to treat AS providing the patient has conserved liver function, and has no comorbidity which is a contraindication for surgery, and with bile cast associated with the stricture. Although the groups are not comparable, the low morbidity associated with hepaticojejunostomies must be highlighted. It has been suggested that morbidity associated with hepaticojejunostomy in patients whose previous surgical treatment has not been successful is similar to that of patients in which surgery is indicated from the beginning.[23] However, the possibility of morbidity

after ultrasound and/or radiological procedures must be taken into account, especially considering that both of these procedures result in an increased risk of bactibilia. Therefore, we consider that with cases with little possibility of being resolved with non-surgical procedures, it is better to treat the patients with surgery without prior manipulation. In our opinion, these are cases of AS with associated lithiasis or bile cast. The type of stricture, the moment of diagnosis, hepatic function, and especially the association or not of bile casts are aspects to be taken into account when deciding how to treat AS.[24] Another aspect to be mentioned is the high percentage of radiological treatment (PTC) performed compared with endoscopic treatment (ERCP) in our centre. This is only a consequence of local availability and the experience of the interventional radiology team. In general, the results of radiological treatment are similar to those obtained with endoscopic treatment.[21]

To be more specific, in our current treatment algorithm, in cases of AS, if the patient has no comorbidity and has bile casts associated with the stricture or a stricture too near to the biliary bifurcation (<1 cm), surgery is the first choice treatment. In patients with a short stricture not associated with a bile cast which is over 1 cm from the bifurcation, endoscopic dilation and stent placement is attempted. If this is not possible, does not provide a resolution or the patient relapses after 2 sessions of dilation+stent, surgical treatment is indicated. When there is an underlying pathology which is a contraindication to surgery or makes it difficult, prosthesis placement via PTC or ERCP is the treatment of choice.

4) *Non-anastomotic strictures:* the second large group of BC analyzed and for which there is controversy over the treatment are NAS. Conservative treatment has not obtained good results,[14] thus, Koneru et al[8] suggest that clinical doctors should not insist too much on treating patients with NAS with conservative radiology instead of retransplantation. Likewise, in our opinion, once there is a clear diagnosis of NAS, radiological and/or endoscopic treatment only increase the possibility of bactibilia, and with it cholangitis. The real value of radiological/endoscopic treatment in the evolution of NAS has not been proven. It does not seem to slow down its evolution or reduce the need for retransplantation. Therefore, we recommend retransplantation in all symptomatic NAS cases (clinical symptoms or analyses), except in selected cases of hilar NAS in which the radiological and/or surgical (hepaticojejunostomy) treatment can be assessed.[26] In all cases of diffuse NAS,[26] once contraindications for retransplantation are ruled out, we try not to manipulate the bile duct to avoid septic complications, and we recommend retransplantation. Thus, with this approach we have performed retransplants on 29 of 46 patients with NAS (63%). Post-transplant mortality was low, but it should be highlighted that in both cases the NAS was diagnosed early (less than one month post-op).

In conclusion, from our experience, surgical treatment still has an important role to play in the management of post-transplant BC, particularly in AS. Radiological/endoscopic treatment can not be considered to be the standard of care for all cases across the board; the management of each patient and their BC must be considered on an individual basis. In the treatment of NAS, retransplantation without prior radiological manipulation provides good results.

## Conflict of interest

The authors affirm that they have no conflicts of interest.

## Acknowledgements

We would like to thank Raquel Lastra for her help with the collection of data.

REFERENCES

1. Verdonk RC, Buis CI, Porte RJ, Haagsma EB. Biliary complications after liver transplantation: a review. Scand J Gastroenterol. 2006;41:89-101.
2. Pascher A, Neuhaus P. Biliary complications after deceased-donor orthotopic liver transplantation. J Hepatobiliary Pancreat Surg. 2006;13:487-96.
3. Sharma S, Gurakar A, Jabbour N. Biliary strictures following liver transplantation: past, present and preventive strategies. Liver Transpl. 2008;14:759-69.
4. Grief F, Bronsther OL, Van Thiel DH, Casavilla A, Iwatsuki S, Tzakis A, et al. The incidence, timing and management of biliary tract complications after orthotopic liver transplantation. Ann Surg. 1994;219:40-5.
5. Verdonk RC, Buis CI, Porte RJ, Van der Jagt E, Limburg AJ, Van den Ber AP, et al. Anastomotic biliary strictures after liver transplantation: causes and consequences. Liver Transpl. 2006;12:726-35.
6. Zoepf T, Maldonado-Lopez EJ, Hilgard P, Dechene A, Malago M, Broelsch CE, et al. Balloon dilatation vs balloon dilatation plus bile duct endoprosteses for treatment of anastomotic biliary strictures after liver transplantation. Liver Transpl. 2006;12:88-94.
7. Lee SH, Ryu JK, Woo SM, Park JK, Yoo JW, Kim YT, et al. Optimal interventional treatment and long-term outcomes for biliary stricture after liver transplantation. Clin Transpl. 2008;22:484-93.
8. Koneru B, Sterling MJ, Bahramipour PF. Bile duct strictures after liver transplantation: a changing landscape of the Achilles' heel. Liver Transpl. 2006;12:702-4.
9. Valls C, Alba E, Cruz M, Figueras J, Andia E, Sanchez A, et al. Biliary complications after liver transplantation: diagnosis with MR cholangiopancreatography. AJR. 2005;184:812-20.
10. Putnam CW, Beart RW, Bell RM, Starzl TE. "The Achilles' heel of liver transplantation is bile duct reconstruction" Hepatic Transplantation, 1975. Postgrad Med J. 1976;52:104-8.
11. Scatton O, Meunier B, Cherqui D, Boillot O, Sauvenet A, Boudjema K, et al. Randomized trial of choledochocholedocostomy with or without a T tube in orthotopic liver transplantation. Ann Surg. 2001;233:432-7.
12. Amador A, Charco R, Martí J, Navasa M, Rimola A, Calatayud D, et al. Clinical trial on the cost-effectiveness of T-tube use in an established deceased donor liver transplantation program. Clin Transpl. 2007;21:548-53.

13. Verdonk RC, Buis CI, Van der Jagt E, Gouw ASH, Limburg AJ, Sloof MJH, et al. Nonanastomotic biliary strictures after liver transplantation, Part 2: Management, outcome, and risks factors disease progression. Liver Transpl. 2007;13:725-32.
14. Guichelaar MM, Benson JT, Malinchoc M, Krom RA, Wiesner RH, Charlton MR. Risk factors for and clinical course of non-anastomotic biliary strictures after liver transplantation. Am J Transplant. 2003;3:885-90.
15. Buis CI, Hoekstra H, Verdonk RC, Porte RJ. Causes and consequences of ischemic-type biliary lesions after liver transplantation. J Hepatobiliary Pancreat Surg. 2006;13: 517-24.
16. Buis CI, Geuken E, Visser DS, Kuipers F, Haagsma EB, Verkade HJ, et al. Altered bile composition after liver transplantation is associated with the development of nonanastomotic biliary strictures. J Hepatol. 2009;50:69-79.
17. Yska MJ, Buis CI, Monbaliu D, Schuurs TA, Gouw AS, Kahmann ON, et al. The role of bile salt toxicity in the pathogenesis of bile duct injury after non-heart-beating porcine liver transplantation. Transplantation. 2008;85:1625-31.
18. Hertl M, Harvey PR, Swanson PE, West DD, Howard TK, Shenoy S, et al. Evidence of preservation injury to bile ducts by bile salts in the pig and its prevention by infusions of hydrophilic salts. Hepatology. 1995;21:1130-7.
19. Solmi L, Cariani G, Miracolo A, Nigro G, Roda E. Results of endoscopic retrograde cholangiopancreatography in the treatment of biliary tract complications after orthotopic liver transplantation: our experience. Hepatogastroenterology. 2007;54:1004-8.
20. Holt AP, Thorburn D, Mirza D, Gunson B, Wong T, Haydon G. A prospective study of standardized nonsurgical therapy in the management of biliary anastomotic strictures complicating liver transplantation. Transplantation. 2007;84:857-63.
21. Pasha SF, Harrison ME, Das A, Nguyen CC, Vargas HE, Balan V, et al. Evolving treatment of biliary strictures following liver transplantation. Gastrointest Endosc. 2007;66:44-51.
22. Davidson BR, Rai R, Nandy A, Doctor N, Burroughs A, Rolles K. Results of choledocojejunostomy in the treatment of biliary complications after liver transplantation in the era of nonsurgical therapies. Liver Transpl. 2000;6:201-6.
23. Alazmi WM, Fogel EL, Watkins JL, MvHenry L, Tector JA, Fridell J, et al. Recurrence rate of anastomotic biliary strictures in patients who have had previous successful endoscopic therapy for anastomotic narrowing after orthotopic liver transplantation. Endoscopy. 2006;38:571-4.
24. Gradiadei IW, Schwaighofer H, Koch R, Nachbaur K, Koenigsraimer A, Margreiter R, et al. Long-term outcome of endoscopic treatment of biliary strictures after liver transplantation. Liver Transpl. 2006;12:718-25.
25. Lee HW, Suh KS, Shin WY, Cho EM, Yi NJ, Lee JM, et al. Classification and prognosis of intrahepatic biliary stricture after liver transplantation. Liver Transpl. 2007;13:1736-42.