Transplant International

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Biliary reconstruction, its complications and management of biliary complications after adult liver transplantation: a systematic review of the incidence, risk factors and outcome

Nobuhisa Akamatsu,[1,2] Yasuhiko Sugawara[2] and Daijo Hashimoto[1]

1 Department of Hepato-biliary-pancreatic Surgery, Saitama Medical Center, Saitama Medical University, Saitama, Japan

2 Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, Tokyo, Japan

Keywords

biliary leakage, biliary stricture, risk factor, systematic review, T-tube.

Correspondence

Yasuhiko Suagwara, Department of Surgery, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Tel.: 81-3-3815-5411; fax: 81-3-5684-3989; e-mail: yasusuga-tky@umin.net

Conflicts of Interest

The authors have declared 'no conflicts of interest'.

Received: 14 August 2010

Revision requested: 7 October 2010

Accepted: 12 November 2010

Published online: 10 December 2010

doi:10.1111/j.1432-2277.2010.01202.x

Summary

Biliary reconstruction remains common in postoperative complications after liver transplantation. A systematic search was conducted on the PubMed database and 61 studies of retrospective or prospective institutional data were eligible for this review. The study comprised a total of 14 359 liver transplantations. The overall incidence of biliary stricture was 13%; 12% among deceased donor liver transplantation (DDLT) patients and 19% among living donor liver transplantation (LDLT) recipients. The overall incidence of biliary leakage was 8.2%, 7.8% among DDLT patients and 9.5% among LDLT recipients. An endoscopic strategy is the first choice for biliary complications; 83% of patients with biliary stricture were treated by endoscopic modalities with a success rate of 57% and 38% of patients with leakage were indicated for endoscopic biliary drainage. T-tube placement was not performed in 82% of duct-to-duct reconstruction. The incidence of biliary stricture was 10% with a T-tube and 13% without a T-tube and the incidence of leakage was 5% with a T-tube and 6% without a T-tube. A preceding bile leak and LDLT procedure are accepted risk factors for anastomotic stricture. Biliary complications remain common, which requires further investigation and the refinement of reconstruction techniques and management strategies.

Introduction

Biliary complications are considered the technical 'Achilles heel' of liver transplantation because of their high frequency, the need for long-term, repeated treatment and the potential detrimental effects on graft and patient survival. In early reports, morbidity rates up to 50% and related mortality rates up to 25–30% were reported [1–5]. Recent improvements in organ selection, preservation, immunosuppression and standardization of the methods of biliary reconstruction, however, have contributed to dramatically reduce the incidence of this complications [6–9]. Biliary reconstruction nevertheless remains the most common site of postoperative complications in liver transplantation. In this sense, it is critical to summarize and validate recent studies addressing biliary complications in an effort to understand and reduce these complications.

Biliary stricture and leakage are common complications. Ischaemic-type biliary lesions, sphincter of Oddi dysfunction, haemobilia and biliary obstruction by cystic duct mucoceles, stones, sludge, or casts are also observed [9]. These complications include a variety of contributing factors, including the reconstruction technique, use of biliary splintage, type of liver transplant procedure, organ preservation, chronic rejection, hepatic arterial thrombosis and other recipient and donor characteristics. Among these, strictures related to anastomotic procedures coupled with leakage in association with the reconstruction technique are the most common and also the most controversial in the recent literature.

Another topic in biliary complication after liver transplantation is the management strategy. Although surgical revision used to be the standard treatment [5,10,11], nonoperative management of biliary complications has become the standard practice over the last two decades, using endoscopic techniques as the preferred diagnostic and therapeutic modalities and obviating the need for surgery in a majority of patients [7,9,12,13].

Here we reviewed the literature focusing on biliary complications related to biliary reconstruction to systematically describe the reported incidence. An additional aim was to demonstrate the different treatment modalities for biliary complications and their outcomes and to update and summarize the associated risk factors for biliary complications.

Materials and methods

Basically, the present study was conducted along with the guideline proposed by Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group [14].

Search strategy

A systematic search was conducted on the PubMed database, provided by the National Center for Biotechnology Information, US National Library of Medicine, by one of the authors (A.N.). The search terms were; ([biliary complication] OR [biliary complications] AND [liver transplantation]), ([biliary stricture] OR [biliary stenosis] AND [liver transplantation]) and ([biliary leakage] AND [liver transplantation]). References of the identified studies were also searched to identify further studies.

Inclusion and exclusion criteria

All studies published between 1990 and 2009, limited to the English language and humans, were considered for this review. We included only papers addressing biliary complications after adult liver transplantation. Articles dealing with transplant cases before 1990 were excluded because of the advances in organ preservation, perioperative management, immunosuppression and recipient selection, which have had a great impact on the incidence of biliary complications and survival after liver transplantation. Papers of an undefined transplant period, an inclusion period outside the range of the abovementioned study periods, reporting biliary problems without the discrimination of nonanastomotic origin and reporting treatment outcome of biliary complications without background clarification or overall incidence of biliary complications were excluded. Case reports, review articles, or studies describing fewer than 30 transplants were also excluded from the study. Papers describing nonanastomotic stricture, split-liver transplant, pediatric population and adults and children together without discrimination were also excluded from the study.

The key variables included were as follows; number of recipients receiving a liver transplantation, type of population described [deceased donor whole liver transplantation (DDLT), living donor liver transplantation (LDLT), or both], biliary reconstruction strategy, incidence and/or day of detection of biliary stricture or biliary leakage, documented treatment modalities and outcomes after those treatment modalities, retransplantation rates and assessment of possible risk factors. The identified variables derived from the selected publications were entered into a database for subsequent statistical analysis. Considering the critical differences of the graft type and the surgical technique, papers dealing with DDLT and those dealing with LDLT were summarized and analysed separately and in addition, comparison between DDLT and LDLT groups was performed for each variable.

Definitions

Biliary stricture was defined as a segmental narrowing around the biliary anastomosis or splintage tube insertion demonstrated by endoscopic retrograde cholangiography, percutaneous transhepatic cholangiography, or intraoperative direct confirmation. Patients with nonanastomotic strictures or ischaemic-type biliary lesions (documented as secondary to hepatic artery thrombosis or stenosis, reperfusion injury, recurrence of primary sclerosing cholangitis, acute/chronic rejection, cytomegalovirus infection, or ABO incompatible transplantation) were excluded from the analysis.

Biliary leakage was diagnosed on the basis of a bile leak through abdominal drains or a significant intra-abdominal collection of bile requiring ultrasound or radiological guided puncture. Alternatively, the leakage was proven by endoscopic retrograde cholangiography or X-ray cholangiography via splinting tubes.

Statistical analysis

Continuous values are expressed as means ± standard deviation. Statistical analysis was performed using SPSS (Chicago, IL, USA) 15.0 for Windows. Categorical variables were analysed by chi-square test or Fisher's exact test, as appropriate. Continuous variables were analysed by Student's *t*-test or the Mann–Whitney test, as appropriate. A *P*-value of <0.05 was considered statistically significant.

Results

After the systematic search, 61 studies were eligible for review [15–75]. Figure 1 shows the number of excluded studies with the reasons for the exclusion. Only studies describing retrospective or prospective institutional data with or without controls were found. Cross-references of the identified studies did not reveal any further papers.

The studies included in this systematic review comprised 61 papers, including 41 DDLT populations and 21 LDLT populations (one paper included both DDLT and LDLT population, which were analysed separately) and 14 359 liver transplantations, including 11 547 DDLT patients and 2812 LDLT patients. All variables retrieved from this review are summarized in Table 1.

Biliary reconstruction was performed in a duct-to-duct (DD) manner in the majority of patients (88%) in both DDLT and LDLT populations, whereas bilioenterostomy [choledochojejunostomy (CJ) or hepaticojejunostomy (HJ)] was more frequently adopted in LDLT patients (31%) than in DDLT patients (8%, $P < 0.0001$).

Biliary stricture

Incidence

All 14 359 transplant patients were analysed for biliary stricture in this systematic review, of which 1844 cases were complicated with biliary stricture. The mean overall incidence of biliary stricture was 12.8%. The onset of biliary stricture ranged widely, from 7 days to 11 years after transplantation.

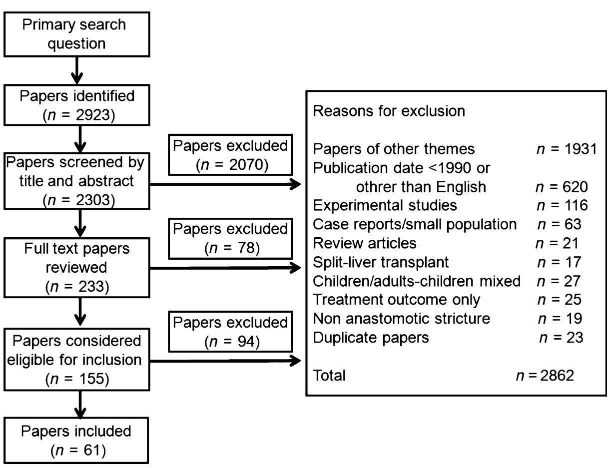

Figure 1 Search process and number of studies excluded with the reasons for exclusion.

The incidence of biliary stricture was 12% (1314/11 547) among DDLT patients, whereas it was 19% (530/2812) among LDLT recipients, a significantly higher rate ($P < 0.0001$).

Management

The management of postliver transplant biliary strictures was divided into three modalities: endoscopic retrograde cholangiogram guided drainage (ERCD), percutaneous transhepatic biliary drainage (PTBD) and surgical revision including re-transplantation.

Pre-established strategies were clearly described in 1640 cases of 52 papers, 33 papers of DDLT and 19 papers of LDLT. ERCD and balloon dilation with or without stenting was the first choice of treatment for biliary stricture in the majority of institutes, comprising 58% (32/52) in this review and was indicated for 83% of patients (1367/1640). The success rate of ERCD treatment was 57% (776/1367). Mean attempted ERCD for cure was 3.5 ± 2.1 times.

On the other hand, 15% (8/52) and 4% (2/52) of institutes first adopted PTBD or surgical revision for treatment of biliary stricture, respectively, and the remaining 19% (10/52) chose the modality case by case without any pre-established policy. PTBD or surgical revision was chosen as the first choice more frequently in LDLT (42%) than in DDLT (3%) populations ($P = 0.0007$).

Finally, 98% cases of biliary stricture were salvaged by either single or combined strategies described above and 19 cases (1%) required re-transplantation and 21 cases (1%) were lost as a result of subsequent deterioration.

Biliary leakage

Incidence

A total of 55 papers, comprising 11 397 cases, documented postoperative biliary leakage. Of the 11 397 cases, 936 were complicated with biliary leakage. The mean incidence of biliary leakage was 8.2%. The onset of biliary leakage ranged from 1 day to 6 months after transplantation. The incidence was 7.8% (668/8585) among DDLT patients and 9.5% (268/2812) among LDLT recipients. The difference between the two groups was not significant.

Management

The management of biliary leakage was described in 46 papers, 27 DDLT papers and 19 LDLT papers. The treatment strategy was the same as that for stricture in every institute. Among 551 leakages with a clearly described treatment modality, ERCD, surgical revision, PTBD and observation were applied for 38%, 28%, 10% and 34% of the cases, respectively. No re-transplantation was

Table 1. Variables retrieved from this systematic review.

	Total	DDLT	LDLT
Papers included [15–75]	62	41	21
Transplantations	14 359	11 547	2812
Reconstruction			
Papers of DD only	36	30	6
CJ/HJ included	25	11	14
Papers of CJ/HJ only	1	0	1
Cases with DD reconstruction	12 579 (88)	10 624 (92)	1955 (70)
Cases with CJ/HJ reconstruction	1785 (12)	923 (8)	862 (31)*
Biliary stricture			
Papers included [15–75]	62	41	21
Transplantations	14 359	11 547	2812
Cases of biliary stricture	1844 (13)	1314 (12)	530 (19)†
Biliary leakage			
Papers included [15–24,27–39,42–44,47–52,54–75]	55	34	21
Transplantations	11 397	8585	2812
Cases of biliary leakage	936 (8)	668 (8)	268 (10)
Management of biliary stricture			
Papers included [14–28,30–33,35–37,39–41, 45–51,54–75]	52	33	19
Cases of stricture	1640	1110	530
Managed by ERCD	776	640	136
Managed by PTBD	600	410	190
Managed by Surgical revision	178	46	132
Re-transplantation	19	14	5
Mortality	21	12	9
Management of biliary leakage			
Papers included [15–24,27,28,30–33,35–37, 39, 47–51,54–65,67–71,73–75]	46	27	19
Cases of leakage	551	283	268
Managed by ERCD	207	167	40
Managed by PTBD	53	13	40
Managed by Surgical revision	157	56	101
Re-transplantation	0	0	0
Mortality	13	10	3

Values shown are *n* (%) except where otherwise stated.
DDLT, deceased donor liver transplantation; LDLT, living donor liver transplantation; DD, duct-to-duct anastomosis; CJ, choledochojejunostomy; HJ, hepaticojejunostomy; ERCD, endoscopic retrograde cholangiogram guided drainage; PTBD, percutaneous transhepatic biliary drainage.
P-values LDLT versus DDLT; $*P < 0.0001$, $\dagger P < 0.0001$.

required, but 13 cases (1%) were lost because of secondary sepsis.

T-tube and splinting of the biliary anastomosis

T-tube placement, which has been a source of major debate in DD reconstruction in DDLT, was not performed in the majority of recent DD reconstruction cases [82% (5126/6235) of cases, 41% of institutes never use T-tube or stent], based on studies reporting better or not impaired outcome of biliary complications of DD reconstruction without T-tube. Adding up cases of studies clarifying DD reconstruction with or without an indwelling T-tube [15–24,26,28–30,33,34,36–40,43, 44,47–50,52,54,55], the incidence of biliary stricture and biliary leakage was 9.7% (108/1109) and 4.7% (52/1109) with T-tube, whereas 12.5% (640/5126) and 6.3% (258/4126) without a T-tube, respectively. Studies comparing the biliary complications after DD reconstruction with and without a T-tube are summarized in Table 2. On the other hand, many institutes prefer to place splinting stents over DD reconstruction in LDLT (81%, 17/21).

Risk factors

Risk factors for the development of biliary stricture, biliary leakage, or both were retrieved from those studies, in

Table 2. Prospective and retrospective studies comparing biliary complications after liver transplantation with duct-to-duct reconstruction with a T-tube (T-tube) and without a T-tube (non T-tube).

Comparative studies: Author (Ref. no)	Stricture			Leakage			Biliary complications/total		
	T-tube	Non T-tube	*P*-value	T-tube	Non T-tube	*P*-value	T-tube	Non T-tube	*P*-value
Cons for T-tube									
Randall [18]	8/59 (14%)	7/51 (14%)	ns	5/59 (8%)*	0	<0.005	13/59 (22%)	7/51 (14%)	0.01
Scatton [28]*	3/90 (3%)	6/90 (7%)	ns	9/90 (10%)	2/90 (2%)	ns	30/90 (33%)	14/90 (15%)	<0.005
Amador [47]*	1/53 (2%)	3/54 (6%)	ns	20/53 (38%)	3/54 (6%)	ns	32/53 (60%)	6/54 (11%)	0.001
Wojcicki [54]	3/35 (9%)	2/49 (2%)	ns	6/35 (17%)	2/49 (4%)	ns	11/35 (31%)	4/49 (8%)	0.008
Equivocal results									
Vougas [17]*	2/30 (7%)	6/30 (20%)	ns	1/30 (3%)	0	ns	5/30 (10%)	6/30 (20%)	ns
Kusano [39]	16/63 (25%)	7/52 (13%)	ns	8/63 (14%)	4/52 (8%)	ns	24/63 (38%)	11/52 (21%)	ns
Pros for T-tube									
Rabkin [22]	7/124 (6%)	10/44 (23%)	<0.05	36/124 (29%)	1/44 (2%)	ns	43/124 (35%)	11/44 (25%)	ns
Nuno [21]*	1/50 (2%)	6/48 (13%)	ns	3/50 (6%)	8/48 (17%)	ns	5/50 (10%)	16/48 (33%)	0.01
Weiss [52]*	7/99 (7%)	8/95 (8%)	ns	5/99 (5%)	9/95 (9%)	ns	27/99 (27%)	50/95 (53%)	0.0005

ns, not statistically difference.
*Prospective randomized trials.

Table 3. Documented risk factors of biliary complications in deceased donor liver transplantation based on individual reports.

Risk factor	Versus	Analysed for	Number of cases (*n*)	Univariate analysis (*P*-value)	Multivariate analysis (*P*-value)	Ref. no.
Recipient factor						
Advanced recipient age		Both	291	0.03		23
Preoperative bilirubin level, mg/dl; 19.3 (0.94–72.5)	6.2 (0.23–56.8)	Both	241	0.003	<0.05	38
Preoperative PT-INR; 2.0 (1.0–10.0)	1.6 (1.0–10.0)	Both	241	0.04		38
High MELD score, mean (SD); 25 (7)	Low; 22 (6)	Leakage	256	0.02		44
Advanced recipient age, mean (SD); 50 (20)	Younger; 41 (11)	Leakage	256	0.005		44
Graft factor						
Female donor	Male donor	Stricture	531	0.02	0.01	40
Advanced donor age, mean (SD); 42 (16)	Younger; 32 (18)	Leakage	256	0.003		44
Macrovascular steatosis >25%	<25%	Both	117		0.002	50
Operative factor						
DD reconstruction	CJ reconstruction	Both	502	0.008	0.008	20
DD reconstruction	CJ reconstruction	Leakage	256	0.02		44
Splintage over anastomosis; yes	No	Both	241	0.02	<0.05	38
Splintage over anastomosis; no	Yes	Stricture	256	0.04	0.07	44
Longer warm ischaemia time, mean (SD) min; 49 (23)	Shorter; 42 (16)	Leakage	256	0.03	0.04	44
Use of UW solution	HTK solution	Stricture	256	0.014	0.005	44
Pressurization of epoprostenol added UW solution	UW solution	Stricture	403	0.0001		53
Flushing of donor bile duct; no	Yes	Stricture	403	0.00001		53
Intraoperative FFP transfusion, Units; 12 (1–48)	10 (0–66)	Both	241	0.03		38
Re-transplant	First transplant	Both	502	0.03		20
Transplant era; recent	Previous	Stricture	531	0.01	0.006	40
Postoperative factor						
Proceeding bile leakage; yes	No	Stricture	256	0.0001	0.001	44
Preceding bile leakage; yes	No	Stricture	531	0.006	0.001	40
Chronic rejection	Without chronic rejection	Both	502	0.0006	0.001	20
Rejection episode; yes	No	Stricture	403	0.03		53
ICU stay, days; shorter 2 (2–7)	Longer 4(2–8)	Stricture	531	0.02		40

PT-INR, prothrombin time-international normalized ratio; MELD, model for end-stage liver disease; DD, duct-to-duct anastomosis; CJ, choledochojejunostomy; HKT, histidine-tryptophan-ketoglutarate; UW, University of Wisconsin; FFP, fresh frozen plasma; ICU, intensive care unit.

Table 4. Documented risk factors of biliary complications in living donor liver transplantation based on individual reports.

Risk factor	Versus	Analysed for	Number of cases (*n*)	Univariate analysis (*P*-value)	Multivariate analysis (*P*-value)	Ref. no.
Recipient factor						
High MELD score; high ≥ 35	low < 35	Both	41	0.04	0.032	60
Advanced recipient age		Stricture	283	0.03	0.04	69
Graft factor						
Advanced donor age; 50<	≤50	Stricture	130	0.003	0.003	67
Graft type; right	left	Both	259	0.02		63
Graft type; right lateral sector graft	other types	Stricture	83	0.006		73
Bile duct diameter, mean (SD) mm; 2.8 (0.7)	4.5 (2.1)	Stricture	83	0.02		73
Bile duct diameter		Stricture	283	0.003	0.02	69
Bile duct multiplicity	Single	Stricture	239		0.02	74
Operative factor		Both				
DD reconstruction for duct <4 mm	Other reconstructions	Both	259	0.02		63
DD reconstruction	HJ reconstruction	Stricture	310	0.0009		71
DD reconstruction	HJ reconstruction	Stricture	321	<0.01		62
HJ reconstruction	DD reconstruction	Leakage	321	<0.01		62
Reconstructions other than single DD anastomosis	Single DD anastomosis	Leakage	156	0.03	0.01	72
Conventional biliary anastomosis	Microsurgical anastomosis	Both	88	<0.05		70
Longer cold ischemia time, min	Shorter	Stricture	283	<0.001	0.001	69
Longer warm ischemia time, mean (range) min; 56 (37–76)	Shorter; 48 (30–76)	Both	90	0.02		61
Use of UW solution	HTK solution	Stricture	283	0.001		69
Postoperative factor						
Preceding bile leakage; yes	no	Stricture	80	0.0001	0.001	68
Preceding bile leakage; yes	no	Stricture	156	0.006	0.01	72
Preceding bile leakage; yes	no	Stricture	239		0.002	74
Preceding bile leakage; yes	no	Stricture	130	0.002	0.002	67
Preceding bile leakage; yes	no	Stricture	283	<0.001	0.001	69
Basiliximab-based immunosuppression; No	yes	Stricture	80	0.04		68
Basiliximab based immunosuppression; no	yes	Leakage	80	0.03	0.005	68
Higher serum creatinine at POD5		Leakage	156	0.05		72
CMV infection; yes	no	Both	321	<0.01		62
Hepatic artery thrombosis; yes	no	Stricture	239		0.002	74
Hepatic artery thrombosis; yes	no	Both	321	<0.01		62

MELD, model for end-stage liver disease; DD, duct-to-duct anastomosis; HJ, hepaticojejunostomy; HKT, histidine-tryptophan-ketoglutarate; UW, University of Wisconsin; FFP, fresh frozen plasma; CMV, cytomegalovirus.

which a significant contributing factor was described. These risk factors are categorized in Tables 3 and 4.

Discussion

Biliary reconstruction

The choice of biliary reconstruction is likely influenced by multiple factors, such as underlying liver disease, graft type (partial or whole size), size of donor and recipient bile ducts and prior transplant or other biliary surgery. DD reconstruction and CJ/HJ with a Roux-en-Y loop are the two most fundamental biliary reconstruction methods. According to some early studies of DDLT, biliary complications are more frequent after CJ reconstruction than after DD reconstruction [5,16,76], whereas some LDLT studies indicate that DD reconstruction is a significant risk factor for developing biliary complications [63,71,74].

In the present review, a DD reconstruction was the procedure of choice in most institutions (73%) and in most cases (92%) in DDLT populations, whereas many institutes (71%) still adopted bilioenterostomy for considerable number of cases (31%) in LDLT populations (Table 1).

The benefits of DD reconstruction include preservation of a physiological bilioenteric continuity and the sphincter of Oddi, less frequent colonization of the biliary tract, shorter operative time, fewer anastomoses [5,77] and the availability of endoscopic treatment as a salvage option if biliary complications develop [7,13]. Roux-en-Y bilioenterostomy is currently used only under specific conditions, such as gross disparity between the sizes of the ducts and diseased or unavailable ducts and for revision surgery in DDLT [9,78–83]. It will be the same with LDLT populations in near future.

Biliary stricture

Anastomotic biliary strictures were among the most common complications of a liver transplant and in the early days affected up to a third of patients with high mortality [3–5,10]. Recent advances, however, have dramatically decreased their incidence, which was 12.8% in the present study. Although anastomotic biliary stricture can present at any time after transplantation as noted in the present study, the majority seem to present within 1 year with a mean interval of the time of presentation of 5–8 months after transplantation [5,12,33,37,84–86].

As pointed out in previous reports [42,55,87], the incidence of biliary stricture is higher in LDLT than in DDLT, which used to be explained by devascularization of the bile duct at the hilar dissection of the graft, bile leakage from cut surface, which causes fibrotic change around the anastomosis and technically challenging biliary reconstruction (e.g., small-size ducts, multiple ducts). In this review, five LDLT studies [67–69,72,74] demonstrated bile leakage as a significant risk factor for subsequent stricture, whereas three studies [69,73,74] evaluated size and multiplicity of bile duct as a risk factor. Actually, our systematic review revealed a significantly higher incidence of biliary stricture (19%) in LDLT.

Although we focused on anastomotic stricture in this review and excluded cases of documented nonanastomotic stricture to the greatest possible extent, a limitation of this study was that still some nonanastomotic cases might have been included. Anastomotic and nonanastomotic stricture should strictly be analysed separately in future articles concerning biliary complications after transplantation.

The management of anastomotic stricture has dramatically improved over the last two decades. There has been an exponential transition in the primary management of anastomotic strictures from predominantly surgical management to primarily endoscopic treatment. Although a percutaneous transhepatic approach still has a critical role in cases with Roux-en-Y reconstructions [12,88], surgical revision is now reserved for patients who have failed those interventional treatments and retransplantation is the final option when all others fail [7,9–13,25]. Indeed, 67% of DDLT institutes and 58% of all institutes have adopted ERCD as the primary treatment for anastomotic stricture with the overall success rate of 57% in this review. The success rate of ERCD varied from 40% to 92% in our review, yet a recent aggressive endoscopic approach has achieved an 80–90% success rate [89–92]. Recurrent anastomotic strictures after ERCD develop in approximately 20% of patients and can still be effectively treated by interventional dilation and/or stenting [25,93,94]. A significantly high proportion of institutes continue to utilize surgical revision or a percutaneous approach as the primary option in LDLT in this review (42%, $P = 0.0007$), which might be due in part to the high rate of bilioenterostomy in LDLT and the reported inferior success rate of ERCD for anastomotic stricture in an LDLT population compared with that of a DDLT population [68,86,95–97]. With the increase in DD reconstruction and technical refinement of ERCD in LDLT, however, an endoscopic approach is the first choice in the majority of institutes.

The major drawbacks of endoscopic dilation with placement of one or more stents as the standard management of anastomotic strictures are the need for multiple procedures repeated over extended periods of time and the risk of associated complications such as cholangitis and pancreatitis [13,84–86] but these seem minimal when compared with the risks of emergent revision surgery [7,9,12,13,25,98].

Biliary leakage

Biliary leakage is the second most common complication after transplantation. The incidence of biliary leakage was 8.2% in this study, without a statistical difference between DDLT (7.8%) and LDLT (9.5%). There are three different entities in biliary leakage: leakage from anastomotic site, leakage from the cut surface of the partial graft and leakage after T-tube removal. Some of the studies in our review clarified the leakage origin but others did not and we strongly propose that future studies will discriminate the types of leakage.

The majority of biliary leakages could be managed conservatively with indwelling abdominal drains, splinting bile drains, or percutaneous radiology-guided drainage, as 34% of cases in the present study were cured without aggressive treatment. When treatment for biliary leakage is necessary, an endoscopic approach including sphincterectomy and stenting or nasobiliary drainage emerged as the preferred treatment option for every type of leakage, restricting surgery to patients with frank peritonitis and/or major leaks [7,27,99–102], as was the case with strictures. In the present survey, endoscopic treatment was applied to one half of the leakages requiring intervention.

Use of T-tube

There is ongoing debate regarding the use of a T-tube for DD reconstruction in DDLT. T-tube drainage in DD reconstruction in DDLT is traditionally performed for the following reasons; it provides easy access to the biliary tree, lowers the pressure in the biliary system, aids in monitoring the quality and output of bile and might reduce the incidence of anastomotic stricture [9,103]. Some authors have demonstrated the advantages of an indwelling T-tube [21,22,52], however, along with the accumulation of retrospective and prospective papers describing safe, efficacious, cost-effective, or at least a not-impaired outcome without T-tube placement (Table 2) and in other papers [104–106], a growing number of centres have abandoned T-tube in DD reconstruction, resulting in 41% of centres with a non-T-tube policy and consequently 82% of DD reconstruction cases in the present study were performed without a T-tube.

The major limitation of T-tube placement is biliary leakage after its removal, which is reported to occur in 5–33% of cases [16,100–102,107–109]. The aggregate calculation of the present study, however, revealed an comparable incidence of biliary leakage (4.7% vs. 6.3%) with and without a T-tube, while the incidence of biliary stricture tended to be higher in the non-T-tube group (9.7% vs. 12.5%). These findings seems to be consistent with the most recent study of a well-conducted meta-analysis of five randomized controlled studies [17,21,28,47,52] by Riediger *et al.* [110]. They concluded that biliary reconstruction with a T-tube prevents the occurrence of biliary strictures and that may have the potential to reduce long-term morbidity with respect to late stricture, while there is no clear evidence in favour of using a T-tube during DDLT in terms of overall biliary complications.

In addition, according to some authors, biliary decompression with a splinting tube may be more indicated in DD reconstruction with a partial-liver graft transplant, where it may reduce the risk of both cut surface and anastomotic biliary leaks [9,87,96,111,112]. Actually, 81% of centres in this review routinely utilized splinting tubes in LDLT. The efficacy of this procedure has not yet been validated in a prospective randomized study.

Risk factors

A variety of factors related to the recipient, graft, operative procedure and postoperative course are associated with anastomotic biliary stricture and biliary leakage, as summarized in Tables 3 and 4. Among the preoperative recipient factors, advanced recipient age and recipients with more impaired liver function seem to be at risk of developing biliary complications [23,38,44,60,69].

Graft and operative risk factors should be discussed separately for DDLT and LDLT because of the essential differences in the graft nature and operative procedures. LDLT itself is a significant risk factor for biliary complications, both according to the present study and previous literature [42,55,87]. Some reports [69,73,74] demonstrated that a small duct size and the presence of multiple duct orifices are risk factors for the development of biliary complications. Other postulated factors such as the devascularization of the bile duct at the hilar dissection of the graft might contribute to a higher incidence in LDLT [113–115]. We believe that these entities are interlinked and a large number of cases may be required to determine the statistical significance. An indwelling T-tube is a matter of debate, as discussed above [17,18,21,22,28,39,47,52,54] Other operative factors, including ischaemia-reperfusion injury with prolonged warm/cold ischaemic time and difference in the preservation methods/solutions had been reported as risk factors [44,53,61,69], but according to recent reports, those factors seem to be more associated with ischaemic-type, nonanastomotic strictures than with anastomotic complications, which is preferred to be dealt as a distinct entity [116–123]. At the same time, eliminating these factors might contribute to reduce anastomotic strictures [124].

Among postoperative factors, biliary leakage has emerged as one of the most important factors in the causation of the biliary stricture [40,44,67–69,72,74]. Other documented factors, hepatic artery thrombosis [62,74,125–127], ABO incompatibility [128,129], cytomegalovirus infection [62,130,131] and chronic/acute rejection episodes [20,53,132,133] are reported to be possible risk factors for biliary complications in historical studies. Yet, these factors are relatively minimized in contemporary series as viral prophylaxis has improved; and events such as ABO incompatibility and hepatic artery thrombosis are infrequent. Moreover, recent perceptions are that these factors are strongly associated with ischaemic-type, nonanastomotic strictures rather than anastomotic complications [116,117,124].

Publication bias is an issue for all systematic reviews. In general, this bias exists when studies report only positive or substantial differences. It is possible that we inadvertently omitted selecting studies containing valuable data. The language bias might have also affected our conclusions because we limited this review to reports published in the English language. Most importantly, considering our strategy combining observational studies, heterogeneity of populations, study designs and outcomes is the critical limitation of this study. Yet, we believe that updating and summarizing recent published observational studies might be of value for the future management of biliary reconstruction and its complications.

This review revealed some problems that might have interfered with the systematic analysis of biliary complications. First, although we excluded cases of nonanastomotic biliary complications to the greatest possible extent, the

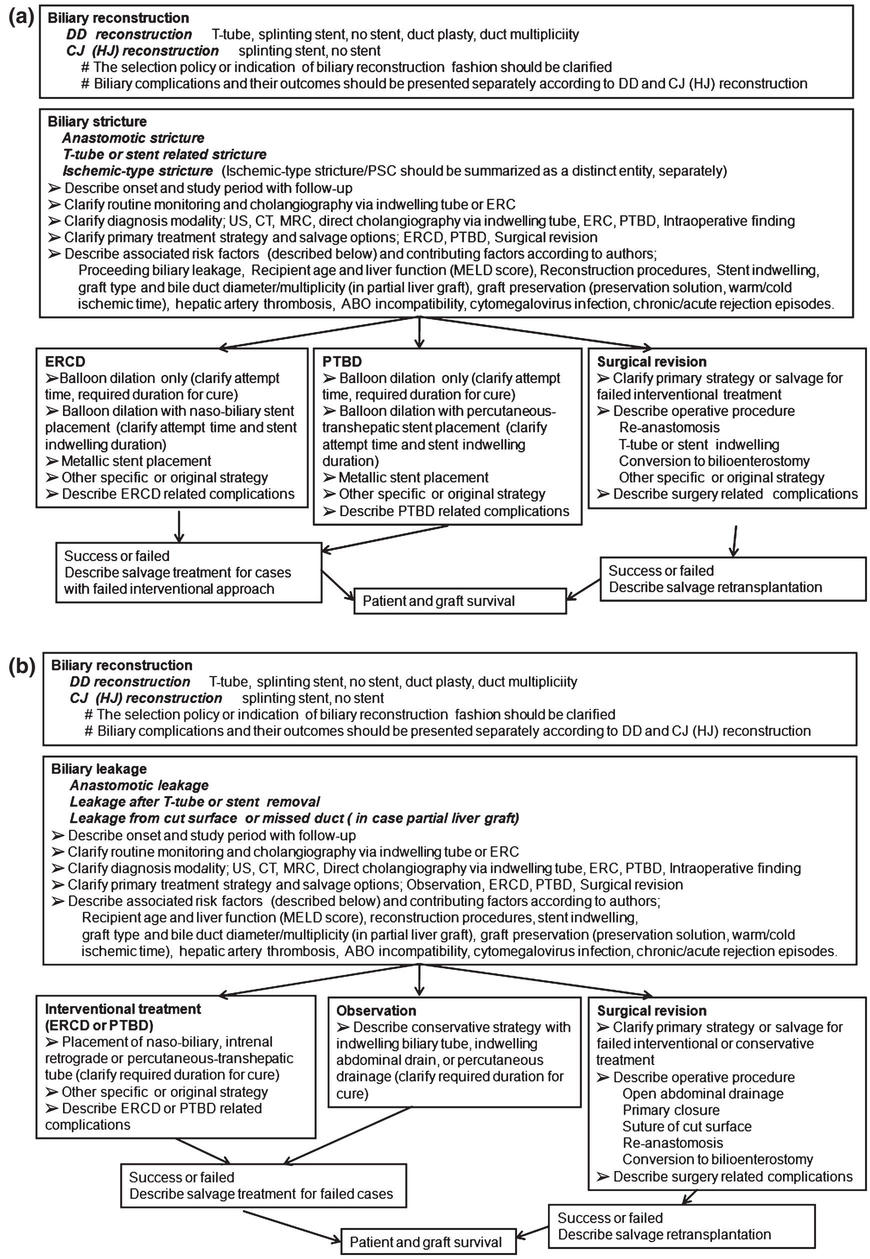

Figure 2 Guidelines for future studies reporting biliary stricture (a) and biliary leakage (b). CJ, choledochojejunostomy; DD, duct-to-duct anastomosis; HJ, hepaticojejunostomy; PSC, primary sclerosing cholangitis; ERC, endoscopic retrograde cholangiography; US, ultrasonography; CT, computed tomography; MRC, magnetic resonance cholangiography; ERCD, endoscopic retrograde cholangiogram guided drainage; PTBD, percutaneous transhepatic biliary drainage; MELD, model for end-stage liver disease.

present study might still include such cases to some extent. Second, the type of leakage was not clarified in some studies: from anastomotic site, after T-tube removal, or from cut surface. Third, stricture or leakage proved by cholangiography via a splinting tube may bias the results when inclusively analysed with cases using a no-tube strategy. Fourth, many centres did not describe the follow-up program and treatment strategy for biliary complications. Based on these revealed problems and in order to permit reliable comparisons of studies on biliary complications, we advocate guidelines for future studies reporting on this topic (Fig. 2).

Conclusions

In conclusion anastomotic stricture and leakage contribute significantly to morbidity after liver transplantation; but with advances in both operative and therapeutic modalities, these complications have become better controlled.

With the growing number of centres adopting DD biliary reconstruction, endoscopic treatment has become the standard strategy for biliary complications after transplantation with satisfactory results.

This systematic review revealed that biliary complications remain a common source of morbidity, which requires further technical refinement and established management strategy.

Authorship

YS and DH designed research/study. NA performed study, collected and analysed data and wrote the paper.

Funding

None to be disclosed.

Acknowledgements

The authors thank Dr H. Yasunaga who performed critical review of statistical analysis of this study.

References

1. Williams R, Smith M, Shilkin KB, Herbertson B, Joysey V, Calne RY. Liver transplantation in man: the frequency of rejection, biliary tract complications, and recurrence of malignancy based on an analysis of 26 cases. *Gastroenterology* 1973; **64**: 1026.
2. Calne RY, McMaster P, Portmann B, Wall WJ, Williams R. Observations on preservation, bile drainage and rejection in 64 human orthotopic liver allografts. *Ann Surg* 1977; **186**: 282.
3. Evans RA, Raby ND, O'Grady JG, *et al.* Biliary complications following orthotopic liver transplantation. *Clin Radiol* 1990; **41**: 190.
4. Starzl TE, Putnam CW, Hansbrough JF, Porter KA, Reid HA. Biliary complications after liver transplantation: with special reference to the biliary cast syndrome and techniques of secondary duct repair. *Surgery* 1977; **81**: 212.
5. Greif F, Bronsther OL, Van Thiel DH, *et al.* The incidence, timing, and management of biliary tract complications after orthotopic liver transplantation. *Ann Surg* 1994; **219**: 40.
6. Testa G, Malagò M, Broelseh CE. Complications of biliary tract in liver transplantation. *World J Surg* 2001; **25**: 1296.
7. Thuluvath PJ, Pfau PR, Kimmey MB, Ginsberg GG. Biliary complications after liver transplantation: the role of endoscopy. *Endoscopy* 2005; **37**: 857.
8. Pascher A, Neuhaus P. Biliary complications after deceased-donor orthotopic liver transplantation. *J Hepatobiliary Pancreat Surg* 2006; **13**: 487.
9. Wojcicki M, Milkiewicz P, Silva M. Biliary tract complications after liver transplantation: a review. *Dig Surg* 2008; **25**: 245.
10. Lerut J, Gordon RD, Iwatsuki S, *et al.* Biliary tract complications in human orthotopic liver transplantation. *Transplantation* 1987; **43**: 47.
11. Lopez RR, Benner KG, Ivancev K, Keeffe EB, Deveney CW, Pinson CW. Management of biliary complications after liver transplantation. *Am J Surg* 1992; **163**: 519.
12. Sharma S, Gurakar A, Jabbour N. Biliary strictures following liver transplantation: past, present and preventive strategies. *Liver Transpl* 2008; **14**: 759.
13. Williams ED, Draganov PV. Endoscopic management of biliary strictures after liver transplantation. *World J Gastroenterol* 2009; **15**: 3725.
14. Stroup DF, Berlin JA, Morton SC, *et al.* Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; **283**: 2008.
15. Neuhaus P, Blumhardt G, Bechstein WO, Steffen R, Platz KP, Keck H. Technique and results of biliary reconstruction using side-to-side choledochocholedochostomy in 300 orthotopic liver transplants. *Ann Surg* 1994; **219**: 426.
16. O'Connor TP, Lewis WD, Jenkins RL. Biliary tract complications after liver transplantation. *Arch Surg* 1995; **130**: 312.
17. Vougas V, Rela M, Gane E, *et al.* A prospective randomised trial of bile duct reconstruction at liver transplantation: T tube or no T tube? *Transpl Int* 1996; **9**: 392.
18. Randall HB, Wachs ME, Somberg KA, *et al.* The use of the T tube after orthotopic liver transplantation. *Transplantation* 1996; **61**: 258.
19. Hintze RE, Adler A, Veltzke W, Abou-Rebyeh H, Felix R, Neuhaus P. Endoscopic management of biliary complications after orthotopic liver transplantation. *Hepatogastroenterology* 1997; **44**: 258.
20. Verran DJ, Asfar SK, Ghent CN, Grant DR, Wall WJ. Biliary reconstruction without T tubes or stents in liver transplantation: report of 502 consecutive cases. *Liver Transpl Surg* 1997; **3**: 365.
21. Nuño J, Vicente E, Turrión VS, *et al.* Biliary tract reconstruction after liver transplantation: with or without T-tube? *Transplant Proc* 1997; **29**: 564.
22. Rabkin JM, Orloff SL, Reed MH, *et al.* Biliary tract complications of side-to-side without T tube versus end-to-end with or without T tube choledochocholedochostomy in liver transplant recipients. *Transplantation* 1998; **65**: 193.
23. Sawyer RG, Punch JD. Incidence and management of biliary complications after 291 liver transplants following the introduction of transcystic stenting. *Transplantation* 1998; **66**: 1201.
24. Davidson BR, Rai R, Kurzawinski TR, *et al.* Prospective randomized trial of end-to-end versus side-to-side biliary reconstruction after orthotopic liver transplantation. *Br J Surg* 1999; **86**: 447.
25. Davidson BR, Rai R, Nandy A, Doctor N, Burroughs A, Rolles K. Results of choledochojejunostomy in the treatment of biliary complications after liver transplantation in

the era of nonsurgical therapies. *Liver Transpl* 2000; **6**: 201.
26. Mosca S, Militerno G, Guardascione MA, Amitrano L, Picciotto FP, Cuomo O. Late biliary tract complications after orthotopic liver transplantation: diagnostic and therapeutic role of endoscopic retrograde cholangiopancreatography. *J Gastroenterol Hepatol* 2000; **15**: 654.
27. Pfau PR, Kochman ML, Lewis JD, *et al.* Endoscopic management of postoperative biliary complications in orthotopic liver transplantation. *Gastrointest Endosc* 2000; **52**: 55.
28. Scatton O, Meunier B, Cherqui D, *et al.* Randomized trial of choledochocholedochostomy with or without a T tube in orthotopic liver transplantation. *Ann Surg* 2001; **233**: 432.
29. Abouljoud MS, Escobar F, Douzdjian V, Moonka D, Shick L, Brown KA. Successful strategy for reducing biliary complications after liver transplantation. *Transplant Proc* 2001; **33**: 2714.
30. Němec P, Ondrásek J, Studeník P, Hökl J, Cerný J. Biliary complications in liver transplantation. *Ann Transplant* 2001; **6**: 24.
31. Gómez R, Moreno E, Castellón C, González-Pinto I, Loinaz C, García I. Choledochocholedochostomy conversion to hepaticojejunostomy due to biliary obstruction in liver transplantation. *World J Surg* 2001; **25**: 1308.
32. Shah SR, Dooley J, Agarwal R, *et al.* Routine endoscopic retrograde cholangiography in the detection of early biliary complications after liver transplantation. *Liver Transpl* 2002; **8**: 491.
33. Rerknimitr R, Sherman S, Fogel EL, *et al.* Biliary tract complications after orthotopic liver transplantation with choledochocholedochostomy anastomosis: endoscopic findings and results of therapy. *Gastrointest Endosc* 2002; **55**: 224.
34. Barkun JS, Tzimas GN, Cantarovich M, *et al.* Do biliary endoprostheses decrease biliary complications after liver transplantation? *Transplant Proc* 2003; **35**: 2435.
35. Patkowski W, Nyckowski P, Zieniewicz K, *et al.* Biliary tract complications following liver transplantation. *Transplant Proc* 2003; **35**: 2316.
36. Thuluvath PJ, Atassi T, Lee J. An endoscopic approach to biliary complications following orthotopic liver transplantation. *Liver Int* 2003; **23**: 156.
37. Thethy S, Thomson BN, Pleass H, *et al.* Management of biliary tract complications after orthotopic liver transplantation. *Clin Transplant* 2004; **18**: 647.
38. Qian YB, Liu CL, Lo CM, Fan ST. Risk factors for biliary complications after liver transplantation. *Arch Surg* 2004; **139**: 1101.
39. Kusano T, Randall HB, Roberts JP, Ascher NL. The use of stents for duct-to-duct anastomoses of biliary reconstruction in orthotopic liver transplantation. *Hepatogastroenterology* 2005; **52**: 695.
40. Verdonk RC, Buis CI, Porte RJ, *et al.* Anastomotic biliary strictures after liver transplantation: causes and consequences. *Liver Transpl* 2006; **12**: 726.
41. Vandenbroucke F, Plasse M, Dagenais M, Lapointe R, Lêtourneau R, Roy A. Treatment of post liver transplantation bile duct stricture with self-expandable metallic stent. *HPB (Oxford)* 2006; **8**: 202.
42. Liu CL, Fan ST, Lo CM, *et al.* Operative outcomes of adult-to-adult right lobe live donor liver transplantation: a comparative study with cadaveric whole-graft liver transplantation in a single centre. *Ann Surg* 2006; **243**: 404.
43. Alsharabi A, Zieniewicz K, Michałowicz B, *et al.* Biliary complications in relation to the technique of biliary reconstruction in adult liver transplant recipients. *Transplant Proc* 2007; **39**: 2785.
44. Welling TH, Heidt DG, Englesbe MJ, *et al.* Biliary complications following liver transplantation in the model for end-stage liver disease era: effect of donor, recipient, and technical factors. *Liver Transpl* 2008; **14**: 73.
45. 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.
46. Pasha SF, Harrison ME, Das A, *et al.* Endoscopic treatment of anastomotic biliary strictures after deceased donor liver transplantation: outcomes after maximal stent therapy. *Gastrointest Endosc* 2007; **66**: 44.
47. Amador A, Charco R, Martí J, *et al.* Clinical trial on the cost-effectiveness of T-tube use in an established deceased donor liver transplantation program. *Clin Transplant* 2007; **21**: 548.
48. Buczkowski AK, Schaeffer DF, Kim PT, *et al.* Spatulated end-to-end bile duct reconstruction in orthotopic liver transplantation. *Clin Transplant* 2007; **21**: 7.
49. Castaldo ET, Pinson CW, Feurer ID, *et al.* Continuous versus interrupted suture for end-to-end biliary anastomosis during liver transplantation gives equal results. *Liver Transpl* 2007; **13**: 234.
50. Baccarani U, Isola M, Adani GL, *et al.* Steatosis of the hepatic graft as a risk factor for post-transplant biliary complications. *Clin Transplant* 2010; **24**: 631.
51. Sanna C, Saracco GM, Reggio D, *et al.* Endoscopic retrograde cholangiopancreatography in patients with biliary complications after orthotopic liver transplantation: outcomes and complications. *Transplant Proc* 2009; **41**: 1319.
52. Weiss S, Schmidt SC, Ulrich F, *et al.* Biliary reconstruction using a side-to-side choledochocholedochostomy with or without T-tube in deceased donor liver transplantation: a prospective randomized trial. *Ann Surg* 2009; **250**: 766.
53. Pirenne J, Monbaliu D, Aerts R, *et al.* Biliary strictures after liver transplantation: risk factors and prevention by

donor treatment with epoprostenol. *Transplant Proc* 2009; **41**: 3399.
54. Wojcicki M, Lubikowski J, Klek R, *et al.* Reduction of biliary complication rate using continuous suture and no biliary drainage for duct-to-duct anastomosis in whole-organ liver transplantation. *Transplant Proc* 2009; **41**: 3126.
55. Gómez CM, Dumonceau JM, Marcolongo M, *et al.* Endoscopic management of biliary complications after adult living-donor versus deceased-donor liver transplantation. *Transplantation* 2009; **88**: 1280.
56. Fan ST, Lo CM, Liu CL, Tso WK, Wong J. Biliary reconstruction and complications of right lobe live donor liver transplantation. *Ann Surg* 2002; **236**: 676.
57. Fondevila C, Ghobrial RM, Fuster J, Bombuy E, García-Valdecasas JC, Busuttil RW. Biliary complications after adult living donor liver transplantation. *Transplant Proc* 2003; **35**: 1902.
58. Settmacher U, Steinmüller TH, Schmidt SC, *et al.* Technique of bile duct reconstruction and management of biliary complications in right lobe living donor liver transplantation. *Clin Transplant* 2003; **17**: 37.
59. Gondolesi GE, Varotti G, Florman SS, *et al.* Biliary complications in 96 consecutive right lobe living donor transplant recipients. *Transplantation* 2004; **77**: 1842.
60. Liu CL, Lo CM, Chan SC, Fan ST. Safety of duct-to-duct biliary reconstruction in right-lobe live-donor liver transplantation without biliary drainage. *Transplantation* 2004; **77**: 726.
61. Zoepf T, Maldonado-Lopez EJ, Hilgard P, *et al.* Endoscopic therapy of posttransplant biliary stenoses after right-sided adult living donor liver transplantation. *Clin Gastroenterol Hepatol* 2005; **3**: 1144.
62. Kasahara M, Egawa H, Takada Y, *et al.* Biliary reconstruction in right lobe living-donor liver transplantation: comparison of different techniques in 321 recipients. *Ann Surg* 2006; **243**: 559.
63. Hwang S, Lee SG, Sung KB, *et al.* Long-term incidence, risk factors, and management of biliary complications after adult living donor liver transplantation. *Liver Transpl* 2006; **12**: 831.
64. Ramacciato G, Varotti G, Quintini C, *et al.* Impact of biliary complications in right lobe living donor liver transplantation. *Transpl Int* 2006; **19**: 122.
65. Giacomoni A, Lauterio A, Slim AO, *et al.* Biliary complications after living donor adult liver transplantation. *Transpl Int* 2006; **19**: 466.
66. Mita A, Hashikura Y, Masuda Y, *et al.* Nonsurgical policy for treatment of bilioenteric anastomotic stricture after living donor liver transplantation. *Transpl Int* 2008; **21**: 320.
67. Shah SA, Grant DR, McGilvray ID, *et al.* Biliary strictures in 130 consecutive right lobe living donor liver transplant recipients: results of a Western center. *Am J Transplant* 2007; **7**: 161.
68. Tashiro H, Itamoto T, Sasaki T, *et al.* Biliary complications after duct-to-duct biliary reconstruction in living-donor liver transplantation: causes and treatment. *World J Surg* 2007; **31**: 2222.
69. Park JB, Kwon CH, Choi GS, *et al.* Prolonged cold ischemic time is a risk factor for biliary strictures in duct-to-duct biliary reconstruction in living donor liver transplantation. *Transplantation* 2008; **86**: 1536.
70. Lin TS, Concejero AM, Chen CL, *et al.* Routine microsurgical biliary reconstruction decreases early anastomotic complications in living donor liver transplantation. *Liver Transpl* 2009; **15**: 1766.
71. Kyoden Y, Tamura S, Sugawara Y, *et al.* Incidence and management of biliary complications after adult-to-adult living donor liver transplantation. *Clin Transplant* 2010; **24**: 535.
72. Melcher ML, Pomposelli JJ, Verbesey JE, *et al.* Comparison of biliary complications in adult living-donor liver transplants performed at two busy transplant centers. *Clin Transplant* 2010; **24**: E137.
73. Marubashi S, Dono K, Nagano H, *et al.* Biliary reconstruction in living donor liver transplantation: technical invention and risk factor analysis for anastomotic stricture. *Transplantation* 2009; **88**: 1123.
74. Seo JK, Ryu JK, Lee SH, *et al.* Endoscopic treatment for biliary stricture after adult living donor liver transplantation. *Liver Transpl* 2009; **15**: 369.
75. Marsh JW, Gray E, Ness R, Starzl TE. Complications of right lobe living donor liver transplantation. *J Hepatol* 2009; **51**: 715.
76. Colonna JO II, Shaked A, Gomes AS, *et al.* Biliary strictures complicating liver transplantation. Incidence, pathogenesis, management, and outcome. *Ann Surg* 1992; **216**: 344.
77. Sung JY, Costerton JW, Shaffer EA. Defense system in the biliary tract against bacterial infection. *Dig Dis Sci* 1992; **37**: 689.
78. Hiatt JR, Quinones-Baldrich WJ, Ramming KP, Brems J, Busuttil RW. Operations upon the biliary tract during transplantation of the liver. *Surg Gynecol Obstet* 1987; **165**: 89.
79. Vallera RA, Cotton PB, Clavien PA. Biliary reconstruction for liver transplantation and management of biliary complications: overview and survey of current practices in the United States. *Liver Transpl Surg* 1995; **1**: 143.
80. Welsh FK, Wigmore SJ. Roux-en-Y Choledochojejunostomy is the method of choice for biliary reconstruction in liver transplantation for primary sclerosing cholangitis. *Transplantation* 2004; **77**: 602.
81. Feith MP, Klompmaker IJ, Maring JK, *et al.* Biliary reconstruction during liver transplantation in patients with primary sclerosing cholangitis. *Transplant Proc* 1997; **29**: 560.
82. Heffron TG, Smallwood GA, Ramcharan T, *et al.* Duct-to-duct biliary anastomosis for patients with sclerosing cholangitis undergoing liver transplantation. *Transplant Proc* 2003; **35**: 3006.

83. Moser MA, Wall WJ. Management of biliary problems after liver transplantation. *Liver Transpl* 2001; **7**: S46.
84. Graziadei IW, Schwaighofer H, Koch R, *et al.* Long-term outcome of endoscopic treatment of biliary strictures after liver transplantation. *Liver Transpl* 2006; **12**: 718.
85. Bourgeois N, Deviére J, Yeaton P, *et al.* Diagnostic and therapeutic endoscopic retrograde cholangiography after liver transplantation. *Gastrointest Endosc* 1995; **42**: 527.
86. Park JS, Kim MH, Lee SK, *et al.* Efficacy of endoscopic and percutaneous treatments for biliary complications after cadaveric and living donor liver transplantation. *Gastrointest Endosc* 2003; **57**: 78.
87. Freise CE, Gillespie BW, Koffron AJ, *et al.* Recipient morbidity after living and deceased donor liver transplantation: findings from the A2ALL Retrospective Cohort Study. *Am J Transplant* 2008; **8**: 2569.
88. Sung RS, Campbell DA Jr, Rudich SM, *et al.* Long-term follow-up of percutaneous transhepatic balloon cholangioplasty in the management of biliary strictures after liver transplantation. *Transplantation* 2004; **77**: 110.
89. Morelli G, Fazel A, Judah J, Pan JJ, Forsmark C, Draganov P. Rapid-sequence endoscopic management of posttransplant anastomotic biliary strictures. *Gastrointest Endosc* 2008; **67**: 879.
90. Morelli J, Mulcahy HE, Willner IR, Cunningham JT, Draganov P. Long-term outcomes for patients with postliver transplant anastomotic biliary strictures treated by endoscopic stent placement. *Gastrointest Endosc* 2003; **58**: 374.
91. Mahajan A, Ho H, Sauer B, *et al.* Temporary placement of fully covered self-expandable metal stents in benign biliary strictures: midterm evaluation (with video). *Gastrointest Endosc* 2009; **70**: 303.
92. Costamagna G, Pandolfi M, Mutignani M, Spada C, Perri V. Long-term results of endoscopic management of postoperative bile duct strictures with increasing numbers of stents. *Gastrointest Endosc* 2001; **54**: 162.
93. Porayko MK, Kondo M, Steers JL. Liver transplantation: late complications of the biliary tract and their management. *Semin Liver Dis* 1995; **15**: 139.
94. Alazmi WM, Fogel EL, Watkins JL, *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.
95. Tsujino T, Isayama H, Sugawara Y, *et al.* Endoscopic management of biliary complications after adult living donor liver transplantation. *Am J Gastroenterol* 2006; **101**: 2230.
96. Yazumi S, Yoshimoto T, Hisatsune H, *et al.* Endoscopic treatment of biliary complications after right-lobe living-donor liver transplantation with duct-to-duct biliary anastomosis. *J Hepatobiliary Pancreat Surg* 2006; **13**: 502.
97. Shah JN, Ahmad NA, Shetty K, *et al.* Endoscopic management of biliary complications after adult living donor liver transplantation. *Am J Gastroenterol* 2004; **99**: 1291.
98. Kuo PC, Lewis WD, Stokes K, Pleskow D, Simpson MA, Jenkins RL. A comparison of operation, endoscopic retrograde cholangiopancreatography, and percutaneous transhepatic cholangiography in biliary complications after hepatic transplantation. *J Am Coll Surg* 1994; **179**: 177.
99. Sheng R, Sammon JK, Zajko AB, Campbell WL. Bile leak after hepatic transplantation: cholangiographic features, prevalence, and clinical outcome. *Radiology* 1994; **192**: 413.
100. Saab S, Martin P, Soliman GY, *et al.* Endoscopic management of biliary leaks after T-tube removal in liver transplant recipients: nasobiliary drainage versus biliary stenting. *Liver Transpl* 2000; **6**: 627.
101. Osorio RW, Freise CE, Stock PG, *et al.* Nonoperative management of biliary leaks after orthotopic liver transplantation. *Transplantation* 1993; **55**: 1074.
102. Johnston TD, Gates R, Reddy KS, Nickl NJ, Ranjan D. Nonoperative management of bile leaks following liver transplantation. *Clin Transplant* 2000; **14**: 365.
103. Shaked A. Use of T tube in liver transplantation. *Liver Transpl Surg* 1997; **3**: S22.
104. Rouch DA, Emond JC, Thistlethwaite JR Jr, Mayes JT, Broelsch CE. Choledochocholedochostomy without a T tube or internal stent in transplantation of the liver. *Surg Gynecol Obstet* 1990; **170**: 239.
105. Rolles K, Dawson K, Novell R, Hayter B, Davidson B, Burroughs A. Biliary anastomosis after liver transplantation does not benefit from T tube splintage. *Transplantation* 1994; **57**: 402.
106. Shimoda M, Saab S, Morrisey M, *et al.* A cost-effectiveness analysis of biliary anastomosis with or without T-tube after orthotopic liver transplantation. *Am J Transplant* 2001; **1**: 157.
107. Ostroff JW, Roberts JP, Gordon RL, Ring EJ, Ascher NL. The management of T tube leaks in orthotopic liver transplant recipients with endoscopically placed nasobiliary catheters. *Transplantation* 1990; **49**: 922.
108. Shuhart MC, Kowdley KV, McVicar JP, *et al.* Predictors of bile leaks after T-tube removal in orthotopic liver transplant recipients. *Liver Transpl Surg* 1998; **4**: 62.
109. Grande L, Pérez-Castilla A, Matus D, *et al.* Routine use of the T tube in the biliary reconstruction of liver transplantation: is it worthwhile? *Transplant Proc* 1999; **31**: 2396.
110. Riediger C, Müller MW, Michalski CW, *et al.* T-Tube or no T-tube in the reconstruction of the biliary tract during orthotopic liver transplantation: systematic review and meta-analysis. *Liver Transpl* 2010; **16**: 705.
111. Renz JF, Emond JC, Yersiz H, Ascher NL, Busuttil RW. Split-liver transplantation in the United States: outcomes of a national survey. *Ann Surg* 2004; **239**: 172.

112. Wojcicki M, Silva MA, Jethwa P, *et al.* Biliary complications following adult right lobe ex vivo split liver transplantation. *Liver Transpl* 2006; **12**: 839.
113. Ohkubo M, Nagino M, Kamiya J, *et al.* Surgical anatomy of the bile ducts at the hepatic hilum as applied to living donor liver transplantation. *Ann Surg* 2004; **239**: 82.
114. Ishiko T, Egawa H, Kasahara M, *et al.* Duct-to-duct biliary reconstruction in living donor liver transplantation utilizing right lobe graft. *Ann Surg* 2002; **236**: 235.
115. Lee KW, Joh JW, Kim SJ, *et al.* High hilar dissection: new technique to reduce biliary complication in living donor liver transplantation. *Liver Transpl* 2004; **10**: 1158.
116. Sanchez-Urdazpal L, Gores GJ, Ward EM, *et al.* Diagnostic features and clinical outcome of ischemic-type biliary complications after liver transplantation. *Hepatology* 1993; **17**: 605.
117. Fisher A, Miller CH. Ischemic-type biliary strictures in liver allografts: the Achilles heel revisited? *Hepatology* 1995; **21**: 589.
118. Moench C, Otto G. Ischemic type biliary lesions in histidine-tryptophan-ketoglutarate (HTK) preserved liver grafts. *Int J Artif Organs* 2006; **29**: 329.
119. Canelo R, Hakim NS, Ringe B. Experience with hystidine tryptophan ketoglutarate versus University Wisconsin preservation solutions in transplantation. *Int Surg* 2003; **88**: 145.
120. Erhard J, Lange R, Scherer R, *et al.* Comparison of histidine-tryptophan-ketoglutarate (HTK) solution versus University of Wisconsin (UW) solution for organ preservation in human liver transplantation. A prospective, randomized study. *Transpl Int* 1994; **7**: 177.
121. Moench C, Moench K, Lohse AW, Thies J, Otto G. Prevention of ischemic-type biliary lesions by arterial back-table pressure perfusion. *Liver Transpl* 2003; **9**: 285.
122. Pirenne J, Van Gelder F, Coosemans W, *et al.* Type of donor aortic preservation solution and not cold ischemia time is a major determinant of biliary strictures after liver transplantation. *Liver Transpl* 2001; **7**: 540.
123. Scotté M, Dousset B, Calmus Y, Conti F, Houssin D, Chapuis Y. The influence of cold ischemia time on biliary complications following liver transplantation. *J Hepatol* 1994; **21**: 340.
124. Buis CI, Verdonk RC, Van der Jagt EJ, *et al.* Nonanastomotic biliary strictures after liver transplantation, part 1: radiological features and risk factors for early vs. late presentation. *Liver Transpl* 2007; **13**: 708.
125. Abbasoglu O, Levy MF, Vodapally MS, *et al.* Hepatic artery stenosis after liver transplantation – incidence, presentation, treatment, and long term outcome. *Transplantation* 1997; **63**: 250.
126. Sanchez-Urdazpal L, Gores GJ, Ward EM, *et al.* Ischemic-type biliary complications after orthotopic liver transplantation. *Hepatology* 1992; **16**: 49.
127. Tung BY, Kimmey MB. Biliary complications of orthotopic liver transplantation. *Dig Dis* 1999; **17**: 133.
128. Sanchez-Urdazpal L, Batts KP, Gores GJ, *et al.* Increased bile duct complications in liver transplantation across the ABO barrier. *Ann Surg* 1993; **218**: 152.
129. Lo CM, Shaked A, Busuttil RW. Risk factors for liver transplantation across the ABO barrier. *Transplantation* 1994; **58**: 543.
130. Halme L, Hockerstedt K, Lautenschlager I. Cytomegalovirus infection and development of biliary complications after liver transplantation. *Transplantation* 2003; **75**: 1853.
131. O'Grady JG, Alexander GJ, Sutherland S, *et al.* Cytomegalovirus infection and donor/recipient HLA antigens: interdependent co-factors in pathogenesis of vanishing bile-duct syndrome after liver transplantation. *Lancet* 1988; **2**: 302.
132. Lautenschlager I, Höckerstedt K, Jalanko H, *et al.* Persistent cytomegalovirus in liver allografts with chronic rejection. *Hepatology* 1997; **25**: 190.
133. Ludwig J, Wiesner RH, Batts KP, Perkins JD, Krom RA. The acute vanishing bile duct syndrome (acute irreversible rejection) after orthotopic liver transplantation. *Hepatology* 1987; **7**: 476.