GENERAL SURGERY

Ann R Coll Surg Engl 2017; **99:** 210–215
doi 10.1308/rcsann.2016.0293

Complications of biliary-enteric anastomoses

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ABSTRACT

INTRODUCTION Biliary-enteric anastomoses are performed for a range of indications and may result in early and late complications. The aim of this study was to assess the risk factors and management of anastomotic leak and stricture following biliary-enteric anastomosis.

METHODS A retrospective analysis of the medical records of patients who underwent biliary-enteric anastomoses in a tertiary referral centre between 2000 and 2010 was performed.

RESULTS Four hundred and sixty-two biliary-enteric anastomoses were performed. Of these, 347 (75%) were performed for malignant disease. Roux-en-Y hepaticojejunostomy or choledocho-jejunostomy were performed in 440 (95%) patients. Perioperative 30-day mortality was 6.5% (n=30). Seventeen patients had early bile leaks (3.7%) and 17 had late strictures (3.7%) at a median of 12 months. On univariable logistic regression analysis, younger age was a significant risk factor for biliary anastomotic leak. However, on multivariable analysis only biliary reconstruction following biliary injury (odds ratio [OR]=6.84; p=0.002) and anastomosis above the biliary confluence (OR=4.62; p=0.03) were significant. Younger age and biliary reconstruction following injury appeared to be significant risk factors for biliary strictures but multivariable analysis showed that only younger age was significant.

CONCLUSIONS Biliary-enteric anastomoses have a low incidence of early and late complications. Biliary reconstruction following injury and a high anastomosis (above the confluence) are significant risk factors for anastomotic leak. Younger patients are significantly more likely to develop an anastomotic stricture over the longer term.

KEYWORDS

Stricture – Leak – Fistula

Accepted 7 August 2016

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While a variety of techniques are available to restore biliary-enteric continuity, the biliary tree is most commonly anastomosed to the jejunum (either as a Roux-en-Y anastomosis or a simple loop) or less commonly to the duodenum. The anastomosis may be performed to the bile duct, common hepatic duct, first or second order hepatic duct branches, or less commonly to the gallbladder. Anastomoses may be performed in an end-to-side or side-to-side fashion, using continuous or interrupted sutures. Stents may be deployed across the anastomosis.[1]

Specific complications of biliary-enteric anastomoses include early postoperative anastomotic leak and delayed biliary stricture. Both of these complications have an adverse impact on patient outcome and can contribute to long-term morbidity or mortality.[2–5] The reported incidence of complications following biliary reconstruction ranges between 3% and 43%.[2–5]

The aim of this study was to review a single-institution experience of biliary-enteric anastomosis with regard to the indications, the types of anastomoses performed, early and late complications, and long-term patency and outcomes.

Methods

Patients

Data for 2000 to 2010 were collected from a prospectively maintained database on the indication, operation performed and type and level of biliary enteric anastomosis, as well as preoperative biliary dilatation and drainage procedures, histopathology, bile leak, biliary stricture, interventions for biliary stricture, patency, non-biliary complications, chemotherapy and length of follow up. All patients who underwent biliary-enteric anastomosis, either alone or as part of a different hepato-pancreatico-biliary procedure, were included in the study. Missing information was completed using paper and electronic records.

Surgical technique

The preferred method of reconstruction of the biliary-enteric anastomosis was an end-to-side configuration for resectional procedures and side-to-side configuration for patients undergoing palliative bypass. A single layer monofilament absorbable suture (polydioxanone, polyglactin or polyglyconate) of appropriate diameter (2/0–5/0) was used to perform the anastomosis with mucosal apposition, either in a continuous or interrupted fashion. A closed drain without suction was placed next to all biliary anastomoses. Trans-anastomotic stents were not routinely used, although the trans-hepatic tube was left across the anastomosis for a short period where preoperative percutaneous biliary drainage had been performed.

Complications

Biliary anastomotic leak was defined as bile within an intra- or postoperatively placed percutaneous intraperitoneal drain and/or a radiologically confirmed anastomotic leak. In patients who had a pancreatoduodenectomy or liver resection, radiological confirmation of the site of the leak was obtained to differentiate between a true biliary-anastomotic leak, a pancreatic anastomotic leak and a leak from the transected liver parenchymal surface. Anastomotic stricture was defined as a radiologically demonstrated narrowing of the biliary-enteric anastomosis in the presence of symptoms (jaundice, cholangitis or deranged liver function tests), for which the patient required percutaneous, endoscopic or surgical treatment.

Follow-up

Patients were followed up in line with agreed local protocols. Those with cancer were seen regularly at 3 months, 6 months, 12 months and annually thereafter for a minimum of 5 years. Patients with benign pathology were followed up at 3 months, 6 months and 12 months and discharged unless otherwise clinically indicated.

Statistical methods

Univariate analysis was performed using Mann-Whitney U test for continuous data and a chi-squared test was applied to categorical data (all other variables). Univariable and multivariable logistic regression analyses were performed to determine the risk factors for early and late complications. Multivariable logistic regression analyses used a forward stepwise selection procedure. SPSS Statistics version 21 (IBM, Armonk, New York, USA) was used for logistic regression analysis, with $p<0.05$ considered statistically significant.

Results

A total of 462 patients had biliary-enteric anastomoses during the 10-year study period. Follow-up data was 96.2% complete. The median follow up for patients with cancer was 20 months (range 0–78), while that for patients with benign disease was 13 months (range 0–70). The median age was 61 years (range 16–86) and 230 (49.8%) were women.

In 347 patients (75%), the indication for surgery was a malignant process. Of those, 190 (41%) had pancreatic ductal adenocarcinoma (PDAC), 46 (10%) had cholangiocarcinoma, 38 (8%) had ampullary carcinoma and 73 (16%) had other forms of cancer. Of the 115 (25%) patients with benign disease, 24 (5%) had chronic pancreatitis, 22 (5%) had iatrogenic bile duct injury and 69 (15%) had another benign pathology (Table 1).

In terms of procedures performed, 247 patients (54%) underwent pancreaticoduodenectomy, 129 (28%) had palliative biliary and/or gastric bypass, 37 (8%) had extrahepatic bile duct excision, 22 (5%) had reconstruction following iatrogenic injury and 27 (6%) had a combination of procedures, such as re-do biliary-enteric anastomosis, total pancreatectomy and/or liver resection. The preferred level of anastomosis with the jejunum was at the hepatic duct. Hepatico-jejunostomy was performed in 268 (58%) patients. Choledocho-jejunostomy was performed in 138 (30%) patients, and in 21 (5%) patients it was unclear from the records if the common bile duct or common hepatic duct had been used. Anastomoses above the biliary confluence to lobar or segmental ducts were performed in 21 (5%) patients. Only seven patients had anastomoses to more than one biliary duct.

Biliary tree dilatation, defined as a bile duct diameter >6mm,[6] was identified preoperatively in 319 (69%) patients. Preoperative biliary drainage, with or without stenting, via percutaneous transhepatic cholangiography (PTC) or endoscopic retrograde cholangiopancreatography (ERCP), was performed in 274 (59%) patients. Of these, ERCP was performed in 226 (85%) patients, while 38 (14%) underwent PTC and three had combined ERCP/PTC.

There were 212 complications in 121 (26%) patients, of which 60 were grade 2 and above on the Clavien-Dindo scale (Figure 1). Thirty-day mortality was 6.5% (n=30).

Anastomotic leak

There were 17 anastomotic bile leaks (3.7 %, Table 1), all of which were detected during the immediate postoperative period (within the first 5 days). Of these patients, 10 were managed either by an intraoperatively placed drain or a radiologically directed percutaneous drain. Five patients had external biliary drainage via PTC and two had to undergo re-laparotomy and re-anastomosis. There were two deaths following bile leaks, one from sepsis and one from multi-organ failure. The rate of bile leak in patients undergoing reconstruction for biliary injury was 24% versus 2.8% overall for non-injury related procedures ($p<0.01$).

On univariable logistic regression analysis, younger age, biliary reconstruction following biliary injury and anastomosis above the biliary confluence were significant risk factors for short term complications from biliary leak (Table 2). Thirteen of the 17 patients with bile leak were aged <60 years. Three (16%) of the 19 anastomoses

Table 1 Distribution of risk factors for biliary anastomotic leak and anastomotic stricture

	Total (n=462)		Biliary anastomotic leak (n=17)		Anastomotic stricture (n=17)	
	N	%	N	%	N	%
Age (mean)	60		52.7		52.8	
Sex						
Male	232	50.2	6	35.3	11	64.7
Female	230	49.8	11	64.7	6	35.3
Diagnosis / Pathology						
Malignant	347	75.1	9	52.9	10	58.8
Benign	115	24.9	8	47.1	7	41.2
Procedure						
Pancreatoduodenectomy	247	53.5	5	29.4	9	52.9
Biliary and/or gastric bypass	129	27.9	3	17.6	2	11.8
Liver resection/bile duct excision	37	8.0	2	11.8	1	5.9
Reconstruction due to injury	22	4.8	4	23.5	3	17.6
Other	27	5.8	3	17.6	2	11.8
Level of anastomosis						
HJ	268	58.0	6	35.3	12	70.6
CDJ	138	29.9	7	41.2	2	11.8
Unspecified (HJ or CDJ)	21	4.5	0		0	
Above confluence	21	4.5	3	17.6	3	17.6
Other	14	3.0	1	5.9	0	0.0
Number of biliary anastomoses						
1	455	98.5	15	88.2	16	94.1
2	4	0.9	2	11.8	0	0.0
3	2	0.4	0	0.0	1	5.9
>3	1	0.2	0	0.0	0	0.0
Bile leak	17	3.7		0.0	2	11.8
Stricture	17	3.7		0.0		0.0
CBD diameter						
Dilated	319	69.0	11	64.7	10	58.8
Not dilated	143	31.0	6	35.3	7	41.2
Chemotherapy						
Yes	128	27.7		0.0	3	17.6
No	331	71.6		0.0	14	82.4
Stent ERCP/PTC						
Yes	274	59.3	7	41.2	7	41.2
No	188	40.7	10	58.8	10	58.8

HJ = hepatico-jejunostomy; CBD = common bile duct; CDJ = choledochojejunsotomy; ERCP = endoscopic retrograde cholangiopancreatography; PTC = percutaneous transhepatic cholangiography

Table 2 Binary logistic regression analysis for biliary anastomotic leak

Variable	Univariable models OR (95% CI)	p	Multivariable (forward stepwise) model OR (95% CI)	p
Age	0.96 (0.93, 0.99)	0.01	-	
Male Sex	1.86 (0.68, 5.11)	0.23	-	
Number of anastomoses >1	4.57 (0.52, 40.25)	0.17	-	
Dilated bile duct	0.82 (0.30, 2.25)	0.69	-	
Preoperative biliary stent	0.47 (0.17, 1.25)	0.13	-	
Malignant pathology	0.45 (0.17, 1.20)	0.11		
Procedure performed (Biliary reconstruction for injury)	7.30 (2.16, 24.62)	.001	6.84 (1.97, 23.69)	0.002
Anastomosis above the confluence	5.08 (1.31, 19.28)	0.02	4.62 (1.16, 18.49)	0.03

CI = confidence interval; OR, odds ratio

Table 3 Binary logistic regression analysis for biliary stricture

Variable	Univariable models OR (95% CI)	p	Multivariable (forward stepwise) model OR (95% CI)	p
Age	0.96 (0.93, 0.99)	0.01	0.96 (0.93, 0.99)	0.01
Male Sex	0.53 (0.19, 1.45)	0.21	-	
Number of anastomoses >1	4.50 (0.51, 39.61)	0.18	-	
Bile leak	3.76 (0.79, 17.94)	0.10	-	
Dilated bile duct	0.62 (0.23, 1.67)	0.34	-	
Chemotherapy	0.56 (0.16, 1.97)	0.36	-	
Preoperative biliary stent	0.47 (0.17, 1.25)	0.13	-	
Malignant pathology	0.45 (0.17, 1.20)	0.11	-	
Procedure performed (Biliary reconstruction for injury)	4.73 (1.25, 17.85)	0.02	-	
Anastomosis above the confluence	2.94 (0.63, 13.79)	0.17	-	

CI = confidence interval; OR = odds ratio

performed above the level of the biliary confluence developed a leak, compared to 14 (3.3%) of 421 anastomoses performed below the level of the biliary confluence. Preoperative stenting was not a risk factor for bile leak in this series (2.6% versus 6.1%; p=0.13). However, multivariable stepwise logistic regression analysis showed that only biliary reconstruction following biliary injury (odds ratio [OR] =6.84; p=0.002) and anastomosis above the biliary confluence (OR=4.62; p=0.03) were significant risk factors for biliary leak. Patients who underwent biliary reconstruction for injury had a six-fold higher risk of biliary leak compared to the rest of the cohort, while those who had an anastomosis above the confluence had a four-fold higher risk.

Anastomotic stricture

There were 17 (3.7%) anastomotic strictures (Table 3) detected at a median duration of 12 months (range 1–84). These patients were managed with either primary or repeated dilatation and/or stenting (plastic stents, meshmetal stents and retrievable covered stents, n=20) or dilatation only (n=4). Seven patients underwent surgical revision of the hepatico-jejunostomy.

On univariate analysis (Table 3), younger age (below 60 years) and biliary reconstruction following injury were significant risk factors for a subsequent stricture. There was a trend towards postoperative bile leak as a risk factor for later development of anastomotic stricture (11.8% versus

Table 4 Comparison of contemporary studies evaluating bile leak and stricture after biliary-enteric anastomosis

	Study type	Anastomosis	Pathology	n	follow up (months)	Mortality (%)	Morbidity (%)	Bile leak (%)	Stricture (%)
Current study	Retrospective	BEA	Benign & malignant	462	20	6.5	30	3.7	3.7
Burkhart 2013[4]	Retrospective	HJ	Benign & malignant	715	24	2	42	2.2	N/A
Zafar 2011[2]	Retrospective	BEA	Benign	79	N/A	5	49	10	N/A
Antolovic 2007[3]	Prospective	HJ	Benign & malignant	509	N/A	1.3	34	5.6	N/A
Walsh 2007[15]	Retrospective	BEA	Post-LC injury	84	67	4	40	4	11
Reid-Lombardo 2007[13]	Retrospective	HJ	benign (PD)	122	48	4	32	6.6	7.4
House 2006[5]	Retrospective	HJ	Pancreatic benign & malignant	1595	27	N/A	30	3	2.6
de Castro 2005[20]	Retrospective	HJ	Benign & malignant	1033	N/A	N/A	N/A	2.4	N/A
Sicklick 2005[8]	Prospective	BEA	Post-LC injury	172	N/A	2.7	42.9	4.6	N/A
Schmidt 2004[12]	Retrospective	HJ	Post-LC injury	54	61	6	N/A	9	17
Suzuki 2003[21]	Retrospective	HJ	Pancreatic benign & malignant	107	N/A	N/A	N/A	8	N/A

BEA = biliary-enteric anastomosis; HJ = hepatico-jejunostomy; LC = laparoscopic cholecystectomy; N/A = not applicable; PD = pancreaticoduodenectomy.

3.5%), but this did not reach statistical significance (p=0.08). Multivariate stepwise logistic regression analysis showed that only younger age (OR=0.96; p=0.01) was an independent risk factor for the development of anastomotic stricture.

Discussion

Anastomosis of the common hepatic duct or common bile duct to a loop of jejunum (usually a Roux loop) with a single layer of monofilament absorbable sutures is now the standard technique of biliary-enteric anastomosis in most centres. Anastomotic biliary leaks and strictures remain significant, though uncommon, complications. Some contemporaneous studies have been summarized in Table 4. Morbidity and 30-day mortality rates in our study, at 26% and 6.5% respectively, are comparable to those of other contemporary series,[3,5,7,8] especially given the greater proportion of high-risk patients within the current study.[6,9]

The incidence of biliary anastomotic leaks in our cohort compares with the rates of 2.2%–10.0% reported in the literature. Fewer studies report long-term follow-up and comment on biliary strictures. The reported stricture rates of 2.6%–17% are comparable to that in our series. As we did not record 'non-intervention' events, we cannot comment accurately on the incidence of subsequent cholangitis and cholangiocarcinoma that some others have reported.[10]

In our study, reconstruction following biliary injury and anastomosis above the biliary confluence were found to be the most significant risk factors for biliary anastomotic leaks. The incidence of biliary anastomotic leaks was 24%, while that of strictures was 18%, in patients who had prior biliary injury. Following a bile duct injury (usually iatrogenic), reconstruction is performed on a non-dilated biliary tree in the presence of inflammation, complex damage to the duct, often inflicted by diathermy, and associated vascular injury. We speculate that this is the reason why these patients suffer a higher incidence of anastomotic leak. The biliary tree above the confluence gets progressively narrower and thinner, making anastomosis to these ducts technically more challenging. We hold this to be responsible for the significantly higher leak rate in this group.

Our analysis showed that younger age was the only significant risk factor for late strictures. Surprisingly, others have reported older age as a risk factor.[9,11,12] Bile duct injuries being more common in younger patients may be a reason for our finding that they are at a higher risk for stricture formation. There is evidence that preoperative biliary drainage increases the incidence of septic complications.[7,13] Endoscopic biliary stenting (as opposed to percutaneous biliary drainage) has also been reported to be protective.[3] Younger patients with injury and benign disease usually have non-dilated bile ducts and are less likely to have received preoperative biliary drainage than those undergoing surgery for malignancy (53% versus 67%). That, too, may be a factor.

Given that patients who underwent biliary reconstruction for injury had a six-fold higher risk and those who had an anastomosis above the confluence had a four-fold higher risk of biliary leak compared to the rest of the cohort, it may be reasonable counsel to these patients accordingly, and to keep a closer eye on these patients in the perioperative phase. Placement of more than one subhepatic drain, or placement of an intra-anastomotic stent, may be useful considerations, although we have no evidence to say if such measures might be useful.

A non-significant trend for an association between biliary anastomotic leak and subsequent stricture was noted. This seems plausible, but may also be due to a type II error, as the incidence of both these complications in the current series was very low and this trend was not seen on multivariable analysis.

Though reported rates of stricture formation after reconstruction following biliary injury are higher than those reported in series of surgery for pancreatic cancer,[3,7,9,14] when we compared the larger group of all patients with benign disease against those who had malignancy, we found no difference in the incidence of anastomotic strictures. Two patients (one with cholangiocarcinoma, one with PDAC) developed further strictures due to recurrence of malignancy. Similarly, there was no relationship between the level of biliary-enteric anastomosis and the development of stricture,[15–17] despite reports describing better results with hepaticojejunostomy than with choledochojejunostomy,[18] and others showing that high biliary injuries are associated with vascular injury.[9,14,19] Postoperative chemotherapy was not associated with an increased risk of stricture,[3] with a median time to biliary stricture of 12 months, when most of the patients were alive. With a median follow up of 11 months (range 0–78), it is likely that the actual rate of stricture may be higher, even though most strictures occur within the first 2 years.[14]

Percutaneous balloon dilatation and stenting form the mainstay of treatment for strictures of biliary-enteric anastomoses. Multiple procedures are often required, over a period of several months, to achieve good long-term patency.[3,14] However, a proportion of patients inevitably require surgical revision of their anastomoses.

While patients with cancer are kept under surveillance to detect recurrence, those with benign disease are often discharged from follow-up after 12 months. Given our findings, it would seem sensible to keep young patients who have undergone a high biliary reconstruction after iatrogenic injury under surveillance for a longer period.

Conclusions

Bile leak and anastomotic stricture are uncommon complications in patients following a biliary-enteric anastomosis, although overall morbidity is considerable due to the complexity of other aspects of the procedure. Biliary reconstruction following injury and a high anastomosis (above the confluence) are significant risk factors for anastomotic leak. Younger patients are significantly more likely to develop an anastomotic stricture over the longer term.

Conflicts of interest

No conflicts of interest to declare.

Acknowledgement

The research was presented in part at the International Hepato-Pancreato Biliary Association 10th World Congress in Paris, 2012.

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