



## ERCP for the treatment of bile leak after partial hepatectomy and fenestration for symptomatic polycystic liver disease

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### Abstract

**AIM:** To describe endoscopic treatment of bile leaks in these patients and to identify risk factors in these patients which can predict the development of bile leaks.

**METHODS:** Retrospective case-control study examining consecutive patients who underwent partial hepatectomy for polycystic liver disease (PLD) and developed a postoperative bile leak managed endoscopically over a ten year period. Each case was matched with two controls with PLD who did not develop a postoperative bile leak.

**RESULTS:** Ten cases underwent partial hepatectomy with fenestration for symptoms including abdominal distention, pain and nausea. Endoscopic retrograde cholangiopancreatography (ERCP) showed anatomic abnormalities in 1 case. A biliary sphincterotomy was performed in 4 cases. A plastic biliary stent was placed

with the proximal end at the site of the leak in 9 cases; in 1 case two stents were placed. The overall success rate of ERCP to manage the leak was 90%. There were no significant differences in age, gender, comorbidities, duration of symptoms, history of previous surgery or type of surgery performed between cases and controls.

**CONCLUSION:** ERCP with stent placement is safe and effective for management of post-hepatectomy bile leak in patients with PLD.

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**Key words:** Polycystic liver; Hepatectomy; Bile leak; Endoscopic retrograde cholangiopancreatography

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### INTRODUCTION

Polycystic liver disease (PLD) is a rare inherited disorder characterized by multiple cysts in the liver, often associated with autosomal dominant polycystic kidney disease (ADPKD)<sup>[1,2]</sup>. The cysts develop as progressive dilation of biliary microhamartomas<sup>[3,4]</sup> which communicate with the hepatic sinusoids and the portal tree. Mature cysts

do not communicate with the biliary tree but are lined by biliary epithelium<sup>[5]</sup>. These cysts grow slowly but can become large and produce massive hepatomegaly. Most patients with PLD are asymptomatic until significant hepatomegaly develops. The commonest symptoms are abdominal pain, dyspnea from diaphragmatic compression, and lower extremity edema. Medical therapy is largely ineffective for the management of these symptoms and therefore, surgical treatment aimed at reduction in hepatic volume is the treatment of choice. These modalities include surgical fenestration or unroofing of cysts, partial hepatectomy or a combination.

Bile leaks are a common complication of surgical management of PLD and occur in 6%<sup>[6]</sup> to 15%<sup>[7]</sup> of patients. Management of bile leaks can be conservative, surgical, or by the use of endoscopic retrograde cholangiopancreatography (ERCP) with placement of a biliary stent with or without a biliary sphincterotomy. Although ERCP has been reported to be used successfully to manage bile leaks in patients without PLD following hepatectomy<sup>[8-12]</sup> there are no reports on endoscopic management of biliary leaks in patients with PLD following surgery. Hence, we hope to define the use of ERCP in these patients.

In this report, we describe endoscopic treatment of bile leaks following surgical management of PLD. We also sought to determine if there were patient or procedural factors in patients with PLD which can predict the development of bile leaks.

## MATERIALS AND METHODS

IRB consent was obtained from the Mayo Clinic Institutional Review Board prior to initiation of the study. We performed a retrospective case control study. All patients with PLD undergoing surgical treatment between January 1, 1998 and September 30, 2008 were identified. These patients were referred for surgery because they were symptomatic from the PLD, with the commonest symptoms being abdominal pain and early satiety. Patients were included only if they underwent fenestration and/or hepatectomy or wedge resection to address these symptoms. PLD was defined as having at least 20 simple cysts larger than 1 cm in diameter in the liver excluding any infectious, parasitic or traumatic causes. Only patients with research authorization were then further studied. Cases were defined as patients having a clinical diagnosis of bile leaks as identified by review of the medical record. Controls were defined as patients who underwent a similar surgery for PLD, matched by date of surgery within 4 months before or after the surgery of the case, without development of a post-operative bile leak. Two controls were chosen for each case. Demographic data including age and gender were abstracted. Charlson score<sup>[13]</sup> was assessed for each patient as also the duration of disease at the time of surgery. Surgical procedural details including type of surgery performed, hepatic lobe(s) removed, and concomitant surgeries performed such as cholecystectomy were noted. The exact classification of hepatic

resection was limited because of anatomic distortion in the livers of patients with PLD<sup>[7]</sup>. The need for ERCP was decided by the surgeon in consultation with the performing endoscopist based upon clinical symptoms and presence and/or volume of ongoing bile leakage from surgical or percutaneous drains. Endoscopic procedural details including time between surgery and ERCP, the leak site identified, performance of a sphincterotomy or placement of a biliary stent, and development of complications were identified. The outcome of ERCP was assessed from chart review and resolution of symptoms, removal of drains, follow-up non-invasive imaging studies or by follow-up ERCP.

## Statistical analysis

Descriptive statistics were used to describe the case patient characteristics and ERCP outcomes. For comparative statistics for the case control portion of the study, a standard unpaired *t*-test or Mann Whitney *U* test was used to compare parametric and nonparametric continuous variables respectively, and the Fischer's exact test was used to compare dichotomous variables. A *P* value  $\leq 0.05$  was considered statistically significant.

## RESULTS

### Case series description

10 patients developed a post-operative bile leak after surgery for symptomatic PLD treatment between January 1, 1998 and September 30, 2008 and were treated endoscopically (Table 1). Of these 10 patients, all were women, with a mean age of  $48.3 \pm 9.7$  years. The median duration of symptoms prior to the index surgery was 12 years (range 2-30 years), and 3 had had previous fenestration or alcohol sclerosis of cysts. All patients underwent partial hepatectomy with fenestration for symptoms including abdominal distention, pain and nausea. The exact classification of hepatic resection was limited because of anatomic distortion in the livers of patients with PLD<sup>[7]</sup>. Half had right hepatectomy and half had left hepatectomy. All the surgeries were performed by one highly experienced surgeon (David M Nagorney). All were open laparotomy and at least 1 percutaneous drain was placed. Seven patients had concomitant cholecystectomy.

Bile leak was diagnosed and ERCP performed after a mean of  $17^{[12]}$  postoperative days. Bile leak was suspected when persistent bilious drainage was noted from the percutaneous drains. Computed tomography confirmation was obtained in two cases. ERCP showed the exact site of leak in 5 (50%) cases and in three more cases a leak of contrast was noted to communicate with the surgical drain but the exact site could not be determined. In two patients, no leak was seen. Leaks occurred from the common hepatic duct and the right intrahepatic ducts in one patient each and the other three arose from the left intrahepatic ducts. None of the patients had a previous sphincterotomy; biliary sphincterotomy was performed in 4 (40%) cases. A 10 French plastic biliary stent was placed

**Table 1** Characteristics of 10 patients with polycystic liver disease who underwent endoscopic retrograde cholangiopancreatography management of post-hepatectomy bile leaks

Patient	Duration of diagnosis prior to surgery (yr)	Surgery performed in addition to fenestration	Cholecystectomy performed?	Time to ERCP (d)	Leak site	Sphincterotomy performed?	Outcome
1	30	Extended left hepatectomy <sup>1</sup>	Yes	8	Not specified <sup>2</sup>	No	Success on repeat ERCP
2	2	Extended right hepatectomy	Yes	16	Common hepatic duct	No	Died 10 d after ERCP
3	17	Right hepatectomy	Yes	21	Left intrahepatic	No	Success clinically
4	6	Extended right hepatectomy	No	28	Left intrahepatic	No	Success clinically
5	8	Right hepatectomy	Yes	7	No leak seen	No	Success clinically
6	4	Left hepatectomy	Yes	20	Not specified	No	Success clinically
7	4	Right hepatectomy	Yes	15	Left intrahepatic	Yes	Success on repeat ERCP
8	26	Left hepatectomy	No	43	Not specified	Yes	Success clinically
9	30	Extended left hepatectomy	Yes	4	No leak seen	Yes	Success on repeat ERCP
10	20	Left hepatectomy	No	6	Right intrahepatic	Yes	Success on repeat ERCP

<sup>1</sup>Extended included removal of segments 4A and/or 4B of the liver; <sup>2</sup>Leak noted into percutaneous drain, but no specific site identified. ERCP: Endoscopic retrograde cholangiopancreatography.

**Table 2** Risk factors for bile leak development

	Cases (n = 10)	Controls (n = 20)	Effect	P value
Age (yr) (mean ± SD)	48.3 ± 9.7	52.2 ± 9.2	-3.9	0.30
Duration of symptoms (yr) (mean ± SD)	14.7 ± 11.3	13.4 ± 7.6	1.3	0.71
Previous surgery (Y/N) n (%)	3 (30)	4 (20)	OR: 1.71, 95% CI: 0.3-9.78	0.66
Charlson score median (range)	1.5 (0-4)	1.5 (1-5)	No difference	0.60
Wedge resection n (%)	2 (20)	10 (50)	OR: 0.25, 95% CI: 0.04-1.48	0.24
Post-op drains median (range)	1 (1-2)	1 (1-2)	No difference	0.67
Concomitant cholecystectomy n (%)	7 (70)	17 (85)	OR: 0.41, 95% CI: 0.07-2.56	0.37

OR: Odds ratio; CI: Confidence interval; Y/N: Yes/no.

with the proximal end at the site of the leak when identified or into the common bile duct in 9 (90%) cases; in 1 (10%) case two stents were placed. None of the patients developed post-ERCP complications. A repeat ERCP was performed in 5 patients after a mean (range) of 26 (8-47) d, 4 of which had resolved the leak. The one patient who in who the leak had not resolved underwent a second ERCP 8 d later for worsening jaundice and suffered fatal fulminant hepatic failure 3 d later. One more patient (20% total) died of liver failure after clinical resolution of bile leak but prior to repeat ERCP. Three cases were lost to follow up in terms of removal of the biliary stent but clinically did well with regards to the bile leak, and in one case the stent passed spontaneously without complication. Overall, 9 of the 10 patients (90%) were deemed to have successful treatment of the bile leak by ERCP management. The patient who died of hepatic decompensation with an ongoing leak was counted as a failure of therapy though

death was not directly related to the bile leak or treatment.

### Risk factors for bile leak development

In order to determine if there were any patient or procedural factors predictive of developing a post-operative bile leak, the above 10 cases were matched retrospectively 1:2 to control patients with PLD who underwent similar surgical procedures within 4 mo of the matched case patient, but who did not develop a post-operative bile leak. All the controls were female and all but three underwent fenestration along with hepatectomy; one patient had only fenestration performed and two had fenestration with wedge resections. When comparing cases to controls, there was no significant difference in age ( $48.3 \pm 9.7$  years *vs*  $52.2 \pm 9.2$  years,  $P = 0.30$ ), duration of symptoms ( $14.7 \pm 11.3$  years *vs*  $13.4 \pm 7.6$  years,  $P = 0.70$ ), history of previous surgical resection [odds ratio (OR): 1.71, 95% confidence interval (CI): 0.30-9.78,  $P = 0.66$ ], Charlson score [median 1.5 (range: 0-4) *vs* 1.5 (range: 1-5),  $P = 0.61$ ], performance of wedge resection (OR: 0.25, 95% CI: 0.04-1.48,  $P = 0.24$ ), number of post-operative drains [median 1 (range: 1-2) *vs* 1 (range: 1-2),  $P = 0.67$ ] or concomitant cholecystectomy (OR: 0.42, 95% CI: 0.07-2.56,  $P = 0.37$ ) (Table 2). All the surgeries were performed by a single highly experienced surgeon (David M Nagorney). Thus, no factors could be identified that would predict development of a bile leak in patients with PLD undergoing surgical fenestration of hepatectomy.

## DISCUSSION

PLD is a disease where multiple cysts develop in the liver and grow with age. When these cysts are significantly enlarged, they cause symptoms including abdominal pain, shortness of breath, and early satiety with resultant adverse affect on quality of life. Surgical manage-

ment of symptomatic cysts includes fenestration of the cysts, wedge resection of the most affected areas of the liver (for limited cystic involvement) or hepatectomy to remove the most enlarged areas. Bile leaks are the commonest complication from hepatectomy and it can be surmised that patients with PLD who have distorted anatomy because of the presence of cysts might be at an even higher risk for this complication. In fact, the risk of biliary complications in patients with PLD undergoing surgery is as high as 15%<sup>[7]</sup>. The incidence of biliary complications following hepatectomy in patients without PLD is 4.8% to 8.1%<sup>[14]</sup>.

Traditionally, management of post-hepatectomy bile leaks in patients with PLD has been exploratory laparotomy or conservative management. However, a laparotomy significantly increases morbidity and costs. Conservative management results in a much longer recovery process<sup>[14]</sup> and is not always successful<sup>[8]</sup>. Nagano *et al.*<sup>[14]</sup> reported that patients who underwent biliary drainage with a naso-biliary tube had markedly shorter healing times compared to those who did not (30 d *vs* 179 d). However, naso-biliary tubes are more cumbersome for patients and technically more difficult to place than indwelling biliary stents. Endoscopic therapy has been used successfully to treat biliary leaks that occur after cholecystectomy<sup>[15]</sup> and also in patients without PLD following liver surgery<sup>[16]</sup>. However, there are no data to support its use in patients with PLD where theoretically, bile leaks may be more difficult to treat given the altered anatomy. Thus, our aim was to publish experience with ERCP in the treatment of post-hepatectomy bile leaks.

Our findings show that ERCP may be an effective therapy for post-hepatectomy bile leaks in patients with PLD. Nine of 10 patients had successful healing of bile leaks. The patient who died with a persistent leak died of hepatic failure, not as a result of complications from the leak.

Bile leaks were treated with and without endoscopic biliary sphincterotomy based upon endoscopist preference. A 10 French biliary stent was used in all cases and the proximal end was placed in the branch of the hepatic duct where the leak was seen to originate. No complications including pancreatitis, perforation or bleeding occurred after ERCP.

The case-control comparison was performed to determine if patient or procedural factors could predict the risk of post-operative bile leak. Previous studies in patients without PLD have determined that age, gender, cut surface area and other operative factors, presence of hepatitis B or C, baseline laboratory studies and the presence of cirrhosis can affect the risk of development of a bile leak<sup>[14]</sup>. In our cohort of patients with PLD, all the cases and controls were women, of similar ages, had no other liver disease or cirrhosis. PLD causes symptoms by mechanical effect and therefore laboratory studies were mostly normal. There is a risk of hepatic decompensation following large hepatectomy because the remaining liver volume may be insufficient though synthetic function

is not affected at baseline. There was also no significant difference between cases and controls in duration of disease, whether right or left hepatectomy was performed, and whether a wedge resection was performed.

There are several limitations to the study. Because of its retrospective nature, there is inherent selection bias. Also, the numbers of patients are small. This is not unusual given that the prevalence of symptomatic PLD is low. The case-control comparison may not be sufficiently powered to detect a difference in risk factors but over 10 years, only 10 patients were identified with clinically important bile leaks. Also, operative details were not prospectively collected and hence not available for review in all cases. Certain operative details such as difficulty of resection, amount of blood loss, and intra-operative damage and repair of bile ducts could have impacted the risk of developing a bile leak.

In summary, we conclude that ERCP with placement of an internal biliary stent is a safe and effective treatment for post-hepatectomy bile leaks in patients with PLD. ERCP should be considered as a therapeutic option when bile leak is suspected clinically due to persistent biliary drainage from percutaneous tubes in these patients. No patient factors can be identified as risk factors to predict development of bile leaks in these patients. Further prospective studies could be performed to assess risk factors.

## COMMENTS

### Background

Polycystic liver disease (PLD) is a rare inherited disorder characterized by multiple cysts in the liver, and surgical treatment aimed at reduction in hepatic volume is the treatment of choice. Bile leaks are a common complication of surgical management of PLD. Here, the authors describe the use of endoscopic retrograde cholangiopancreatography (ERCP) to manage bile leaks in these patients.

### Research frontiers

In the area of management of bile leaks in polycystic liver disease, the research hot spot is in determining the safest and most effective modality of treatment, whether medical, surgical or endoscopic.

### Innovations and breakthroughs

Previously, endoscopic therapy had been used successfully to treat biliary leaks that occur after cholecystectomy, and also in patients without PLD following liver surgery. The innovation described in this report is in the successful use of endoscopic therapy in a novel patient population.

### Applications

The study demonstrates that ERCP may be an effective therapy for post-hepatectomy bile leaks in patients with PLD.

### Terminology

PLD is a disease where multiple cysts develop in the liver and grow with age. When these cysts are significantly enlarged, they cause symptoms including abdominal pain, shortness of breath, and early satiety with resultant adverse affect on quality of life.

### Peer review

Although the endoscopic treatment in patients with biliary leaks after hepatectomy is a well recognized procedure, the authors report their experience, as case series, concerning a subset of patient with hepatic cysts.

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