Percutaneous Biliary Drain Complications in Transplanted versus Native Liver: A Comparative Retrospective Study

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Abstract

Purpose The aim of this study was to assess the rate of complications of percutaneous transhepatic biliary drain in transplanted versus native livers.

Materials and Methods A retrospective chart review was performed of all percutaneous transhepatic biliary drains completed at our institution from 2009 to 2018. Chart review of complications and interventions was recorded. Chi-squared and Fisher's exact tests were used to compare percutaneous transhepatic biliary drains performed in patients with liver transplants (n = 62) to those with native livers (n = 285).

Results There was a statistically significant difference in the frequency of complications of percutaneous transhepatic biliary drains in patients with liver transplants (61%) compared with those with native livers (13%), $\chi^2(1) = 9.59$, $p<0.01$. There was a statistically significant increased frequency of worsening liver function, sepsis, bile leak, arterial and portal venous bleeds, and secondary complications in those with liver transplants. The median number of days until the complication occurred for those with liver transplants was nearly three times longer than those with native livers. The most common subsequent intervention for patients with liver transplants was placement of a new drain (53%), whereas those with native livers was drain upsize (70%).

Conclusion Complications including vascular injury, sepsis, bile leak, and worsening liver function after percutaneous transhepatic biliary drains occurred more commonly in patients with liver transplants versus native livers.

► **Keyworks:**
► percutaneous transhepatic biliary drain
► hepatobiliary
► liver transplant

Introduction

Liver transplantation is commonly performed; 8,250 liver transplantations were performed in the United States in 2018.[1] Biliary complications, including leaks and anastomotic strictures, occur in 10 to 40% of liver transplants.[2-4] When they do occur, they have a published mortality rate of up to 10%.[2-4] As liver transplantation frequently involves creation of a hepaticojejunostomy, endoscopic interventions are often difficult to perform. An alternative and less commonly used surgical approach is the creation of a duct-to-duct anastomosis. Therefore, percutaneous transhepatic biliary drains (PTBD) often used to treat biliary complications after

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Table 1 Exclusion criteria explanation

Exclusion criteria	Explanation
Age less than 18 years	Our patient population naturally includes those over the age of 18, as there is a separate pediatric hospital. In addition, the primary research regarding PTBD complications to date has been in the pediatric rather than the adult population
Unsuccessful PTBD placement	We chose to study complications of successful PTBD placement. Although failed attempts of drain placement could also lead to complications, this was not our primary focus
Lack of available follow-up until PTBD removal or 6 months post drain placement	There were occasional cases where a patient from an outside institution had a one-time PTBD placed at our institution and therefore lacked adequate follow-up. There were often cases where adequate follow-up had not been reached by the time of data acquisition. We required that the patient has follow-up for 6 months after PTBD placement or until drain removal, whichever came first. Usually if the drain was not removed, it would have been exchanged routinely by 3 months. Six months was chosen as it extended well beyond the average length of time where complications occurred and a PTBD remained in place

Abbreviation: PTBD, percutaneous transhepatic biliary drain.

transplant. Biliary leaks usually occur in the initial postoperative period. Small leaks can be managed conservatively, whereas larger leaks often require both percutaneous drainage of the fluid collection and PTBDs for diversion.[3] Biliary strictures are treated with PTBDs followed by increasing balloon dilation of the anastomotic stricture with drain upsizing.[3] PTBD is also performed in native livers, with the most common indications being obstruction (either from malignant causes or stones) and cholangitis. While conventional anatomy allows for endoscopic intervention via endoscopic retrograde cholangiopancreatography, this can fail in ~10% of cases.[5]

Table 2 Indications for biliary drain placement in native and transplanted livers

Indication	Native liver, *n* (%)	Transplant liver, *n* (%)
Biliary obstruction	213 (79.8)	43 (70.5)
Cholangitis	40 (15.0)	7 (11.5)
Choledocholithiasis	9 (3.3)	2 (3.3)
Biloma	3 (1.1)	4 (6.6)
Bile leak	2 (0.7)	5 (8.2)

Potential complications after PTBD include infection, pneumothorax, empyema, sepsis, occlusion, dislocation, and bleeding.[2] The reported incidence of post-PTBD bleeding ranges from 0.6[6] to 12%.[7] Sepsis or transient bacteremia is reported in 2% of patients after biliary intervention.[1011] The Society of Interventional Radiology consensus guidelines recommend in the native liver a threshold for major complications of 10%.[1,8,9] Though complications regarding PTBDs in native and transplanted livers have been previously established in the literature, there is minimal research regarding the rate of complication and comparison of PTBD placement in native to transplanted livers at a single institution. Established risk factors for PTBD's in both native and transplanted livers include malignancy, prior complications, and bilateral biliary drainage.[2]

Though these established risk factors are well known, the comparison of native to transplanted livers allows for greater insight into the type of complications, timeline, and further interventions that may be necessary in transplanted livers. In addition, given the suppressed immunity and altered anatomy, we hypothesized that liver transplant patients would have a higher rate of complications after PTBD.

Materials and Methods

After obtaining institutional review board approval, a retrospective review was performed of all PTBD placed at a single institution between 2009 and 2018 (n = 547). All interventions were performed by interventional radiologists. Exclusion criteria included age < 18, unsuccessful PTBD placement, and lack of available follow-up for a minimum of 6 months post-PTBD placement (►**Table 1**). Indications for PTBD placement, demographics (►**Table 2**), and complications were recorded for both groups. There was no statistical significance between the two groups from the obtained demographics. The chi-squared and Fisher's exact test analyses were used to compare the two groups. Analyses were performed via Microsoft Excel.

Broad indications for liver transplants and native livers were obtained but largely were due to biliary obstruction, which included congenital such as biliary atresia, acquired, malignant, and infectious causes (►**Table 2**). Given the overwhelming majority of cause for biliary drain placement being biliary obstruction, further analysis was not obtained. Patients were not separated by the type of liver transplant (living vs. diseased donor) that they received.

The following complications were sought via retrospective review of the electronic medical record and picture archiving and communications system for 6 months after initial PTBD: vascular injury including portal venous and arterial injury, bleeding including significant hemobilia (volume or rate of bleeding externally through the PTBD catheter or into the gastrointestinal lumen through biliary ducts to warrant intervention) intraperitoneal and hepatic parenchymal bleeds, bile leak, worsening liver function, fulminant liver failure, sepsis, abscess formation, and death. Complications that did not fit within the above categories were defined as "other." Vascular injury was determined with imaging

evidence of either by computed tomography (CT), angiographic, or pull-back cholangiography. Worsening liver function was defined as a rising bilirubin or increase in liver enzymes by at least two times their baseline level, without a subsequent downtrend after the procedure.[12] Abscesses were confirmed by CT, magnetic resonance imaging, or ultrasound. If complications occurred, subsequent interventions were also analyzed including embolization, tube upsize, and additional PTBD placement. These interventions were then followed for further complications for an additional 6-month time period. Finally, the location of PTBD drain placement (e.g., left vs. right side of the liver) was also recorded if the information was available.

Results

Of the initial 547 patients, 200 were excluded for the reasons discussed in ►**Table 1**, with the primary reason for exclusion being lack of available follow-up. Only successful placement of PTBD placements was included and therefore unsuccessful attempts and their associated complications were not recorded. Of the 347 included patients, 285 were in patients with native livers and 62 in transplanted livers. Baseline characteristics are shown in ►**Table 3**.

Baseline demographic characteristics were similar between the native and transplanted livers. The indications for biliary drain placement were also similar between the groups with the most common indication being biliary obstruction.

There was nearly a fivefold increased risk of complications in liver transplant patients undergoing PTBD compared with native liver (61%; n = 38 with complications, n = 24 without complications) versus (13%; n = 38 with complications, n = 247 without complications) (χ^2 (1) = 68.5, $p < 0.01$). The most common complication overall in both groups was worsening liver function (►**Table 4**). There was no statistically significant difference between the two groups regarding hepatic parenchymal bleeds, abscess formation, fulminant liver failure, death, and other complications.

Complications occurred significantly sooner after PTBD in native livers versus transplanted livers; the median number of days until the complication for the liver transplant group was 16 days, whereas those without liver transplants was 5.5 days (p = 0.012, two tailed t-test). More unplanned interventions were required in the liver transplant group, requiring an average of 3.1 versus 1.4 interventions within a 6-month time period for those with liver transplants and native livers, respectively (p = 0.005, McNemar's chi-squared test). The most common intervention differed between the two groups; for patients with liver transplants, it was subsequent additional PTBD placement of the same drain size (53%), whereas those with native livers most often required a drain upsize (64%). Embolization was required in 10% transplanted livers who had a complication that necessitated an intervention, whereas no embolizations were performed in native livers.

We also analyzed whether the PTBD location (left vs. right side of the liver) was associated with an increased rate of complications and found no difference in complications of drain placement between left and right side in either transplanted (χ^2 (1) = 2.24, p = 0.13) or native livers (χ^2 (1) = 0.04, p = 0.84).

Discussion

There was a statistically significant higher frequency of complications in patients with liver transplants undergoing PTBD compared with those with native livers. This included bleeding (both arterial and portal venous) (see ►**Figs. 1** and **2**), worsening liver function, bile leaks, and to become septic. These differences may be due to immunosuppression, poorer healing, and/or greater fragility of the biliary system in transplanted livers, whose vascular supply is dependent solely on hepatic arterial supply.[14,15] It is hard to fully attribute whether the increased rate of complications after PTBD placement is due to the drain itself versus related to the liver transplant. However, complications such as bleeding, bile leaks, and sepsis postprocedure are more likely to be associated with the drain placement due to the timing of the complications. Timing of complications for both groups was generally seen

Table 3 Demographics: Sex reported by percent male and female.

	Sex (% of male and female)	Age	Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Alkaline phosphatase (U/L)	Creatinine (mg/dL)	Biliary ductal dilation (%)
Native liver	51% male, 49% female	M = 61.6, SD = 14.6 95% ±1.7	M = 7.4, SD = 7.0 ±0.8	M = 132.6, SD = 177.7 ±20.6	M = 128.7, SD = 141.9 ±16.5	M = 532.5, SD = 452.0 ± 2.5	M = 1.02, SD = 0.76 ±0.09	15
Liver transplant	51% male, 49% female	M = 51.6, SD = 17.5 ±4.4	M = 3.4, SD = 5.3 ±1.3	M = 67.9, SD = 53.8 ±13.4	M = 79.5, SD = 77.8 ± 19.4	M = 645.5, SD = 795 ±197.9	M = 1.21, SD = 0.70 ±0.17	34

Abbreviation: AST, aspartate transaminase; ALT, alanine transaminase; M, mean; SD, standard deviation.

Table 4 Comparisons of complication types in native versus transplant livers and the increased rate observed in transplanted livers

Complication type	Native (%)	Transplant (%)	Statistic (increased rate observed in transplanted livers)
Worsening liver function	4.2	22.6	5.4x higher $p = 0.02$[a]
Vascular injury (portal venous and arterial)	1.4	9.7	6.9x higher $p = 0.02$[a]
Bile leak	3.5	14.5	4.1x higher $p<.01$[a]
Sepsis	1	8	8x higher $p<.01$[a]
Overall complications	13	61	4.7x higher $p<0.01$[a]
Parenchymal bleeds	0.7	1.6	$p = 0.45$
Intrahepatic abscess formation	0	1.6	$p = 0.18$
Fulminant liver failure	0	0	N/A
Death	0.35	0	$p = 1$
Other complications	2.1	3.2	$p = 0.64$

Abbreviation: N/A, not available.
[a]Statistically significant.

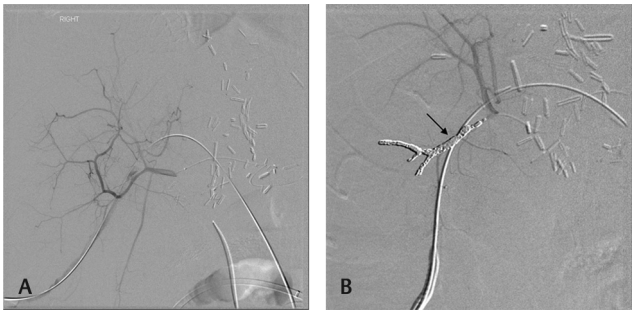

Fig. 1 A 51-year-old man with a history of autoimmune hepatitis after liver transplant complicated by biliary leak who underwent percutaneous transhepatic biliary drain 2 days prior. The patient had ~2 L of bloody output from his biliary drain over 2 hours with concomitant hypotension. He received packed red blood cell and request was made for emergent angiogram and possible embolization. Image (**A**) shows findings from the angiogram, and image (**B**) shows findings post coil embolization.

as less than 2 weeks after placement. In addition, postsurgical liver anatomy after transplant allows for more tortuous vessels, alternate anatomy, and established increased rate of vasculature and biliary strictures. These findings are not unforeseen consequences of the liver transplant surgery, but a likely expected result of the nature of the disease and new anatomy.[2] In addition, the complication of worsening liver function post drain placement may not be fully attributed to the PTBD itself. Possible confounding issues such as simply requiring a PTBD may imply that the transplanted liver is suffering and by nature would have increasing liver enzymes. This may be cause for the higher rates of complications seen from that variable. When comparing native to transplanted complications overall, our rates of PTBDs were slightly higher than previously reported in the literature.[8,9] In addition, we chose to look only at successful attempts at biliary drain placement. Given that there were 200 biliary drain placements excluded primarily due to lack of follow-up or failed attempt

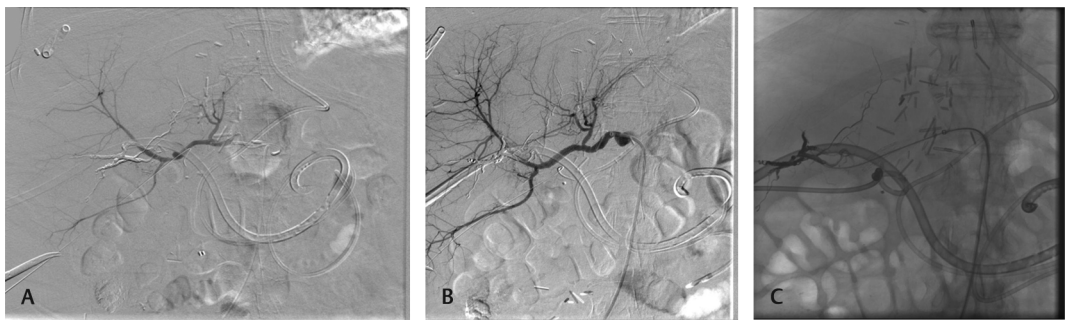

Fig. 2 A 61-year-old female with a history of decompensated nonalcoholic steatohepatitis cirrhosis who underwent deceased donor liver and kidney transplantation that was complicated by a biliary enteric stricture. Six weeks after initial liver transplantation, the patient underwent right-sided percutaneous transhepatic biliary drain placement. Thirty-five days after drain placement, the patient had significant hemobilia with falling hematocrit and hemodynamic instability. Onyx embolization was performed for arterioportal fistula. Angiography showed a pseudoaneurysm in the right hepatic artery (**A**), which was treated with a 5 mm Lifestream balloon expandable stent placement **(B** and **C)**.

at placement, we may be not fully capturing complications (or lack thereof) from those patients. Further prospective studies would benefit from including all complications from failed attempts in both liver transplant and native liver patients.

For primary placement of the PTBD, those with liver transplants were more likely to have complications on average over 2 weeks after placement, whereas those with native livers had complications just under a week. As noted previously, the complications may not be fully attributed to the PTBD placement itself, but rather the nature of the disease. The most common complication and subsequent reason requiring further intervention was worsening liver function. Portal venous bleeds, arterial bleeds, and sepsis presented more readily, as would be expected. Native livers have a shorter time window on average prior to complication.

Nondilated biliary systems are a known risk factor for complications post-PTBD.[13] However, we found no statistically significant increase in complications in nondilated versus dilated systems in either the native or transplanted liver populations. We also found no difference in complications between left- versus right-sided biliary drain placement that is counter to other reports that showed higher rates of complications with left-sided versus right-sided drains.[16]

Our findings underscore that extra caution and care should be undertaken while performing PTBDs in patients with liver transplants. Close clinical follow-up in these patients is warranted. Additionally, given that post-PTBD complications in liver transplant patients may present in a delayed manner, longer active follow-up by the interventional radiology (IR) team is recommended.

Limitations of this study include that this is a single-center and retrospective review design. In addition, it is challenging to fully characterize whether the increased rate of complications is due solely to placement of PTBD in the transplanted liver. Many patients with liver transplants have progression of their disease, significant comorbidities, and differing indications for liver transplant.

Conclusions

Posttransplant patients were nearly five times more likely to have complications after PTBD than those with native livers. These findings may not solely be attributed to placement of a PTBD; however, they expose some complications that may arise in the short postprocedure timeframe that the interventional radiologist should be aware of. Therefore, patient consent process, expectations from patients, and referring physicians and management after PTBD should be adjusted accordingly. Further research into uncovering the underlying mechanisms to explain this marked difference is needed.

Financial and Competing Interests' Disclosure

None.

Ethical Conduct of Research

There was appropriate institutional review board approval through our institution's institutional review board and maintenance of protected patient health information.

Funding

None.

Conflicts of Interest

No relevant conflicts of interest.

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