INTRODUCTION

Bile duct injuries can have substantial medical and psychological impact on patients and can require significant healthcare resources for diagnosis and management. Iatrogenic injury during surgery is the most common etiology, but both blunt and penetrating trauma can cause bile duct injuries as well. There is a significant prevalence of variant biliary anatomy that poses a risk for biliary injury during surgery. Bile duct injuries are most commonly treated using endoscopic techniques but may require a multidisciplinary approach with percutaneous and surgical approaches as well. The topic of bile duct injuries pertains to several medical specialties including general and transplant surgery, gastroenterology, interventional radiology, and general medicine services which may work as a multidisciplinary team to formulate an individualized plan for each patient.

CAUSES OF BILE DUCT INJURIES

Laparoscopic Cholecystectomy

Bile duct injuries most commonly occur during surgery, and the surgery most frequently implicated is laparoscopic cholecystectomy. Bile ducts can be accidentally clipped, lacerated, avulsed, or completely transected during surgery, with the most severe injuries being the least common. Cystic duct remnant injuries have been and remain the most common injury following cholecystectomy. (Figure 1) The laparoscopic approach to cholecystectomy was introduced in the late 1980s, and although it provides many advantages over open cholecystectomy, it has been associated with a higher rate of biliary complications. The rate of bile duct injury for open cholecystectomy has been reported to be 0.1-0.2% (although it has been reported...
to be as high as 0.75%.

Due to intra-operative difficulties, surgeons convert about 4.7-8.2% of laparoscopic cholecystectomies to open procedures. The principal reason for converting in these cases is poor or limited visualization, distorted anatomy due to inflammation, and to control bleeding. Patients with a history of upper abdominal surgery often have distorted anatomy as well and are more likely to require conversion to open cholecystectomy. There is a learning curve associated with the technical skill required to perform laparoscopic cholecystectomies. One study found that novice surgeons who have performed less than ten laparoscopic cholecystectomies endure a bile duct injury rate of 0.49%, but surgeons with a tally greater than a hundred have a rate of only 0.04%.

A newer laparoscopic approach, known as single-port laparoscopic cholecystectomy, is typically performed through a single incision site in the umbilicus and poses additional opportunities and challenges for surgeons. This new approach is less invasive and potentially results in quicker recovery time, less post-operative pain, and better cosmetic results for patients. A recent meta-analysis of eleven randomized controlled trials revealed a nonsignificant difference in the bile duct injury rate comparing the single-port technique (0.4%) with conventional laparoscopic cholecystectomy (0%) with use of three or four ports. However, the authors recognized that only two of the included trials in the meta-analysis offered evaluation of bile duct injuries, which limits the validity of the results.

ORTHOTOPIC LIVER TRANSPLANT

Anastomotic Injuries

Liver transplant patients, both recipients and living donors, are at risk for bile duct injuries. Despite advances in surgical technique, biliary complications are still reported in 10-39% of liver transplant recipients, including strictures, leaks, anastomotic dehiscence, or a combination thereof. Strictures can occur at the site of the bile duct anastomosis or at distant locations in the biliary tree, and bile leaks can result from a failed anastomosis or direct injury to bile ducts. The anastomosis of the bile ducts between the donor liver and recipient can occur via a duct-to-duct, end-to-end choledochocholedochostomy, or via hepaticojejunostomy, and strictures occur with any of these approaches. Anastomotic strictures can result from surgical technique or bile duct ischemia that results in fibrosis and stenosis of the anastomosis. (Figure 2) The risk of developing an anastomotic stricture increases with time from transplant surgery, with a rate of 6.6% at 1 year and 12.3% at 10 years.

The following risk factors have been associated with the development of anastomotic strictures after orthotopic liver transplant: the presence of a post-operative bile leak, female donor-male recipient transplant combination, and a more recently performed transplant (although this may reflect improved diagnosis and increased graft survival which allows more time...
for anastomotic strictures to develop). A direct duct-to-duct anastomosis has been associated with a higher risk of post-transplant biliary complication than Roux-en-Y hepaticojejunostomy. Anastomotic strictures have a high recurrence rate of nearly 20% after initial successful treatment. Patients at risk for recurrent anastomotic strictures are those who experience a bile leak or have a longer time to presentation.13

Non-anastomotic Injuries

Non-anastomotic biliary strictures following orthotopic liver transplant can occur for several reasons. Bile duct ischemia from hepatic artery thrombosis is a recognized cause of non-anastomotic strictures. Ischemic-type biliary lesions, characterized by diffuse intrahepatic biliary strictures and dilatations in the absence of hepatic artery thrombosis, occur in 5-15% of orthotopic liver transplant patients and are not completely understood. Proposed risks for ischemic-type biliary lesions include compromised blood flow to the peri-biliary capillaries, immunologic injuries, and cytotoxic injuries from bile salts. Efforts to provide better perfusion of the small peri-biliary capillaries at the time of graft retrieval have resulted in a decreased incidence of ischemic-type biliary lesions. Other known causes of non-anastomotic strictures include ABO blood type incompatibility and immunologic rejection.9

Adult Living Donor Liver Transplant (ALDLT)

Approximately 1/3 of adult living donor liver transplantation recipients will develop some sort of biliary injury, although this rate has been reported in some centers to be as high as 67%. The incidences of bile duct leaks and strictures are similar in ALDLT recipients. For right hepatic lobe recipients, the anastomosis of the donor right hepatic duct to recipient common hepatic duct is associated with the lowest incidence of biliary complication when compared to all other anastomosis types. When donor liver grafts have more than one bile duct, a Roux-en-Y hepaticojejunostomy anastomosis is often used. Three-duct donor grafts have been associated with increased biliary complications when compared to single-duct donor grafts. The difference likely reflects a higher risk of bile duct ischemia when several small ducts are involved rather than a single large duct.11

The donors of ALDLT can also experience bile duct injuries. Bile leaks occur in 4-6% of living liver donors and are more common than bile strictures.16,17

Figure 3. ERCP image of a peripheral, intrahepatic duct injury with an associated leak in a patient who experienced blunt abdominal trauma and a liver laceration following an all-terrain vehicle (ATV) rollover accident.

Right lobe donors endure a higher bile leak rate and overall complication rate than left-sided donors. Right lobe grafts provide more liver parenchyma that can accommodate increased portal vein flow to the recipient, however this comes at the cost of a larger resection margin with increased risk of bile leak in the donor. A prospective study showed bile leaks in 7% of right hepatectomies and in 4% in left lateral hepatectomies and left lobe hepatectomies. Repeat operations are required in 1-4.5% of all living donors to address the most severe complications, but most bile leaks are controlled with less invasive techniques such as endoscopic retrograde cholangiography with stent placement, percutaneous transhepatic drainage or ultrasound-guided drainage.15,19

Transcatheter Arterial Chemoembolization (TACE) and Chemoinfusion (TACI)

Transcatheter arterial chemoembolization (TACE) and chemoinfusion (TACI) are interventional radiology procedures used to treat solid hepatic malignancies. These procedures are most often used to treat hepatocellular carcinoma (HCC) but are also used for other hepatic tumors as well. TACE consists of infusing iodized oil mixed with a chemotherapeutic agent directly into the tumor, followed by the infusion of gelatin sponge particles to embolize the blood vessels surrounding the tumor. Subcapsular bilomas and

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focal bile duct strictures are potential complications of TACE, and they often present in the context of serious bacterial infections such as cholangitis. Leaks and, more commonly, strictures in these patients can present in an acute or delayed manner.

Bile duct injury from TACE can occur in hepatic lobes separate from the tumor location. The iodized oil with the chemotherapeutic agent is often injected via the common hepatic artery, which can lead to bile duct necrosis with biloma or stricture formation in any segment of the liver. The hypertrophied peri-biliary capillaries in a cirrhotic liver may act as a vascular shunt that protects against bile duct ischemia after TACE. In fact, Child-Pugh class A patients have a higher rate of bile duct injury (15.2%) following TACE when compared with Child-Pugh class B and C patients (2.7%). Bile duct injury from TACE is also more common with non-hepatocellular carcinoma tumors (38.9%) compared to HCC tumors (11.3%). TACI, which involves chemoinfusion without embolization, has a significantly lower risk of bile duct injury than TACE.

Resection and Radiation of Hepatic Tumors

Patients may undergo partial hepatectomy as definitive treatment for hepatocellular carcinoma. Bile leaks are common post-operative complications and occur in up to 12.8% of cases. Pre-operative treatments such as TACE or radiofrequency ablation do not increase the risk for development of a post-hepatectomy bile leak per se. However, if these pre-operative treatments were complicated by a bile leak or stricture, then the patient is at increased risk for a post-hepatectomy bile leak as well. Prolonged operative time has also been identified as a risk factor for bile leak after hepatectomy.

Patients with either primary or metastatic liver tumors may receive radiation therapy as an element of their cancer treatment. Delivery of radiation to these tumors creates a risk of developing fibrosis and bile duct strictures. Stereotactic body radiation therapy (SBRT), which involves accurate delivery of radiation directly to the tumor, is a potential therapy for tumors in high-risk areas such as the hepatic hilum that cannot otherwise be treated safely with surgery, TACE, or radiofrequency ablation. When specific radiation doses are used (40 Gy or less), SBRT has been associated with minimal biliary toxicity and is a viable option for treatment of tumors within the hepatic hilum.
Traumatic Bile Ducts Injuries

Penetrating and blunt trauma can result in injuries to the structures of the portal triad, including the extrahepatic bile ducts, hepatic arteries, and portal vein. Traumatic injuries to these structures are infrequent but are associated with high mortality rates ranging 50-52% for vascular injuries but reported as high as 75% for portal vein injuries.25,26,27,28,29 Trauma resulting in extrahepatic bile duct injury carries a mortality rate of 10-31%, and high-grade traumatic injury to the liver has a mortality rate up to 37.5%.28,29 The majority of these mortalities occur on day of admission while in the operating room due to exsanguination from vascular injuries.25,28

The most common causes of penetrating trauma to bile ducts include gunshot wounds, stab wounds, and shrapnel injuries. Penetrating trauma often results in a partial bile duct laceration rather than a complete transection, although transection can be seen in some patients as well.25 Blunt trauma to biliary system is most often secondary to motor vehicle crashes but also includes falls and assaults. (Figure 3) Blunt force to the abdomen can also result in hematoma formation, which can cause extrinsic compression of bile ducts and lead to biliary obstruction.31

Trauma to the liver can result in bile duct injuries. Liver lacerations due to stab wounds or gun shot wounds can result in intrahepatic biliary complications in the form of a biloma or biliary fistula. A recent study of hepatic trauma identified that bile leaks occur more commonly in patients with penetrating trauma, those undergoing operative management, damage control surgery with packing of the liver and those with higher-grade liver injury.30 High-grade liver injuries (grade 3-4 on American Association for the Surgery of Trauma Organ Injury Scale) are associated with bile duct injuries in up to 25% of cases.28 Approximately 2.8-7.4% of patients who experience blunt hepatic traumas of all grades have a biliary complication, most commonly bile leaks with associated biloma formation.28,31

Variant Biliary Anatomy

The existence of aberrant biliary anatomy and anatomic variations of the biliary tree creates an increased risk for iatrogenic bile duct injury. Surgeons may or may not be aware of aberrant biliary anatomy at the time of surgery depending on the type of preoperative imaging obtained.

The duct of Luschka was first described in 1863 as a thin bile duct passing through the gallbladder fossa to join the right hepatic or common hepatic duct, although this can also manifest as a small duct that connects to peripheral right intrahepatic branches.32 The prevalence of the duct of Luschka has been reported in 4.6-30% of dissected liver specimens. The ducts are typically thin, measuring 1-2mm in diameter, with variable sites of origination within the liver and sites of union with the biliary tree.32,33

Magnetic resonance cholangiopancreatography (MRCP) of patients suspected of having pancreaticobiliary disease demonstrated anatomic variations in 24.2% of patients. These anatomic variations included an aberrant right hepatic duct in 4.8%, right posterior hepatic duct in 5.7%, trifurcation in 0.8%, low medial cystic duct insertion in 3.8%, long and short cystic ducts in 1.7% and 0.63% respectively, vascular compression of the common hepatic duct in 2.5%, and 2.3% of patients had more than one anatomic variation.34 Bile duct injuries originating from aberrant biliary anatomy have proven difficult cases for providers that necessitate multiple diagnostic modalities and, in some cases, a multidisciplinary approach, to diagnose and treat the underlying injury associated with the aberrant anatomy.35

DIAGNOSIS OF BILE DUCT INJURIES

Clinical Presentation of Bile Duct Injuries

The most common presenting symptom experienced by patients with bile leaks is abdominal pain, often accompanied by fever, due to the inflammation of the peritoneum caused by bile which may or may not become secondarily infected. Patients may also have abnormal liver function tests at presentation, although patients who have leaks alone often have normal serum bilirubin levels as the bile is pooling within the abdomen.2 An increase in serum bilirubin without elevation of transaminases may represent the presence of a bile duct injury, particularly a bilio-venous fistula where bile can flow down its pressure gradient and into the venous system.36

Biliary strictures often have a more insidious clinical onset with cholestatic symptoms such as jaundice and pruritus. The median time to presentation for patients with biliary strictures is 7 to 9.6 months but ranges as early as 6 days and as late as several years following the inciting surgery.37,45 Patients with biliary strictures can present acutely with cholangitis and serious bacterial infections as well.21 Patients may have concomitant
biliary strictures and leaks depending on the severity of the injury. (Figure 4)

**Diagnostic Imaging Modalities**

The biliary tree can be imaged by multiple modalities, including MRCP, hepatobiliary scintigraphy (HIDA scan), and cholangiograms obtained by endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiography (PTC), and intraoperative cholangiogram (IOC). Several studies have investigated the efficacy of IOC during laparoscopic cholecystectomy, and overall they have concluded that obtaining an IOC in every cholecystectomy reduces the rate of bile duct injury from 0.42% to 0.21% and increases the rate of intra-operative detection of bile injuries from 21.7% to 76.9%. Opponents of universal IOC during cholecystectomy caution against the increased operative time, cost, and limited practical use of the procedure. One large study found that only 82.7% of attempted IOCs were successful, and the estimated additional operating to perform IOC was only 19 minutes.

Bile duct injuries are most often diagnosed from a cholangiogram performed during ERCP or PTC, however many noninvasive imaging techniques, such as MRCP and HIDA scan, can be employed to evaluate the biliary tree as well. MRCP has been utilized to assess the biliary anatomy of donor livers prior to living donor liver transplantations and can detect variant biliary anatomy with a sensitivity of 85.6%. HIDA scan is a noninvasive nuclear medicine study used to evaluate the vascular flow and biliary drainage of the liver and extrahepatic bile ducts. The sensitivity of HIDA scan to diagnose bile leaks after laparoscopic cholecystectomy and liver transplantation has been reported to be between 83-100%. HIDA scan has proven to be successful at diagnosing traumatic bile leaks as well. Biliary strictures can also be detected by HIDA scan with a reported sensitivity of 75% and specificity of 97%, often manifesting as a failure of the radiotracer to reach the duodenum after protracted amounts of time.

**Treatment of Bile Duct Injuries**

The treatment of bile duct injuries can often require a multidisciplinary approach with several therapeutic possibilities including surgery, endoscopy, and interventional radiology approaches. Bile duct injuries can be managed surgically by re-establishing biliary continuity through reconstructive surgery or by suturing open injuries, although in current practice most biliary injuries are primarily treated endoscopically if at all possible. If patient outcomes are the same, then nonsurgical approaches are preferred.

**ERCP for Bile Duct Injuries**

ERCP with dilation and stent placement and/or sphincterotomy (as needed) has proven to be a successful method of treating bile leaks and strictures and is the current gold standard and first line treatment for most biliary injuries. These therapies can open up strictures, and allow for stent placement to reduce the pressure gradient across a stricture or the sphincter of Oddi, which directs bile to flow downstream into the proximal duodenum and not out of the leak site. Directing the flow of bile away from the site of injury allows the defect to subsequently heal.

In patients with low-grade bile leaks (defined as bile leaks that are visualized during ERCP only when there is full opacification of the intrahepatic biliary tree with contrast, indicating that more pressure is required to force contrast and bile out of the duct injury site), endoscopic sphincterotomy alone has been reported to lead to successful resolution of the bile leak in 91% of patients, although many patients will receive a stent alone in this situation as stent placement is (continued on page 64)
a lower risk maneuver than biliary sphincterotomy. Patients with high-grade bile leaks (visualized during ERCP before intrahepatic biliary tree opacification, indicating a more brisk flow of bile through the leak site) require either stenting or (rarely) surgical ligation for successful resolution of the leak. The reported success rate of treating post-surgical bile leaks with endoscopic placement of biliary stents ranges from 77-100%. As one would imagine, less severe bile duct injuries have higher success rates with stenting than more severe or complex injuries. Of the Strasberg classification of bile duct injuries, Class A injuries (leak of cystic duct or small accessory duct) have reported success with ERCP and stent placement in 99% of cases. More severe Class E1 through E5 bile duct injuries (stricture or complete transection of the common bile duct or common hepatic duct) have a reported successful treatment in 77% of attempted ERCPs, but the majority require immediate surgical intervention.

Bile duct strictures due to surgical injury often require long-term stenting with multiple follow-up ERCPs to obtain resolution of the strictures. Success rates of 71% and 74% have been reported after six and eleven months of stent therapy, respectively. Anastomotic strictures following OLT and ALDLT are successfully treated by endoscopic dilation and stenting in 74-88.9% of cases. However, up to 18% of patients have stricture recurrence after successful initial treatment of the anastomotic stricture, and they may require anywhere from one to four additional ERCPs for successful treatment. The simultaneous presence of both a bile duct stricture and a bile leak following surgery is a well-documented risk factor for recurrent strictures.

Endoscopists have long used plastic stents in the treatment of benign, post-operative biliary strictures. Uncovered metal stents, commonly used in the palliative treatment of malignant bile duct strictures, were trialed in 1990s for the treatment of benign post-surgical strictures as an alternative to plastic stents. Although they helped reduce the frequent stent exchanges required with plastic stents, metal stents encountered high rates of stent occlusion and stricture relapse due to ductal mucosal hypertrophy through the stent mesh with resulting recurrent obstruction which proved to be difficult to treat. Covered self-expandable metal stents (C-SEMS) that are removable have been developed to prevent stent occlusion and may be used for temporary stenting of benign bile duct strictures. Success rates of 88-90% have been reported for C-SEMS in the treatment of benign biliary strictures that were initially refractory to plastic stent treatment. Recurrence rates of 7.1-12% were reported within 16 months of stent removal. Post-liver transplant anastomotic strictures are often stented using an increasing number of plastic stents to progressively dilate the stricture, although this practice is much less common in the era of fully covered metal biliary stents. Fully covered metal stents, which can provide a similar dilation diameter as several plastic stents, have achieved similar resolution rates in anastomotic strictures. Metal stents do carry a risk of migration (ranging 16-24.2%) but most often migrate distally into the duodenum and are expelled without causing clinical complications. Furthermore, migration is not always to be considered a negative event as it may signify resolution of the underlying stricture.

**Percutaneous Transhepatic Catheter (PTC) Drainage for Bile Duct Injuries**

PTC is a non-surgical approach that is often attempted after failure of ERCP to treat bile duct injuries. PTC is also performed when bile ducts cannot be accessed by ERCP, often due to post-surgical bowel anatomy (most commonly in patients with a Roux-en-Y gastric bypass). PTC is performed by interventional radiologists and provides the same physiologic treatment as ERCP, via dilation and stent placement, but through a percutaneous transhepatic approach. PTC with a biliary-enteric stent placed across the sphincter of Oddi has a reported success rate of 77.2-80% at treating bile leaks. This success rate is seen with nondilated intrahepatic bile ducts as well, which were once thought to be a contraindication to PTC due to difficult percutaneous accessibility. The success rate of treating post-surgical bile duct strictures with PTC dilation and stenting has been reported from 58.8-81%.

**Management of Traumatic Bile Duct Injuries**

Patients with blunt and penetrating traumatic injuries to the biliary system can often be safely managed nonsurgically via ERCP. Patients with bile leaks secondary to gunshot wounds and stab wounds have had successful resolution of bile leaks when managed nonsurgically with sphincterotomy and/or stent placement.
Bile Duct Injuries: Multidisciplinary Evaluation and Treatment

It is the standard of care to manage patients with blunt hepatic trauma non-surgically. One study evaluated non-operative management of severe, grade 4 and grade 5, blunt liver injuries (parenchymal disruption of 25-75% and >75% of a hepatic lobe, respectively) and found that ERCP successfully treated 81% of bile leaks in these cases. Two independent predictors for failed non-operative management were identified: admitting systolic blood pressure less than 100mmHg and presence of additional abdominal organ injury. Failure of non-operative management was seen in 23% of patients with both of these predictors and only 4% with neither. Complex bile duct injuries, such as complete transection or strictures of the common bile duct, common hepatic duct, or disruption at the level of hepatic duct bifurcation, almost always require surgical intervention after diagnosis by ERCP. (Figure 5)

Surgical Reconstruction as Treatment of Bile Duct Injuries

Referral to a tertiary medical center for surgical intervention is often necessary with severe bile duct injuries. Primary end-to-end anastomosis may be performed when the loss of tissue from the bile duct transection is not significant. This technique has been associated with a high rate of stricture formation at the anastomosis site, but nearly two-thirds of these strictures can be successfully managed endoscopically without further surgery. When end-to-end anastomosis is not possible, a Roux-en-Y hepaticojejunostomy (RYH) is the preferred treatment. Strictures can occur with RYH as well, but the stricture rate is reduced when the anastomosis is performed more proximally where right and left bile ducts join, rather than at a more distal site in the common hepatic duct. Patients with severe bile duct injuries may rarely develop chronic complications such as secondary sclerosing cholangitis with associated cirrhosis or acute liver failure; rarely, liver transplant can be required.

Morbidity and Quality of Life after Bile Duct Injuries

Bile duct injuries and the subsequent therapies can result in short term and sometimes life long complications for patients. One study followed patients after surgical reconstruction for bile duct injuries, reporting a mean hospital stay of 17 days following surgery, with 38% requiring acute readmissions within the first year most commonly for cholangitis. At one year follow up, 62% of patients remained asymptomatic, 28% continued to have episodic cholangitis, and 10% had persistently elevated liver function tests but were asymptomatic. Another study evaluated patients at a mean of 70 months after treatment of bile duct injury following laparoscopic cholecystectomy, reporting 93% of endoscopic treatments and 84-94% of Roux-en-Y hepaticojejunostomies remained functionally successful without need for additional surgery. Despite the promising reports of these treatment success rates, the patients reported on questionnaires a significantly poorer quality of life on mental and physical scales compared to controls.

CONCLUSION

Biliary injury can occur via many routes. Laparoscopic cholecystectomy and liver transplantations are the most common surgeries associated with bile duct injuries, but other treatments for hepatic malignancy such as TACE, partial hepatectomy, and radiation may result in bile duct injuries as well. ERCP remains the principal method of diagnosis and treatment using plastic or covered metal stents. Percutaneous and surgical approaches can be utilized as well to properly treat each individual case, and complex bile duct injuries often require multidisciplinary treatment.

References

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