Review

PERCUTANEOUS TRANSHEPATIC INTERVENTION FOR MALIGNANT BILIARY OBSTRUCTION

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ABSTRACT

Biliary obstruction is a serious clinical condition resulting from either benign or malignant etiologies. For malignant obstruction, curative resection is rarely performed due to disease progression, thus decompression drainage is the management of choice. Percutaneous transhepatic drainage and stenting are effective alternative treatments to surgical bypass and endoscopic biliary drainage when these two modalities are contraindicated. Percutaneous biliary intervention is safe and effective in both drainage and restoration of bile flow with high successful rate and acceptable risk of complication. Multidisciplinary approach, proper patient selection, careful image review and comprehensive knowledge of available techniques, success rates and complications are utmost importance for a successful procedure.

Key words: *malignant biliary obstruction, percutaneous transhepatic biliary drainage, stenting*

I. INTRODUCTION

Biliary obstruction is a serious condition that can occur in the setting of both benign and malignant pathologies, leading to life quality impairment, pruritus, cholangitis and liver failure [1-3]. Malignant biliary obstruction most commonly results from pancreatic adenocarcinoma and cholangiocarcinoma, followed by gallbladder carcinoma, hepatocellular carcinoma, lymphoma, liver metastasis and perihilar lymphadenopathy [4,5].

Curative resection is the primary goal of treatment but rarely possible because of local invasion and distant metastases at the time of diagnosis [2,4]. Therefore, palliative decompression of advanced malignant obstruction by biliary catheterization or stent placement remains a key component in the management of these patients [4]. Decompression of the biliary system relieves pain, decreases jaundice and risk of cholangitis, improves liver function prior to curative therapy, and provides a bridge to palliative chemotherapy [6]. Restoration of the biliary to bowel transit also allows physiological bile flow [6]. Biliary drainage can be achieved from surgical bypass, endoscopic biliary drainage (EBD) or percutaneous transhepatic cholangiography depending on the etiology and the chance for cure [2,4]. Importantly, the most

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effective strategy to manage malignant biliary obstruction should combine a multidisciplinary team of hepatobiliopancreatic surgeons, medical oncologists, diagnostic radiologists, surgical oncologists, gastroenterologists, and interventional radiologists [4].

Percutaneous transhepatic biliary drainage (PTBD) is a therapeutic procedure that includes the sterile cannulation of a peripheral biliary radicle or an intrahepatic duct (IHD) after percutaneous puncture followed by imaging-guided wire and catheter manipulation. Placement of a tube or stent for external and/or internal drainage completes the procedure. Percutaneous therapy of biliary lesions is often staged, requiring several sessions to achieve the therapeutic goals [7]. Since its introduction in the late 1960s, PTBD has been used globally to treat biliary obstruction of both benign and malignant causes [1,8]. The procedure is especially beneficial for patients who are not candidates for curative operation or endoscopic intervention. Surgical bypass demonstrated low rates of recurrent jaundice (2-5%), however, the surgery itself carries an appreciable risk of postoperative morbidity and mortality, in up to ¼ of the patients in some trials [5]. In cases of malignant biliary obstruction, the first choice of treatment worldwide is EBD. However, EBD is not always feasible due to duodenal obstruction or previous surgery that has altered the anatomy. Under these circumstances, and in cases where prior EBD has been insufficient or failed, PTBD is often a suitable treatment option [9,10]. This procedure is a potential option for any case of biliary obstruction, but always first line for malignant lesions above the level of the common hepatic duct, particularly for advanced unresectable hilar malignant biliary obstruction [2,4]. This article aims to highlights the perspectives of radiological intervention for malignant biliary obstruction. Clinical cases from Hue University of Medicine and Pharmacy Hospital are also illustrated.

II. INDICATIONS AND CONTRAINDICATIONS OF PTBD

PTBD is performed as a preoperative procedure for resectable malignancies, prior to neoadjuvant chemotherapy or as a palliative technique [6]. Indications of PTBD are based on the practice guideline of the Society of Interventional Radiology [7], as followed:

- Provide adequate biliary drainage

+ Decompress obstructed biliary tree

+ Divert bile from and place stent in bile duct defect

- Provide a portal of access to the biliary tract for therapeutic purposes that include but are not limited to:

+ Dilate biliary strictures

+ Remove bile duct stones

+ Stent malignant lesions

+ Brachytherapy/phototherapy

+ Endoluminal tissue sample or foreign body retrieval

- Provide a portal of access to the biliary tract for mid-to long-term diagnostic purposes (lower-risk cholangiography)

Coagulopathy is a relative contraindication to PTBD. Every effort should be made to correct or improve coagulopathy before the procedure. In patients with persistent coagulopathy, these procedures may still be indicated if they are associated with a lower expected morbidity rate than alternative methods of diagnosis or treatment [7]. Other relative contraindications include INR >1.5, platelet count < 50,000 x 10^9/L, ascites and multiple hepatic cysts [11].

III. TECHNIQUES OF PTBD

Patient consent must be obtained prior to any procedure. Prophylactic antibiotic should be instituted before and after the procedure, as manipulations in obstructed system carry the risk of cholangitis and sepsis. For pain alleviation, intravenous analgesics can be administered or optionally the procedure can be performed under conscious sedation. Fasting for at least 4 h prior to the procedure is necessary [11].

We routinely perform PTBD using Seldinger technique (Figure 1) with a micro puncture set (Neff set, Cook medical, Bloomington, IN, USA).

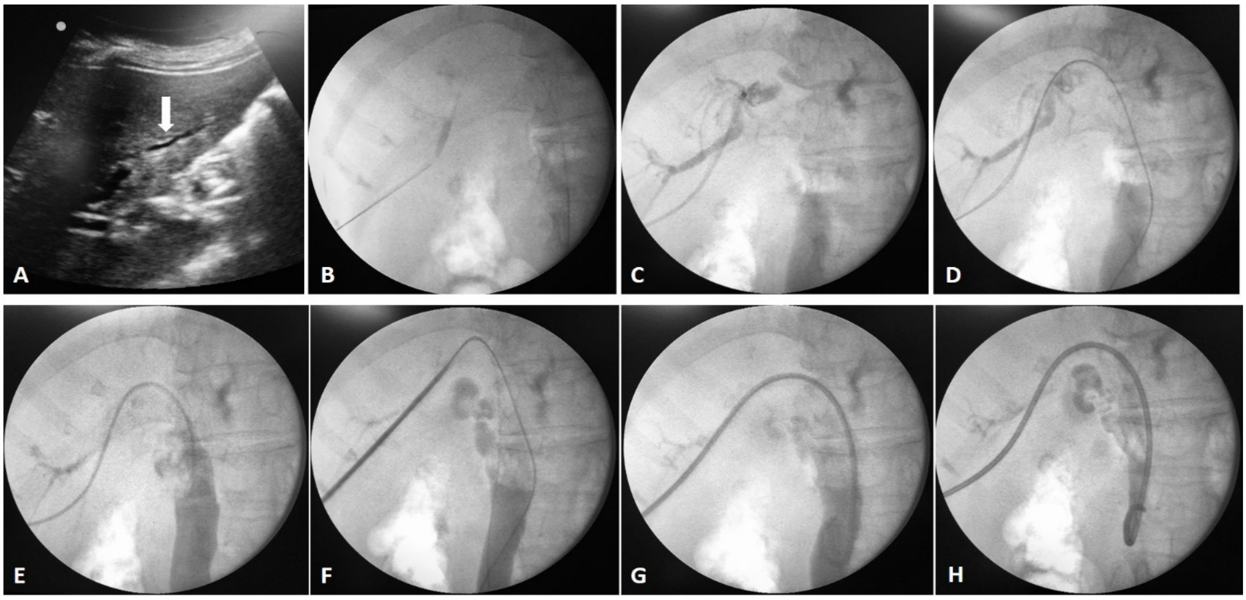

Figure 1: Pre-operative PTBD using Seldinger technique in a patient with ampullary cancer. (A) A segmental IHD dilatation was seen on ultrasound (arrow). (B) Ultrasound-guided puncture of the selected IHD. Contrast medium was injected to confirm the IHD and a 0.018" hair wire was advanced to the distal common bile duct (CBD) under fluoroscopic guidance. (C) A 5F sheath was introduced over the wire and cholangiography was performed to evaluate the biliary tree anatomy and pathologies. (D) A 0.035" J tip hydrophilic wire was manipulated across the obstruction site to the distal CBD followed by an introduction of an angiographic catheter. (E) Cholangiography of the downstream CBD was done. (F) The tract was dilated with an 8F dilator. (G) An 8F pigtail drainage catheter was advanced over the wire and positioned in the distal CBD. (H) Completion cholangiography and aspiration were performed to confirm the desired catheter position and function.

- Patient is in supine position. After sterile preparation, local anesthesia is given at the expected puncture site.

- A dilated peripheral duct is targeted using a 22G Chiba needle under ultrasound guidance. A small amount of contrast medium is injected to confirm the bile duct. A 0.018" hair wire is then advanced through the needle to the bile duct under fluoroscopic guidance.

- A small skin incision is made and the tract is created followed by an introduction of a 5F sheath. Cholangiography is performed to evaluate the biliary tree (anatomy, obstruction site, type of obstruction, filling defect, common bile duct patency, bile leak…).

- A 0.035" hydrophilic wire (Terumo, Tokyo, Japan) is used to cross the obstruction. An angiographic catheter (usually Cobra 5F) can be used to help manipulate the guide wire. Once the wire is across the stricture and in the duodenum, the catheter is pushed over the wire into the duodenum. The soft wire is then replaced by a Super Stiff Amplatz guide wire (Boston scientific, Natick, MA, USA) over which the tract and stricture are dilated with an 8F dilator. Finally, a drainage catheter (8F, 10F) is positioned across the stricture. A completion cholangiography and aspiration are performed to confirm the position and the function of the catheter.

- The catheter can be placed proximally to the obstruction site for external drainage or distally for internal-external drainage (Figure 2). In the latter case, multiple side holes are created on the drainage catheter to ensure effective drainage of both upstream and downstream biliary tract.

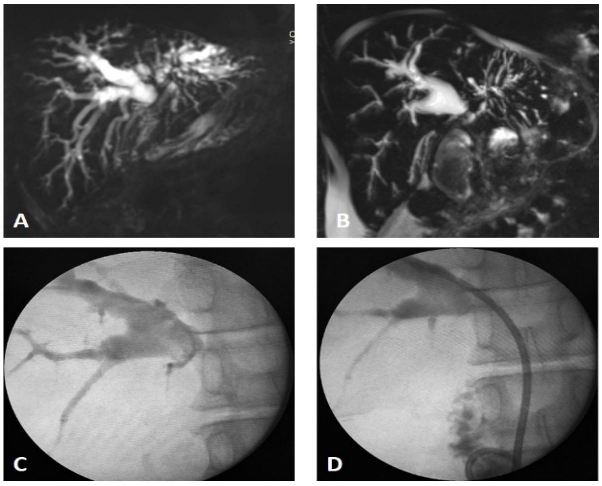

Figure 2: External drainage and external-internal drainage of the same patient. (A, C): Magnetic retrograde cholangiopancreatography (MRCP) image and cholangiogram of an external drainage for a malignant hilar obstruction. (B, D): Follow-up MRCP and external-internal drainage catheter was exchanged. Multiple side hole were created along the catheter to optimize drainage efficacy.

Depending on the type and extent of the obstruction, patient status, unilateral or bilateral drainage (T vs. Y configuration) will be decided (Figure 3, 4). Multiple segment drainage may also be performed when secondary confluence is involved. In case of chronically obstructed biliary segments with parenchymal atrophy, except for biliary infection, drainage is usually ineffective since improvement of liver function is unlikely [6].

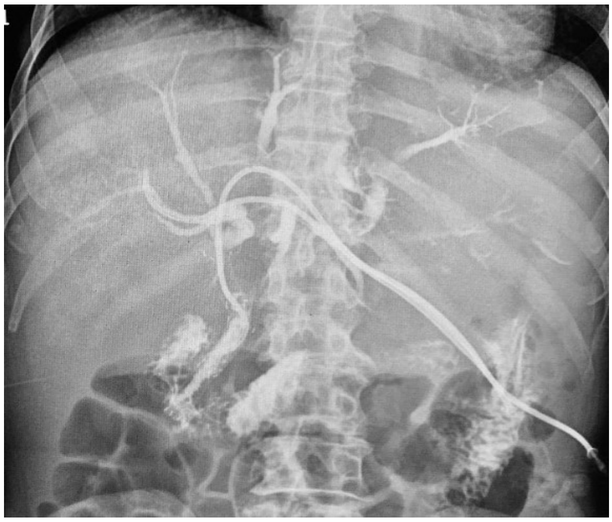

Figure 3: Unilateral PTBD with T-configuration catheter in a patient with multiple liver metastases. The biliary tree was approached from the segment 3 (B3), from which 2 drainage catheters were inserted, one to the right IHD and the other to the CBD. Multiple side holes were also created. Noted a good passage of contrast medium through 2 previously inserted CBD metallic stents.

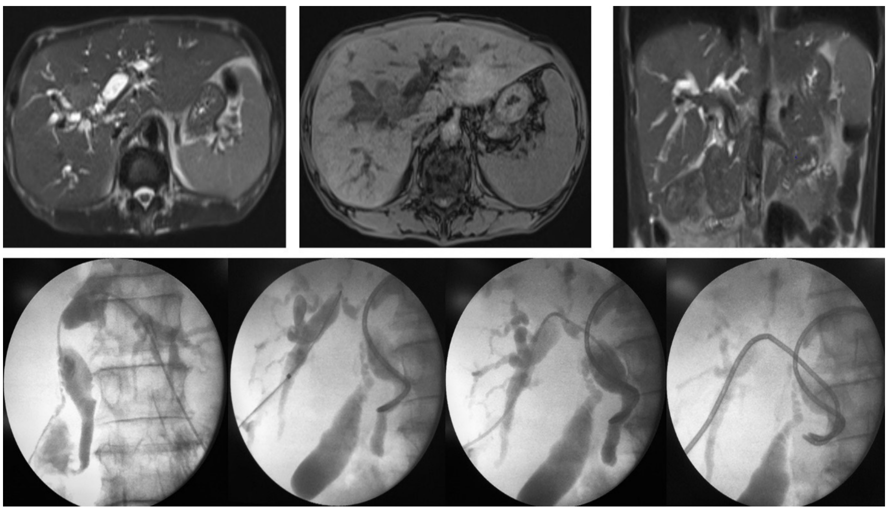

Figure 4: Bilateral PTBD with Y-configuration drainage catheters for the management of a type II Klatskin tumor. Left IHD was accessed from segment 3 and right IHD from segment 6. Catheter tips were positioned in the distal CBD across the hilar obstruction. Multiple side holes were made to ensure external-internal drainage.

- The drainage catheter is secured to the skin and attached to a urine bag through a 3-way stopcock to facilitate daily irrigation or sampling. Saline irrigation is recommended twice daily thereafter.

Left vs. right-sided PTBD

The procedure can be performed either via right (subcostal or intercostal) or left ductal (subxiphoid) approach. Selection of appropriate sided duct is down to operator preference, although there are certain advantages and disadvantages of both (Table). Castiglione found that right access is associated with intercostal pain and respiratory difficulties whereas left access for PTBD provides a better Quality of Life for patients who underwent PTBD as palliative treatment for the management of malignant obstructive jaundice and could be considered as the approach of choice in case of distal obstruction [12]. Reviewing ultrasound prior to biliary puncture is crucial for assessing the suitability of puncture as well as any contraindication to the procedure [11].

Table 1: Comparison between left-sided vs. right-sided IHD puncture

	Left-sided puncture	**Right-side puncture**
Advantages	Easier to puncture Better patient's compliance More preferable in ascites	Less radiation exposure to operator's hand More liver segment drainage
Disadvantages	More radiation exposure to operator's hand	More painful due to continuous irritation of intercostal nerves More chances of accidental catheter dislodge due to constant motion of the drainage catheter in the intercostal space during respiration

Biliary stenting

Once the obstruction is traversed, stent can be deployed to recanalize bile flow. Self-expandable metallic stents are more preferable due to their higher patency rates (Figure 5). We usually insert stents 1-2 weeks after the 1st PTBD to prevent complication (cholangitis) (Figure 6). The proximal and distal ends of the stent should be at least 1 cm and preferably 2 cm from the proximal and distal ends of obstruction, respectively [6].

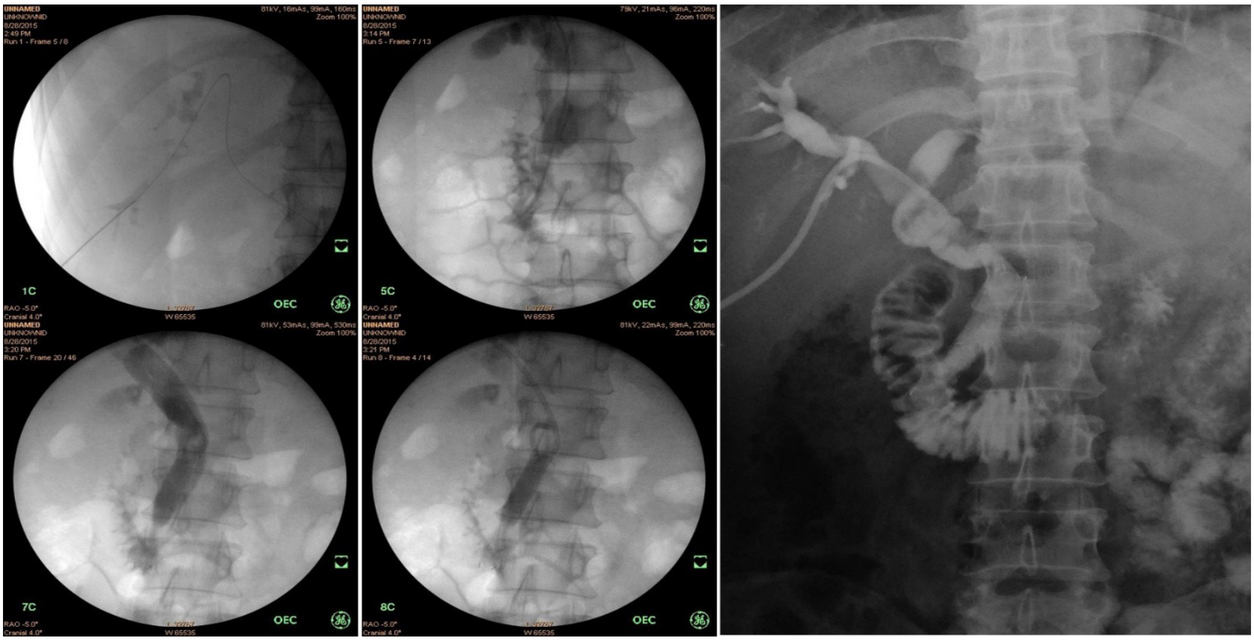

Figure 5: Biliary stenting in a patient with distal CBD cancer. Follow-up cholangiogram through a pigtail catheter confirmed the patency of the bile flow.

We sometimes pre-dilate the obstruction site with low pressure balloon to facilitate stent passage. The metallic stents have thermal memory and expand to their maximum width when they reach the body temperature, usually occurring in 2448h. If the expansion is not adequate after 48h, dilatation of the stent with balloon catheter may be needed for successful drainage. Self-expandable metallic stents can be either covered or uncovered. Uncovered stents are usually preferred due to their lower costs, very low incidence of migration and lower complications of cholangitis and pancreatitis but have higher incidence of tumor ingrowth [6]. The patency rate for uncovered stents is about 70% at 6 months and 50% at 1 year.

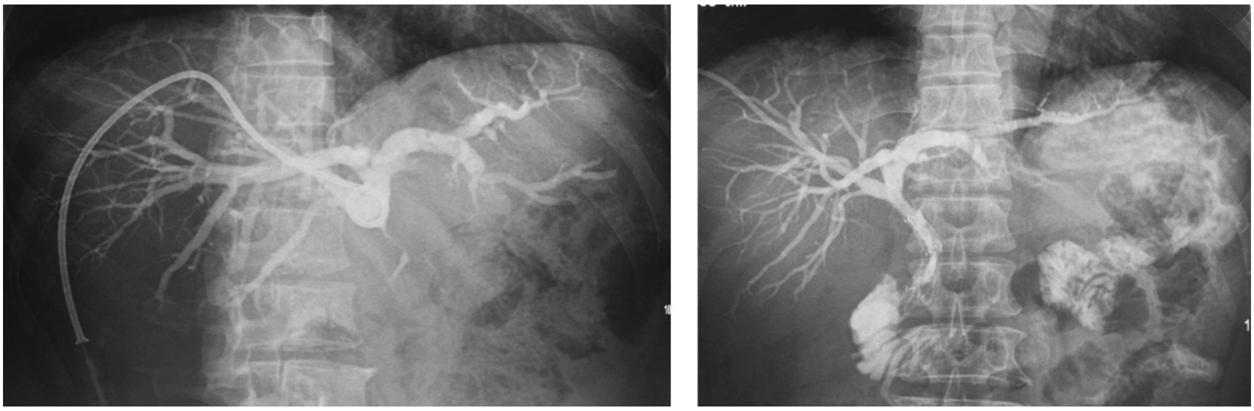

Figure 6: PTBD and CBD stenting in a patient presented with biliary septic shock. He was previously treated with surgical bypass due to pancreatic head cancer. PTBD was performed for decompression followed by CBD stents deployment to maintain the bile flow.

One study showed that performing PTBD and stenting as a "one-stage" procedure is useful, safe, and cost-effective with a high percentage of technical success and a similar occurrence of complications compared to the two-stage procedure [13]. Like PTBD, stent can be inserted unilaterally or bilaterally with a T or Y-configuration (Figure 7, 8, 9).

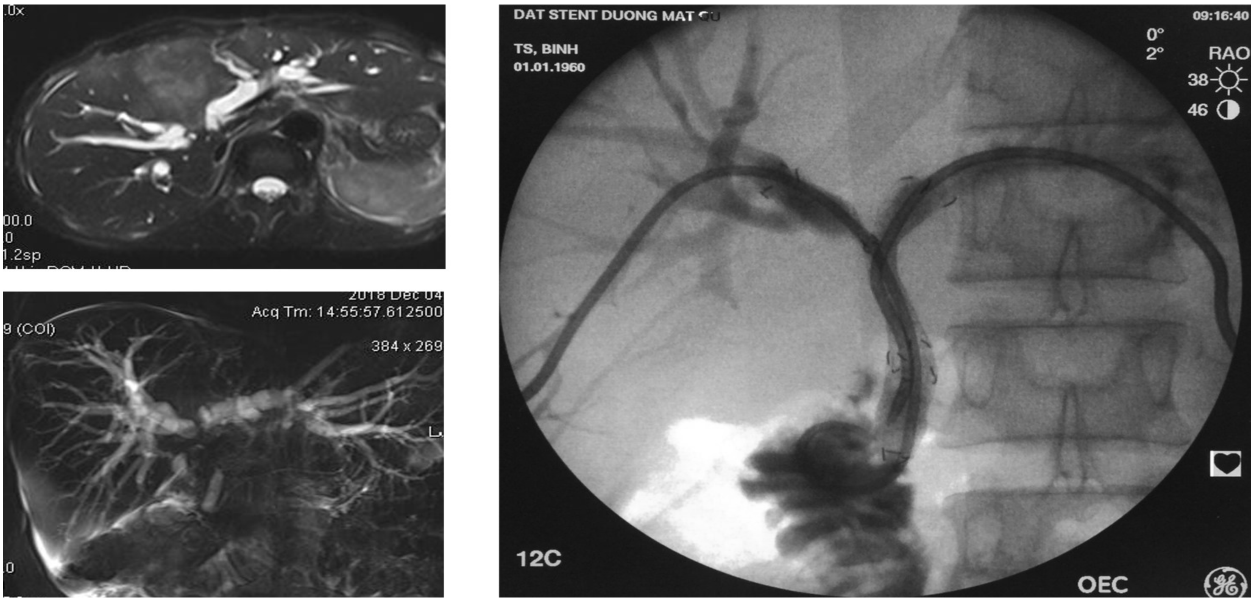

Figure 7: Bilateral biliary stenting with Y-configuration in a patient with type II Klastkin tumor. Noted that 2 drainage catheters were left in place for at least 1 week post stenting to ensure full expansion of the metallic stents.

IV. OUTCOMES OF PTBD

Technical success rate of PTBD is 95% for dilated duct and 70% for non-dilated duct [7] and clinical success is >75% [12]. A recent study reported technical success of PTBD was 91.2% in high risk patients and concluded that PTBD can be effectively and safely performed even in situations which potentially increase risk of adverse events [10]. Drainage of 25%30% of normal liver is adequate to improve jaundice and liver functions [6].

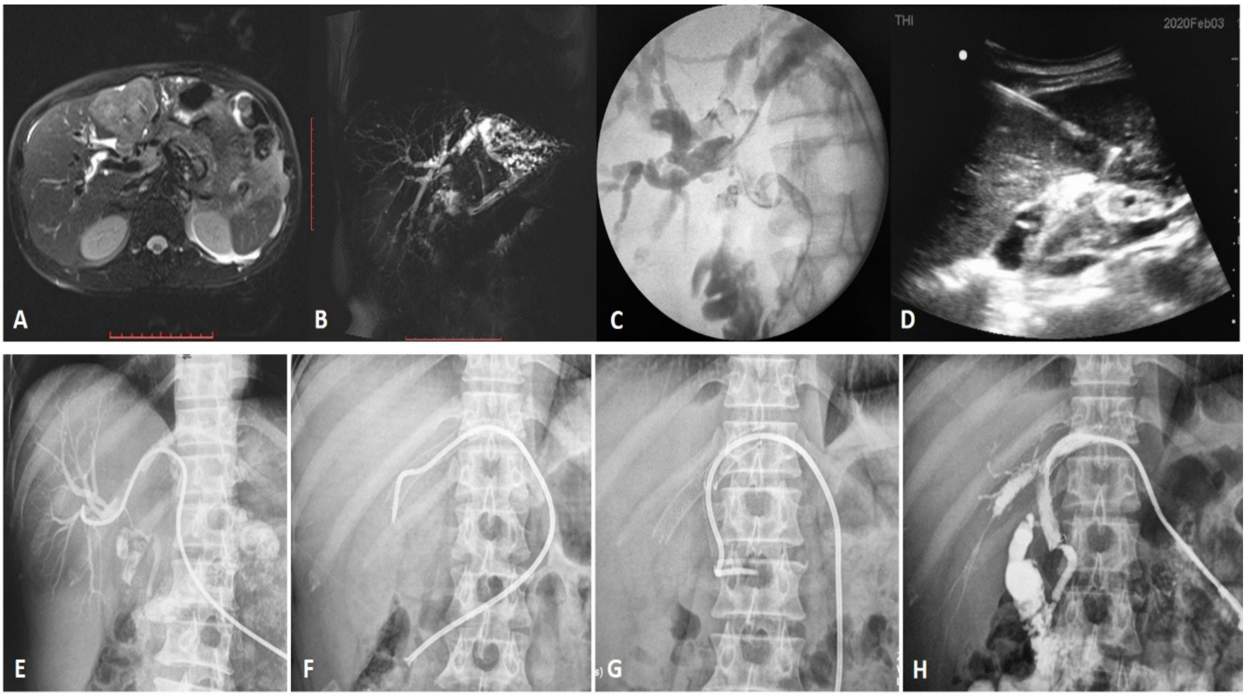

Figure 8: Bilateral T-stent for the management of type II hilar obstruction. (A, B) T2W FS MRI and MRCP showed a mass-forming and an intraductal tumor causing prominent left IHD dilatation. (C) A left-to-right PTBD was performed with multiple side holes. Cholangiogram demonstrated a filling defect at the confluence. (D) Intraoperative biopsy was performed which later confirmed the diagnosis of cholangiocarcinoma. (E, F) A left-to-right stent was deployed. Cholangiogram showed patency of stent. Note the filling defect within the stent (tumor ingrowth) and severe stricture of the common hepatic duct and proximal CBD. (G) A left-to-CBD stent was subsequently inserted through the struts of the initial stent. (H) Follow-up cholangiogram confirmed the stent patency without IHD dilatation. The drainage catheter was removed shortly.

Data comparing PTBD and EBD as an initial procedure prior to surgery are inhomogeneous. A meta-analysis shows that PTBD has a lower rate of complications than EBD as an initial procedure and is associated with less conversion and lower rates of pancreatitis and cholangitis [14]. Conversely, Mori et al concluded that PTBD is significantly associated with shorter survival and peritoneal recurrence and should not be performed for patients undergoing pancreatoduodenectomy [15]. Another study observed a similar median decrease in total bilirubin levels after biliary drainage between PTBD vs. EBD and these 2 modalities had similar long-term disease-specific survival and recurrence-free survival [16]. However, another study found that bilirubin decreased from 237 µmol/l (31-634) to 180 µmol/l (17-545) within the first week after PTBD and only 25% reached a level below the double upper reference value while adverse events are common [17].

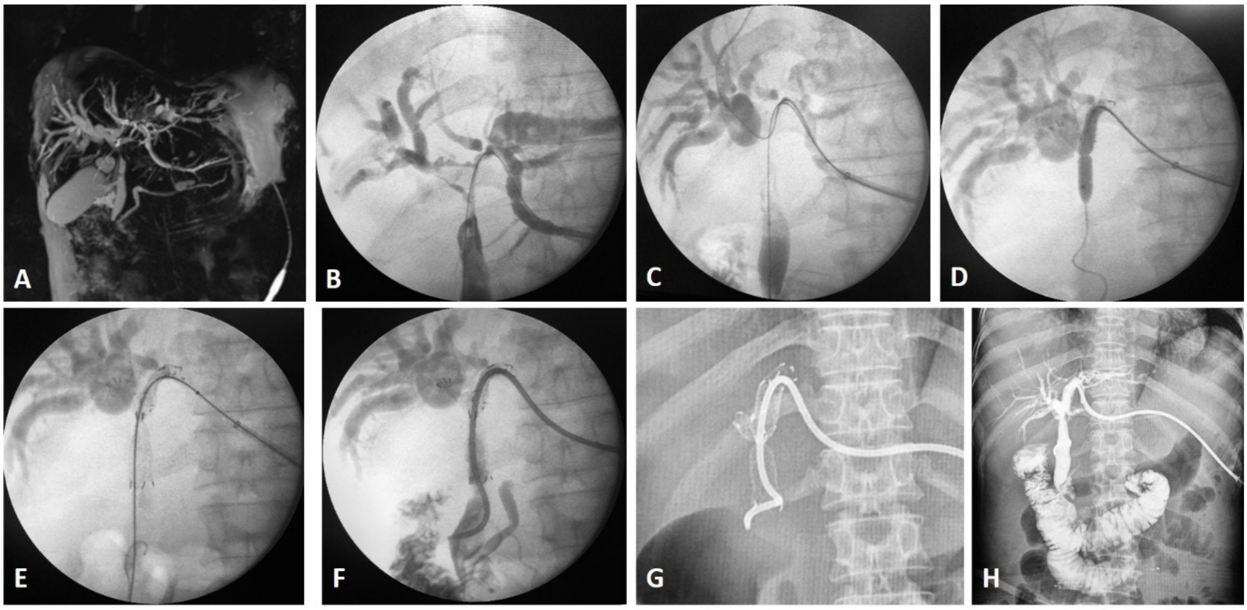

Figure 9: PTBD and bilateral stenting using T-configuration. (A) MRCP image showed extensive IHD dilatation due to type IV Klatskin tumor. (B). Cholangiogram demonstrated severe stricture at the confluence extended to the bilateral lobar hepatic duct, consistent with type IV Klatskin cholangiocarcinoma. (C) An 8F vascular sheath was placed at the segment 3 IHD followed by an introduction of 2 hydrophilic wire (double wire technique), one to the right IHD and the other to the distal CBD. (D) A left-to-right metallic stent was deployed and post-dilated with a balloon. (E) Next, a left-to-CBD stent was deployed across the mesh of the 1st stent. (F) A drainage catheter was remained in the CBD stent. (G) Spot image of the bilateral T-stent. (H) Follow-up cholangiogram showed full stent expansion and good bile flow without evidence of IHD dilatation. The drainage catheter was removed thereafter.

A study group enrolled 643 patients with malignant biliary obstruction found that median overall survival (OS) after PTBD was 2.6 months (95% CI 2.2–3.0), and 108 patients (16.8%) were alive at 12 months post-drainage [9]. Median overall survival was better in patients with biliary obstruction due to primary cancer compared to patients with biliary obstruction due to metastases ((3.5 months vs. 1.5 months, respectively) [9]. Survival is 2–6 times better in patients with good performance status and who can undergo chemotherapy after biliary drainage compared to patients unable to receive chemotherapy [18].

A large scale national cohort reported high 30-day mortality rate (23.1%) after PTBD for malignant biliary obstruction, in which 5.2% died within 7 days and 15.3% died in hospital [2].

V. ASSOCIATED FACTORS OF BETTER OUTCOME POST DRAINAGE

Factors associated with 30- day mortality were age (≥81 years), increasing comorbidity, pre-existing renal dysfunction and non- pancreatic cancer [2]. Higher median survival was associated with age ≤ 75 years, lower ASA class, lower ECOG performance status, obstruction due to primary cancer, and bilirubin level <60.0 µmol/L [9]. ECOG PS was an independent factor for predicting OS [9]. Prognosis was extremely poor for patients with an ECOG PS of 3 or 4 (median OS was 0.9 months) and better for those with an ECOG of 2 (median OS was 1.7 months) [9]. In clinical practice, patients with ECOG PS of >2 are generally not candidates for chemotherapy and are treated with palliative care and minimal interventions.

Post-drainage bilirubin level < 60 µmol/L was associated with longer survival, thus this parameter can be used to predict survival [9]. Patients with high bilirubin levels before drainage can achieve clinically relevant bilirubin reduction. High bilirubin levels are usually a contraindication for chemotherapy, and thus a reduction in bilirubin level may enable future chemotherapy treatment [9]. However, Thornton et al. reported that only 31% of patients achieved post-drainage bilirubin levels low enough to permit chemotherapy.

VI. POTENTIAL COMPLICATIONS

Generally, percutaneous biliary tract interventions are associated with complication rates ranging from 3% to 10% and procedural mortality rates ranging from 0.1% to 0.8% [19]. Although safe, PTBD and stenting of malignant biliary obstruction is associated with immediate, early (within 30 days) or late complications. The incidence of complications ranges from 8%42% in which 5.9% of patients suffered a complication within 7 days of their PTBD and 20% within 3 months [2,7]. Infection was the most common complication with 2.4% of patients experiencing this within a week, and 9% within a month (cholangitis 3.9%, sepsis 3.9%, bacterial infection of unspecified site 0.8%, cholecystitis 0.4%) [2,19]. Minor complications are pain at the puncture site, bile leak with risk of biliary peritonitis and biloma formation and catheter related problems like kinking or dislocation [6]. Major complications include sepsis (2.5%), haemobilia (2.5%), arterial injury (1-2%), overall inflammation (abscess, peritonitis, cholecystitis, acute pancreatitis: 1.2%), pneumothorax (0.5%), acute kidney injury (0.9%) and death (1.7%) [2,7,11,19].

The reported rate of significant bleed after PTBD varies from 0.6% to 12% [20]. For patient requiring hemostasis correction, the risk of bleeding is also acceptable (15.8%) [21]. Bile leak is another common complaint (6%) in clinical setting [3,11]. The causes are various including ascites, catheter blockage or malposition [3,6,11]. A cholangiogram is needed to evaluate the catheter position and patency. Based on the findings, reposition, change or larger bore catheters upgrade will be considered. Seeding metastasis has been reported elsewhere but has a high incidence in Japan (4-40.4%) [22]. A meta-analysis showed that EBD was associated with fewer seeding metastasis than PTBD (10.5% vs. 22.0%, P< 0.01) [22].

Stent blockage may occur due to tumor ingrowth, tumor overgrowth or sludge. This needs repeat procedure. PTBD can be done again and a ring biliary catheter or another stent can be placed through the blocked stent [6]. Recurrent cholangitis due to stent occlusion is seen in about 30% cases, which needs repeat stenting [6]. The stent patency rates are higher for metallic stents (85%) compared with plastic stents (67.6%) [23]. The recommended overall procedure threshold for all major complications of PTBD is 10% [7].

VII. CONCLUSION

Percutaneous management of malignant biliary obstruction is a well-established method of treatment. Although long-term prognosis remains dismal in malignant obstructive jaundice, percutaneous biliary intervention is the recommended standard of palliative care as it improves quality of life with definite immediate survival benefits and facilitate resection or adjuvant chemotherapy. Careful image reviewing, appropriate pre-procedure planning and multidisciplinary discussions are crucial for optimal patient management. A comprehensive knowledge of the available techniques, success rates and risk of complications is needed for a successful procedure.

VIII. DISCLOSURE

The authors declare no potential conflict of interest.

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