

Should preoperative biliary drainage be routinely performed for obstructive jaundice with resectable tumor?

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Abstract: Obstructive jaundice is a common clinical manifestation of malignant lesions adjacent to extrahepatic bile duct, ampulla or pancreatic head. Animal experiments and some clinical observations have demonstrated that preoperative biliary drainage could improve liver function as well as reduce endotoxemia, thereby reducing the incidence of perioperative complications. However, a number of randomized, controlled studies have found that preoperative biliary drainage failed to improve prognosis or reduce the incidence of perioperative complications; in contrast, it might increase the incidence of complications and cause extra financial burden on patients. Thus, whether preoperative biliary drainage should be performed or not is controversial. Since clinical randomized controlled studies are more relevant in clinical setting, we believe that preoperative biliary drainage should not be routinely performed for obstructive jaundice with resectable tumors. More randomized, controlled, prospective studies should be conducted for further exploration.

Keywords: Obstructive jaundice; preoperative biliary drainage



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Obstructive jaundice is a common clinical manifestation of malignancy in extrahepatic bile duct, ampulla or pancreas. When obstructive jaundice happens, symptoms and signs such as yellow skin and sclera, skin itching, dark urine, and light color stool will present accompanied by progressive liver damage and even liver failure. For jaundice caused by unresectable tumors, options usually include bypass surgery, endoscopic biliary stent placement, percutaneous stent placement, and chemotherapy (1). However, for jaundice caused by resectable tumors, radical surgery is the only effective treatment. In general, obstruction can be divided into the upper and the lower obstruction based on its location. For the upper obstruction, complete resection of cholangiocarcinoma in combination with partial hepatectomy is often required. In case of the lower obstruction, pancreaticoduodenectomy is usually performed. Given the facts that patients with obstructive

jaundice often have poor nutritional status, severe liver dysfunction, and perioperative complications, a practical consideration is to improve patient tolerance of surgery by reducing preoperative bilirubin levels. However, whether there should be a routine preoperative biliary drainage remains controversial. It is still debatable on whether the procedure truly benefits the patients. In this paper, we reviewed recently published literatures with an aim to further analyze and discuss the dispute.

Concept of the preoperative biliary drainage

In 1935, Whipple *et al.* suggested that poor nutritional status in patients with obstructive jaundice and severe liver damage may greatly affect patient's tolerance to a one-step removal of ampullary tumors. A staged surgery, which consists of gallbladder gastric anastomosis (*Figure 1*)

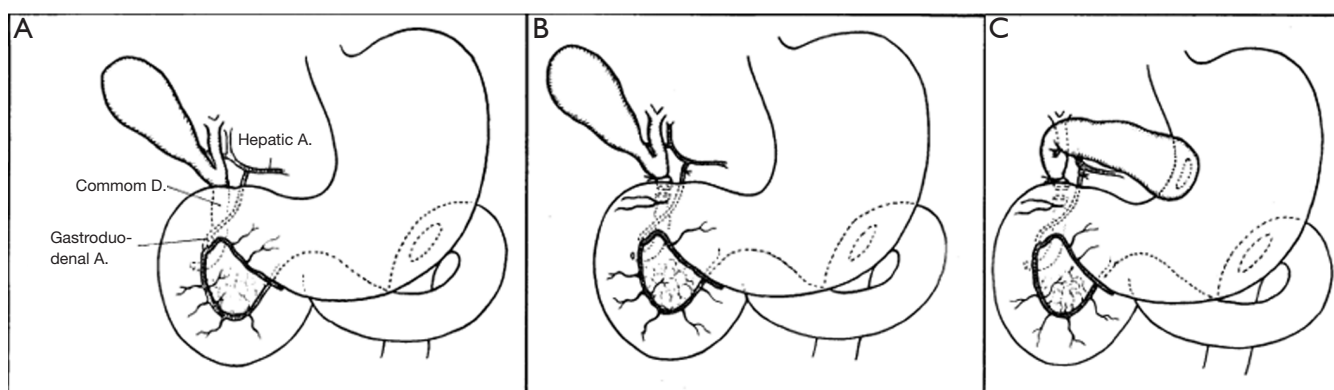


Figure 1 Schematic illustration of stage I surgery procedure for obstructive jaundice caused by ampullary tumor (2). (A) Ligation of the pancreatic artery and gastroduodenal artery; (B) Gastrointestinal anastomosis and disconnection of the common bile duct; (C) Gallbladder and stomach wall anastomosis.

followed by tumor resection 3-4 weeks afterwards, was proposed (2). The concept of preoperative biliary drainage, therefore, was first established.

Methods for preoperative biliary drainage

In the early days, biliary drainage was achieved mainly through surgery (2,3). In the 1950s Carter *et al.* brought percutaneous transhepatic cholangiography (PTC) technology into the clinical application (4). In late 1960s, McCune proposed endoscopic retrograde cholangiopancreatography (ERCP) technique (5), which significantly reduced the surgical trauma of preoperative biliary drainage. The procedure can be divided into internal drainage and external drainage, referring to the bile being drained to the inside and outside of the intestine respectively. Major complications related to the procedure consist of pancreatitis, cholangitis, perforation, bleeding, and stent restructure (6). Comparing with ERCP, PTC generates fewer complications, and is superior in the speed of bilirubin reduction (7), and has a relatively lower cost (8). ERCP may lead to the emergence of duodenal flora migration that could result in cholangitis, especially in the cases of proximal obstruction; therefore it is not the first choice (9). Although PTC seems to be advantageous over ERCP, there has been no randomized controlled clinical study for a solid conclusion. The choice of methods relies mainly on the experience of individual professional.

Efficacy of preoperative biliary drainage

The benefits of biliary drainage were mainly observed

in animal studies. Studies have shown that obstructive jaundice in animal models leads to lack of bile salts in the digestive tract, disorder of intestinal flora, and the increase of endotoxin concentration in portal system. It also causes damage to intestinal barrier which leads to the increase of mucosal permeability (10-12). The function of Kupffer cells can also be impaired, so is the cellular immune function due to the increased levels of tumor necrosis factor (TNF), interleukin-6 (IL6) and other inflammatory cytokines (13-16); increasing the probability of bacterial infection and tumor metastasis (17,18). However, all these effects are mainly associated with elevated endotoxin levels (19), and have little to do with hyperbilirubinemia (15). Intestinal barrier dysfunction may be caused by significantly decreased intestinal epithelial cell proliferation and the disruption of tight junction protein expression during obstructive jaundice (20,21). Several natural and synthetic reagents, including turmeric, glutamate (22), *Lactobacillus plantarum* (23), and *Astragalus* (24), were shown to protect small intestine and its barrier function, thereby reducing inflammation.

Studies have shown that after undergoing biliary drainage procedure, liver function was significantly improved, endotoxemia reduced, cytokine release decreased (16,25), and immune function restored (26). The internal drainage is significantly better than external drainage in reducing endotoxemia (16). Result could be more satisfied by applying *Lactobacillus plantarum* with the internal drainage (27).

Clinically, it was found that hepatocellular apoptosis and bile lake were reduced after biliary drainage procedure (28),

whereby liver function was protected. The surgical delay of 4-6 weeks due to biliary drainage procedure did not significantly affect survival (29).

In addition to liver function, other organ function can be impacted by obstructive jaundice as well. The elevated bile acid level inhibits hepatic glucocorticoid metabolism, suppresses the hypothalamic-pituitary-adrenal axis activity (30). Clinical studies found that levels of atrial natriuretic peptide (ANP) increased in obstructive jaundice patients (31), and decreased following the internal drainage, indicating the improved heart function (32). Kidney failure is another common complication of obstructive jaundice (33,34) with acute tubular necrosis and venous dilatation as pathological manifestations (35). Rehydration therapy alone often cannot relieve such renal failure. Either internal drainage (36) or external drainage (34) may lead to significant improvement of renal function.

Although it is evident that biliary drainage brings favorable outcome pathophysiologically, it is not a clear cut when the clinical perioperative morbidity and mortality are considered. Surgical complications often include pancreatic anastomotic fistula, postoperative bleeding, delayed gastric emptying, biliary fistula, gastrojejunostomy anastomotic fistula, intra-abdominal abscess, wound infection, portal vein thrombosis, pneumonia, cholangitis, and myocardial infarction (6).

During 1980s, several randomized controlled clinical studies found that the external drainage would not improve prognosis, but rather increase the incidence of complications (37-39), thus raising the hospitalization and costs (39). However, questions were also raised about credibility of these studies. Pisters *et al.* argued that the Evidence-Based Medicine concept was only well established after the mid-1990s, and considered these studies not performed methodological strictly. They believed that these studies employed outdated technology that resulted in low resection rate (16%) and high perioperative mortality (12%). Therefore, these findings needed to be reviewed carefully (40). Meanwhile, their own retrospective study indicated that preoperative biliary drainage (stenting) increased the risk of postoperative wound infection, but not the risk of major postoperative complications or mortality (41). Povoski *et al.* reported that preoperative biliary drainage is the only factor associated with postoperative infection, intra-abdominal abscess, and postoperative mortality. The preoperative biliary drainage should therefore be avoided

for resectable pancreatic head tumor or other adjacent tumors (42). van der Gaag reported in a randomized controlled study of pancreatic head cancer that the preoperative biliary drainage group (either ERCP or PTC) incurred 47% postsurgical complications in contrast to the 37% in the direct surgery group. Thus, preoperative biliary drainage is not recommended for obstructive jaundice caused by pancreatic head mass (6). Meta-analysis by some scholars has found that although preoperative biliary drainage induces higher incidences of complications it does not affect postoperative mortality. There is no definite evidence to support or against preoperative biliary drainage (43-45).

The benefits in pathophysiology and the adversities in perioperative complications for preoperative biliary drainage are clearly hard to reconcile. One of the possible explanations can be that the animal model of obstructive jaundice was obtained through bile duct ligation which caused acute obstructive jaundice. The manifestations of the animal model and their pathophysiological process can be very different from the chronic progressive jaundice caused by malignant obstructive. Although several clinical studies did point out the benefits of preoperative biliary drainage in patients concerning pathophysiology (32,34-36), overwhelming evidences from randomized, controlled clinical studies pointed to the unfavorable outcomes in perioperative complications caused by the procedure. Taking all current domestic and international clinical studies into consideration, we believe that malignant obstructive jaundice does not require routine preoperative biliary drainage (*Figure 2*).

Conclusions

Currently, there is still no definite conclusion on whether it is needed for preoperative jaundice alleviation through biliary drainage. Although the benefit in pathophysiology is evident, the clinical studies have revealed many adversities for this procedure. In light of currently available information, we believe that the adversities in perioperative complications resulted from preoperative biliary drainage clearly outweighs its benefits in alleviating pathophysiological symptoms. Thus, we believe that obstructive jaundice does not require routine preoperative biliary drainage. However, large-scale clinical randomized, controlled, prospective studies are still needed for a clear and un-ambivalent answer.

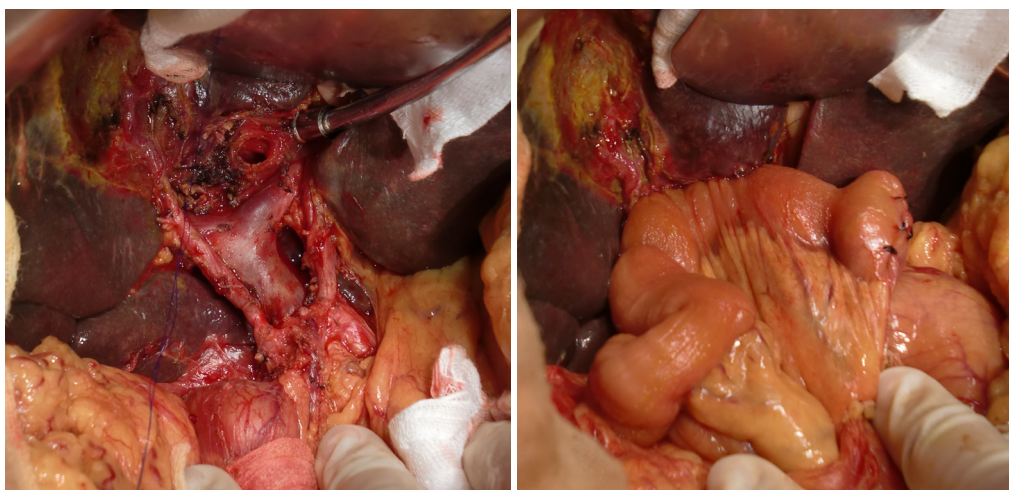


Figure 2 Surgical site of hilar cholangiocarcinoma: malignant obstructive jaundice does not require routine preoperative biliary drainage.

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