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Operable malignant jaundice: To stent or not to stent before the operation?

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Abstract

Traditionally, pre-operative biliary drainage (PBD) was believed to improve multi-organ dysfunction, and for this reason, was practiced worldwide. Over the last decade, this concept was challenged by many reports, including meta-analyses that showed no difference in morbidity and mortality between surgery with, and surgery without PBD, in operable malignant jaundice. The main disadvantages of PBD are seen to be the additional cost of the procedure itself, and the need for longer hospitalization. In addition, many studies showed the significance of specific complications resulting from PBD, such as recurrent jaundice, cholangitis, pancreatitis, cutaneous fistula, and bleeding. However, the results of these studies remain inconclusive as to date there has been no perfect study that equally randomized comparable patients according to the level of obstruction and technique used for PBD. Generally, endoscopic stent insertion (ES) is preferred for common duct obstruction, whereas endoscopic nasobiliary drainage and percutaneous biliary drainage is reserved for hilar obstruction, since ES in hilar block confers a high rate of cholangitis. Although, there is no guideline which either supports or refutes this approach, certain

subgroups of patients, including those with symptomatic jaundice, cholangitis, impending renal failure, hilar block requiring preoperative portal vein embolization, and those who need pre-operative neoadjuvant therapy, are suitable candidates for PBD.

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INTRODUCTION

Liver, gallbladder, bile duct and pancreas share a common embryologic origin and also play their parts as the common etiologies for resectable biliary related tumors^[1]. Malignant biliary obstruction presents mainly as jaundice and pruritus. In a prolonged obstruction, multi-organ dysfunction including renal failure, cardiac dysfunction, pulmonary dysfunction, poor hepatic metabolism and hemostasis impairment^[2-7] may develop. This, in turn, can compromise the outcome of surgery. For years, it has been a routine practice to achieve pre-operative biliary drainage (PBD), either by means of an endoscopically placed stent (a plastic stent, nasobiliary tube, or a removable metallic stent) or by means of a percutaneously placed catheter (either externally or a combination of external and internal drainage). However, the benefit of PBD has not

been confirmed and some studies^[8,9] reported that many patients may be harmed by developing procedure-related complications. Conversely, other^[10-13] showed a lower rate of intra-abdominal abscess in the PBD group.

OVERVIEW

There are 2 early meta-analyses^[14,15] which reported on the overall morbidity, stent-related morbidity, post-operative morbidity and mortality in obstructive jaundice patients with or without PBD, who underwent surgery. The first meta-analysis demonstrated no difference in mortality rate between the two groups; however the overall complication rate was shown to be adversely affected by PBD^[14]. By contrast, another meta-analysis reported no adverse effects after preoperative endoscopic biliary stent placement when compared with direct surgery^[15]. Another 2 recent meta-analyses^[16,17] neither supported nor refuted pre-operative biliary drainage, since they also found no difference in mortality between the 2 groups. More importantly, these 2 analyses showed similar results on stent-related complications, and these were observed to be the significant cause for the higher rate of the overall morbidity^[16,17]. After excluding stent related complications, the meta-analysis focusing on the endoscopically drained patients showed that post-surgical complications were significantly less in the stented group^[16]. The other meta-analysis^[17] showed no difference in the overall morbidity. However, it demonstrated a higher incidence of post-procedural cholangitis from the endoscopically treated group. It is thought that the higher rate of endoscopically-related morbidity in this analysis was due to the inclusion of a study^[18] that contained a significant number of patients with hilar obstruction who had had a failed endoscopic drainage.

There are many factors that limit the usefulness of these analyses for current practice. Firstly, different types of biliary drainage were used, so that the patient-groups who underwent internal or external biliary drainages were not homogeneous. Theoretically, the physiology of enterohepatic circulation is disrupted by external drainage, and this, in turn, may result in disruption of intestinal barrier integrity^[19,20]. It is thought that, compared to internal drainage methods, external drainage may possibly increase the patient's risk of developing intestinal bacterial translocation. Secondly, there was a mixture of patients with different types of malignant tumors in those studies and, more importantly, the locations of the biliary obstruction varied. There were a significant number of patients with proximal biliary obstruction who underwent PBD. We know that the rate of post endoscopic drainage cholangitis is quite high in patients with proximal biliary obstruction^[18,21,22]. Inadequate subsegmental drainage is the main cause of this complication. Thirdly, variation in preoperative and post-operative care among different institutions may also have contributed to varying results in the overall complication rates. For instance, preoperative biliary drainage is associated with a higher rate of bacterial contamination and a different

pattern of antibiotic resistance of the bacteria cultured from bile^[23]. *Enterobacteriaceae* is typically found in non-stent patient whereas mixed organisms, including the *Enterococcus* species can be found more commonly in bile from patients with stent^[23,24]. Hence use of more broad spectrum antibiotics, which cover both *Enterobacteriaceae* and *Enterococcus* can result in better bacterial coverage in the stented group. Lastly and most importantly, the heterogeneity of patients and methods of recruited articles in those analyses is our biggest concern^[14-17]. The early two meta-analyses contain a majority of non-randomized controlled trials (RCT). There were 18 retrospective cohort studies in the total 23 recruited trials in the Sewnath *et al*^[14] analysis, and there were 8 retrospective cohort studies amongst the total 10 recruited trials in the Saleh *et al*^[15] analysis. Another meta-analysis from Mumtaz *et al*, contained only 2 RCTs^[16]. The latest meta-analysis by Wang *et al*^[17] recruited 5 RCTs, and this analysis seems to contain the best quality of trials, however, key components of trial methodology (allocation sequence, allocation concealment, and follow-up) in those trials were considered to pose a significant risk of bias.

In addition, post ERCP pancreatitis was an important contributory factor in the calculation of the morbidity rate in those who underwent PBD during 1982-2000^[14,16,17]. In those days, temporary pancreatic stenting in difficult cannulation was not routinely performed. Currently, this technique has become a common means of decreasing the rate of post-ERCP pancreatitis^[25]. If those PBD studies were repeated nowadays, and included prophylactic temporary pancreatic stenting, the results would not be the same, and the PBD method might be supported more widely.

Overall, the standard practices for PBD at different centers vary, and this in turn can yield a wide margin for the differences in success rate and morbidity. Nevertheless, the authors still believe that there is a balance between pros and cons of PBD in malignant biliary obstruction. Careful selection of each patient in order to select appropriate candidates for PBD is very important before sending any patient to surgery. Later, special preparation, care, and management tailored to the needs of each individual patient undergoing PBD, must be implemented.

THE CASE TO GO FOR PBD

Although PBD may not be beneficial in all malignant biliary obstructed patients, certain patients may be selected to undergo PBD (Table 1).

Symptomatic jaundiced patient

Whilst awaiting surgery, intractable pruritus is a devastating condition. Despite the use of many agents and plasmapheresis to relieve pruritus, biliary diversion sometimes is the only way to improve this condition, as it reduces the serum bile salt level in the enterohepatic cycle^[26]. Although the role of bile acid reduction after biliary drainage in the mediation of pruritus has not been confirmed^[27], there have nevertheless been some

Table 1 Indication for pre-operative biliary drainage

Symptoms
Pruritus
Renal impairment
Acute cholangitis
Hilar block requiring portal vein embolization prior to surgery
Pancreatic cancer undergoing preoperative chemotherapy
Delay in surgery

reports which demonstrate a transient relief of pruritus within 24 h after biliary drainage^[28,29].

Fluid and electrolyte balance have to be precisely maintained in all biliary obstructed patients undergoing surgical resection. Lactulose and a bile salt supplement can offer renal protection^[30]. However, in patients with pre-existing renal impairment, these measures may not be enough to prevent the development of acute renal failure. Some surgeons may therefore advocate the patient undergoing PBD prior to surgery.

Patients with acute cholangitis

Although de novo case of acute cholangitis in patients with malignant biliary obstruction is quite unusual, ampullary tumors, intraductal papillary mucinous neoplasm (IPMN), and biliary papillomatosis are certain conditions that acute cholangitis may develop spontaneously^[31-33]. For this subgroup of patients, biliary decompression plays an important role in the management of acute cholangitis and this, in turn, can reduce the operative mortality and morbidity^[34].

Certain hilar obstructed patients

In the past, central hepatectomy was the standard surgical technique for hilar cholangiocarcinoma. With the use of surgery and the introduction of portal vein embolization (PVE), typical major hepatectomies including right or left hepatectomy, and right or left trisectionectomy have increasingly been performed^[35-37]. After PVE of the affected lobe, the enlarged contralateral lobe that is preserved from embolization is supposed to carry out all hepatic functions^[38]. A report from Nagoya, Japan, showed that the risk of post-operative liver failure in the group who underwent PVE dropped from 33% to 23%^[38]. However, a delay of at least 3 wk is advised before the contralateral lobe is fully able to compensate and the patient is ready for hepatectomy^[39]. PBD is therefore needed as a bridge for this package. Practically, unilateral PBD in a hilar block is sufficient and the preferred side for drainage is the future remnant lobe^[40]. However, bilateral drainage is considered in the following situations: patients with pre-existing cholangitis; patients who develop post-procedural cholangitis, despite board-spectrum antibiotics, and additional drainage from the same side; and patients with persistent jaundice. Apart from the discomfort from nasal irritation, endoscopic nasobiliary drainage (ENBD) is the preferred initial technique that has replaced percutaneous transhepatic

biliary drainage (PTBD) in many Japanese endoscopy centers^[40-42] and PTBD is currently reserved as a salvage method in patients with suboptimal endoscopic drainage who develop subsegmental cholangitis. In addition, because of the higher risk of cholangitis reported in advanced hilar blocks^[21,22] and the fear that duodenal fluid could flow back into the biliary tree, endoscopic stent placement (ES) is not recommended in this group.

Patients requiring neoadjuvant therapy

Traditionally, radio-chemotherapy for pancreatic cancer was administered post-operatively. Unfortunately, this strategy had limited success. Recently, these neoadjuvant agents have been given pre-operatively, with the objective of tumor down-staging and in the expectation of a higher number of complete resections^[43]. To minimize the toxicity from chemotherapy, many of these patients with obstructive jaundice will benefit from PBD prior to the treatment protocol. However, to date, no randomized trials comparing neoadjuvant with no adjuvant therapies given preoperatively have yet been conducted.

THE DISADVANTAGES OF PBD

The disadvantages of PBD can be reviewed in terms of morbidity, mortality, and cost of treatment when compared with the group without PBD.

The majority of studies did not demonstrate any difference in the overall morbidity and mortality between those patients undergoing PBD and those with no drainage. Only an early study from UCLA in 1985 showed a slightly, but not significantly, higher rate of morbidity in patients having undergone PBD than the no PBD group (57% *vs* 53%)^[44]. In addition, the total number of days for hospitalization was longer in the PBD group (31.4 d *vs* 23.1 d), and in 1985 the estimated cost relating to both the additional stay in hospital and the cost of the procedure was more than \$US 8000^[44]. In contrast, a study reported by a group from New York University^[45] demonstrated a shorter hospital stay in the PBD group than in non-PBD group (13.5 d *vs* 19 d, $P = 0.02$). Moreover, PBD group tended to have fewer overall complications ($P = 0.054$). This study suggested that “the increased cost of preoperative ERCP and PBD may be offset by the decreased length of hospitalization and decreased complication rate”^[45]. The important difference between the two studies was the technique for PBD. The first study used PTBD, and the second, ES. Better fluid and electrolyte control and an improvement in immune response resulting from ES may play an important role in the different results found. Of note, the majority of the cases in these two studies involved patients with common bile duct obstruction.

Post-operative fistula is a common complication of bilio-pancreatic resection, leading to prolonged hospitalization, increased cost of treatment and delayed further adjuvant therapy. The largest retrospective study^[46] by a group from John Hopkins on patients who underwent pancreaticoduodenectomy ($n = 567$) reported

a higher incidence of pancreatic fistula (10% *vs* 4%, $P = 0.02$) and wound infection (10% *vs* 4%, $P = 0.02$) in the PBD group, whereas other smaller studies ($n = 38-257$) have not shown significant incidence of fistula development in PBD groups^[44,47-49].

Intra-operative hemorrhage is an important factor in morbidity and mortality of patients undergoing surgery. Only one small study^[50] reported a higher volume of intra-operative bloodloss in the PBD group than the undrained group (1207 mL *vs* 1122 mL), whereas other larger studies have failed to demonstrate the different effects of PBD or the lack of PBD on these issues^[45,46,48,49].

CONCLUSION

In conclusion, a routine PBD for every patient undergoing bilio-pancreatic surgery is not recommended. PBD carries with it risks of recurrent cholangitis, pancreatitis, cutaneous fistula development, and intra-operative hemorrhage. These can result in a prolonged hospital stay and increase in the total cost of therapy. However, the rate of pancreatitis may be reduced by temporary pancreatic stenting. At this moment we can advocate PBD only in a certain subset of patients, including those with symptomatic jaundice, cholangitis, impending renal failure, hilar block requiring PVE, and those who need pre-operative neoadjuvant therapy.

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