

# Operable severe obstructive jaundice: How should we use pre-operative biliary drainage?

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Obstructive jaundice is a common surgical problem, and surgery in jaundiced patients is associated with a higher risk of postoperative complications than surgery in non-jaundiced patients. However, the efficacy of pre-operative biliary drainage (PBD) for patients with obstructive jaundice remains controversial. Many studies have been unable to confirm the benefit of PBD and have suggested that it should not be performed routinely. While we agree that routine PBD is not recommended for all jaundiced patients, we believe that it is useful for certain subgroups; however, there are no clear guidelines regarding its application in these subgroups. We suggest that further large and detailed randomised control studies should focus on formulating codes and standards of PBD for patients with operable conditions causing severe obstructive jaundice.

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Obstructive jaundice is a common surgical problem that occurs when there is blockage of the passage of conjugated bilirubin from liver to intestine. In most benign biliary diseases, jaundice is intermittent and incomplete. Only a few diseases (e.g. primary sclerosing cholangitis) result in persistent obstructive jaundice, or even in biliary cirrhosis and portal hypertension, and most cases are related to stone obstruction and/or cholangitis,<sup>[1,2]</sup> usually with a serum total bilirubin level  $<100 \mu\text{mol/l}$ ,<sup>[3]</sup> which does not cause significant problems during surgery. In contrast, malignant obstructive jaundice (caused by malignant diseases of the extrahepatic distal or proximal biliary tract) is usually chronic, and obstruction is more severe and often accompanied by older age, a weakened immune system, chronic organ dysfunction, and many other problems.

## Effects of obstructive jaundice

Jaundiced patients have marked systemic pathophysiological changes such as hyperbilirubinaemia, endotoxaemia, blood coagulation and liver function disorders, and renal, cardiac or pulmonary dysfunction.<sup>[4-9]</sup> Of these changes, hyperbilirubinaemia and endotoxaemia have been identified as being of most prognostic importance in surgical patients.<sup>[10-12]</sup> Prolonged and progressive obstructive jaundice results in hepatic dysfunction due to bile stasis and cholangitis, eventually leading to hepatic failure, which is a major cause of postoperative death.<sup>[13,14]</sup> Surgery is associated with a higher risk of postoperative complications in jaundiced patients than in non-jaundiced patients,<sup>[15-17]</sup> including sepsis, hypotension, gastrointestinal bleeding, anastomotic leakage, abdominal abscess and liver or renal failure. How to manage

patients with severe obstructive jaundice is therefore a complicated problem that surgeons have to face.

## Debate about pre-operative biliary drainage for obstructive jaundice

The increased risk of surgery in jaundiced patients was recognised as early as 1935 by Whipple *et al.*,<sup>[18]</sup> who proposed a two-stage procedure for surgery in severely jaundiced patients. The first stage consisted of a drainage procedure in the form of cholecystogastrostomy to decompress the biliary tract and improve liver function, followed 4 weeks later by radical resection of the tumour.<sup>[18]</sup> In the late 1970s, studies on pre-operative biliary drainage (PBD) reported that it reduced the postoperative death rate in jaundiced patients.<sup>[19-22]</sup> In the 1980s, the effect of PBD was questioned in many retrospective and prospective studies, and focus shifted towards the negative effects of PBD, such as an increase in the rate of infectious complications. From then on, numerous studies, both randomised and non-randomised and both retrospective and prospective, have compared outcomes of surgery with and without PBD.<sup>[23-27]</sup> Proponents advocate routine PBD in an attempt to reduce the incidence of hepatic dysfunction and peri-operative complications in patients with obstructive jaundice,<sup>[28-31]</sup> while opponents consider that it does not significantly reduce postoperative complications and mortality,<sup>[32-34]</sup> can even result in major complications that can delay surgery and increase hospital costs,<sup>[35-37]</sup> and therefore should not be performed routinely.<sup>[13,37-48]</sup>

We have noted that almost all the above studies on the effects of PBD have the following limitations and methodological flaws: (i) most patient data were collected retrospectively, so there is a risk of selection bias;<sup>[44,47,48]</sup> (ii) in some studies, no distinction

was made between different levels of biliary obstruction;<sup>[48-50]</sup> (iii) in many studies, no distinction was made between different types of operations;<sup>[36,44,48,51]</sup> (iv) often no distinction was made between different methods and durations of PBD;<sup>[45,47,49,52]</sup> and (v) most importantly, these studies did not take advances in surgical skills and techniques (e.g. improved methods of anastomosis and use of the electrocutter and ultrasonic scalpel), intra-operative management and postoperative care into account.<sup>[36,44,47-56]</sup> There is no doubt that these advances reduce postoperative complications.<sup>[57]</sup> Such methodological and reporting deficiencies would make it difficult to draw objective conclusions, and may be one of the reasons why controversy exists. In contrast, in animal experiments we can control differences between individual animals, severity of jaundice and types of operations. Experiments in which PBD was used before surgery in animal models showed it to have benefits such as improved liver function and nutritional status, a reduction in systemic endotoxaemia and cytokine release and an improved immune response, resulting in significantly reduced mortality.<sup>[58-65]</sup>

### Debate about method of PBD

The development of minimally invasive techniques has meant that conventional surgical PBD is rarely used today. The two methods most widely used for the relief of obstructive jaundice are percutaneous transhepatic biliary drainage (PTBD) and endoscopic biliary drainage (EBD), including endoscopic nasobiliary drainage (ENBD) and endoscopic biliary stenting (EBS). Although PTBD and ENBD can relieve biliary obstruction they do not restore bile flow to the duodenum, so the enterohepatic circulation is still disrupted, and impaired intestinal barrier integrity may continue.<sup>[59,66]</sup> EBS helps stabilise the internal environment, but can have complications such as migration of stents, pancreatitis, bacterial contamination from stents, and cholangitis due to clogging.<sup>[41,42]</sup> Biliary stenting also generates a severe inflammatory response in the wall of the bile duct, which probably increases the risk of bile leakage from the bilio-intestinal anastomosis.<sup>[33,43,67]</sup> Each of the above drainage procedures is known to have been associated with infection or other complications.<sup>[26,32,41,42,68-70]</sup> Although complication rates in major medical centres have been reduced to very low levels indeed, the therapeutic effect of PBD, either by means of PTBD or EBD, has been extensively debated in recent decades.<sup>[32,47,58,65,71,72]</sup> Experimental studies have proved that internal biliary drainage improves nutritional status,<sup>[73]</sup> reduces endotoxaemia<sup>[59,64]</sup> and has other benefits.<sup>[74-76]</sup> However, a retrospective review by Sohn *et al.*<sup>[43]</sup> analysed whether internal drainage was better than external drainage, and concluded that there was no difference in terms of death or complications.

PBD is widely used in Japan and the Netherlands, and the Japanese literature<sup>[66,71,72,77]</sup> is unanimous in emphasising its benefits. Mortality rates after major liver resection for hilar cholangiocarcinoma in Japan are currently low (0 - 9%), and many attribute this to PBD being regarded as an essential element in pre-operative management.<sup>[72,78,79]</sup>

We consider that the key question is not which method of PBD is better, because in each case the specific clinical situation, the

technical proficiency of the operator, the costs involved and the patient's personal requirements will differ. All these factors should be considered in choosing the most appropriate method and the one that will achieve the best outcome.

### Clinical and laboratory parameters

In series of studies from the 1980s, a bilirubin level of 170 - 200  $\mu\text{mol/l}$  was clearly shown to indicate a risk of postoperative complications.<sup>[11,21,22]</sup> More recent studies have shown that postoperative mortality in patients with a total bilirubin level  $>342 \mu\text{mol/l}$  was significantly higher than in those with a total bilirubin level of  $<342 \mu\text{mol/l}$ .<sup>[80-82]</sup> Many researchers therefore propose that PBD should be used when the bilirubin level is  $>342 \mu\text{mol/l}$ , but others consider  $>500 \mu\text{mol/l}$  a more reasonable level.<sup>[83]</sup> As an evaluation index of PBD the bilirubin level seems to be rising with advances in medical technology, but experience indicates that the role of liver function in jaundiced patients is also an important factor affecting prognosis. Prolonged pre-operative jaundice is associated with increased postoperative morbidity and mortality after hepatic resection as a result of severe cholestatic liver dysfunction.<sup>[84-87]</sup> Evaluation of probable postoperative residual liver function is therefore indicated for patients requiring major curative hepatic resection, as well as for those with operable malignant obstructive jaundice.<sup>[77,88]</sup>

In addition to the pre-operative bilirubin level and liver function, advanced patient age<sup>[89]</sup> is an important factor. Tian *et al.*<sup>[90]</sup> combined bilirubin level with age and calculated a formula,  $\text{age (years)} \times 3 + \text{total bilirubin } (\mu\text{mol/l}) > 450$ , which can be used after doing PBD for patients with malignant obstructive jaundice. According to the formula, the operation can proceed if the total bilirubin level declines steadily by more than 30% for 2 weeks after PBD - it is not necessary for it to go down to normal. When the initial level is less than  $450 \mu\text{mol/l}$  the operation can be done immediately, without PBD.<sup>[90]</sup> Of course, this formula needs to be supported by further clinical experience, and other laboratory parameters, such as prothrombin, creatinine, haemoglobin and haematocrit, should also be taken into account.<sup>[81]</sup>

### Conclusion

In certain specific subgroups of jaundiced patients, including those with acute suppurative cholangitis,<sup>[91]</sup> severe malnutrition, impending renal failure or hilar block requiring portal vein embolisation,<sup>[13,92,93]</sup> and those who need pre-operative neo-adjuvant therapy,<sup>[29]</sup> urgent PBD is indicated and can be life-saving. However, although several reports have been published, there are still no clear guidelines regarding use of PBD in those patients.<sup>[13,81]</sup> Whether or not to use PBD before surgery for severe obstructive jaundice currently depends mainly on local expertise. We believe that if the complications of the procedure itself can be reduced and the enterohepatic circulation can be restored (e.g. with PTBD plus bile replacement<sup>[66]</sup>), PBD is of benefit, but this needs to be validated by further research. We suggest that future large and detailed randomised control studies should focus on formulating codes and standards of PBD for operable severe obstructive jaundice, to guide clinicians in their management of these patients.

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