



Preoperative biliary drainage for resectable or borderline resectable periampullary tumor: what is the best management?

Julie Perinel^{1,2}, Mustapha Adham^{1,2}

¹Service de chirurgie Digestive, Hôpital Edouard Herriot, Hospices Civils de Lyon, Lyon, France; ²Faculté de Médecine de Lyon, Université Claude Bernard Lyon 1 (UCBL1), Lyon, France

Correspondence to: Dr. Julie Périnel. Hôpital Edouard Herriot, Service de Chirurgie Digestive, 5 Place d'Arsonval, 69437 Lyon Cedex 03, France. Email: julie.perinel@chu-lyon.fr.

Comment on: Sandini M, Honselmann KC, Birnbaum DJ, *et al.* Preoperative Biliary Stenting and Major Morbidity After Pancreatoduodenectomy: Does Elapsed Time Matter?: The FRAGERITA Study Group. *Ann Surg* 2018;268:808-14.

Submitted Mar 01, 2019. Accepted for publication Mar 08, 2019.

doi: 10.21037/hbsn.2019.03.15

View this article at: <http://dx.doi.org/10.21037/hbsn.2019.03.15>

Management of preoperative biliary drainage (PBD) in patients undergoing pancreaticoduodenectomy (PD) is still debated. Obstructive jaundice is associated with a proinflammatory state, impaired immune function and disturbances in coagulation. Patients with jaundice are at high risk to develop renal dysfunction and bacteriobilia. In this context, PBD was traditionally performed before surgery to improve postoperative outcomes. Older studies have demonstrated that PBD may reduce the risk of infection, restore immune function and improve the nutritional status (1,2). PBD can be achieved by an internal or external approach. Endoscopic retrograde cholangiopancreatography is currently performed to place an endobiliary stent in the common bile duct. External approach with percutaneous transhepatic drainage is performed alternatively. However, more recently, the benefits of routine PBD have been questioned. Several meta-analyses concluded that PBD was associated with increased postoperative complications, including wound complications, without a difference in mortality when compared to surgery first (3-6). A Cochrane review published in 2012 included six trials and reported that PBD may increase the rate of serious adverse events. The authors also underlined a high risk of bias in all trials (7). van der Gaag *et al.* confirmed in a multicenter randomized controlled trial (RCT) that early surgery without PBD did not increase the risk of complications (8). In this context, routine PBD is no longer mandatory. Current guidelines recommend selective indications for PBD including the

following: cholangitis, neoadjuvant treatment, delayed surgery for technical reasons and bilirubin level equal or greater than 15 mg/dL (9).

When PBD is required, the optimal duration of PBD before surgery is still debated. Experimental data and animal studies suggested that adequate recovery of hepatic function required a minimum of 4 to 6 weeks after PBD (10). It depends on the duration of biliary decompression and the severity of obstructive jaundice. Kawarada *et al.* showed that PBD is necessary for more than 3 weeks to improve hepatic function (11). In the RCT of van der Gaag, the authors chose a delay of 4 to 6 weeks between the PBD and the surgery (8). Only two studies have been published on the topic (12,13). Son *et al.* evaluated 120 patients who underwent curative surgery for periampullary tumors after PBD for severe obstructive jaundice (12). They concluded that PBD duration less than 2 weeks are more appropriate. Indeed, while the morbidity and the mortality did not differ between the two groups, patients in the short group (<2 weeks) had significantly less PBD related complications. Sandini *et al.* reported in 312 patients that short elapsed time between PBD and surgery (<4 weeks) was associated with increased major morbidity, surgical morbidity, biliary fistula rate and infectious complications (13). However, negative biliary cultures were more frequent in the short group with lowest incidence of drug resistance. In multivariate analysis, less than 4 weeks from PBD to surgery were independent risk factor of major complications. The median time from stent placement to surgery was 37 days [2-559]. The

authors suggest that a delay of 4 to 6 weeks is required from PBD to surgery to improve postoperative outcomes after PD. Both studies had some limitations (12,13). First, these are non-randomized comparative studies. The first study included a majority of biliary tumor and only patients with severe obstructive jaundice (12). In the second one, there is a risk of selection bias in the elapsed time from stent to surgery (13). Why 91 patients had to wait more than 8 weeks to reach surgery? Only 13 patients had neoadjuvant treatment and only 14 patients had benign lesion with chronic pancreatitis. What were the characteristics of the other patients? Secondly, the level of serum bilirubin before PBD was not reported. Indeed, it has been suggested that adequate recovery of hepatic function depends on the severity of the obstructive jaundice before the surgery (11). Finally, the authors used the ALBI score to estimate liver function. This score was validated in the management of HCC and chronic liver disease. It is probably not suitable for periampullary tumors.

To date, the optimal duration of PBD before surgery has not been established. While Sandini *et al.* (13) suggested that an elapsed time of less than 4 weeks is probably not enough to obtain an adequate recovery of hepatic function, a long period may also be deleterious due to the increased risk of bacteriobilia and stent related complications. The incidence of complications is also responsible of delayed surgery. In this context, a RCT is required to confirm these results.

The elapsed time between PBD and surgery also raises the issue of the oncological outcomes. There is no data on survival in the study of Sandini *et al.* (13). One multicenter RCT has demonstrated in 113 patients undergoing PD for pancreatic head cancer that delay in surgery after PBD does not impair or benefit survival rate (14). In this study, the mean time from randomization to surgery in patients undergoing PBD was 5.1 [4.8–5.5] weeks.

Last issue regarding PBD concerns the type of stent used: the metal stent versus the plastic stent. Plastic stents are commonly used for endoscopic procedure. In the meta-analysis of Crippa *et al.*, less than one third of the patients underwent metal stents (15). Metal stents were associated with significantly lower rate of endoscopic reintervention and pancreatic fistula. There was no significant difference regarding overall surgical complications and mortality. More recently, Lee *et al.* concluded that the level of evidence is actually insufficient to determine the best strategy of PBD among plastic stent and metal stent (6). Further RCT are necessary to confirm the superiority of

metal stent when PBD is required and especially in patients undergoing neoadjuvant treatment.

Early surgery without PBD is recommended as standard treatment in patients with resectable periampullary tumors and asymptomatic jaundice. Nevertheless, PBD is warranted in case of neoadjuvant treatment, cholangitis and delayed surgery due to technical reasons or the need for further investigations. Current guidelines (9) recommend PBD if the serum bilirubin level is superior to 250 $\mu\text{mol/L}$. However, most of the studies included patients with lower serum bilirubin level. In the RCT of van der Gaag, the mean bilirubin level was 150 $\mu\text{mol/L}$ in both groups. For patients with asymptomatic jaundice and high bilirubin level, which patients will really benefit from PBD? This indication should be precised in future studies.

Despite these recommendations, more than 50% of the patients still undergo PBD when there are referred to expert pancreatic centers, and more than 75% of those patients receive PBD before surgical consultation (5). The high incidence of endoscopic staging and biopsy before surgery increased the rate of PBD.

To date, PBD is not recommended for surgically fit patients with asymptomatic jaundice and bilirubin level $<250 \mu\text{mol/L}$. When indicated, an elapsed time of 4 to 6 weeks is required before surgery to recover optimal liver function and to avoid PBD related complication due to prolonged stenting. Besides, recent data suggested that metal stents were superior to plastic stents with a reduction of stent related complications. In both situations, the level of evidence remains low. Future RCT should confirm the optimal elapsed time between PBD and early surgery and also the superiority of metal stents. Indeed, to change practice, a high level of evidence is necessary to drop the dogma.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Roughneen PT, Gouma DJ, Kulkarni AD, et al. Impaired specific cell-mediated immunity in experimental biliary

- obstruction and its reversibility by internal biliary drainage. *J Surg Res* 1986;41:113-25.
2. Gouma DJ, Coelho JC, Fisher JD, et al. Endotoxemia after relief of biliary obstruction by internal and external drainage in rats. *Am J Surg* 1986;151:476-9.
 3. Wang CC, Kao JH. Preoperative drainage in pancreatic cancer. *N Engl J Med* 2010;362:1343; author reply 1345.
 4. Chen Y, Ou G, Lian G, et al. Effect of Preoperative Biliary Drainage on Complications Following Pancreatoduodenectomy: A Meta-Analysis. *Medicine (Baltimore)* 2015;94:e1199.
 5. Scheufele F, Schorn S, Demir IE, et al. Preoperative biliary stenting versus operation first in jaundiced patients due to malignant lesions in the pancreatic head: A meta-analysis of current literature. *Surgery* 2017;161:939-50.
 6. Lee PJ, Podugu A, Wu D, et al. Preoperative biliary drainage in resectable pancreatic cancer: a systematic review and network meta-analysis. *HPB (Oxford)* 2018;20:477-86.
 7. Fang Y, Gurusamy KS, Wang Q, et al. Pre-operative biliary drainage for obstructive jaundice. *Cochrane Database Syst Rev* 2012;9:CD005444.
 8. van der Gaag NA, Rauws EA, van Eijck CH, et al. Preoperative biliary drainage for cancer of the head of the pancreas. *N Engl J Med* 2010;362:129-37.
 9. Lassen K, Coolson MM, Slim K, et al. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *World J Surg* 2013;37:240-58.
 10. Hirazawa K, Hazama S, Oka M. Depressed cytotoxic activity of hepatic non-parenchymal cells in rats with obstructive jaundice. *Surgery* 1999;126:900-7.
 11. Kawarada Y, Higashiguchi T, Yokoi H, et al. Preoperative biliary drainage in obstructive jaundice. *Hepatogastroenterology* 1995;42:300-7.
 12. Son JH, Kim J, Lee SH, et al. The optimal duration of preoperative biliary drainage for periampullary tumors that cause severe obstructive jaundice. *Am J Surg* 2013;206:40-6.
 13. Sandini M, Honselmann KC, Birnbaum DJ, et al. Preoperative Biliary Stenting and Major Morbidity After Pancreatoduodenectomy: Does Elapsed Time Matter?: The FRAGERITA Study Group. *Ann Surg* 2018;268:808-14.
 14. Eshuis WJ, van der Gaag NA, Rauws EA, et al. Therapeutic delay and survival after surgery for cancer of the pancreatic head with or without preoperative biliary drainage. *Ann Surg* 2010;252:840-9.
 15. Crippa S, Cirocchi R, Partelli S, et al. Systematic review and meta-analysis of metal versus plastic stents for preoperative biliary drainage in resectable periampullary or pancreatic head tumors. *Eur J Surg Oncol* 2016;42:1278-85.

Cite this article as: Perinel J, Adham M. Preoperative biliary drainage for resectable or borderline resectable periampullary tumor: what is the best management? *HepatoBiliary Surg Nutr* 2019;8(4):398-400. doi: 10.21037/hbsn.2019.03.15