



Unmet needs in preoperative biliary stenting for patient candidates for pancreaticoduodenectomy: a viewpoint

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We read with great interest the article published in *Annals of Surgery*, “Preoperative Biliary Stenting and Major Morbidity After Pancreatoduodenectomy: Does Elapsed Time Matter? The FRAGERITA Study Group” (1). The timing of preoperative biliary stenting (PBS) and its impact on postoperative outcomes after pancreaticoduodenectomy (PD) are ever-burning issues for pancreatologists dealing with jaundice due to periampullary tumors.

To investigate the association between the duration of PBS and postoperative morbidity, a retrospective analysis of five prospectively maintained international databases was performed. A cohort of 312 patients was subdivided into three groups according to the duration of PBS before PD: short (<4 weeks), intermediate (4–8 weeks), and long (>8 weeks). The authors found that, when possible, PD should be postponed to up to 1 month after PBS. Indeed, the short group showed higher rates of major morbidity after PD, as well as an increase in the length of stay. This finding has been widely explained by the beneficial effects of time in the restoration of liver function and the immune system.

In 2018, we performed a study that assessed the role of PBS on postoperative outcome after PD. Also, we aimed at establishing a cut-off value for bilirubin levels to recommend PBS in patient candidates for PD. Retrospectively analyzing a large cohort of 1,500 patients, we found that PBS *per se* does not increase major morbidity after surgery, but that it is associated with higher rates of surgical site infection. Furthermore, we identified that a value of bilirubin greater than 7.5 mg/dL (128 μ mol) might segregate those patients to submit to PBS [AUC =0.82 (0.77–0.870)] (2).

The impact of PBS on postoperative outcomes after PD

has been underestimated. Only one randomized controlled trial is currently available (3), and this dates back to 10 years ago (when novel findings on bile colonization after PBS were not available and biliary stents were different).

Several aspects make this topic very difficult to investigate. Thus, the results published become hardly comparable. First, the bile colonization after PBS, especially by multi-drug resistant bacteria, might be responsible for poorer postoperative outcomes (4,5). Furthermore, the microbiological flora that can colonize the bile is affected by different geographical variations (6). The role of a proper antibiotic prophylaxis/therapy in this setting is still under debate, and further investigation is needed. Second, the liver function is difficult to evaluate, and the lab tests commonly adopted to assay it (e.g., coagulation tests, protein synthesis analysis, or bilirubin levels) might not adequately reflect the true function of the organ. Third, and linked to the previous aspect, the immune system is hardly explorable in a cohort of patients with malignancy, especially in those patients that are going to receive chemotherapy. Fourth, there is no clear consensus on the type of biliary stent to use (plastic or metallic) as no randomized controlled trials are available. Also, complications of PBS, such as stent displacement or occlusion with persistent jaundice with or without cholangitis, are common in clinical practice and impact negatively on the course of the drainage of jaundice. Fifth, the mechanisms behind the harmful effects of hyperbilirubinemia are not fully understood. Therefore, it is not easy to presume from which value on hyperbilirubinemia would become able to impact negatively on the clinical status. Fifth, some logistics and

psychological reasons have to be taken into account. Unless stronger evidence becomes available, in case of resectable periampullary neoplasms, it is not easy to explain to a patient that the postoperative outcomes would likely be negatively impacted by a short time between PBS and PD, and that a delay of surgery would be beneficial.

Considering the high prevalence of jaundiced patients among those with periampullary cancers to treat with PD, we believe that this topic should be deeply investigated with a multicenter randomized controlled trial, that could definitively shed light on the proper timing and potential benefits of PBS, as well as on the type of biliary stent to adopt.

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Footnote

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

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