



# Post-hepatectomy biliary fistula: from risk factors to the role of drain placement and management—still a lot to be answered

Guido Costa, Matteo Donadon, Guido Torzilli

Department of Hepatobiliary and General Surgery, Humanitas University & Humanitas Clinical and Research Center – IRCCS, Rozzano, Milan, Italy

*Correspondence to:* Matteo Donadon, MD, PhD. Department of Hepatobiliary and General Surgery, Humanitas Clinical and Research Center – IRCCS, Via Manzoni 56, 20089, Rozzano, Milan, Italy. Email: [matteo.donadon@hunimed.eu](mailto:matteo.donadon@hunimed.eu).

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Hepatic resection represents the gold-standard treatment for different liver diseases. Among postoperative complications, bile leak remains one of the most common sources of morbidity, which can lead to an increase of hospital stay, need of invasive procedure and potentially death (1). The definition and acknowledge of risk factors for the development of biliary fistula as well as its early detection and optimal management is, in this sense, of crucial importance.

We read with great interest the paper published by Spetzler *et al.* (2). In a single-center cohort of prospectively collected patients, they identified some preoperative and intraoperative predictors of bile leak. These predictors included: preoperative patients' characteristics, comorbidities and type of surgical indications and surgical procedures. Interestingly, the authors found that fragile and soft liver, such in cases of extensive use of preoperative systemic chemotherapy, was associated with increased risk of bile fistula. Conversely, hard and fibrotic liver, such in cases of cirrhosis, was deemed to be a protective factor. Notably, these results are very important and consistent with previously published studies (3-6). Indeed, one of the increasing indications for hepatectomy is the presence of colorectal liver metastases (CLM) that, as known, are usually operated after systemic chemotherapy. Thus, the finding of an increased risk of bile leak in some cases of chemotherapy-associated liver injury is worthy to be mentioned when deciding the indication and duration of preoperative systemic chemotherapy. Moreover, the developing tendency

to adopt parenchyma-sparing surgery for the treatment of multiple bilateral CLMs (7), which reduce the amount of resected healthy liver and therefore the risk of postoperative liver failure, can lead to the performance of more complex and wider resection planes with the exposure of major Glissonean pedicles. Then, such type of surgery may be associated with increased risk of bile leak both for the use of preoperative chemotherapy and for the type of resection.

Looking further into surgical factors that showed an association with the development of bile leak, it was found an increased risk for those patients who had interventions on the biliary tract before surgery and for those who received biliary anastomoses. These associations have been already reported in the literature, and they usually require an extra-care in the intraoperative and postoperative management as well as separate reports in surgical series. Indeed, attention should be paid when comparing different surgical series because there is a lack of uniformity in reporting definitions and management of post-hepatectomy bile leak. In this sense, we believe that is difficult to compare results when different protocols for drain placement and management are adopted. The International Study Group of Liver Surgery (ISGLS) definition of low-grade fistula is based on the ratio between the bilirubin concentration in the drained fluid and in the serum (i.e., at least 3 on or after post-operative day 3) (8); this means that low-grade fistulas can be detected and reported only if a surgical drain is placed in the abdomen after liver resection. This is partially in contrast with the most recent tendency of not placing drains after elective

hepatectomy. In fact, it can be argued that these low-grade leaks, not detectable without a surgical drain, may not be clinically relevant and therefore that systematic drainage of hepatic resection can even be a wasteful habit. This is actually supported by some randomized controlled trials (RCT) (9). However, it is important to note that a rigorous protocol of drain placement and long-term maintenance (more than five days) is usually associated with lower rates of post-operative radiological intervention and reoperation for bile leaks or fluid collections (4,10). These results (0.9% rate of percutaneous puncture and 1.1% rate of reoperation for the series of Kyoden *et al.* and 1.8 and 0% respectively for the series of Donadon *et al.*) are better than those results reported in both drained and not-drained arms of the published RCTs. This suggests that drainage after hepatectomy has an important role in the recognition and treatment of biliary fistulas and that not only the role of the drain placement but also its optimal management is a key-factor.

In conclusion, we believe that the widening indications for hepatic resection, the increasing amount of chemotherapy given to patients before surgery and the growing complexity of surgical procedures impose a cautious attitude towards the risk of development of bile leakages and related complications. The literature has answered some of the question regarding risk factors and optimal management but it is still lacking robust and standardized evidence.

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## Footnote

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

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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