Editorial

Kinetics of remnant liver volume and function after a major hepatectomy

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Liver regeneration after a major hepatectomy (MH) is crucial for the patient postoperative recovery, with the first postoperative month (1M) being a critical period for the liver regeneration course. The risk of post hepatectomy liver failure (PHLF), which is the leading cause of death, is usually anticipated in the preoperative period by the measurement of the future remnant liver volume (RLV) via computed tomography (CT) with volumetry. Nevertheless, the efficacy of this preoperative work-up is restricted by the lack of correlation between the volume of the future remnant liver and its function assessed via hepatobiliary scintigraphy (HBS), as reported following portal vein embolization (PVE) (1). Hence, patients with similar preoperative RLV developed differently postoperative complications and PHLF.

Recently, Rassam *et al.* (2) reported a similar lack of correlation between volume and function gain, though this time in the postoperative period. In 18 patients who had one-stage MH, function and volume of the remnant liver had raised significantly on the 5th postoperative day (POD), in comparison to baseline. After 4–6 weeks, liver function showed no significant additional increase, in contrast to RLV that had further increase. Moreover, patients with serious complications (≥ Clavien-Dindo 3a) had delayed functional regeneration, while showing significant volumetric gain of the remnant. In parallel, the authors analyzed the liver stiffness using fibroscan. Between baseline and the first five POD, they reported a significant gain in liver elasticity of the remnant liver, which progressively recovered after 4–6 weeks. There was no significant difference in terms of liver elasticity at baseline when comparing patients with versus without serious complications.

Likewise, we previously analyzed the kinetics of (future) RLV and function in 125 patients undergoing MH (3) via sequential CT and HBS assessments performed preoperatively and postoperatively on POD7 and 1M as a critical period for the liver regeneration process. Our data showed that the remnant liver function gain following MH correlated poorly with the RLV gain, in accordance with the results of Rassam *et al.* (2). On average, the function gain was slower than the volume gain. Moreover, the changes in remnant liver function were correlated with the postoperative course, in particular PHLF, whereas the kinetics of RLV were comparable between patients with and without PHLF or severe complications. In particular, four patients who died from PHLF displayed a significant volumetric gain of the remnant liver despite no function increase. These findings were confirmed after

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matching patients on preoperative RLV, as the rate of liver regeneration depends on the RLV.

Desynchronized changes in volume and function in the early phase of liver regeneration have been suggested by several experimental and clinical studies (4-7). Hence, in a dog model of 70% hepatectomy, the remnant liver weight increased rapidly up to baseline values at 2 weeks after surgery, while bile flow went on rising for 12 weeks. In 27 donors undergoing right hepatectomy for living donation, functional recovery assessed via galactose elimination capacity occurs much more gradually than volume and liver biochemistries recovery (7). This delayed functional recovery at the early phase of liver regeneration could be related to an increase in size of proliferating immature hepatocytes (8,9). The time interval between hepatocytes replication that occurs early (i.e., within 24 h) and replication of non-epithelial and ductal cell types that starts later, may be another contributing mechanism (10).

Altogether, these data emphasize the need for functional assessment of liver regeneration rather than volumetric one in patients undergoing MH. On the other hand, the current techniques of functional assessment of the remnant, mainly ICG and HBS may be directly influenced by the postoperative hepatic function, rendering their interpretation difficult; indeed, there is a competition between bilirubin and the tracers used in such techniques on hepatocytes receptors. The present findings further suggest that MH [in one or two stages like Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS)] and PVE imply distinct regeneration pathways. Indeed, differences in volume versus function changes after MH went in the same direction to what was reported after ALPPS (11,12), but in the opposite direction to what was observed after PVE, where the liver function gain exceeded the liver volume gain (1).

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