French Editorial from the ACHBPT

Comment on: liver venous deprivation (LVD) or associating liver partition and portal vein ligation for staged hepatectomy (ALPPS)? A retrospective multicentric study

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We read with interest the recently published paper by Chebaro *et al*. (1). The authors compared liver venous deprivation (LVD) and associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) which are two novel techniques used to achieve increased hypertrophy of the future liver remnant (FLR) in view of extensive liver resections (2,3).

Portal vein embolization (PVE) is currently the standard of care to increase the FLR and to allow safe resection by decreasing risk of posthepatectomy liver failure (4). The main drawback is that increase of the FLR size requires a mean delay of 6–8 weeks which may lead to patient dropout because of tumor progression (5). The ALPPS strategy overcomes PVE shortcomings by accelerating FLR growth (+80% increase within 10 days) and allowing liver resection in nearly all patients. However, unacceptable mortality and morbidity rates reported during the initial ALPPS experience incited the surgical community to refine the indications and improve patient selection (6).

The LVD technique associates concomitant portal vein and hepatic vein (HV) embolization in the liver to be resected (7). The technique is less invasive than ALPPS and the resulting hypertrophy of the FLR which is superior to PVE (2). In patients at risk of PVE failure, LVD and ALPPS appear as the main competitors to reduce risks of post-hepatectomy liver failure but their respective indications are still a matter of debate.

In this retrospective study Chebaro *et al*. (1), used a composite primary end point (successful resection rate, i.e., resection rates without mortality on postoperative day 90) to compare 124 patients who received LVD to 85 patients who underwent ALPPS. Time to surgery was significantly longer (median 37 *vs*. 10 days) and the successful resection rate significantly lower (73% *vs*. 91%) after LVD while the FLR hypertrophy was faster (KGR: +2%/day *vs*. +7%/day; P<0.001) after ALPPS. Operative morbidity and mortality were similar in both groups. Successful resection rates remained higher in the ALPPS compared to the LVD group (93.2% *vs*. 79.2%, P=0.028) on subgroup analysis of patients with colorectal liver metastases (CRLM) only. Altogether these findings led the authors to suggest that in patients at risk of PVE failure, ALPPS should be preferred to LVD.

One major concern with this study is group comparability. Selection bias is introduced by the retrospective nature of the study and by the fact that the choice of treatment depends on the preferences of the surgeon and/or the center. Moreover, there was a significantly higher number of patients with perihilar cholangiocarcinoma (PHCC) in the LVD group and this is a major confounding factor hindering the interpretation of the results. These patients are subject to jaundice or/and sepsis and require iterative biliary drainage as hypertrophy of the cholestatic liver is slower; as a result, risk of morbidity, tumor progression and death before surgery are greater for PHCC than for CRLM patients. Indeed, analysis of the international ALPPS registry showed unacceptable

morbidity and mortality rates in PHCC patients suggesting that ALPPS should not be performed for this indication (8). However, in order to overcome this bias, the authors carried out a subgroup analysis on patients with CRLM. Again, the successful resection rate of LVD patients remained below that of ALPPS (79% *vs*. 93%) suggesting that ALPPS should also be favoured CRLM patients.

In this study, 90-day postoperative mortality rates after LVD and ALPPS were similar (8.4% *vs*. 9.4%). However, as the authors concede, the benefit of ALPPS was ultimately related to higher rates of cancelled resections after LVD because of tumour progression. This fact calls to caution in the interpretation of long-term results. It is generally accepted that surgery does not benefit patients with progression of CLRM (9). Of course, higher dropout rate after LVD is due to longer delay in surgery but it is questionable whether this should be interpreted as LVD failure or just improved patient selection. The only way to get a reliable answer is to perform a survival analysis in the CRLM group.

The study design is original and is the first report to date that compares LVD and ALPPS with the purpose to refine their respective indications. The authors confirmed that in experienced hands ALPPS is a safe and effective tool for the management of CLRM patients; their findings are in accordance with recent publications on the topic and validate the use of ALPPS in this setting (10). The study also reports one of the largest LVD cohorts in the literature providing important information on the dynamics of FLR hypertrophy and outcomes.

In conclusion, the study is of importance because it is the first to report comparison between patients undergoing ALPPS and LVD-prepared major hepatectomy for malignant liver tumours. However, selection bias induced by the retrospective design and voluntary data reporting as well as the lack of group comparability hinder meaningful interpretation of the main endpoints. We look forward to the see the survival analysis that would validate the oncological benefit of ALPPS and LVD in patients with CRLM.

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Footnote

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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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