Liver venous deprivation before major hepatectomy—promising but still a work in progress

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In December 2024, Boubaddi *et al.* reported the results of a multicenter French collaboration retrospectively analyzing the outcomes of 192 patients with liver malignancies who underwent liver venous deprivation (LVD) prior to major hepatectomy (1). This study focused on the feasibility, efficacy and safety of LVD, demonstrating a 100% technical success rate, a low rate of severe post-embolization complications (2.6%), a mean kinetic growth rate (KGR) of 6% per week, and a resection rate of 83.8%. This collaboration represents the second-largest single-arm cohort of patients undergoing LVD reported to date and provides valuable real-world data from seven expert centers.

For patients with liver malignancies, tumor eradication through local treatment is vital. Although local treatment options continue to expand with the rise of thermal ablation, parenchymal-sparing resection, radioembolization, and even transplantation, anatomical liver resection remains an essential facet of local therapy, particularly for patients with extensive hepatic disease. For those with extensive disease, major liver resection carries the risk of an insufficient future liver remnant (FLR) and, consequently, an increased risk of post-hepatectomy liver failure (PHLF), necessitating preoperative FLR enhancement (2).

Although portal vein embolization (PVE) is the standard FLR hypertrophy-inducing procedure, the addition of ipsilateral hepatic vein embolization (HVE), first described in 2016, has rapidly gained traction (3,4). The technique has acquired multiple aliases, including double-vein embolization, bi-embolization, LVD, or combined PVE and HVE (PVE/HVE). Technically, LVD typically involves selective HVE using both vascular plugs and glue, whereas PVE/HVE refers to HVE performed with vascular plugs only, without glue (5). The LVD approach, with glue in the hepatic veins, was used exclusively in the cohort described by Boubaddi *et al.* To date, there is no clear evidence favoring one technique over the other. Each has its respective disadvantages: risk of glue migration through venous collaterals in LVD versus potentially increased procedural cost due to multiple plug placement advised for a complete PVE/HVE.

The extent and completeness of embolization is another critical and largely unreported factor (5,6). Segment 4

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embolization was not performed in this study, and only 10.4% of patients received both right and middle HVE, despite nearly half ultimately undergoing extended right hepatectomy. Moreover, no centralized imaging assessment was done to objectify embolization completeness. As with earlier research into PVE optimization, evaluation of LVD technique in relation to FLR growth, safety, and cost-effectiveness is key for future research (7).

Boubaddi *et al.* demonstrate that LVD can induce significant FLR growth, with a mean %FLR volume increase of 59.2%. This is substantially higher than the volume increase of 37.9% observed after PVE (8). The KGR seen after a mean of four weeks is also noteworthy. The 6%/week shown in this cohort surpasses KGRs reported in the recently published DRAGON 1 trial (3.9% after three weeks), the EuroLVD registry (3.4% after 3–4 weeks), and the MSKCC cohort from Choubey *et al.* (3.3% after 3 weeks) (9-11). Notably, as part of their single-arm retrospective study, Choubey *et al.* also demonstrated that the hepatic artery infusion pump chemotherapy has no influence on FLR growth after embolization (11). Despite the high KGR, the authors note that the median time from embolization to hepatectomy remained quite long at 40 days, which is comparable to the EuroLVD results, but nine days longer than in the DRAGON 1 trial (9,10). As Boubaddi *et al.* also hypothesize, logistical issues can hamper timely planning of resection and standardized protocols for earlier FLR assessment have yet to be widely adopted. In the DRAGON 1 trial, FLR assessment one week after embolization was stipulated in the trial protocol, at which point 27% of patients could already be planned for surgery (9). These results certainly suggest that implementing standardized FLR assessment intervals and stricter surgical planning may reduce the time to resection and the number of patients deemed unresectable after embolization due to disease progression. In this study, disease progression was indeed the reason for non-resectability in 14.7% of patients. Overall resection rates are comparable to previous retrospective LVD data, slightly higher than those reported after PVE (80%), and slightly lower than the 90% resection rate observed in the DRAGON 1 trial for colorectal liver metastases only (8,9,12).

With the publication of this study, the first EuroLVD results and the prospective DRAGON 1 trial, all in the past year, the safety and feasibility of LVD are certainly confirmed. The findings of no embolization-related mortality and low severe complication rates of 2–3% are consistent across the recent evidence (10). However, considering its occurrence in both this cohort and DRAGON 1, vascular plug migration is a potential severe complication of HVE that needs to be highlighted. Oversizing vascular plugs by at least 50% is thus an important step to mitigate the risk of this serious complication.

Even after LVD, the risk of PHLF remains significant. In this cohort, clinically significant PHLF (ISGLS grade B or C) occurred in 21.1% of patients and was the main cause of 90-day mortality (4.3%). These results bear resemblance to the 22% observed in DRAGON 1, which resulted in total 90-day mortality of 8%. It would be interesting to examine the distribution of PHLF and mortality across this study's inclusion period (2016 to 2023), as some incidence may be attributable to a learning curve in LVD performance and work-up towards resection. Even more importantly, the lack of functional FLR assessment in both studies is apparent, and the addition of such assessment with 99mTc-mebrofenin hepatobiliary scintigraphy (HBS) will probably improve safety (13). It is important in future FLR regenerative research to incorporate HBS and other assessment tools mentioned by the authors, such as the KGR cut-off of >2%/week and the aspartate aminotransferase/platelet ratio index (APRI)/albumin-bilirubin (ALBI) score, into a risk evaluation algorithm (14,15).

Even though there is growing support for incorporating FLR function into decision-making, with FLR function cut-offs of 2.69%/min/m2 measured using HBS, the number of centers that have implemented HBS as standard of care is still rather low. Since all centers have single-photon emission computed tomography (SPECT) available, implementation should be high on the priority list. For now, FLR volume assessment remains the prevailing standard in clinical practice (13). CIRSE Standards of Practice suggest rather optimistic FLR volume cut-offs (FLR/total liver volume ratio) of >20% in normal livers, >30% in livers with prior chemotherapy, and >40% in cirrhotic or cholestatic livers (5). However, these cut-offs are not consistent across literature or between centers, as illustrated by a nationwide survey of 46 Italian centers in which FLR thresholds for healthy livers ranged from 20% to 40% (4). Boubaddi *et al.* report cut-offs of >25% for normal livers and >30% for diseased livers. Importantly, PHLF risk rises sharply as the FLR decreases, increasing from an 11% risk with an FLR larger than 30% to an alarming 29% when FLR falls below 30% (2). This underscores the importance of determining whether the current cut-offs should be revised and whether FLR enhancement should be employed more liberally.

The coming years will hopefully bring exciting results to look forward to. According to ClinicalTrials.gov, the HYPER-LIV01 trial (NCT03841305) evaluating percentage change in FLR after PVE versus LVD, completed inclusion in October 2024. The DRAGON randomized controlled trials (RCTs) are also actively recruiting. The DRAGON 2 RCT (NCT05428735) in colorectal liver metastases examines split primary endpoints of: FLR sufficient for resection 3 weeks after embolization, and five-year overall survival after PVE versus PVE/HVE. The DRAGON PLC (primary liver cancer) (NCT06914648) started accrual in April 2025, with identical outcomes to DRAGON 2.

We congratulate Boubaddi *et al.* on this important study, which contributes meaningfully to the growing body of evidence regarding LVD outcomes. We fully agree with the authors that the LVD technique requires further standardization and optimization, and that its precise indication remains to be defined, especially considering increased radiation exposure, as well as increased procedural time, materials, hospital resources, and thus cost. Functional FLR assessment using HBS should also be integrated into standard clinical practice.

As demonstrated by this study and recent publications, LVD has great potential in terms of FLR growth and resectability, but until now, prospective comparative evidence to the standard, PVE, is severely lacking, and safety outcomes after hepatectomy must be improved. We need prospective evidence from RCTs to move the field forward, an effort that will only be achievable through multicenter collaboration.

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