



New evidence for liver venous deprivation: safety and feasibility for extended liver resections

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For many primary and metastatic liver tumors, hepatectomy is the treatment of choice that can effectively extend the survival time of patients. Among different factors, the expected residual liver volume after resection, also known as future liver residue (FLR), is one important aspect affecting the prognosis of patients (1,2). Many patients lose the chance of liver resection due to too little FLR. Portal vein embolization (PVE) is one of the most common techniques for increasing FLR. It is usually performed percutaneously with a microguidewire entering the right hepatic vein under ultrasound guidance, a Berenstein catheter is then inserted into the portal vein with the guide wire, and portogram is performed. After 3D portography, the portal vein branches are embolized with a mixture of n-butyl cyanoacrylate and lipiodol in the appropriate ratio (3). Since the first use of PVE to increase FLR and successfully completed surgery in patients previously considered to be intolerant to liver resection, PVE has been widely investigated to increase FLR before liver resection (4).

However, patients after PVE usually need to wait 4–6 weeks before the liver is hypertrophic to a sufficient volume for safe liver resection. During this waiting time, as many as 20% of patients suffering tumor progression (mainly bilobar colorectal liver metastases) is the main disadvantage of PVE (5). Therefore, new technologies have been developed to increase FLR in a shorter period of time, including association of liver distribution and portal vein ligation (ALPPS) and liver vein deprivation (LVD). ALPPS

is a surgical technique involving parenchymal transection combined with ligation of the right portal vein and branches of the portal vein before resecting the diseased liver (6), it can increase FLR in a much shorter time, but has higher mortality. LVD is mainly through the jugular vein to avoid direct puncture through the right liver and the right hepatic vein embolization is also performed in addition to the right PVE described in PVE (3). LVD could achieve faster FLR growth without affecting mortality, but as a new tool the data are limited (7).

A recent study published in the *Journal of Hepatobiliary Surgery and Nutrition* by Dr. Fabrizio *et al.* compared the FLR between 16 patients receiving PVE and 13 patients receiving LVD (8). This study included the largest number of patients in the current series of studies. They compared intraoperative, preoperative and postoperative results of LVD and PVE in patients undergoing standard right hepatectomy: no statistically significant differences were observed in the two groups in terms of intraoperative bleeding, hepatic ischemia time, operative time, postoperative biliary leakage, liver atrophy, liver necrosis and sinusoidal dilatation. In addition to clinical indicators, the secondary endpoint of the study was the evaluation of histological specimens in order to compare the morphological changes of hepatocytes and sinusoidal endothelial cells between the two groups. The frequency of hepatocyte atrophy and necrosis was slightly higher in the LVD group, but had no statistical difference. Besides,

sinusoidal dilatation occurred in 6 and 7 patients after PVE and LVD respectively. They concluded that LVD was a promising and safe procedure for inducing rapid FRL hypertrophy, with similar mortality/morbidity during and after surgery compared to PVE. Liver regeneration depends on the stimulation of the injury and the condition of the liver parenchyma, but its molecular and cellular mechanisms have not been clearly defined. Sinusoidal cells and hepatocytes play a key role in liver regeneration while hepatocyte growth factor, transforming growth factor- α and epidermal growth factor have been proven to be important participating factors (2,9).

We want to discuss some parts of this article, which may be useful for further designing experiments in this area. Firstly, as far as we know, all articles comparing PVE and LVD are retrospective studies, so a randomized controlled trial (RCT) is needed to confirm the benefits of LVD (the authors also mentioned two ongoing RCTs, which may provide new strong evidence).

Moreover, although the hypertrophy rate of LVD is better than that of PVE at the same time, recent studies have compared the efficacy and safety of LVD and PVE at the same waiting time. For patients with malignant tumors, especially those with advanced liver cancer, early liver resection can reduce the risk of tumor progression. Therefore, further research is needed to investigate the efficacy and safety with shorter intervals after LVD. In addition, some studies have reported that the complications of ALPPS have decreased significantly with increasing operating experience and more stringent indications (5). We expect a comparative study between improved ALPPS, PVE and LVD. By choosing the most appropriate technology for different patients, this result may provide new evidence for future personalized medicine.

Finally, the study also included several Child-A patients, and the effects of LVD and PVE were similar to normal patients. Patients who require liver resection are often accompanied by different degrees of cirrhosis. Because of impaired liver function and structure, patients with severe cirrhosis may not be suitable for LVD or PVE. However, whether PVE, LVD, ALPPS, or other new technologies can benefit patients with mild or moderate fibrosis requires further research.

In summary, this study provided new evidences for the safety and efficacy of LVD through rigorous patient selection and broader comparison issues. Based on the comments shown above, future studies on the effect and safety of shorter interval LVD and including patients with

mild to moderate fibrosis may be beneficial for more people.

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