Editorial

Editorial on "Uncommon indications for associating liver partition and portal vein ligation for staged hepatectomy: a systematic review"

Anastasia Murtha-Lemekhova[1,2], Katrin Hoffmann[1,2]

[1]Department of General, Visceral, and Transplantation Surgery, Heidelberg University Hospital, Heidelberg, Germany; [2]RELIVE Initiative, Heidelberg, Germany

Correspondence to: Professor Katrin Hoffmann, MD, MBA. Department of General, Visceral, and Transplantation Surgery, Heidelberg University Hospital, Im Neuenheimer Feld 420, 69120, Heidelberg, Germany. Email: Katrin.Hoffmann@med.uni-heidelberg.de.

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Associating Liver Partition and Portal vein ligation for Staged hepatectomy (ALPPS), an innovative procedure in liver surgery, capacitated resection of previously unresectable liver tumors. Originally ALPPS was predominantly applied in patients suffering from extensive colorectal liver metastases (CRLM) with good results (1). ALPPS is thought to exploit liver's ability to regenerate upon mechanical injury, while safeguarding against liver failure by temporarily leaving a deportalized and detached portion of the liver afflicted with disease. The non-tumorous tissue of the diseased portion is entrusted to support liver function during the regeneration process, thus preventing overexertion of the hepatocytes in the remnant that would otherwise cause their demise.

As ALPPS has facilitated surgery in otherwise incurable patients, many indications and modifications have emerged (2-4). With this, a strong heterogeneity of reports has appeared, describing low individual caseloads and mortality rates reaching up to 50% (5). Ultimately, a decade since the initial description of the technique, there is no evidence-based consensus on criteria for patient selection or exclusion criteria based on comorbidities and performance status. Although some patients with CRLM and hepatocellular carcinoma (HCC) seem to benefit from the procedure, patients suffering from less prevalent conditions are only described anecdotally. Rare liver lesions have habitually been at a disadvantage as clear treatment guidelines are missing; case reports and small series provide limited evidence, whereas randomized-controlled trials are not feasible. Additionally, after disappointing experiences and high morbidity and mortality rates in some indications such as cholangiocarcinoma, ALPPS has become controversial. The initial excitement, the number of applications in major hepatobiliary centres, and, consequently, the number of published reports have subsided. Presently, it is debatable if ALPPS should be applied wherever technically feasible or if it should merely be a second choice conditioned on failure of portal vein embolization (5).

In their article in *HepatoBiliary Surgery and Nutrition*, Lai *et al.* presented the results of a systematic review on ALPPS for uncommon liver lesions. Authors reviewed and synthesized current reports concluding that despite 136 cases reported so far, clarity on recommendation has not yet been achieved (6). The review provides the best body of evidence on feasibility of this technique in curing uncommon diagnoses.

Liver metastasis from cancers other than colorectal was the most common diagnosis preceding ALPPS. Not surprisingly, as patients have shown favourable outcome after ALPPS for CRLM that other secondary malignant lesions may benefit from it as well (7). However, benefit of resecting non-colorectal secondary liver lesions at all is still under debate, and although some reports provide supportive evidence, a selection bias must be anticipated as particularly young and otherwise healthy patients are preferred for treatments outside the mainstream (8,9).

Although strong evidence for resection of liver metastasis from neuroendocrine tumors is lacking, this was the second most common indication for ALPPS with 1-year overall survival of 73–95% (6). While reports of primary resection of neuroendocrine tumor (NET) liver metastasis state 5-year overall survival of 68%, it is unclear how ALPPS will influence this statistic (10). Despite a favourable overall survival, a third of patients developed serious complications (Clavien-Dindo grade III or higher) and two died within the first 2 months.

Similar trends with high complications are seen in patients with gastrointestinal stromal tumor (GIST) metastasis; two out of three patients developed serious complications. It is unclear how ALPPS can be applied in patients with other secondary lesions to the liver. Although 43 patients with various metastases have undergone the procedure, the follow-up was reported in only eight and ranged from 2 to 40 months. This substantially limits possible conclusion on ALPPS application.

A particularly problematic cancer to treat is gallbladder carcinoma, as it is often detected late and, due to anatomical considerations, resection is difficult. From 15 ALPPS cases with 90-day follow-up, 60% died. However, extent of the tumor was unclear and can only be assumed to involve large portion of the liver to necessitate ALPPS at all. Still, with high mortality and generally high positive resection margins, a benefit of an extensive hepatectomy, such as ALPPS, in gallbladder carcinoma can only be indicated in highly selected cases after rigorous consideration (11).

Short follow-up is one of the biggest limitations in the majority of ALPPS reports. Additionally, it is unclear which criteria can be used to select patients with uncommon tumors for ALPPS. With 18 countries contributing reports on 136 cases comprising 31 diagnoses, the selection criteria will remain difficult for the foreseeable future. This highlights the need for systematic synthesis of evidence on treatment of rare liver lesions (12).

We commend authors on their interesting manuscript and although it remains unclear which patients with uncommon liver tumors benefit from ALPPS, the systematic review shows that it is a promising treatment for some. We agree that multi-central analyses focusing on patient selection and safety are needed.

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Footnote

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