Editorial

Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS)—a fine balance

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We read with interest the paper by Li *et al.* entitled "*Associating liver partition and portal vein ligation for staged hepatectomy versus sequential transarterial chemoembolization and portal vein embolization in staged hepatectomy for HBV-related hepatocellular carcinoma: a randomized comparative study*" (1). In this single-centre randomised comparative study, 76 patients with unresectable hepatitis B virus (HBV) related hepatocellular carcinoma (HCC) due to inadequate future liver remnant (FLR) volumes were randomly assigned to undergo Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) or Trans arterial chemoembolization (TACE) and portal vein embolization (PVE) for staged hepatectomy.

Patients in the ALPPS group were reported to have a higher rate of resection (97.4% *vs.* 65.8%, P<0.001). While the three-year overall survival (OS) rate was reported to be higher in the ALPPS group, there was no significant difference in the OS when comparing only those who underwent resection in both groups. Importantly, the rate of major complications (Clavien-Dindo Grade ≥3A) after hepatectomy was also found to be significantly higher in the ALPPS group (54.1% *vs.* 20.0%, P=0.007). One major limitation of this study is patients first underwent TACE prior to PVE so direct comparison to ALPPS as a method of liver hypertrophy and oncological control needs to be taken with caution.

It has now been a decade since ALPPS was first described for primary liver tumours (2,3), and utilisation of this technique has been used predominantly in the context of the resection of colorectal liver metastasis (4). Although the authors report this to be the first randomised comparative study of ALPPS versus PVE in HBV-related HCC patients, perhaps unsurprisingly, the results bring up the same debate surrounding ALPPS. It is now well-documented that ALPPS induces rapid liver hypertrophy and allows for an earlier second-stage hepatectomy. ALPPS as reported in this study also leads to a higher resection rate but at the expense of appreciably higher rates of morbidity and mortality (5,6). The long-term oncological and survival benefit is unproven.

The feasibility of ALPPS in patients diagnosed with initially inoperable HBV-related HCC has previously been demonstrated (7,8). Recent literature comparing ALPPS to TACE in the treatment of HBV-related HCC, reports contrasting results. Propensity score matching analysis in one study with 23 patients reported no difference in OS rates in patients who underwent ALPPS compared to TACE (9) for HBV-related HCC. While other larger comparative studies reported significant OS benefit in patients who underwent ALPPS for HBV-related HCC (8) compared to

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TACE. Importantly, the long-term survival for patients who underwent ALPPS is no different to those who underwent one-stage liver resection (7). So, the question remains, is it worth the risk?

These reported findings in combination with the fact that the authors reported no difference in OS in those who underwent resection in both groups suggest a complete resection is a key factor in improved outcomes. It is still uncertain whether more rapid resections achieved with ALPPS confers any overall benefit. If we are able to achieve an R0 resection or complete tumour response with a less risky procedure, then that method should still be first considered.

Two factors would help inform both clinicians and patients when trying to select the appropriate procedure. Firstly, we currently still do not fully understand what factors potentiate or impact liver hypertrophy response to PVE (10). Secondly, efforts have been made to generate predictive scoring systems for the prediction of risk and outcomes following ALPPS (11,12). Such scoring systems consider patients' pre-operative comorbidities. If validated and proven reliable when applied to the appropriate cohorts, this will be an important tool in selecting the appropriate procedure tailored to each individual patient.

This paper by Li *et al.* adds to the literature that ALPPS can improve rates of resection but at the expense of higher rates of major complications. Complete resection of the tumour achieved by any method is the key determinant of long-term survival. Currently, whether it is a primary liver tumour or hepatic metastasis, using PVE to increase FLR remains the accepted compromise between liver hypertrophy leading to safe hepatectomy and rates of morbidity and mortality (5). ALPPS or modifications of ALPPS (13) whilst effective, should only be performed in highly selected patients at specialist centres or considered as a rescue procedure in incidences of failed PVE on a case-by-case basis.

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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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