



The ALPPS procedure—As Limited Procedures as Possible, leads to improved Survival

Ruben Ciria, Javier Briceño

Unit of Hepatobiliary Surgery and Liver Transplantation, University Hospital Reina Sofía, Córdoba, Spain

Correspondence to: Ruben Ciria, MD, PhD, FEBS. Unit of Hepatobiliary Surgery and Liver Transplantation, University Hospital Reina Sofía, Córdoba, Spain. Email: rubenciria@gmail.com.

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The history of procedures for liver regeneration in the context of extended resections changed with the incorporation of Associating Liver Partition to Portal Vein Ligation in Two-Stage Hepatectomy (ALPPS) (1). The main well-known advantages of the ALPPS procedure are a fast and feasible increase in liver volume within a short period of time which leads to a second-stage procedure in 2–3 weeks. Contrary to other techniques such as the classic portal vein embolization (PVE) is the reduced time to second stage hepatectomy with the theoretical “oncological” advantage of reduced disease progression after first stage (2).

The main advantages of ALPPS were not so strong after the first series in which it was observed that such a strong aggression to the liver led to a moderate number of patients in which regeneration did not happen (mostly because of complications, bile leaks, or marked liver insufficiency). Interestingly, it was clearly defined as well that ALPPS needed a very strict selection process in which patients with impaired liver function, with non-controlled oncological disease and/or with hilar cholangiocarcinomas and cholestasis shall be discarded for this procedure. The use of ALPPS needs to be based on the main pillars: first, adequate preoperative liver function for a proper regeneration; second, precise oncological study with neoadjuvant control if necessary; and third, avoidance of any kind of surgery leading to bile leak or increased risk of infection/decompensation (3). Moreover, liver surgeons should always keep in mind both alternatives and variations of ALPPS, as they may offer same results with less aggression, mainly minimally invasive procedures (*Figure 1*) (4).

The main indication proposed for ALPPS has been colorectal liver metastases (5,6). Several series have clearly showed that ALPPS may offer a significant benefit in patients otherwise discarded for any surgical option. However, it should be noted that this kind of extensive resection should not overcome the two main principles which are the current standard of care in surgery for liver metastases: first, to preserve as much parenchyma as possible; and second, to achieve complete R0 resection. The number of procedures that have been described range from a wide variety: since the less aggressive till the most radical one, which is the full liver transplant.

The manuscript from Lai *et al.* is the perfect example that in surgery, sometimes less is more (7). This is a well-conducted manuscript that highlights uncommon indications of ALPPS, including benign tumours, gallbladder cancer, liver metastases from neuroendocrine tumours (NET), gastrointestinal stromal tumor (GIST) or other malignancies and a subset in the paediatric population. Data from 45 studies were obtained and 136 cases were collected.

Considering primary liver malignancies, twenty-seven cases of gallbladder cancer (GBC) infiltrating the liver parenchyma treated with ALPPS have been reported. The only information reported about survival shows that 60% of the patients died within 90 days from the second stage. Chemotherapy was a marginal strategy both in the neoadjuvant and adjuvant settings. These results show that such an aggressive surgical strategy in one of the most lethal tumours without adequate oncological control and very

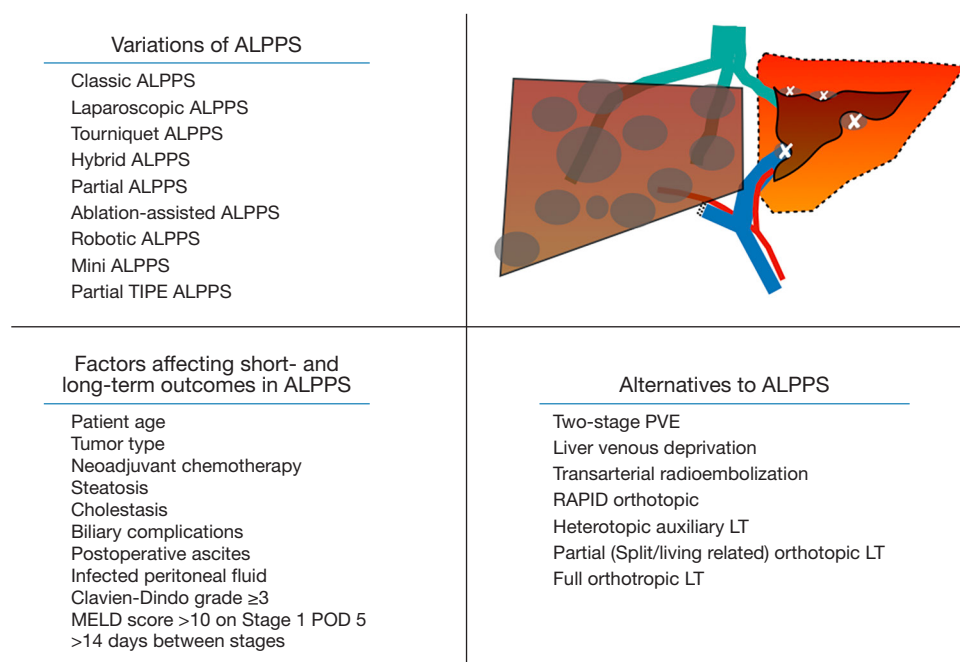


Figure 1 Summary of variations of ALPPS, alternatives to ALPPS and factors affecting short- and long-term outcomes. ALPPS, Associating Liver Partition to Portal Vein Ligation in Two-Staged Hepatectomy; POD, postoperative day; PVE, portal vein embolization; RAPID, Resection And Partial Liver Segment 2/3 Transplantation with Delayed total hepatectomy; LT, liver transplantation; MELD, Model For End-Stage Liver Disease.

likely with main vascular structures affected, leads to results that may be worse than supportive care.

Another set of cases was reported in liver secondary malignancies. Forty patients were resected using ALPPS technique for liver metastases from primary neuroendocrine tumor (NET). Insufficient oncological data are reported but most of them had the primary tumour resected before the surgery and most of them had been on any kind of neoadjuvant strategy. One-year overall survival rates were 73–95% and recurrence rates were around 45% (60% hepatic). These data are quite interesting and probably, in very carefully selected patients, and considering the strict criteria for liver transplantation in metastatic NET, it could be an option to be considered in patients with high metastatic tumor burden. Another 6 cases of metastatic GIST and 43 from other malignancies were reported. Data from the GIST cases, although just 6 cases, show promising results in terms of mid-term recurrence-free survival. The rest of the cases are a mixture of indications from which no clear conclusions can be obtained.

The last interesting indication analyzed in this manuscript is ALPPS in the pediatric population. Nine cases have been

reported from which 6 cases were hepatoblastomas. Only 2 cases have reported long-term outcomes, from which one early recurrence was observed. This is an unexplored field which may be an option considering the extremely healthy remnant liver and the high regenerative potential of these cases. A reinforcement of the collaboration between adult HPB and pediatric surgeons shall be promoted to consider the potential of ALPPS in this population.

Considering all the above mentioned unusual indications, we strongly agree with the authors that restriction is the key to have proper results in ALPPS. The success of long-term outcomes in oncological liver tumours is based on proper selection and lack of perioperative complications. In ALPPS, this balance is difficult to be achieved and a bad indication may lead to poor inadequate results. In our group, ALPPS is mainly indicated for patients in which 3 conditions have to be fulfilled: liver disease is considered not resectable by combining less aggressive multiple resections; second, liver disease has been controlled by any kind of neoadjuvant chemotherapy for metastases or preoperative locoregional strategy for hepatocellular carcinoma (HCC); and third, patients should be fit for surgery with no cholestasis (8). It is

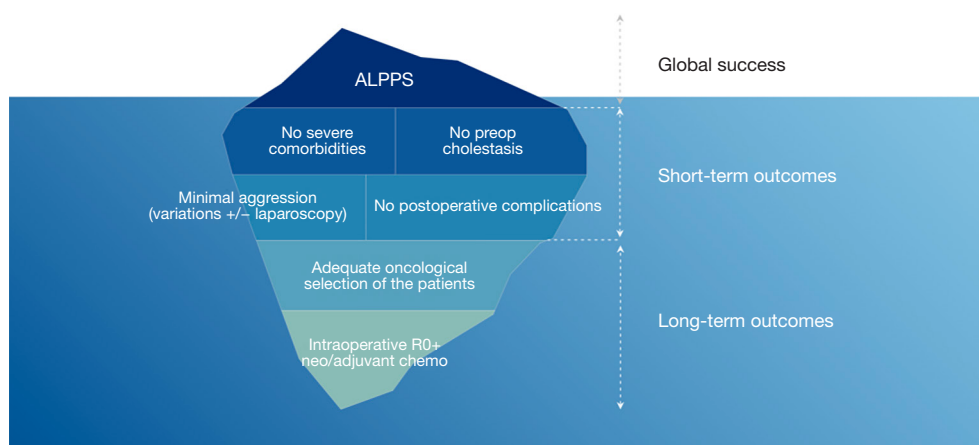


Figure 2 The Iceberg of ALPPS. What is hidden below the tip of the iceberg to achieve success is 6 principles that may be followed to reduce impact on both short- and long-term outcomes. ALPPS, Associating Liver Partition to Portal Vein Ligation in Two-Staged Hepatectomy.

also our policy to attempt minimally invasive techniques and ALPPS variations rather than classic one to reduce biliary complications and bleeding (*Figure 2*) (9,10). Anyhow, even our Unit is a referral Unit with more than 150 liver cases per year, the number of ALPPS is less than 1–2%. This is, from our point of view, the place where ALPPS belongs: a very strict indication which, in good hands, may lead to improved survival.

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appropriately investigated and resolved.

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