

VIEWPOINT

Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy

A Better Approach to Treat Patients With Extensive Liver Disease

Eduardo de Santibañes, MD, PhD

General Surgery Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Victoria Ardiles, MD

General Surgery Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Fernando A. Alvarez, MD

General Surgery Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.



Viewpoint

Corresponding

Author: Eduardo de Santibañes, MD, PhD, General Surgery Service, Hospital Italiano de Buenos Aires, Esmeralda 1319, 4to piso, 4to cuerpo, CP 1007 Buenos Aires, Argentina (eduardo.desantiban.es @hospitalitaliano.org.ar).

jamasurgery.com

Liver resection is the treatment of choice and a hope for cure for patients with malignant liver tumors. Resection is many times limited by the amount of future liver remnant, with liver failure being the most severe complication after major resections. To minimize this risk and expand resectability, portal vein occlusion of the tumor-bearing lobe is used to redistribute portal flow and induce hypertrophy of contralateral healthy parenchyma. Right portal vein embolization (PVE) is best used before surgery when the future liver remnant is tumor free, while portal vein ligation (PVL) is usually applied as part of 2-stage procedures for patients with bilobar disease who initially require tumor removal in the liver remnant. Around 20% to 40% hypertrophy can be achieved in 8 to 12 weeks with these strategies. However, up to 40% of patients never arrive to tumor resection either because of disease progression or insufficient hypertrophy during these long interval periods.

The associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) approach has emerged as an innovative 2-stage hepatectomy developed in Germany and characterized by a short interval between both surgical procedures.¹ Briefly, during the first stage, the liver parenchyma is divided in 2 hemilivers and PVL of the diseased hemiliver is performed. Once sufficient hypertrophy is achieved, which usually takes 7 to 10 days, the diseased hemiliver is resected. Although ALPPS has been increasingly applied to achieve tumor resection in patients with small future liver remnant, the surgical community is still debating its clinical application owing to high morbidity and mortality in initial series, as well as uncertain oncological outcomes.^{1,2} In our opinion, ALPPS has the following benefits over the established methods that prompt its inclusion among other treatment modalities for patients with locally advanced liver tumors:

1. Aggressive future liver remnant clean-up: the current paradigm of liver resectability is defined as a complete tumor removal preserving at least 2 contiguous Couinaud segments with intact vascular inflow, outflow, and biliary drainage. The ALPPS approach has challenged this classic concept, demonstrating that single liver segments can be left behind as sufficient liver remnant.³ This constitutes an important paradigm change in liver surgery.
2. Unparalleled future liver remnant hypertrophy: ALPPS induces a rapid and large future liver remnant hypertrophy.^{1,3} In a previous series, the median hypertrophy was 90% in 6 days and 80% of patients achieved a sufficient hypertrophy in fewer than 10

days.⁴ This hypertrophy is superior to traditional strategies, especially for patients with initially very small future liver remnants.

3. Fewer adhesions: the tremendous hypertrophy achieved in a brief period allows reducing classic interval periods of 8 to 12 weeks to around 7 to 10 days.⁵ Therefore, early definitive resection is possible with less adhesion formation compared with classic 2-stage approaches.
4. Single hospitalization: in most patients, both stages are possible during the same hospital stay.^{4,5} The potential psychological impact for the patient and the financial implications for the health system have not been evaluated yet.
5. Increased resectability: there is strong evidence indicating that ALPPS has higher resectability rates compared with PVE or PVL in classic 2-stage hepatectomy.²⁻⁶ The dropout reduction can be explained because almost all patients achieve sufficient hypertrophy, the short interval makes tumor progression unlikely, and liver splitting prevents direct tumor infiltration of the future liver remnant. In addition, although there are patients who may be treated with either PVE, the classic 2-stage approach, or ALPPS, it seems that there are patients who do not have another option but ALPPS. Such patients usually have extensive bilateral liver metastases that require an aggressive future liver remnant cleanup, resulting in a very small remnant with tumor close to its boundaries.

6. Rescue of futile portal vein occlusion: up to 9% of portal vein occlusions fail to induce sufficient hypertrophy. The ALPPS approach has been demonstrated to allow further hypertrophy and tumor resection in these patients.⁶ Although there are other alternatives for this scenario, such as hepatic vein or hepatic artery embolization, nowadays it represents an unquestionable indication for ALPPS.

In addition, there are other benefits of ALPPS that in our opinion deserve to be commented on despite being shared with conventional 2-stage resections: (1) abdominal cavity exploration during the first stage allows a more accurate disease staging, (2) the deportalized hemiliver acts as a temporary auxiliary liver contributing to a great proportion of liver function as demonstrated by scintigraphy, and (3) in the setting of synchronous disease, ALPPS has proven to be a feasible alternative to offer sufficient hepatic mass reserve and allow combined colorectal and major liver resection.⁴

Despite these potential benefits, initial reports prompted awareness concerning high morbidity and mortality rates associated with ALPPS. This fact, together with the increased international interest, led to the 1st International Consensus Meeting on ALPPS in Hamburg, Germany, in February 2015. In this meeting, everything seemed to indicate that ALPPS had arrived to stay as a valuable option for selected patients. In terms of safety, the quality of liver parenchyma and its function are clearly future directions to improve patient selection as well as timing of the second stage, both being important determining factors of outcomes. This approach should be performed with caution for indications other than metastatic liver disease and in patients older than 60 years.⁵ In addition, the second stage should be delayed or even abandoned in case of compromised clinical status or liver function to avoid mortality. It is highly possible that ALPPS outcomes will improve in the near future as a consequence of the learning curve, technical improvements, and better patient selection. In fact, a prospective study has demonstrated that ALPPS can be performed with similar perioperative results compared with classic 2-stage resections in specialized centers, suggesting that partial parenchymal transection might reduce morbidity without affecting hypertrophy.⁴

Regarding oncological outcomes, probably the most important question still unanswered is whether higher tumor resectability is latterly translated into improved survival. While the available evidence does not definitively answer this question, previous studies

have suggested that patients with colorectal liver metastases may have similar short-term oncological outcomes compared with patients treated by traditional approaches.⁴⁻⁶ Because outcomes are directly related to patient selection, if we select for ALPPS those patients with extensive bilateral liver disease (probably not the ideal candidate but the true candidate), poor results should not be surprising. It must be taken into account that we are treating a population of patients with an aggressive tumor biology that has the highest possible risk for recurrence. As Tanabe⁷ stated: "Opponents of ALPPS argue that early progression of malignant disease after PVE is beneficial for selection of patients who were not destined to benefit from liver resection. What cannot be assessed in this stance is how often such disease progression saves a patient from an unnecessary operation vs denies a patient from a life-saving operation."

In summary, because the ALPPS approach can be performed with acceptable patient safety in experienced centers, the benefits mentioned here favor it as a treatment option for patients with failure of PVE/PVL or extensive bilateral disease where an extremely small future liver remnant might result from tumor clean-up, especially if there is tumor close to future liver remnant boundaries. It seems that ALPPS will never replace PVE for patients with a tumor-free future liver remnant, but it might replace classic 2-stage liver resections in certain cases if future evidence demonstrates better or equal long-term outcomes.

ARTICLE INFORMATION

Published Online: August 26, 2015.
doi:10.1001/jamasurg.2015.1643.

Conflict of Interest Disclosures: None reported.

REFERENCES

- de Santibañes E, Clavien PA. Playing Play-Doh to prevent postoperative liver failure: the "ALPPS" approach. *Ann Surg*. 2012;255(3):415-417.
- Schnitzbauer AA, Lang SA, Goessmann H, et al. Right portal vein ligation combined with in situ splitting induces rapid left lateral liver lobe hypertrophy enabling 2-staged extended right hepatic resection in small-for-size settings. *Ann Surg*. 2012;255(3):405-414.
- Schadde E, Malagó M, Hernandez-Alejandro R, et al. Monosegment ALPPS hepatectomy: extending resectability by rapid hypertrophy. *Surgery*. 2015;157(4):676-689.
- Alvarez FA, Ardiles V, de Santibañes M, Pekolj J, de Santibañes E. Associating liver partition and portal vein ligation for staged hepatectomy offers high oncological feasibility with adequate patient safety: a prospective study at a single center. *Ann Surg*. 2015;261(4):723-732.
- Schadde E, Ardiles V, Robles-Campos R, et al; ALPPS Registry Group. Early survival and safety of ALPPS: first report of the International ALPPS Registry. *Ann Surg*. 2014;260(5):829-836.
- Schadde E, Ardiles V, Slankamenac K, et al. ALPPS offers a better chance of complete resection in patients with primarily unresectable liver tumors compared with conventional-staged hepatectomies: results of a multicenter analysis. *World J Surg*. 2014;38(6):1510-1519.
- Tanabe KK. Commentary on "Can we improve the morbidity and mortality associated with the associating liver partition with portal vein ligation for staged hepatectomy (ALPPS) procedure in the management of colorectal liver metastases?" *Surgery*. 2015;157(2):204-206.