

# ALPPS and the endless pursuit of hepatic resectability

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Division of Transplantation and Hepatobiliary Surgery, Department of Surgery, University of Rochester Medical Center, Rochester, NY, USA *Correspondence to:* Roberto Hernandez-Alejandro, MD. Division of Transplantation and Hepatobiliary Surgery, Department of Surgery, University of Rochester Medical Center, 601 Elmwood Avenue, Box SURG, Rochester, NY 14642, USA. Email: Roberto\_Hernandez@urmc.rochester.edu. *Comment on:* Lai Q, Mennini G, Larghi Laureiro Z, *et al.* Uncommon indications for associating liver partition and portal vein ligation for staged hepatectomy: a systematic review. Hepatobiliary Surg Nutr 2021;10:210-5.

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Associated liver partition and portal vein ligation for staged hepatectomy (ALPPS) is an established resection strategy well into its teenage years. After initial controversy, it has proven to be an effective and safe approach for primary unresectable liver remnant anatomy in high volume centers (1-5). ALPPS involves portal vein ligation and parenchymal split to obtain rapid, enhanced hypertrophy of the future liver remnant and resection during second stage of the operation (6). This allows for resection with liver remnants as small as 20% of original volume (7,8). It is the most rapid tool in achieving hypertrophy compared to other modalities (9-11). Nevertheless, ALPPS remains a contentious topic in the HPB literature (12-15). We believe that ALPPS is an excellent option for highly selected patients with expanded indications, especially when conducted by experienced surgical teams (5,16).

The ALPPS Registry, developed in 2014, has been a resource for the liver surgeon in decision making for curative resection (14). This tool, along with improved technique and refinement in patient selection, has yielded positive results in hepatocellular carcinoma, cholangiocarcinoma and colorectal cancer liver metastases (1,4,13,17,18). Recent publications have shown that ALPPS can be safely used for a broader range of indications (5,19). Lai *et al.* have conducted an excellent review on some of the less common indications treated with ALPPS. This group explored the literature and ALPPS registry and published an excellent article on outcomes from ALPPS application in neuroendocrine tumor liver metastasis (NELM), gallbladder

cancer, gastrointestinal stromal tumor, adult primary and secondary malignant, adult benign and pediatric indications.

This group's findings are especially intriguing in use of ALPPS to treat neuroendocrine liver metastasis (20). NELM are divided into three classes—type I: single metastasis, type II: bilobar metastatic bulk, and type III: disseminated metastases. In this study, 40 patients have been reported in the literature as being treated with ALPPS for NELM, all type II (bilobar). These patients had favorable outcomes with 73–95% 1-year survival and 73–83% 1-year disease free survival. Consistent with other ALPPS indications, this review found a major complication rate of 33% in these patients. The authors also provide a brief review of patient selection and outcomes in liver transplantation for NELM (21)—offering the potential for study focusing on the direct comparison of these modalities.

We would caution the reader from applying the information found in this review towards pediatric and benign indications. For the pediatric patients, the *a priori* search criteria included articles among the adult (age >18) human population and may have restricted this studies ability to report on pediatric outcomes of ALPPS. For benign pathology, given the low power (four patients) and limited follow-up information of the study we would also caution the reader from making any significant clinical decisions with these results. Most importantly, we would encourage the application of these results to patients with good functional status and normal liver function tests (22). In the very rare benign pathologic case with no

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other liver resection strategy, we would encourage ALPPS to be performed by high volume centers with extensive experience.

Our group is encouraged by findings provided by this review and the opportunity for ALPPS to be used for a broader set of indications. Our center is experienced with this procedure and our surgeons have had excellent outcomes in our patients (16). In our practice, more than fifty ALPPS cases have been performed with one single mortality at 90 days with acceptable disease free and overall survival rates. We attribute our success to careful patient selection and the accelerated hepatic hypertrophy. We are confident in the procedure's hypertrophic potential with similar recurrence rates in well selected patients as compared to two-stage hepatectomy (19,23). Most importantly, we are comfortable with the safety and efficacy of this procedure and would be interested in expanding the understanding and clinical use in highly selected patients for a broader range of indications. We would encourage patients and referring physicians to seek second and third opinions with experienced centers regarding the resectability of their disease.

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#### References

- Hasselgren K, Røsok BI, Larsen PN, et al. ALPPS Improves Survival Compared With TSH in Patients Affected of CRLM: Survival Analysis From the Randomized Controlled Trial LIGRO. Ann Surg 2021;273:442-8.
- Sandström P, Røsok BI, Sparrelid E, et al. ALPPS
   Improves Resectability Compared With Conventional
   Two-stage Hepatectomy in Patients With Advanced
   Colorectal Liver Metastasis: Results From a Scandinavian
   Multicenter Randomized Controlled Trial (LIGRO Trial).
   Ann Surg 2018;267:833-40.
- Petrowsky H, Linecker M, Raptis DA, et al. First Longterm Oncologic Results of the ALPPS Procedure in a Large Cohort of Patients With Colorectal Liver Metastases. Ann Surg 2020;272:793-800.
- 4. Alvarez FA, Ardiles V, de Santibañes M, et al. 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;261:723-32.
- Wanis KN, Linecker M, Madenci AL, et al. Variation in complications and mortality following ALPPS at earlyadopting centers. HPB (Oxford) 2021;23:46-55.
- 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;255:405-14.
- Pawlik TM, Schulick RD, Choti MA. Expanding criteria for resectability of colorectal liver metastases. Oncologist 2008;13:51-64.
- 8. Guglielmi A, Ruzzenente A, Conci S, et al. How much remnant is enough in liver resection? Dig Surg 2012;29:6-17.
- Croome KP, Hernandez-Alejandro R, Parker M, et al.
   Is the liver kinetic growth rate in ALPPS unprecedented when compared with PVE and living donor liver transplant? A multicentre analysis. HPB (Oxford) 2015;17:477-84.
- 10. Petrowsky H, Fritsch R, Guckenberger M, et al. Modern therapeutic approaches for the treatment of malignant liver

- tumours. Nat Rev Gastroenterol Hepatol 2020;17:755-72.
- 11. Fernandez H, Nadalin S, Testa G. Optimizing future remnant liver prior to major hepatectomies: increasing volume while decreasing morbidity and mortality. Hepatobiliary Surg Nutr 2020;9:215-8.
- 12. Olthof PB, Schnitzbauer AA, Schadde E. The HPB controversy of the decade: 2007-2017 Ten years of ALPPS. Eur J Surg Oncol 2018;44:1624-7.
- Hernandez-Alejandro R, Ruffolo LI, Alikhanov R, et al. Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS) procedure for colorectal liver metastasis. Int J Surg 2020;82S:103-8.
- Schadde E, Ardiles V, Robles-Campos R, et al. Early survival and safety of ALPPS: first report of the International ALPPS Registry. Ann Surg 2014;260:829-36.
- 15. Belghiti J, Dokmak S, Schadde E. ALPPS: Innovation for innovation's sake. Surgery 2016;159:1287-8.
- 16. Wanis KN, Ardiles V, Alvarez FA, et al. Intermediateterm survival and quality of life outcomes in patients with advanced colorectal liver metastases undergoing associating liver partition and portal vein ligation for staged hepatectomy. Surgery 2018;163:691-7.
- 17. Viganò L, Cimino MM, Adam R, et al. Improving the Safety of ALPPS Procedure: The Optimal Compromise Between Dropout and Mortality Risk. Comment on Schadde E et al Prediction of Mortality After ALPPS Stage-1: An Analysis of 320 Patients From the International ALPPS Registry. Ann Surg. 2015;262: 780-786. Ann Surg 2017;266:e101-2.

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- 18. Chan ACY, Chok K, Dai JWC, et al. Impact of split completeness on future liver remnant hypertrophy in associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) in hepatocellular carcinoma: Complete-ALPPS versus partial-ALPPS. Surgery 2017;161:357-64.
- 19. Li J, Moustafa M, Linecker M, et al. ALPPS for Locally Advanced Intrahepatic Cholangiocarcinoma: Did Aggressive Surgery Lead to the Oncological Benefit? An International Multi-center Study. Ann Surg Oncol 2020;27:1372-84.
- Linecker M, Kambakamba P, Raptis DA, et al. ALPPS in neuroendocrine liver metastases not amenable for conventional resection - lessons learned from an interim analysis of the International ALPPS Registry. HPB (Oxford) 2020;22:537-44.
- 21. Muttillo EM, Mazzarella G, Picardi B, et al. Treatment strategies for neuroendocrine liver metastases: a systematic review. HPB (Oxford) 2022. [Epub ahead of print]. doi: 10.1016/j.hpb.2022.06.009.
- 22. Linecker M, Björnsson B, Stavrou GA, et al. Risk Adjustment in ALPPS Is Associated With a Dramatic Decrease in Early Mortality and Morbidity. Ann Surg 2017;266:779-86.
- 23. Bednarsch J, Czigany Z, Sharmeen S, et al. ALPPS versus two-stage hepatectomy for colorectal liver metastases—a comparative retrospective cohort study. World J Surg Oncol 2020;18:140.