

Response to reviewers

Name of journal: *World Journal of Hepatology*

ESPS Manuscript NO: 20552

Editor Comments

Title should be less than 12 words.

The title is now less than 12 words (page 1)

A short running title of less than 6 words should be provided.

A short running title is now provided (page 1)

Please offer the postcode! Thank you!

The postcode has been added (page 1)

Any article describing a study (basic research, clinical research, and case report) involving human and/or animal subjects is required to have the institutional review board (IRB) name, whether institutional (part of the author(s)' academic/medical institution, such as the Oak Grove Children's Hospital Institutional Review Board) or commercial/independent/private (contracted for-profit organizations, such as the ClinicCare Coalition for Human Rights Institutional Review Board), stated explicitly in the title page.

An Institutional review board statement, Informed consent statement and conflict of interest statement have been added to the title page (page 2). An official document with these statements has been attached along with the revised case report.

Please write a summary of no more than 100 words to present the core content of your manuscript, highlighting the most innovative and important findings and/or arguments.

A core tip has been added (page 2)

Please offer the audio core tip

An audio core tip has been uploaded along with the revised case report

Please write the comments.

A comments section with the ten requested bullet points has now been added (page 9)

Reviewer No. 923850

The authors present a case report of a patient with UNILOBAR liver metastasis in which a right hepatectomy was planned and finally an ALPPS was made:

1. In Figure 1, a very small left lobe is observed, so that the authors should have conducted a preoperative CT volumetry. In this case a preoperative right portal vein embolization had to be made.

We agree that pre-operative volumetry should have been performed. This was a point of major criticism at our institution morbidity and mortality review board. A statement acknowledging this has been added to the discussion. (page 8, paragraph 2). ALPPS was used instead of portal vein embolization because the small future liver remnant was noted intra-operatively and not pre-operatively.

2.- Normally, ALPPS is indicated in multiple and bilobar liver metastases. In this case report the liver metastases were unilobar.

You are correct, and that is why the initial plan was to perform a right sided hemi-hepatectomy (page 5, paragraph 1). The reason ALPPS was performed was that the small size of the future liver remnant was noted intra-operatively.

3.- The authors present an unusual complication after performing ALPPS technique. The occlusion of the right hepatic artery was due to the ALPPS technique or a technical error?

The exact reason for the occlusion of the right hepatic artery is not known. What we found interesting is that it has never been described after ALPPS and that the patient recovered from this potentially fatal complication. While a technical error cannot be excluded no sign of occlusion was noted at the end of Stage 1 (page 8, paragraph 2). This can also be visualized in figure 2.

4.- I believe that the occlusion of the right hepatic artery occurred in this case is not attributable to the ALPPS technique. Complications attributable to the ALPPS technique are necrosis of the segment IV, biliary fistula, infected collections, acute liver failure due to incomplete regeneration, etc.

We disagree with this statement. ALPPS is the only technique within hepatic surgery that involves identification, dissection and banding of the right hepatic artery without ligation. More importantly, preservation of the right hepatic artery is of fundamental importance to the procedure as it allows left-sided hypertrophy while maintaining metabolic functions. What is of interest is that despite occlusion of an artery crucial to the procedure, the patient did well with impressive left sided hypertrophy. You are correct that it is not a known complication, but it is

important to bear in mind that ALPPS is a relatively new technique that has not yet been fully explored and explained.

5.- The presence of vascularization of the right lobe via the portal, is also a strange phenomenon that the authors try to explain with the presence of irrigation through the perihilar route. In conclusion, it is a case with many unknowns and I consider that are not attributable to technical ALPPS

You are correct that portal vascularization of the right lobe is a strange phenomenon but nevertheless a significant finding as it is most probably what kept the patient alive. As it has never been described before, we can only hypothesize as to its cause (page 7, paragraph 4). We, the authors, agree that it is a case of “unknowns” that will hopefully stimulate critical discussion of the ALPPS procedure. We regard that as an important motivation for publishing it.

Reviewer No. 2992649

This case report deserves to be published as it reports an interesting situation in the setting of ALPPS procedure and mechanisms of liver hypertrophy. The authors should indicate the cause of artery occlusion if any. Then, in the discussion Authors need to better develop the part about the different mechanisms to induce an increase of the FLR. Portal vein embolization (PVE) PVE with in situ splitting the liver (ALPPS), and also about procedures such as arterial occlusion and the bile duct occlusion not routinely used. Of these latter there are reports in the past and in animal studies.

We thank the author for his comments. Possible mechanisms to the arterial occlusion and the role of PVE have been added to the discussion (page 8, paragraph 2). The reason we did not discuss the molecular mechanism behind the hypertrophy is that it has previously been well described in the literature. Arterial embolization has been reported as a technique for volume manipulation, but found to be less effective than PVE. It is however regarded as experimental.

Reviewer No 03262112

Arterial ischemia in the deportalized liver following ALPPS; a case report and literary review of a rare post-operative complication. ALPPS is an interesting novel two stage surgical procedure for extended liver tumors with more and more applications described into literature: This article describes a case report of application of ALPPS procedure in a patient intraoperatively judged as not eligible to a right hepatectomy due to unexpected little remnant volume: the attention is focalized on a specific particular postoperative complication, never described previously into literature. The abstract provides a clear delineation into introduction, case presentation, and conclusions, lacking of a section about discussions. Ethics and related aspects of the research are outlined and respected. Introduction is very clear with a summary of ALPPS technique and indications according to literature. Case report is completely exhaustive, well and rationally structured: the planned strategy and technical aspects are aligned with literature. The indications to perform the ALPPS procedure are well explained The surgical technique is the standard one and is properly described and well defined.

The description of any surgical complication, especially during a relatively new surgical performance, is very useful in clinical practice. The most frequent complication described into literature is biliary fistula, surprisingly not found into our case report despite the reported arterial ischaemia. It's very interesting to remark that the patient, despite right liver iscahemia and liver failure, was asymptomatic and that no complication occurred between the first and the second procedure. It has been described into literature patency of venous system but in presence of a correct hepatic arterial flow with possible collateral flows between arterial and venous system that passes through biliary ducts. It's very remarkable and innovative to find at postoperative CT scan venous portal flow in deportalized liver segments, even if right portal branch was transected and right hepatic artery was occluded. This can explain the progressive improvement of serum liver values with the progressive repatency of the venous system. Preoperative and postoperative blood pattern of patient is well synthesized into table 1. Figures are interesting, correctly placed and well organized; very well performed the intraoperative picture. The discussion is well organized with a great effort in reviewing the current literature about the argument. The references are appropriate, relevant and up-to-date. Great best regards and thank You all for the confidence.

We thank the reviewer for his encouraging comments!