

Format for ANSWERING REVIEWERS

March 21, 2017

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 33064-review.doc).

Title: Abdominal cross-sectional imaging of the ALPPS procedure**Authors:** Michele Zerial, Dario Lorenzin, Chiara Zuiani, Andrea Risaliti, Rossano Girometti**Name of Journal:** *World Journal of Hepatology***ESPS Manuscript NO:** 33064

We thank the reviewers 02861186 and 02937578 for their thoughtful and positive comments. The revised manuscript incorporated suggestions of the editor and reviewers, as follows:

- 1 Text format has been updated according to each of the editor's specifications. In particular, we shortened the title as requested (change has been colored in red).
2. We revised English language (please, see the response to reviewer 02937578).
3. We believe we can respond substantively to each of the reviewers' observations and criticism as detailed below. Changes in the text have been highlighted in red.

(a) Reviewer 02861186

(i) *I do miss the typical characteristics of a review: There is no description of the search strategy for the finally selected and evaluated articles. Furthermore, even a "flow-chart diagram" would have been of dramatic benefit for understanding the source of all the information and references. Alternatively: If this review was designed as a "single-center report" it should be described and entitled as it in order to exclude similar expectations and/or confusion. But I could not find a comparable declaration in the supplement or even in the manuscript. If I have misunderstanding a declaration, I want to strongly apologize for mistaking or "having read over" it.*

In our opinion, there was a misunderstanding about the nature of this paper, which has not been submitted/presented as an original research under the form of a "systematic review" or "metanalysis" focused on quantifying the role of radiology in ALPPS (e.g., in terms of pooled sensitivity/specificity). Consequently, the paper does not incorporate the methodology of data collection/analysis required for systemic reviews or metanalyses (data extraction, selection, assessment of homogeneity, QUADAS criteria for inclusion, pooled analysis and son on...). Given the paucity of literature on the specific topic of ALPPS radiology, a systematic review would represent an immature step to be performed.

As properly emphasized by the columns assignment at the beginning of the revised manuscript, this

paper presents like a “minireview”, that is as an invited expert opinion/comment/description of a procedure (e.g., Girometti R et al., World J Gastroenterol 2014;20:6180-6200, or Girometti R et al., World J Radiol 2014;6:424-436). Consequently, we believe that a declaration on the article nature would sound redundant compared to the columns assignment performed by the editorial team. Though an “ordinary” review has not the same level of evidence of a systematic review, we believe our paper is might be of interest in showing to clinicians and radiologists which typical normal and abnormal findings may be expected when ALPPS is performed, and which role imaging can play in this setting.

(ii) *In an internet based search about this special topic “Imaging and ALPPS” I found a similar publication of the above mentioned group of authors. The link promises a poster-presentation held on the European Congress on Radiology in 2016. But in the provided link you will find a well-written manuscript containing similar text and figures like in this manuscript. Imaging of ALPPS procedure: what the Radiologist should know Poster No.: C-0818 Congress: ECR 2016 Type: Educational Exhibit Authors: M. Zerial, D. lorenzin, A. risaliti, M. Bazzocchi, C. Zuiani, R. Girometti; Udine/IT Keywords: Liver, CT, MR, Surgery, Neoplasia DOI: 10.1594/ecr2016/C-0818 Website:http://www.google.de/url?sa=t&rct=j&q=&esrc=s&source=web&cd=4&ved=0ahUKEwi6r_iArI3SAhWCZCwKHTSnAH0QFggxMAM&url=http%3A%2F%2Fposter.ng.netkey.at%2Fesr%2Fviewing%2Findex.php%3Fmodule%3Dviewing_posteraction%26task%3Ddownloadpdf%26pi%3D132769&usq=AFQjCNFjTt_Q0MXc1QZojKAgnHCrG7o8A Maybe I did “read over” a declaration of the authors that a part of the data were demonstrated on the mentioned Congress of Radiology - Then I am really sorry about my mistake and I want to strongly apologize to the authors! However, I would prefer to read a short declaration of the authors about this issue.*

We added the following sentence in the “Conflict-of-interest statement” at the beginning of the review: “This paper has been presented as an electronic poster at the European Congress of Radiology (ECR) 2016 and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) annual meeting 2016.”.

As usual in the radiological community, we tried to disseminate our work in international congresses before publishing it. We presented this paper as an electronic poster to the European Congress of Radiology 2016 and European Society of Gastrointestinal and Abdominal Radiology 2016. A comparison between the poster .pdf and the submitted review will show that the text has been deeply revised, rewritten and re-organized, as well as enriched by additional clinical and radiological content. This reflected on tables and figures organization/presentation too. In summary, this is not a duplicated paper, since it has never been published on other journals and is substantially different from the previous poster.

(iii) *I would consider shortening the chapter introduction and the description of ALPPS, since both contain redundant information.*

We believe that the reviewer’s opinion reflects an “expert point of view” which might conflict with the need of a generic reader (clinician, surgeon or radiologist) to understand what ALPPS is and how it is imaged. E.g., some apparently secondary surgical details might have great impact on the radiological interpretation (e.g., drainage sites).

In this light, we tried to balance the reviewer’s valuable suggestion and potentially relevant information by: i) making no changes to the Introduction (though a bit long, it explains how ALPPS developed); ii) eliminating some unnecessary sentences in the “Indications and technique” paragraph

as highlighted in the revised text.

(iv) *As the title of the manuscript promises a focused view on imaging, I would prefer to read more detailed information about typical, normal and pathological findings in the perioperative time-course after ALPPS. In addition I would like to see corresponding figures illustrating the described findings (see below for the details). - So please, enlarge the chapter about imaging and findings and their correlation to clinical indications as some of the authors belong to the surgical department of the university hospital of Udine. Maybe a table would provide substantial benefit.*

We added a table (Tab. 3 in the revised manuscript) to emphasize expected radiological findings after ALPPS.

On the other hand, we do not completely agree with the reviewer's observation. We acknowledge that typical findings may appear limited in our description. However, many postoperative findings occurring after ALPPS are comparable to well-known ones occurring after other types of liver surgery, being irrelevant from the radiological (and often clinical) point of view. We believe that a detailed description of those findings would be redundant, since our attempt was to focus on what is really radiologically typical after ALPPS and "unexpected" compared to other postoperative conditions (this is especially true for the post-stage 1 imaging) based on personal experience and literature review. Furthermore, there is paucity of prospective radiological studies on ALPPS, suggesting that "the list" of typical post-ALPPS findings is still to be refined. We believe that our work might be an initial contribution to this still uncertain panorama.

(v) *Please check for correct abbreviation for volume of transfusion (I found "min").*

The entire sentence containing this issue was eliminated (see reply to point (iii)).

(vi) *What do you mean with "panoramacity"?*

"Panoramacity" is a technical radiological term indicating the capability of an imaging modality/technique to represent large body volumes within a single image or examination (e.g., a volume-rendering reconstruction of the abdominal aorta or a CT-angiography examination). From this point of view, ultrasonography lacks panoramacity compared to CT or MRI.

We understand this term can sound ambiguous/confusing, so we modified the text in which this word appears first as follows: *"Furthermore, US lacks panoramacity, i.e. the capability to represent a section or a 3D reconstruction of the entire liver within a single image. Consequently, though this technique is useful in initial diagnosis of liver abnormalities, it has no direct role in selecting patients for ALPPS (e.g., by assessing the number of lesions in the FLR or estimating its volume)."*

(vii) *Do you really do a 3D-T1 weighted MRCP with delayed phases to detect biliary leakage? Or do you do it in rare cases of persistent fluid collections in the follow-up after completed ALPPS?*

As an institutional policy, we perform gadoxetic-acid based MRCP whenever a postoperative biliary complication is clinically suspected (regardless of the type of surgical procedure). We found excellent

results in our clinical experience, in accordance with previous literature (e.g., Kantarci M et al., Eur Radiol 2013;23:2713-2722). Of course, small fluid postoperative collections or bile collections within the endobag are not *per se* an indication to gadoxetic-acid based MRCP, so we clarified our procedure at the end of the "Imaging techniques" paragraph as suggested by the reviewer: *"In particular, 3D T1-weighted MRCP acquired in the delayed phase after gadoxetic acid administration is useful in confirming clinical suspicion of biliary leakage (e.g., persisting postoperative fluid collections associated with clinical sign of biliary sepsis) by showing active contrast extravasation^[44]. The presence of endobag after surgical stage 1 can avoid gadoxetic acid-based MRCP, since bile leakage can be actively monitored through the internal surgical drainage."*

(2) Reviewer 02937578

(i) This reviews give many new updated information of the use of ALPPS in surgery. But there are still many mistakes in word spelling.

We thank the reviewer for the positive comment. We corrected grammatical/spelling errors in the text, and made language polishing with the help of an English mother language colleague having the residency in our Institute of Radiology. She was now included in the acknowledgments. All changes incorporated in the re-submitted manuscript are colored in red. Of note, changes are limited to grammar, with no substantial modification of the content compared to the original version of the manuscript. We believe that English language is now suitable for publication.

Thank you again for considering our manuscript for the publication on the *World Journal of Hepatology*.

Sincerely yours,

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