

Response to Reviewer Comments

Reviewer #1

Samuel Han and Coworkers evaluate in their retrospective study the value of ERCP and liver biopsy in the assessment of increase in liver enzymes after liver transplantation. Among 1284 patients who underwent liver transplantation, 96 patients with increased liver enzymes were further analyzed. Overall, the manuscript is written well and the topic of interest, and could be recommended for publication after addressing of several issues as outlined below. Especially the role of MRCP versus ERCP should be further back-up by data.

We thank the reviewer for these comments and we hope this revision sufficiently addresses their concerns.

Was MRCP conducted in all patients prior ERCP? MRCP as a noninvasive approach should also be discussed in more detail in the discussion section, e.g. p. 12 "... are poorly specific for any single diagnosis..." and p. 12, line 9 "ERCP is not only more accurate than MRCP..." this seems to be questionable for MRCP compared to ERCP. Please provide more data, as ERCP nowadays is predominantly selectively conducted when an intervention is planned. Conclusions made by the authors on the recommendation to conduct ercp seems to be to strong and should be balanced with the recommendations for MRCP (p. 14, line 6 "...Transplant physicians should have a lower threshold to perform both LB and ERCP when evaluating abnormal LFTs...")

The reviewer raises a valid issue regarding the use of imaging, particularly MRCP for evaluation of anastomotic strictures prior to ERCP. MRCP was not conducted in all patients prior to MRCP. We have now described in the Results section the breakdown of imaging modalities prior to ERCP. MRCP was utilize in a minority of cases (6.6%) with ultrasound being the commonly used modality, which is now described in the Discussion section as well. We have also rephrased our Discussion to tone down our recommendations.

Did ERCP reveal secondary sclerosing cholangitis in one or more of the patients?

ERCP did not reveal secondary sclerosing cholangitis in any of these patients.

How many patients received immunosuppression with two drugs (or even three), and which combinations were used? Please provide data. Concerning the diagnosis of ACR, where the levels of immunosuppressants measured? Were they adequate?

We have now provided the proportions of immunosuppression combination regimens in the Results section and in Table 1. It is our practice to measure immunosuppressant levels and our subgroup of patients represent a cohort of patients where levels were adequate.

Please provide data. p. 5, line 6 other guidelines available worldwide include the guidelines by the European association for the study of the liver (EASL) should also be included and discussed, as the audience of the journal is worldwide.

We thank the reviewer for this recommendation. We have now also included the EASL guidelines.

Further data on the exclusion (type and quantity of complication) is required: p. 6, line 5: “patients with medication” please explain, this refers to medication-associated liver injury? Please provide data on the specific medication.

Patients with a clearly identifiable cause of elevated liver chemistries - such as drug or medication-related hepatitis, vascular liver disease or infectious hepatitis – and without additional diagnosis/es based on the initial history, labs, or imaging studies were excluded from our analysis. Since these patients were outside of the Hepatology database query, we do not know how many patients there were with these individual complications.

Please also state how many patients suffered from vascular or post-operative complications, and which type those were. How were these complications assessed and excluded?

Patients with a clearly identifiable cause of elevated liver chemistries - such as drug or medication-related hepatitis, vascular liver disease or infectious hepatitis – and without additional diagnosis/es based on the initial history, labs, or imaging studies were excluded from our analysis. Since these patients were outside of the Hepatology database query, we do not know how many patients there were with these individual complications.

Were other complications depicted in Figure 4 present in these patients? Please provide data. A combination of these complications to AS and ACR might occur also, and are not included in this analysis. Please provide more data. p. 11, line 4: rate of complications seems to be very low.

We reported the adverse events of ERCP and liver biopsy in the Adverse Events section. Regarding the other causes of elevated liver function tests, we have now displayed these in the updated Table 2.

Consider to add AUROC curves for both liver biopsy and ERCP.

We thank the reviewer for this comment. Unfortunately, due to the lack of false positives in our data, an AUROC cannot be calculated.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: ERCP is an invasive procedure. Most of liver function abnormality could be diagnosed by liver biopsy. CT or MRCP can diagnose most of anastomotic stricture. ERCP is an useful method as a treatment modality for anastomotic stricture, but it might be over-invasive for a diagnostic modality alone. Authors should show the results of CT or MRI before ERCP.

We have now displayed in the

We agree with the reviewer that the imaging findings are important to report and are part of the standard work-up of abnormal LFTs. We have now displayed the results of pre-test imaging in the Results section.

(1) *Science editor*: 1 Scientific quality: The manuscript describes an observational study of the ERCP vs LB for after LT. The topic is within the scope of the WJH. (1) Classification: Grade C and Grade D; (2) Summary of the Peer-Review Report: The authors evaluate in their retrospective study the value of ERCP and liver biopsy in the assessment of increase in liver enzymes after liver transplantation. Overall, the manuscript is written well and the topic of interest. However, there are some issues should be addressed. CT or MRCP can diagnose most of anastomotic stricture. ERCP is an useful method as a treatment modality for anastomotic stricture, but it might be over-invasive for a diagnostic modality alone. Authors should show the results of CT or MRI before ERCP. The questions raised by the reviewers should be answered; and (3) Format: There are 3 tables and 4 figures. A total of 22 references are cited, including 4 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade B and Grade B. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, and the Institutional Review Board Approval Form. Written informed consent was waived. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and fill out the STROBE checklist with page numbers. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by National Institute of Health.

The topic has not previously been published in the WJH. The corresponding author has not published articles in the BPG.

5 Issues raised:

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