

World Journal of Gastroenterology

Manuscript WJG-50289

Retrospective Cohort Study

Manuscript WJG-50289: **“Segmental Intrahepatic Cholestasis as a Technical Complication of the Transjugular Intrahepatic Porto-Systemic Shunt”**

Dear Prof. Gong,

We thank you and the reviewer for your valuable comments and objective critiques. Furthermore, we are glad to have the opportunity to resubmit our manuscript as revised version to your Journal. All comments have been very useful to us in making the necessary changes needed to improve the manuscript. We hope we have satisfactorily addressed them in the following paragraphs and adapted the manuscript according to the journals guidelines. In addition, all of the extensive comments by the editorial office were incorporated to the revised version. Hopefully, you will find the revised version of the manuscript suitable for publication.

Sincerely,

Marcus Hollenbach

REVIEWER 1:

This retrospective study is interesting and worth reading. However, several issues need to be addressed. The etiology for the development of SIC-T is not convincing. Whether the “atypical” TIPS-placement is the key factor need more evidence.

We thank the reviewer for this advice. We agree that the etiology for SIC-T remains not elucidated yet. Nevertheless, we provided several possible explanations in our discussion section. First, SIC-T was a late complication in most cases and mechanical compression alone or in combination with ischemia might be the best explanation for development of SIC-T. Furthermore, we added more data of logistic regression analysis and found only an TIPS placement other than MHV to RPV as predictor for SIC-T. We highlighted this issue in the discussion.

P3 Actually, establishment of TIPS from the medial hepatic vein or left hepatic vein is considered atypical. In most countries, right hepatic vein is the most preferred approach.

We fully agree with the reviewer that TIPS placement from the right hepatic vein to the right portal vein is considered as typical TIPS placement. Nevertheless, an equivalent approach is placement from the medial hepatic to right portal vein (Rossle M et al NEJM 1994, Rossle M et al Best Prac Res Clin Gastroenterol 2004). As demonstrated by our data, we used the MHV to RPV route. We highlighted this issue in both methods and results section.

P7 Why other pre-TIPS parameter was not included in the logistic regression analysis? For instance, the underlying liver disease PBC and PSC? Biliary injury during TIPS?

We thank the reviewer for this advice and included a new Table 3 to the manuscript. Here we tested different variables for prediction of SIC-T but only a TIPS placement other than

MHV-RPV reached statistical significance. We thoroughly revised the manuscript in this regard. Unfortunately, we were not able to analyze a biliary injury during TIPS as such occurrence was not assessed.

P12 Major TIPS complication rate is exaggerated even it was supported by one study.

We agree the reviewer and revised the corresponding section of the manuscript. Please refer to the introduction section.

REVIEWER 2:

Bucher et al. conducted a systematic, retrospective analysis to provide evidence regarding prevalence and consequences of this TIPS-induced bile duct compression. The manuscript is well written. Thank you for giving opportunity to review this study.

We thank the reviewer for the positive critiques and are glad to have the reviewer convinced with our work.

REVIEWER 3:

To the authors: This is a well written and relevant study for the field, congratulations. I have only some minor comments to improve the readability of your manuscript: Minor comments:

- This sentence is found in the introduction section: "In 2013 we reported a case of a segmental intrahepatic cholestasis caused by intrahepatic bile duct compression as a consequence of the TIPS-stent (SIC-T) [17]. In order to identify prevalence and consequences of SIC-T in a large cohort, we evaluated all consecutive patients who underwent TIPS*

implantation or TIPS-revision at our institution since 2005.” o The sentence should be in the methods section. And only the aim should remain in the introduction.

We thank the reviewer for the positive evaluation of our work. We shifted the indicated sentence to the methods section and revised the manuscript accordingly.

- *This sentence from the results section refers to the selection criteria: “We identified 135 Patients (107 male, 28 female) that met the selection criteria.” o Please add this selection criterion to the methods section.*

The manuscript was revised as suggested.

- *Table 1 and Table 2 have subtitles starting with lowercase such as „indications for TIPS“, it should read „Indications for TIPS“, please check.*

We thank the reviewer for this advice and corrected the Table subtitles.

- *A logistic regression analysis is found, did you add and controlled for other variables or only included the variable „TIPS-placement other than from the medial hepatic vein to the right portal branch“? o I suggest creating a table with the data written in the results, including OR and confidence intervals, and adding information of the complete model, it'll be more easy to read, and it is an important finding.*

We are very thankful for this comment. Please find the univariate logistic regression analysis in new Table 3. We also tested the variables age, gender, etiology of cirrhosis and variceal bleeding indication for TIPS to be predictors for SIC-T. Nevertheless, only atypical TIPS-placement reached statistical significance. In addition, no predictors could be identified in multivariate analysis. We thoroughly revised the manuscript in this regard.