

Ze-Mao Gong
Scientific Editor of
World Journal of Gastroenterology



T +49 3641 – 93 22 302
F +49 3641 – 93 24 233
tony.bruns@med.uni-jena.de

**Dpt. of Internal
Medicine IV**
Hepatology
Dr. Tony Bruns

Dear Dr Gong,

Revision of manuscript no. 21220

16. October 2015

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Dual-Sugar Tests Of Small Intestinal Permeability Are Poor Predictors Of Bacterial Infections And Mortality Cirrhosis: A Prospective Study



Many thanks for providing us the opportunity to submit a revised version of our manuscript for consideration by the *World Journal of Gastroenterology*. We are very grateful for the constructive comments regarding our article and also for providing us with an opportunity to address the issues raised.

The two requested changes in our revised manuscript include:

- Change of the title as requested
- Clarifying skin and soft tissue infections in cirrhosis as including wound infections
- Language editing by an additional native speaker

Attached is a point-by-point response to the individual comments made by the reviewers, as well as a tracked (underlined) revision incorporating the reviewers' recommendations.

In addition, we have provided the following documents:

- Institutional review board statement
- Copyright statement signed by all authors
- Biostatistics statement (André Scherag, Full Professor of Clinical Epidemiology at the Jena University Hospital, Jena, Germany)
- Language certificate from a native speaker (Palak Trivedi, Academic Clinical Lecturer and SPR in Hepatology and Gastroenterology, University of Birmingham, UK)
- Audio core tip (.mp3)

Yours on behalf of the authors

Doctor Tony Bruns, MD
Research Fellow and Specialist in Internal Medicine

**Center for Sepsis
Control and Care**
Erlanger Allee 101
07747 Jena | Germany
T +49 3641 – 9 32 33 74
F +49 3641 – 9 32 33 82
cscs@med.uni-jena.de

Point-by-point responses

Reviewer 39368:

This is well performed and interesting prospective clinical study for analyzing of impact of increased intestinal permeability on mortality and the occurrence of infection in patients with liver cirrhosis. The study was performed in 46 consecutive hospitalized patients with liver cirrhosis and in 16 healthy volunteers. The intestinal permeability was assessed using the lactulose/mannitol test. The authors used ELISA test for assessment of intestinal fatty acid-binding protein (I-FABP), lipopolysaccharide-binding protein (LBP) and IL-6 in serum as markers of inflammation. The authors found that increased small-bowel intestinal permeability, quantified using the lactulose/mannitol test is pronounced in advanced liver cirrhosis and correlates with some parameters of inflammation and Child-Pugh stage. In spite of some limitations of the study described by the authors, this clinical investigation gives an additional knowledge to understand the role of intestinal permeability in prognosis and complications of liver cirrhosis. The study is set up correctly. The paper is written well. Introduction gives a good overview of the study background and the authors raised clearly the aim of the study. The aim of the study is fulfilled. The material studied is large enough and allows to draw the conclusions. The Tables and Figure of high quality give a good overview about the results.

However, the following point needs to be considered: In Results, in paragraph "Development of infections" line 16 it is not clear what does authors means under the skin and soft tissue infection?

Response to reviewer 39368:

We would like to thank the reviewer for his evaluation of our manuscript and for his valuable comment.

Because of an increased prevalence of skin and soft tissue infections (SSTI) in cirrhosis because of edematous skin, poor hygiene standards, malnutrition, frequent hospitalization and frequent invasive procedures and because of the increased mortality associated with skin infections (Rongey C et al. *Open Gastroenterol J.* 2008;2:24–27. Liu BM et al. *J Clin Gastroenterol.* 2008;42:312–316. Pereira et al. *J Hepatol* 2012;56:1040-6.), we pre-specified SSTI as an endpoint for „bacterial infection“ in the study.

In our study, one patient had sternal wound infection after cardiac surgery, and the second patient had an infected leg ulcer (both by *Staphylococcus* species). To address the reviewers concern, we have now added the information in the revised manuscript:

"Less frequently observed infections were purulent skin and soft tissue infections including wound infections (n=2), pneumonia (n=1), campylobacter enteritis (n=1), spontaneous bacterial empyema (n=1), monomicrobial bacterascites (n=1) and severe sepsis with unknown focus (n=1)."

Reviewer 2449040

The authors present a prospective study on an important subject. The results are described and discussed in a clear way. However, since only negative results are presented the title of the study should be changed accordingly.

Response to reviewer 2449040:

We thank the reviewer for his valuable suggestion to indicate the main result of the study within the title.

Therefore, we have changed the title to: **"Dual-Sugar Tests Of Small Intestinal Permeability Are Poor Predictors Of Bacterial Infections And Mortality Cirrhosis: A Prospective Study"**