September 02, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Revised Manuscript NO. 12436).

Title: Paclitaxel-eluting balloon dilation of biliary anastomotic stricture after liver transplantation

Authors: Anna Hüsing, Holger Reinecke, Vito R. Cicinnati, Susanne Beckebaum, Christian Wilms, Hartmut H. Schmidt, Iyad Kabar.

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 12436

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revisions have been made according to the suggestions of reviewer 02723208.

(1) I suggest to specify more clearly whether the included patients were consecutive. In how many patients the intra-hepatic bile ducts appeared dilated on non-invasive imaging?

Answer: Thirteen consecutive eligible patients were included in the study. Four of the 13 patients (30.8%) had dilated intra-hepatic bile ducts on non-invasive imaging examinations.

Changes to the text: Thirteen consecutive eligible patients were enrolled between January 2011 and September 2011, and follow-up was performed until March 2014.
Four of the 13 patients (30.8%) had dilated bile ducts on non-invasive imaging examinations.

(2) More details about the balloon would be welcome, also in this paper focused on follow up data: in particular about the type of polymer the balloon was made of and about the concentration of Paclitaxel (%; or microg/mm2). Was the balloon purposely designed to be used in bile ducts? Is this balloon commercially available by the manufacturer?

Answer: The paclitaxel-eluting balloons were purchased from Eurocor, Germany. The balloons were designed for use during coronary interventions, and were not specially manufactured for use in the bile duct. Technical information about the balloons has been added to the text.

Changes to the text: If AS was diagnosed, endoscopic treatment was performed, comprising sphincterotomy followed by dilation with a PEB (DIOR paclitaxel coated coronary balloon dilatation catheter, paclitaxel 3 μg/mm^2; Eurocor, Bonn, Germany). The PEB was coated with a 1:1 mixture of paclitaxel and shellac that prevented release of paclitaxel in the working channel of the endoscope. Contact of the hydrophilic shellac mixture with a body fluid such as bile opens the structure to allow pressure-induced release of paclitaxel on the inflated balloon.

(3) Long term clinical success was achieved in 12/13 patients. In two of them at least a recurrence after sustained clinical success was observed and it was treated by further dilation sessions. Please specify how many additional endoscopic sessions were required in these patients.

Changes to the text: In each of these two patients, one additional dilation was needed to achieve LTCS.

(4) Patients included in these series underwent an intensive endoscopic follow-up. Do the Author think that a less intensive follow-up schedule could be appropriate in clinical practice?

Answer: Based on our experience, 8-weekly endoscopic re-evaluations of the stricture is reasonable. If there is sustained resolution of the stricture for 6 months, regular endoscopic follow-up can be discontinued and the patient can be observed clinically. If there is laboratory evidence of cholestasis or jaundice, ERCP should be repeated. Additional studies to investigate optimal follow-up are warranted.

(5) Paclitaxel-coated stents were proposed for use in GI and biliary stenosis: the results were not always promising. I guess that the comparison between the two techniques is not pertinent, in particular because available experience with paclitaxel-coated biliary stent was nearly completely limited to malignant stenosis. I wonder whether the Authors believe that the experience with paclitaxel coated stent should be quoted in the discussion section (perhaps the reference to these experiences is not needed).

Answer: As noted, paclitaxel-coated biliary stents have previously been used only to treat malignant biliary strictures caused by cholangiocellular carcinoma or pancreatic carcinoma. There are currently no paclitaxel-eluting stents available that are specifically designed for the treatment of benign strictures. Such stents should ideally be removable, and should release a defined amount of paclitaxel over time.

Reviewer 02438888 made no suggestions for revision.

3 References and typesetting were corrected. The entire manuscript was reviewed by a native English-speaking editor.

Thank you again for considering our manuscript for publication in the *World Journal of Gastroenterology*.

Sincerely yours,

Iyad Kabar, MD
Department of Transplant Medicine
University Hospital Münster
Albert-Schweitzer-Campus 1, Gebäude A14
Münster 48149, Germany
Email: iyad.kabar@ukmuenster.de
Tel: +49-251-8344957
Fax: +49-251-8357771