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To: dr. Jin-Lei Wang Company Editor-in-Chief, World Journal of Gastrointestinal Endoscopy

Date: 06-06-2023

Re: manuscript reference NO: 84972

Dear Dr. Jin-Lei Wang,

Thank you for reviewing our manuscript entitled "*Graft dilatation and Barrett's esophagus in adults after gastric pull-up and jejunal interposition for long-gap esophageal atresia*".

We have carefully studied the comments of the reviewers and revisions have been made according to their suggestions. Enclosed you will find our response to the reviewers' comments. Changes in the manuscript were made with Track Changes.

We sincerely hope our revised manuscript will be suitable for publication in the *World Journal of Gastrointestinal Endoscopy*.

With highest regards,

E. Sofie van Tuyll van Serooskerken, MD  
Gabriele Gallo, MD, PhD  
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J. Westerhof, MD, PhD

L.A.A. Brosens, MD, PhD

S. Zwaveling, MD, PhD

J. Ruitkamp, MD, PhD

J.W. Verweij, MD

J.B.F. Hulscher, MD, PhD

H. G.M. Arets, MD, PhD

A.J.N. Bittermann, MD, PhD

D.C. van der Zee, MD, PhD

S.H.A.J. Tytgat, MD, PhD

M.Y.A. Lindeboom, MD, PhD

**Reviewer #1:**

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors:

I think this study provides clearer insight in terms of long-term physiologic changes after particular type of esophageal reconstruction in EA patients. I have a couple of questions for the authors and it would be beneficial to the readers if the answers or parts of them can be added into the discussion part.

Thank you very much for reviewing our manuscript and for your suggestions. We have carefully studied your suggestions and made changes to the Discussion section accordingly.

Would the type of EA be a factor affecting choice of the reconstruction procedure in your opinion?

The reviewer is correct that the type of EA affects the choice of the reconstruction procedure.

The most common type of EA is Gross type C and a direct anastomosis of the esophageal pouches can be performed. Primary esophageal atresia repair is often not feasible in patients with long-gap esophageal atresia, due to the wide gap between the proximal and distal esophageal pouch.

In LGEA, preservation of the native esophagus is the treatment of choice (elongation techniques), as outlined in the Introduction section, lines 116-120. However, these elongation techniques are technically challenging and should therefore only be performed in experienced centers.

Gastric pull-up requires only one anastomosis and is therefore relatively easy to perform. To date GPU is the most used technique for LGEA worldwide. In our opinion, preservation of the native esophagus is the preferred treatment in LGEA, however, if experience is lacking a GPU procedure can be performed.

We have adjusted the Discussion section, lines 392-396: “Furthermore, treatment for LGEA is being corrected by using the thoracoscopic traction technique in our center. In our opinion, this is now the treatment of choice for LGEA, but only in experienced centers. Alternatively, if experience in this challenging procedure is not available, a GPU can be performed.”

In patients who underwent JI reconstruction, the majority of them developed symptoms of dysphagia and jejunal graft dilatation during the long term follow up. In your opinion, what would be the underlying causes of dysphagia and the graft dilation? Could it be from the dysmotility of the distal esophageal segment?

We agree with the reviewer that this could be more extensively outlined in the Discussion section. In our opinion, the graft dilatation is caused due to the slower motility of the jejunal graft compared to the faster esophageal motility. Stasis of food due to dysmotility of the jejunal graft and the distal esophageal remnant may result in dilatation of the graft and may cause dysphagia symptoms in these patients. Lengthening of the jejunal interposition graft may also contribute to dysmotility and therefore dysphagia due to the siphon shape.

We have clarified this in the Discussion section, lines 356-361.

Do you routinely perform pyloroplasty (or pyloromyotomy) after GPU reconstruction? We routinely performed pyloromyotomy during the GPU procedure. We have clarified this matter in the manuscript, Methods section, line 155.

In your opinion, which type of operation would you prefer or recommend in EA patients?

For Gross type C EA we would recommend a primary anastomosis. For long-gap esophageal atresia we would recommend a lengthening procedure, such as the thoracoscopic traction technique, to preserve the native esophagus. We have outlined this in the Discussion section: “Furthermore, treatment for LGEA is being corrected by using the thoracoscopic traction technique in our center. In our opinion, this is now

the treatment of choice for LGEA, but only in experienced centers. Alternatively, if experience in this challenging procedure is not available, a GPU can be performed.” Discussion section, line 392-396.

**Reviewer #2:**

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors:

This study is a combined prospective and retrospective long-term follow-up study on patients previously reconstructed for long gap esophageal atresia with either a gastric pull-up (9 patients) or a jejunal replacement procedure (11 patients). The number of eligible patients were 24 and there is a good description of the exclusion criteria. The patients had undergone investigations with gastroscopy and peroral contrast studies. The main finding was that gastroesophageal reflux disease was more common in gastric pull up patients, whereas dysphagia was more common in patients with jejunal replacement procedure. Due to the small number of patients a statistical analysis is unreliable.

Thank you very much for reviewing our manuscript and for your suggestions. We have carefully studied your suggestions and made changes accordingly.

It is difficult to read where the information on gastric reflux and dysphagia originates from. Was it from standardized questionnaires or just information, that appeared in the patient's records.

The information on gastric reflux and dysphagia was derived from the routine outpatient follow-up at the Gastroenterology department, as outlined in the Methods section, Clinical assessment, Gastro-intestinal symptoms line 174-175 and in the Discussion section line 326-327: 'In our study, reflux symptoms were assessed at the outpatient clinic by a gastroenterologist.'

In the group with jejunal replacement a dilatation was found in half of the patients and in most of these a graft lengthening is reported. How were these two parameters defined?

Upper gastrointestinal barium contrast studies were analyzed by an experienced radiologist and pediatric surgeon for the following parameters: anastomotic stenosis, stasis of contrast, reflux, graft-dilatation and graft-lengthening (resulting in a siphon shaped graft) of the jejunal interposition. This is outlined in the methods section, contrast study, line 177-181.

This concern is also outlined in the Discussion section, line 400-403: "Furthermore, review of contrast studies is not standardized and therefore subjective. However, all contrast studies were analyzed by an experienced radiologist and pediatric surgeon to minimize bias."

Did the results from the various investigation result in any changes in ongoing treatment or introduction of new treatment modalities and with which result?

The reviewer is correct stating this issue. The results from our study did not result in any changes in the primary treatment, since all patients with LGEA are nowadays treated with the thoracoscopic traction technique in our center. No changes were made in the ongoing treatment. However, we advised the gastroenterologists to observe potential complaints in patients with severely changes in anatomy after surgery.

It is postulated that regular follow-up in these patients is important, but the authors must explain why and how to follow the patients based on their results.

Due to the small patient group, it is not possible to draw firm conclusions for a standardized long-term follow-up. We have made changes to the Conclusion section, in which we clarified that follow-up should entail endoscopic surveillance during adulthood, line 409-410: "Therefore, increased awareness and endoscopic follow-up during adulthood is suggested for LGEA patients after ER."

Because of macroscopic and microscopic abnormalities during follow-up, and especially the increased risk on intestinal metaplasia in GPU patients, we think follow-up of these patients is important.