Author's response to reviews

Title: A comparison of the temporary placement of 3 different self-expanding stents for the treatment of refractory benign esophageal strictures: A prospective multicentre study

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Version: 2 Date: 19 May 2012

Author's response to reviews: see over
19 May 2012

To the Editorial Board
BMC Gastroenterology

Manuscript ID 5558858366888979: A comparison of the temporary placement of 3 different self-expanding stents for the treatment of refractory benign esophageal strictures: A prospective multicentre study

Thank you for allowing us to submit a revision of our manuscript.

The reviews were very helpful in improving the quality of our paper and we thank the reviewers, Dr Young S Oh, and Dr Stuart Gordon for the constructive comments. We revised the manuscript according to the given suggestions and hope that it is suitable for publication in your journal in the present form. In the following, you can find our responses to the comments made by reviewers:

**Reviewer 1: Young S Oh**

Minor Essential Revisions:
1. Under the Clinical effectiveness and evaluation of dysphagia subsection, would add “being” before “...dysphagia-free (esophageal patency)...”.
   
   We made the change (results, page 10)

2. Under the Clinical effectiveness and evaluation of dysphagia subsection, would add a comma between “...stent removal/dysphagia recurrence” and “...differences were significant in the biodegradable stent group...”.
   
   We added a comma (results, page 10)

3. Under the Complications subsection, please clarify in the text that the p=0.086 refers to the difference between tissue hyperplasia with the Ella stent compared to the other two stents.
   
   We agree. We made the change in order to improve readability und understanding; we changed the text to:

   “…Importantly, tissue hyperplasia (ingrowth) was observed in 3 patients submitted to temporary biodegradable stent placement, and was not observed in the patients submitted
to treatment with SEPS or with fully covered SEMS. The statistical value for the comparison between tissue hyperplasia with the Ella stent compared to the other 2 stents was 
\[ P = 0.086 \ldots \]

4. In the Follow-up and reinterventions subsection, please clarify whether stent repositioning after migration was counted as new stent placement (e.g. were some of the 7 SEPS placed in the 3 patients after initial SEPS migration repositioned stents that had migrated?).

The 7 SEPS placed were the number of stent re-placements due to migration, in the 3 patients.
We agree with the reviewer. It is not clear in the text; we changed to:

“...In the 3 patients who were submitted to further stenting with SEPSs, the number 7 stents refers to the total number of stent re-placements; in these patients we did not place a new stent, but we repositioned stents that had migrated...”

5. In the Discussion section, the success rate for the van Hooft study is 60% (6 out of 10 patients had relief of their dysphagia after stent placement and dissolution without need for reintervention) and not 70%.

We agree; In the paper of Jeanine van Hooft is clearly stated in results, page 1045: (Primary endpoint: in 6 patients, placement of the biodegradable stent proved an effective 1-step treatment...). We changed to 60% in our paper, accordingly with the reviewer

6. In the Discussion section, change “alternatively” in “Alternatively, the Polyflex stent has only 1 flared end” to “In contrast, the Polyflex stent has only 1 flared end.”

We made the change (Discussion, page 16)

7. In the Discussion section, change “For example, the estimated time of dysphagia-free...” to “For example, the duration that patients were dysphagia free after temporary stenting with a biodegradable stent or a fully covered SEMS...”.

We made the change (Discussion, page 16)
8. In the Statistical analysis section, consider changing the “…were compared using the Wilcoxon signed-rank test” to “…were compared within each stent group using the Wilcoxon signed-rank test” for clarification.

We made the change. (Methods, statistical analysis, page 9)

9. Please add in the Technique and stents subsection information regarding the dilation diameter performed immediately before esophageal stent insertion. For example, were the RBES dilated large enough only to allow passage of the stent delivery apparatus (e.g. 12-14 mm for the SEPS, 9.4 mm for the Ella stent, 6.2 mm for the SEMS) or was another criteria was used?

This is a very important question. Immediately before esophageal stent insertion, dilatation of RBES, when needed, was performed with a diameter large enough only to allow passage of the stent delivery system. No other criteria were used. To clarify this issue and accordingly with the reviewer suggestion we added in the text:

“…and dilatation was performed as needed using either a balloon dilator or a Savary-Guilliard dilator at the discretion of the operator. The RBES were dilated large enough only to allow passage of the stent delivery apparatus (e.g. 12-14 mm for the SEPS, 9.4 mm for the Ella stent and 6.2 mm for the fully covered SEMS)”.

10. In the Figures section, the pictures and the legends do not correspond. For example, Figure 1 should be Figure 1 (A), Figure 2 should be Figure 1 (B), figure 4 should be Figure 2 (A), etc.

We are aware of that. This wrong numbering of figures was created by the submission system. In our revised submission we made an alert to the editorial office to correct it.

11. In Table 2, the p values of 0.27 and 0.4 are incorrectly listed as 0.27 and 0.4.

We corrected it

12. In the Discussion section, please discuss whether balloon dilation of the Ella stents after deployment, which your group implemented in an attempt to mitigate migration, did decrease migration rates compared to before balloon dilation was implemented.
This is again an important suggestion. After implementation of balloon dilatation of the Ella stent to further embed the stent into the esophageal mucosa and reduce the risk of migration, we had no more migrations, and perhaps this measure can be implemented in future Ella esophageal stent placements. We add some sentences in discussion to further clarify this issue.

“...we began to perform larger balloon dilatation of the stent immediately after deployment to further embed the stent into the esophageal mucosa and reduce the risk of migration. The implementation of balloon dilatation of the Ella stent after deployment did decrease migration rates compared to before balloon dilatation. No other cases of migration were observed and we suggest that this measure can help to mitigate migration after Ella stent deployment...”

Discretionary Revisions

1. Consider splitting the first paragraph in the Introduction section on line 20 between “...from the stents themselves [2-9]” and “To avoid complications of partially...” since the first paragraph is quite long.

We agree. First paragraph is quite long and splitting it improves the flow of the text. We changed it accordingly with the reviewer suggestion

2. In the Introduction section, a brief summary (specific numbers are not necessary since these are presented in the Discussion section) of the previously published experience of biodegradable stents may be useful, particularly since these stents may not be as familiar to endoscopists in countries such as the United States where biodegradable stents are not available. As examples: (1) The similar clinical performance and complication rates for Ella compared to Polyflex esophageal stents as well as the significantly lower reintervention rate for the Ella stent group in the Van Boeckel et al. study. (2) The high migration rate of the PLLA esophageal stent (10/13 cases) reported by Saito et al. (3) Ella stent migration rates of 2/21 (Repici et al) and 4/18 (Van Boeckel et al).

This is a very interesting suggestion and we fully agree with the reviewer. We provided a brief summary of the published experience of biodegradable stents without being exhaustive (large details are provided in discussion)
We changed the new text to: “.....Biodegradable stents have recently been developed and can serve as an alternative for SEPS. Saito et al. reported results from 2 series of patients who received poly-l-lactic esophageal stents [18, 19]. In one study Saito et al. observed a high migration rate (10/13 cases), although no symptoms of re-stenosis were observed within the follow-up period in all cases [19]. Three recent studies have used a novel stent (Ella esophageal stent) composed of the biodegradable polymer polydiaxone [4, 20, 21]. In these 3 studies authors observed low migration rates with the Ella stent (range: 0-22.2%), and encouraging clinical results with clinical success rates ranging from 33% to 60%. One study comparing the Ella stent with the Polyflex stent observed similar clinical performance and complication rates between the 2 stents as well as a significantly lower reintervention rate for the Ella stent group [4]...”

3. In the Discussion section, either add a reference to SEPS in the first sentence of the paragraph starting with “Regarding clinical success, the results of our study...” or combine this paragraph with the last paragraph starting with “There are several case series that have evaluated...” since it is not initially intuitive that the discussion is related to SEPS.

We agree. It is not intuitive. We added a reference to SEPS in the first sentence (Discussion, page 13).

Reviewer 2: Stuart Gordon

Minor Revisions:

1. Since the study is not randomized, please describe more clearly how the type of stent was chosen. Was it at the discretion of the endoscopist, or was it done consecutively (for instance 10 SEPS, then 10 biodegradable, then 10 SEMS)?

This is a very important question and we thank the reviewer for this suggestion. It is not clear in the text. The type of the stent was chosen consecutively and not at the discretion of the endoscopist. To further clarify this issue and to give further detail we changed the text to:....”
The stent used was chosen accordingly with the practice at that time in the participating centre. The placement of the stents was done consecutively (e.g. 10 SEPS, then 10 biodegradable stents and then 10 fully cover SEMS), and not at the discretion of the endoscopist...”
2. Paragraph 6 in Results: would change wording to: "In our study, 30% of patients in the biodegradable stent group were dysphagia free..."

We agree. Improves readability. It is Discussion, paragraph 6, page 14. We changed it

3. Typo in Table 1, column 1 Post-surgical 4 out of 10 should be (40%) not (10%) 

We agree. The typing mistake was corrected

We hope that we satisfactorily replied to all questions/comments/suggestions and the revised manuscript is suitable for publication in the BMC Gastroenterology. Again we acknowledge the reviewers and we kindly ask you to contact us for any further information or suggestions you may require

Yours sincerely,

On behalf of the co-authors

J. M. Canena