

ANSWERING REVIEWERS



June 25th, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11197-review.doc).

Title: Biodegradable stent or balloon dilatation for benign oesophageal stricture: pilot randomised controlled trial

Author: Anjan Dhar, Helen Close, YKS Viswanath, Colin James Rees, Helen Catherine Hancock, Deepak Dwarakanath, Rebecca Maier, Douglas Wardell Wilson, James Meredith Mason

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11197

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

1 Format has been updated

2 Revision has been made according to the suggestions of the administrative reviewer:

(1) Please provide language certificate letter by professional English language editing companies (Classification of manuscript language quality evaluation is B). For manuscripts submitted by non-native speakers of English, please provided language certificate by professional English language editing companies mentioned in 'The Revision Policies of BPG for Article'.

A language certificate letter has not been provided as we are native English speakers and we have thoroughly checked the manuscript. We believe that the language of our manuscript has reached or exceeded Grade A and would like to sign a guarantee indicating that we choose not to have our manuscript edited by an English language editing company.

(2) The title must be informative, specific, and brief (Title should be no more than 10~12 words/60 bytes. Please revise it). Words should be chosen carefully for retrieval purposes. All nonfunctional words should be deleted, such as 'the', 'studies on', 'observations of', and 'roles of', etc.

The title has been shortened and now reads "**Biodegradable stent or balloon dilatation for benign oesophageal stricture: pilot randomised controlled trial**"

A short running title of less than 6 words should be provided

A running title is as shown: "**Biodegradable stent for benign oesophageal stricture.**"

(3) An informative, structured abstracts of no less than 246 words should accompany each paper. Abstracts for original contributions should be structured into the following sections. AIM (no more than 20 words): Only the purpose should be included. Please write the aim in the form: "To investigate/study/...; METHODS (no less than 80 words); RESULTS (no less than 120 words): You should present *P* values where appropriate and must provide relevant data to illustrate how they were obtained, e.g. 6.92 ± 3.86 vs 3.61 ± 1.67 , $P < 0.001$; CONCLUSION (no more than 26 words).

The abstract has been restructured to meet these requirements as follows:

AIM: To undertake a randomised pilot study comparing biodegradable stents and endoscopic dilatation in patients with strictures.

METHODS: This British multi-site study recruited seventeen symptomatic adult patients with

refractory strictures. Patients were randomised using a multicentre, blinded assessor design, comparing a biodegradable stent (BS) with endoscopic dilatation (ED). The primary endpoint was the average dysphagia score during the first 6 months. Secondary endpoints included repeat endoscopic procedures, quality of life, and adverse events. Secondary analysis included follow-up to 12 months. Sensitivity analyses explored alternative estimation methods for dysphagia and multiple imputation of missing values. Nonparametric tests were used.

RESULTS: Although both groups improved, the average dysphagia scores for patients receiving stents were higher after 6 months: BS-ED 1.17 (95% CI: 0.63 to 1.78) $p=0.029$. The finding was robust under different estimation methods. Use of additional endoscopic procedures and quality of life (QALY) estimates were similar for BS and ED patients at 6 and 12 months. Concomitant use of gastrointestinal prescribed medication was greater in the stent group (BS 5.1, ED 2.0 prescriptions; $p<0.001$), as were related adverse events (BS 1.4, ED 0.0 events; $p=0.024$). Groups were comparable at baseline and findings were statistically significant but numbers were small due to under-recruitment. The oesophageal tract has somatic sensitivity and the process of the stent dissolving, possibly unevenly, might promote discomfort or reflux.

CONCLUSION: Stenting was associated with greater dysphagia, co-medication and adverse events. Rigorously conducted and adequately powered trials are needed before widespread adoption of this technology.

(4) **Core tip:** (Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.)

A core tip has been included in the manuscript as follows:

Core tip: Benign oesophageal strictures are managed by endoscopic dilatation using balloons or bougies, often requiring costly repeat procedures. Biodegradable stents do not usually require removal and may reduce the need for repeated endoscopy. This pilot multi-site randomized study demonstrates that stenting was associated with greater dysphagia, co-medication and adverse events. The oesophageal tract has somatic sensitivity and the process of the stent dissolving, possibly unevenly, might promote discomfort or reflux. Groups were comparable at baseline and findings are statistically significant but patient numbers were small. Rigorously conducted and adequately powered trials are needed before widespread adoption of this technology.

(5) **COMMENTS**

Background

To concisely and accurately summarize the related background of the article and to enable the readers to gain some basic knowledge relevant to the article, thus helping them better understand the significance of the article.

Research frontiers

To briefly introduce the hotspots or important areas in the research field related to the article.

Innovations and breakthroughs

To summarize and emphasize the differences, particularly the advances, achievements, innovations and breakthroughs, from the other related or similar articles so as to allow the readers to catch up the major points of the article.

Applications

To summarize the actual application values, the implications for further application and modification, or the perspectives of future application of the article.

Terminology

To concisely and accurately describe, define or explain the specific, unique terms that are not familiar to majority of the readers, but are essential for the readers to understand the article.

Peer review

To provide the comments from peer reviewers that most represent the characteristics, values and significance of the article, and allow the readers to have an objective point of view toward the article.

A comments section is now attached to the submission:

Background: Benign oesophageal strictures are managed by endoscopic dilatation using balloons or bougies, often requiring repeat procedures with their associated risks and costs and discomfort to patients. Biodegradable stents do not usually require removal and may reduce the need for repeated endoscopy.

Research frontiers: No randomized controlled trials comparing biodegradable stents with other stents or with balloon dilatation have been identified. Lack of adequately robust evidence for effectiveness and cost-effectiveness formed the rationale of this trial.

Related publications:

- Lorenzo-Zúñiga V, Moreno-de-Vega V, Marín I, Boix J. Biodegradable stents in gastrointestinal endoscopy. *World J Gastroenterol.* 2014 Mar 7;20(9):2212-2217. <http://dx.doi.org/10.3748/wjg.v20.i9.2212>. PMID:24605020 PMCID:PMC3942826
- Canena JM, Liberato MJ, Rio-Tinto RA, Pinto-Marques PM, Romão CM, Coutinho AV, Neves BA, Santos-Silva MF. A comparison of the temporary placement of 3 different self-expanding stents for the treatment of refractory benign esophageal strictures: a prospective multicentre study. *BMC Gastroenterol.* 2012;12:70. <http://dx.doi.org/10.1186/1471-230X-12-70>. PMID:22691296 PMCID:PMC3447662

Innovations and breakthroughs: This pilot multi-site randomized study demonstrated that stenting was associated with greater dysphagia, co-medication and adverse events. Groups were comparable at baseline and findings are statistically significant but patient numbers are small.

Applications: The oesophageal tract has somatic sensitivity and the process of the stent dissolving, possibly unevenly, might promote discomfort or reflux. Rigorously conducted and adequately powered trials are needed before widespread adoption of this technology.

Terminology:

Benign oesophageal stricture: Narrowing of the oesophagus is often caused by injury or radiation which leads to difficulty swallowing; BS=Biodegradable stent: A hollow structure placed into the oesophagus which gradually dissolves; ED=Endoscopic dilatation: A procedure conducted under anaesthesia to stretch the oesophagus, usually by means of an endoscopic balloon.

Peer review:

This is a good research idea as it is an important clinical entity. This is a nice pilot study that compares biodegradable stents and balloon dilatation. It is a well-designed study that unfortunately was not completed due to lack of included patients.

3 Revision has been made according to the suggestions of reviewer 1:

Dear Editor, Authors. Thank you for sending the study "Biodegradable stent compared to standard balloon dilatation for benign oesophageal stricture: a pilot randomized controlled trial." for revision. Please accept the following comments - good research idea as it is an important clinical entity. - frequent spelling and grammatical mistakes should be revised. - The study has a good design. - Need more number of patients for results confirmation. Thanks

We thank the reviewer for their positive comments. We have thoroughly checked the manuscript and can identify no spelling or grammatical mistakes. However, we would be happy to rectify any specific concerns identified by the editorial team.

4 Revision has been made according to the suggestions of reviewer 2:

General comments: This is a nice pilot study that compares biodegradable stents and balloon dilatation. It is a well-designed study that unfortunately was not completed due to lack of included patients.

We thank the reviewer for these positive comments.

Beside that I have minor remarks: - in the introduction section in the third paragraph eosinophilic esophagitis as a cause of benign esophageal strictures was not mentioned.

Thank you for highlighting this. Eosinophilic oesophagitis has been added to the introduction alongside an appropriate citation (p.5):

“Benign oesophageal strictures are caused by a number of conditions: injury by acid reflux (peptic strictures); injury by ingestion of acid or alkaline caustic agents (corrosive strictures); radiation induced inflammatory strictures; sequelae of therapeutic endoscopic interventions for early oesophageal cancer and Barrett’s oesophagus (such as endoscopic mucosal resection or photodynamic therapy); post surgical anastomotic strictures [7]; and eosinophilic oesophagitis [8].”

- in the part of complications the authors almost didn’t mention thoracic pain as the most frequent complication after stent placement or col- lapse of the biodegradable stent inside the esophageal lumen ?

These complications have now been highlighted in the introduction as follows:

“Self-expanding plastic or metal stents, have been used to dilate benign recurrent oesophageal strictures, as a means of reducing the need for repeated endoscopic balloon/bougie dilatation with mixed results and potential complications of stent migration, hyperplastic tissue ingrowth or overgrowth (metal stents), oesophageal obstruction due to collapsed stent, thoracic pain and disappointing longer-term symptom relief [9,10,11,12,13,14].”

- I strongly believe that Table 2: Baseline Comorbidities should be removed due to lack of included patients.

We have carefully considered this advice but would recommend leaving table 2 in situ in order to conform with standard trial reporting as per CONSORT guidelines (checklist no. 15 “A table showing baseline demographic and clinical characteristics for each group” <http://www.consort-statement.org/>). We feel WJG would want to conform to international reporting practice. The Table is essential so that readers can understand the characteristics of patients participating.

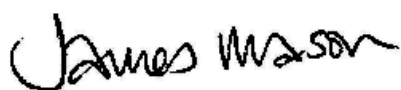
Therefore I classified the manuscript Biodegradable stent compared to standard balloon dilatation for benign oesophageal stricture: a pilot randomised controlled trial into grade B. According to the language evaluation the revised article is evaluated as grade B.

As noted above, we have thoroughly checked the manuscript and can find no spelling or grammatical mistakes. We would be happy to rectify any specific concerns identified by the editorial team.

I conclude that the authors should make above mentioned changes in the article. After they correct the proposed changes, I think you should accept the manuscript for the publication.

5 References and typesetting were corrected.

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



Sincerely yours,

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