

Endoluminal vacuum therapy for rectal anastomosis is safe and does not increase risk of strictures in a swine model

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1st Editorial decision

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Journal of Clinical and Translational Research

Dear Dr. Ostapenko,

Reviewers have now commented on your paper. One reviewer was very positive about your work, while the other two reviewers had recommended a reject. The two unfavorable reviewers are advising that you revise your manuscript, but also raised fundamental concerns about the novelty of the work as well as some technical concerns. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

For your information, reviewer 2 is referring to two clinical papers on the technique, performed in 14 and 1 patient, respectively. The editorial board accepts the reviewers point but feels that there is an overall paucity of studies on EVAT of rectal anastomoses and the number of patients addressed is still very low. We therefore have interest in the study because we feel it can contribute to existing literature. Our decision, however, does not absolve the authors from addressing the comments of these top experts in the field.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Jul 22, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: I have been given a manuscript titled "Endoluminal vacuum therapy for rectal anastomosis is safe and does not increase risk of strictures in a swine model" to review. In my opinion this paper does not require any revisions. Despite I had read this paper many times, I did not find any mistakes. Conceptualization, formal analysis, methodology, project design, the content of the article and figures are of superior quality. I fully accept this manuscript for the publication.

Congratulations to the authors!

Reviewer #2: The manuscript entitled "Endoluminal vacuum therapy for rectal anastomosis is safe and does not increase of risk of strictures in a swine model" investigated the safety of a rectal endoluminal vacuum device and ist effect to prevent an anastomotic leak after low anterior resection.

In their manuscript, the authors have performed low anterior rectal resection in a Yorkshire pig animal model (five experimental pigs and two control pigs). Postoperatively a vacuum device was rectally placed for five days in the experimental group only (n=5). The animals were euthanized on POD 35 and the rectal anastomosis and the sphincter was histologically evaluated for anastomotic healing or strictures or imflammation of the anastomosis.

Major comments:

The manuscript is well written and easy to read. While the aim and purpose of the study show a clinical relevance and might be important to the broad readership of Journal of Clinical and Translational Research, the manuscript lacks novelty and is not specific enough. Moreover, the study has its weakness due to the small collective (5 vs. 2 animals).

1. The abstract and introduction of the manuscript is confusing. It is not clear to the reader if the authors have placed the vacuum device for prophylactic use or as a treatment for anastomotic leakage? The authors should revise these paragraphs and make it more clear.

2. The authors describe in their discussion (page 6, line 27-28) about the novel endoluminal vacuum assisted device to treat anastomotic leaks. However, the treatment of anastomotic leakage of colorectal anastomoses by endo vacuum therapy is already a well known, clinically often performed procedure for anastomotic leakage. Furthermore, in the past two years two studies were published about the prophylactic use of rectal endoluminal vacuum device (Lehwald-Tywuschik et al, The "impossible" rectal anastomosis: a novel use for endoluminal vacuum-assisted therapy, Tech Coloproctol. 2021 Jan;25(1):125-130 and Mandarino et al, The prophylactic use of endoscopic vacuum therapy for anastomotic dehiscence after rectal anterior resection: is it feasible for redo surgery? Tech Coloproctol 2022 Apr;26(4):319-320).

Unfortunately the authors have not mentioned and discussed these already known studies in their manuscript. The introduction and discussion part need to be substantially revised.

3. The collective of five animals and two controls is quite small. The authors should therefore also include a paragraph in the discussion about possible limitations of the study.

4. The authors have used 12 references in their manuscript. However, only 6 references were cited from recent literature of the last 5 years. All other references are quite old. Since the treatment of anastomotic leakage has very much evolved over the last decade and treatment options have changed, we recommend to update the references and add more recent studies. Especially the two citations about prophylactic endovac treatments need to be added.

Reviewer #3: The authors present an experimental study evaluating endoluminal vacuum therapy in rectal anastomosis in an animal model. The authors did not employed the therapy for treating anastomosis defect but on intact anastomosis, since this is not the intended employment of this therapy the authors should clearly state the hypothesis of their work. The aim of the study is not clear: the authors stated that they wanted to investigate the role of vacuum therapy in lowering risk of an anastomotic leak after a low anterior resection in Yorkshire pigs, but immediately after they stated they wanted to study the effects on bowel tissue surrounding an intact anastomosis.

Endoluminal vacuum therapy has been used in rectal and other anastomosis leakage to accelerate the healing process of the perianastomotic cavity, therefore the possible stricture of the anastomosis could be due to the leakage itself and not to the vacuum therapy.

Moreover there was no difference in the histopathology of the experimental and control group, therefore the authors could not state that the therapy was "efficacious"

Authors' response

Reviewers' comments:

Reviewer #1: I have been given a manuscript titled "Endoluminal vacuum therapy for rectal anastomosis is safe and does not increase risk of strictures in a swine model" to review.

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Despite I had read this paper many times, I did not find any mistakes.

Conceptualization, formal analysis, methodology, project design, the content of the article and figures are of superior quality.

I fully accept this manuscript for the publication. Congratulations to the authors!

Thank you for the praise. We have revised the manuscript slightly to address other reviewer feedback.

Reviewer #2: The manuscript entitled "Endoluminal vacuum therapy for rectal anastomosis is safe and does not increase of risk of strictures in a swine model" investigated the safety of a rectal endoluminal vacuum device and its effect to prevent an anastomotic leak after low anterior resection.

In their manuscript, the authors have performed low anterior rectal resection in a Yorkshire pig animal model (five experimental pigs and two control pigs). Postoperatively a vacuum device was rectally placed for five days in the experimental group only (n=5). The animals were euthanized on POD 35 and the rectal anastomosis and the sphincter was histologically evaluated for anastomotic healing or strictures or inflammation of the anastomosis.

Major comments:

The manuscript is well written and easy to read. While the aim and purpose of the study show a clinical relevance and might be important to the broad readership of Journal of Clinical and Translational Research, the manuscript lacks novelty and is not specific enough. Moreover, the study has its weakness due to the small collective (5 vs. 2 animals).

1. The abstract and introduction of the manuscript is confusing. It is not clear to the reader if the authors have placed the vacuum device for prophylactic use or as a treatment for anastomotic leakage? The authors should revise these paragraphs and make it more clear.

Thank you for this feedback. The EVAC was used prophylactically here to demonstrate its safety in Yorkshire pigs and establish that it does not cause anastomotic strictures. Our study is unique in the histopathological evaluation of vacuum therapy. This has been added to the manuscript and emphasized in the abstract.

2. The authors describe in their discussion (page 6, line 27-28) about the novel endoluminal vacuum assisted device to treat anastomotic leaks. However, the treatment of anastomotic leakage of colorectal anastomoses by endo vacuum therapy is already a well known, clinically often performed procedure for anastomotic leakage. Furthermore, in the past two years two studies were published about the prophylactic use of rectal endoluminal vacuum device (Lehwald-Tywuschik et al, The "impossible" rectal anastomosis: a novel use for endoluminal vacuum-assisted therapy, Tech Coloproctol. 2021 Jan;25(1):125-130 and Mandarino et al, The prophylactic use of endoscopic vacuum therapy for anastomotic dehiscence after rectal anterior resection: is it feasible for redo surgery? Tech Coloproctol 2022 Apr;26(4):319-320).

Unfortunately the authors have not mentioned and discussed these already known studies in their manuscript. The introduction and discussion part need to be substantially revised.

Thank you for bringing up these two studies; they have been described in the introduction and incorporated into the discussion. Although these two studies are very recent, they similarly contain few numbers of subjects. We feel that our study contributes to existing literature and has a focus on the histopathological effects of EVACs on tissue, which the previous publications lacked.

3. The collective of five animals and two controls is quite small. The authors should therefore also include a paragraph in the discussion about possible limitations of the study. Mandarino et al

Although this is true, it is consistent with the number of subjects in other publications. (Shada, Amber L., et al. "Endoluminal negative-pressure therapy for preventing rectal

anastomotic leaks: a pilot study in a pig model." *Surgical Infections* 15.2 (2014): 123-130. And Rubicondo, Carolina, et al. "Endoluminal vacuum-assisted closure (E-Vac) therapy for postoperative esophageal fistula: successful case series and literature review." *World Journal of Surgical Oncology* 18.1 (2020): 1-7.). However, we agree with the reviewers that it should be included as a limitation, which was added to the discussion.

4. The authors have used 12 references in their manuscript. However, only 6 references were cited from recent literature of the last 5 years. All other references are quite old. Since the treatment of anastomotic leakage has very much evolved over the last decade and treatment options have changed, we recommend to update the references and add more recent studies. Especially the two citations about prophylactic endovac treatments need to be added.

We have expanded our references to more recent publications and included the two studies mentioned by the reviewer.

Reviewer #3: The authors present an experimental study evaluating endoluminal vacuum therapy in rectal anastomosis in an animal model. The authors did not employed the therapy for treating anastomosis defect but on intact anastomosis, since this is not the intended employment of this therapy the authors should clearly state the hypothesis of their work.

Thank you for this feedback. We adjusted the introduction and discussion to emphasize that the endoluminal therapy was used prophylactically. There are no clear guidelines or specific indications for endoluminal vacuum therapy currently. Some authors have used this therapy for managing anastomotic defects, whereas others have used it prophylactically (Lewald-Tywuschik et al).

The aim of the study is not clear: the authors stated that they wanted to investigate the role of vacuum therapy in lowering risk of an anastomotic leak after a low anterior resection in Yorkshire pigs, but immediately after they stated they wanted to study the effects on bowel tissue surrounding an intact anastomosis.

We clarified our aims in the abstract and introduction. The aim of the study is to assess the safety and efficacy of prophylactic use of endoluminal vacuum therapy and investigate the histopathological changes on the anastomosis from the vacuum.

Endoluminal vacuum therapy has been used in rectal and other anastomosis leakage to accelerate the healing process of the perianastomotic cavity, therefore the possible stricture of the anastomosis could be due to the leakage itself and not to the vacuum therapy. Moreover there was no difference in the histopathology of the experimental and control group, therefore the authors could not state that the therapy was "efficacious".

We changed the wording of the conclusion and delted efficacious as suggested by the reviewer.

2nd Editorial decision
27-Jul-2022

Ref.: Ms. No. JCTRes-D-22-00062R1
Endoluminal vacuum therapy for rectal anastomosis is safe and does not increase risk of strictures in a swine model
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: