

Peer Review File

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Reviewer A

This article reports four consecutive cases of endophytic gastric GIST patients operated with single staple line, tissue-preserving resection. After 12 weeks of follow-up, none of these four patients had complications. This technique is a good method for surgical treatment of endophytic gastric GIST, and this article has potential publication value, however, there are some minor concerns:

Dear Reviewer, thanks for considering our technique valuable. Please find below detailed response to your comments.

1. What is the GAP about endophytic gastric GIST resection? Please introduce the background of laparoscopic wedge resection with one or two sentences and highlight the unique of these case series regarding checklist 3a.

Thanks for your comment. We added to the introduction a short background as follows: “Although rare, GISTs are the most common tumours of mesenchymal origin in the gastrointestinal tract. They can occur anywhere throughout this tract, but the most common location is the stomach. Considering they rarely metastasize to nearby lymph node stations, it is recommended that GISTs undergo complete surgical resection with macroscopically negative margins. Minimally invasive wedge resections have been described as feasible and safe. However, the former often require removal of a large amount of excess tissue, which can result in narrowing and tortuosity of the remnant lumen. We hereby present a tissue preserving technique also applicable for large/bulky tumours”.

We have also added this sentence to the abstract – introduction:

“Minimally invasive wedge resection is a safe technique but often results in resection of an excessive amount of healthy tissue”

2. The methods in Abstract should be more detailed regarding checklist 3b - describe when was it done, by whom and what disease does the patients have?

We have re-structured the abstract and, to address your comment, we have added the following sentence: "All four patients had endoluminal gastric GISTs and were operated at the same institution between 2018 and 2020. The technique was specifically used for endophytic bulky tumours".

3. I fail to find reference in Introduction. The addition of references in the Introduction could give readers a clearer understanding of the background and current status of laparoscopic wedge resection.

Thanks for this comment. The references now appear in the introduction.

4. After the patients were discharged, were there any relevant imaging follow-up?

All the patients followed/will follow national guidance on surveillance determined by the risk stratification used in this disease (Ref: Judson et al. Clin Sarcoma Res (2017) 7:6 DOI 10.1186/s13569-017-0072-8). This information now appears in the manuscript.

We have also added the relevant FU for patient 3 (high risk), who was started on Imatinib therapy one month after the resection and had CT after six months and eighteen months, which did not show any evidence of recurrence.

5. In the Discussion, at present, for laparoscopic wedge resection, are there any other studies reported methods to reduce complications? Compared with this surgical method, what are the advantages and disadvantages? Please add references and discuss in more detail.

We have extended the discussion to include an alternative method that aim at preserving gastric tissue (gastrotomy, eversion of tumour and dual stapling) as well as methods to prevent complications (such as the use of haemostatics).

The advantage of our technique is not to leave an additional endoluminal staple line, which would not be visible at the end of the procedure (and might bleed). Moreover, we do not need to use haemostatic products.

6. The word mentioned in Conclusion that “optimal” is inaccurate. The surgical method is valuable for reducing complications, but the author should be more objective. Meanwhile, I fail to find the limitations about these four cases regarding checklist 7c.

We accept that “optimal” should be changed to “valuable”, as it appears in the new version. With regards to limitations, we added a short paragraph at the end of the discussion mentioning:

- 1. The small number of cases in this series;*
- 2. The fact that not 100% of gastric GISTs can be treated with this technique (for the ones located <2cm from the GOJ the staple lining can be difficult). We mention indeed that our technique allows to resect tumours which are closer to the OGJ compared to wedge resection.*

Reviewer B

The manuscript describes a minimally invasive surgical approach for GIST resection which combines a gastric tissue preserving excision with a single staple line closure. It is a well-constructed paper that reports a series of four cases of localized GIST, which undergo a modified laparoscopic technique (or in open surgery) based on the eversion method, which additionally tries to avoid complications derived from multiple staple lines used in the closure of the wall defect. In this sense, it could become an interesting technique in selected cases, due to its potential effectiveness, safety and reproducibility.

Some specific areas to attend are listed below (my comments on the technique will be based solely on the video description of the manuscript, as I do not have access to the video file).

Dear Reviewer, thanks for your comment and appreciation of the technique and its potential benefits. Please find below a point-to-point response to your specific criticisms.

1- It is advised that “case report” or “case series” should be included in the Keywords following the CARE guidelines.

The word case series was included in the Keywords.

2- No exclusion criteria were included in patient selection. Nevertheless, GIST with ulceration have been described to have potential risk of tumour cell seeding into the abdominal cavity after gastrotomy (exposure procedures). At least 3 patients were found to have ulcerated GIST. Should we assume this risk?

Thanks for this valuable comment. We minimize tumour manipulation by placing stay sutures at both edges. In selected cases, to further decrease intraabdominal seeding risks, an endoscopic bag can be applied to cover the tumour after its complete mobilization and immediately before the resection/stapling. This is now mentioned in the text.

3- Many endophytic GIST are difficult to identify laparoscopically, how did you choose the best site for the vertical gastrotomy?

Thanks for pointing out this missing information in the manuscript. We always have endoscopy available intraoperatively. We recommend mobilization of the stomach according to CT findings to optimize the view, and intraoperative endoscopy if in doubt to identify accurately the tumour borders before the gastrotomy is made.

4- The reader may presume that the 4 excisions were margin free (only included in the abstract). It is said that this technique could be the best way to maintain as much tissue and lumen behind as possible. However, no touch isolation techniques for GIST can be challenging, especially when trying to identify the tumour borders, in order to preserve as much healthy tissue as possible. As a matter of fact, there is a higher risk of margin positive or larger resection size than expected. Did you consider intraoperative endoscopy for marking?

As you kindly pointed out, it can be difficult to identify the margins laparoscopically. As per our reply to comment number 3, we recommend the use of intraoperative endoscopy when in doubt. We think this technique allows better direct visualization of the tumour margins, obtained by extroversion, compared to wedge resection. The information about specimen integrity/oncological completion of resection is now present in the main text.

5- It is reported that this approach could be applicable to tumours anywhere in the stomach. Would you find difficulties in resecting lesions located at the esophagogastric junction or pylorus using a linear stapling device as described?

Thanks for your comment. Using a linear stapler in that anatomical area will be difficult and should be done with caution. We now acknowledge this in the study limitations. As stated above (and in the limitations section) we think with this technique, which preserves as much gastric tissue as possible, we can resect endophytic tumours located closer to the GOJ (or pylorus) than a wedge resection would allow.

6- Could you better describe the follow-up protocol for these patients, was it the same for all despite the histological differences?

Please see response to comment 4 by Reviewer A. The follow up is according to the national UK guidelines and depending on the pathological risk assessment. This information now appears in the manuscript.