

March 15, 2016

Dear Editor,

Thank you for the opportunity to provide revisions to the thorough peer review of our invited manuscript entitled "Safety of Direct Endoscopic Necrosectomy in Patients with Gastric Varices," manuscript number: 24777.

Please find here the point-by-point response and citation for edits based on the reviewers' comments.

Reviewer 00160226

- 1) Were the patients described in this paper included in your previous publication of 60 patients, and were there overlap?
 - a. No, this group of patients with gastric varices was a new subset of patients, not previously reported in the literature.
- 2) If not, could the authors compare the outcomes of patients with those who did not have GV's?
 - a. Thank you for this important revision. While our main focus of this manuscript was to report the safety and feasibility of DEN in patients with gastric varices, we have now added some to the discussion that the safety and outcomes were similar between these two groups.
- 3) What were the indication of DEN?
 - a. This has been explicitly outlined in the materials and methods section.
- 4) Did you allow for a period of transgastric drainage before DEN?
 - a. That is not our practice, and this point is now made in the methods.
- 5) How do you decide to stop DEN?
 - a. We do not proceed with further DEN if the patient is asymptomatic and tolerating full oral diet. This is now described in the methods section.
- 6) How long are stents placed?
 - a. This varies, but the general approach is now outlined in the methods section.
- 7) Out of 15 patients, only 5 had follow up imaging, how can you be sure the collections resolved?
 - a. Our practice is to avoid radiation procedures/imaging if the patient is asymptomatic, which is generally also the patient's preference. While it is our practice to obtain at least one follow up CT or MRI, and all patients were seen to ensure clinical resolution in clinic, not all patients were willing to undergo repeat imaging. This is now described.
- 8) Did any patients receive adjunctive treatment like nasocystic irrigation, ERCP with PD stenting?
 - a. This is an interesting point, which we have elaborated. It is not our practice to provide nasocystic irrigation as we find that quality DEN with removal of necrotic material precludes this. None of these patients had ongoing evidence of PD leak requiring ERCP/PD stent placement.
- 9) Were there any other adverse events after DEN other than bleeding?

- a. All adverse events are reported, and only minor, delayed bleeding in these few cases was noted. Specifically, no sepsis was encountered, possibly due to our routine use of prophylactic antibiotics (this is now in the methods section)
- 10) Can the authors comment on the rate of bleeding?
- a. We have added this to the discussion. Interestingly, as defined in other large DEN studies, these two bleeding events would not have met the requirements for reporting as an adverse event. One bleeding event was discovered incidentally on CT scan and both were self-limited.

Reviewer 00503824

- 1) These selected patients should be placed in context of the experience of the authors.
 - a. Thank you, this was a recurring point of interest of all reviewers and we have attempted to address this issue with an expanded discussion section.
- 2) The duration of follow up should be clarified. How long after pancreatitis did the patients undergo DEN?
 - a. We attempted to address these issues under methods. Unfortunately, many patients at our center come from outside institutions for referral specifically for DEN, as such the index date/episode of pancreatitis is often not known to us making that measure of time difficult to determine.
- 3) Did the authors use systemic antibiotics?
 - a. Thank you, this was an important omission. Yes, and this is now detailed in the methods section.
- 4) What were the criteria for deciding on repeat or index DEN?
 - a. This is now explicitly outlined in the methods section.
- 5) Minor comments/revisions:
 - a. IR was changed to "interventional radiology"
 - b. Referring to the table in the abstract was removed.

Reviewer 00503857

- 1) The authors should clearly define the radiological criteria of pancreatic walled-off necrosis
 - a. Thank you, this has been outlined fully in the methods section.
- 2) The authors should also describe the outcomes of the remaining 75 patients with WON but without gastric varices.
 - a. All reviewers agreed this was not discussed with enough detail, which has been revised in the results and discussion sections. Thank you for this important point.
- 3) The authors should discuss more on the comparative results of patients receiving DEN or surgical drainage.

- a. Thank you, while our manuscript is meant to describe only the safety and feasibility of direct endoscopic necrosectomy in patients with necrotic pancreatic fluid collections in the presence of known gastric varices, it would be interesting to find a center where surgical management of patients with varices has been performed more commonly. Unfortunately, this was outside of the scope of our manuscript and study. We do discuss the potential risks and why we believe that endoscopic necrosectomy may be the preferred treatment modality in patients with WON and varices over surgical or interventional percutaneous routes.

Reviewer 02438659

We were not able to appreciate any suggestions for revision or edits from this review.

It reads in entirety:

“The purpose of this paper is to determine the feasibility and safety of transgastric DEN in patients with WON and gastric varices. The results are feasible, safe and effective. However there are some shortcomings about the paper, such as structure, language.”

We have made no specific changes based on these comments, but appreciate the time of the reviewer.

This concludes our discussion of our revisions after review of the thorough peer review comments. Thank you again for the opportunity to revise the manuscript for publication with your Journal.

Sincerely,

Andrew C Storm, MD

Christopher C Thompson, MD