

We thank the editors and reviewers for their thorough assessment of our work and constructive criticism that helped us improve our manuscript.

Our responses are given in a point-by-point manner below. Changes to the manuscript have been tracked with red underlined color.

AUTHORS' COMMENTS TO THE REVIEWERS

REVIEWER 1

Specific Comments to Authors: I congratulate Markus Brand and his colleagues for this beautiful work. They aimed to find a solution to one of the important problems in direct endoscopic necrosectomy. Any new technology that will reduce the DEN session and provide faster necrosis resolution is valuable. In our own experience, the most important factor in clearing necrosis is the "time after insertion of LAMS." Because over time, the necrosis solidifies and becomes easier to clear.

- 1. It would be better to indicate when the first necrosectomy session was performed in the article.**
 - Thanks for pointing this out. In mean the first necrosectomy session was performed 35.7 (14 - 90) days after the beginning the pancreatitis. We have added this information to the article.

- 2. The fact that there are only three LAMS dislocations is too good to be true, I would like to suggest a review of this data**
 - Thank you for the critical inquiry. We have checked this fact again, indeed only 3 dislocated LAMS were found.

- 3. It is pleasing for therapeutic endoscopy to have excellent results in other indications.**
 - Thank you for the comment. We have therefore presented additional information on these cases in a separate table (Table 2).

REVIEWER 2

Specific Comments to Authors: My recommendation (Reject) The article titled “The Over-The-Scope-Grasper - A new tool for pancreatic necrosectomy and beyond - first multicenter experience” is not acceptable for publication in its current form, with the following additional details mentioned underneath (in Comments to Authors).

General comments This is a retrospective study utilizing descriptive statistics for the utility of Over-The-Scope-Grasper for variety of indications mostly pancreatic necrosectomy in nine European endoscopic centers between November 2020 and October 2021. A total of 56 procedures were performed, with an overall technical success rate of 98%. Most of the procedures were endoscopic pancreatic necrosectomies (33 transgastric, 4 transduodenal). No clinically relevant complications were encountered. The device looks promising but is commercially unavailable at majority of the centers. The topic is appropriate and within the scope of this journal. The authors must be congratulated for conducting this study. However, the rationale for carrying out this study is not understood. The research question of interest looks pointless. The major limitation seems to be the chosen retrospective design of the study. The quality of evidence for such studies is low. Since the use of grasping tool was already published in Innovations and brief communications in Endoscopy in 2021, the authors could have perhaps conducted the current study prospectively.

- We agree with the reviewer that conducting a prospective study on the use of over-the-scope Grasper would be useful and provide better data. There are plans to conduct such a study. However, the present data are from the early launch period of the system and were used to collect initial data on the technical success, safety of the system, and potential areas of application. At this early stage, a structured prospective study was not yet reasonably possible.
- We have added this information to the article.
- At the time of the study, the device was only available in selected centers. After market launch (mid-2021), the device is now already available in many countries.

Comments to authors:

1. The authors did not adequately address the important issue regarding the retrospective study design. What was the method used for missing data? Did the authors use complete case analysis, available case analysis or a mean of the other values?

- Thank you for this objection. Since retrospective data collection was performed shortly after the procedure, complete data sets are available for all cases. We therefore performed a complete case analysis in all 56v procedures. All data mentioned in the manuscript are available and analyzed completely for the respective patient group.

- We have added this information to the article.
2. **With heterogeneous patient populations, different techniques and operator experiences, the multicenter management and retrospective review looks problematic. Details about the number of patients from each site is missing.**
 - This is an important objection. We have supplemented the data in the manuscript (Supplementary data).
 - We also raised this point in the Discussion.
 3. **There is inherent selection bias with these studies. What if the authors would have selected patients who have their outcome of interest?**
 - This is another important objection. We agree with the reviewer. Due to the retrospective study design, we cannot exclude that the data contain a selection bias.
 - We have therefore mentioned this point in the discussion (study limitations).
 4. **Since this is a retrospective study the authors need to mention that waiver of written informed consent was obtained from ethics committee (if yet all it was taken). They can mention that all patients had given their consent for the procedure.**
 - Thank you for pointing this out. We have changed the paragraph accordingly.
 5. **The center is a specialized unit of a tertiary care center which includes select set of referred patients leading to referral bias.**
 - It is true that the leading center is a specialized unit of a tertiary care center. However, of the 9 participating centers, 6 were university centers, so the proportion of specialized unit of a tertiary care is very high. The other 3 centers were also specialized endoscopy centers. Since the endoscopic care of necrotizing pancreatitis is usually provided in such specialized centers, the group of DEN patients certainly corresponds to clinical reality.
 - Nevertheless, we mentioned this point in the discussion (limitations of the study).
 6. **Another limitation relates to inadequate characterization of the study population.**
 - To better characterize the study population (especially the necrosectomy group), we added additional data in Table 1. We also added another table with data on the other indications (Table 2).
 7. **Was ethics approval obtained from every center or IRB approval from coordinating center?**

- The ethics approval was an IRB approval from the coordinating center (Ethics Committee of the University of Würzburg)

8. The term endpoint in retrospective studies looks problematic, outcomes would rather be a better term.

- Thanks for the comment. We have changed the sentences accordingly.

Minor comments:

The methods section in the manuscript needs a lot of changes for better clarity. The details on how the patient details were extracted and details of proforma need to be mentioned.

- Done as suggested.

The references have been accurately written. The figures, illustrations and video have been nicely presented.

- No changes made

REVIEWER 3

Specific Comments to Authors: I read with interest the study by Brand et al. Necrosectomy is still a procedure burdened by the lack of dedicated devices and of the a standardized approach. This new device could represent a valuable device could represent a step forward in the in setting of patients. Not least, this setting could also have several potential indications. This study provide interesting data about the employment of this new device in several setting of patients.

However, I have some concerns:

1. In the introduction author affirmed that no dedicated devices are available for necrosectomy. However, as reported in the discussion, a new motorized device, Endorotor, Has been recently introduced on the market, providing encouraging data [Stassen PMC, de Jonge PJF, Bruno MJ, Koch AD, Trindade AJ, Benias PC, Sejpal DV, Siddiqui UD, Chapman CG, Villa E, Tharian B, Inamdar S, Hwang JH, Barakat MT, Andalib I, Gaidhane M, Sarkar A, Shahid H, Tyberg A, Binmoeller K, Watson RR, Nett A, Schlag C, Abdelhafez M, Friedrich-Rust M, Schlachterman A, Chiang AL, Loren D, Kowalski T, Kahaleh M. Safety and efficacy of a novel resection system for direct endoscopic necrosectomy of walled-off pancreas necrosis: a prospective, international, multicenter trial. *Gastrointest Endosc.* 2022 Mar;95(3):471-479. doi: 10.1016/j.gie.2021.09.025. Epub 2021 Sep 22. PMID: 34562471.]. Author should modified the sentence in the introduction. Endorotor has been mentioned in the discussion, although references should be uptadated.

- Thanks for the tip. We have adjusted the sentence accordingly and added the citation in the introduction discussion.

2. 56 procedures have been included. However for a deeper comprehension, also the number of patient treated with this device should be reported.

- Thanks for the comment. We have added this information to the results.

3. Author should clearly indicate on-label uses and off-lable ones.

- The OTSG-Xcavator is approved for grasping large volumes of tissue and foreign bodies in the gastrointestinal tract. Therefore, no procedures were performed off label. We have added the information in the text.

4. Complications should be classified according the ASGE Lexicon [Cotton PB, Eisen GM, Aabakken L, Baron TH, Hutter MM, Jacobson BC, Mergener K, Nemcek A Jr, Petersen BT, Petrini JL, Pike IM, Rabeneck L, Romagnuolo J, Vargo JJ. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc.* 2010 Mar;71(3):446-54. doi: 10.1016/j.gie.2009.10.027. PMID: 20189503.]

- Thank you for pointing out this publication. We have revised the paragraph accordingly.

5. In table 1, Authors indicated that 26 cases necrosectomy was performed through a LAMS, while in 11 patients no LAMS was present. Which type of stent or stent was present? SEMS? double pig-tail? If double pig-tail why DEN was performed without LAMS placement according the step-up-approach?

- Thank you for this tip. In the 11 cases without SEMS, double pig-tails were used to keep the access to cavity open.
- These cases are, for example, transduodenal procedures where the insertion of a SEMS was not possible due to space restrictions.
- In some cases, the amount of fluid in the necrosis was so high that double pig-tails were used from the beginning.
- In addition, in some necrosectomies during the course, SEMS were removed and subsequent double pig-tails were used, so that follow-up procedures with OTSG were performed without LAMS.
- We have adjusted Table 1 and the text.

6. Authors reported 37 necrosectomies. On how many patients? How many session of DEN were needed for the complete resolution of the collection?

- The 37 DENs were performed in a total of 31 patients. An average of 4.5 sessions of DEN were required, for the complete resolution of the collection.
- We have added these data in the text and in Table 1

7. I suggest to modify Table 1 adding columns indicating dimension of WON and estimated percentage of necrosis within each collection, a number of DEN session for WON resolution.

- Thank you for this note, we have added these data to the text and in Table 1

8. Regarding foreign bodies retrieval, author should provide information regarding type of foreign bodies and location. A table with "other" indication for the use of the over-the-scope grasper should also be provided.

- Thank you for this note, we have added these data to a new Table (Table 2)

9. Pictures or video of each indication, different from necrosectomy, should be provided.

- Pictures or videos of DEN, foreign body removal, and blood coagulation management are included in the publication. Unfortunately, we cannot provide images for OTSG use prior to endoluminal vacuum therapy.

SCIENCE EDITOR:

The study tried to evaluate the Over-The-Scope-Grasper technical and safety of the device in treatment of pancreatic necrosis. It is interesting and useful. But there are some comments for authors.

1. The multicenter management with different techniques and operator experiences may effect the results analysis and details of the patients and surgical procedure need to be listed.

- Thank you for this tip. We have taken up this point in the discussion. Additional data have been added to Table 1 and 2.

2. The authors need to add more information in Table 1 to explain how many patients? How many session of DEN were needed for the complete resolution of the collection? When the first necrosectomy session was performed.

- Thank you for this tip. We have added the requested data to Table 1.

3. The authors also need to provide the details of foreign bodies retrieval.

- We have included another table (Table 2) with data on the removal of foreign bodies.

The authors would like to thank the reviewer for taking the time to read our manuscript. We believe that his/her suggestions have significantly improved its value.