

Responses to reviewer comments

Reviewer 1

This is a systematic review comparing different treatment of pancreatic pseudocyst. I have the following comments/suggestions on this report Please include the indication for treatment of pancreatic pseudocysts Please include the classification of pancreatic fluid collection in a table. What the au meant as “the article was thought to be relevant” How the final decision was made about the inclusion. On the basis of the limitations of the current study, as evidenced by the AU (see discussion) I believe that a clear conclusion comparing the different approaches could not be made at present and this point have to be very clearly evidenced in this paper

Thank you for your comments. Amendments have been made in the text.

Reviewer 2

This is the systematic review comparing percutaneous, endoscopic and surgical drainage of pancreatic pseudocyst. Overall, this paper is well written. Since there is few systematic review in this issue to date, this review is valuable for publication. The references are selected appropriately. I have no further comment for revision.

Thank you for your comments.

Reviewer 3

The manuscript gives an overview of publications on outcome of endoscopic drainage of pancreatic pseudocysts, compared with percutaneous and/or surgical drainage. Figure 1 illustrates that very few comparative studies were found, and table 1 reveal that most studies are “old”. Ie. in four series inclusion ended in 2007, in one 2009, and most of the others are even from the nineties. Another problem with the present manuscript is that some basic concepts might be misunderstood, for example (introduction, line 6): “Pancreatic pseudocysts are traditionally managed by open surgical internal drainage”. This is simply not true – and the focus of the paper becomes inappropriate. Primary and secondary outcome is chosen without inclusion of procedure related complications. There might be an alternative to review the literature again with adjusted focus. Probably can more results be found, if the perspective is expanded.

Thank you for your comments. The reviewer correctly pointed out that the outcomes of the review are dependent on the quality of the included studies. This would be the limitation of the current study. As indicated in the manuscript, only English

comparative studies involving the concerned treatment approaches were included. This was decided to make comparison between the treatment modalities possible. We did not want to include case series to the review, as this will further increase the potential biases included to the study. We understand that there are several options to treatment of pancreatic pseudocyst. From our search, it has been indicated that the traditional management of pancreatic pseudocyst is by open surgical internal drainage. In page 7, the section of Data extraction and outcomes, we have mentioned that the procedure related adverse events was one of the outcome parameters.

Reviewer 4

Your comprehensive well organized manuscript reviews the issue of pseudocyst drainage. This is one of interest to gastroenterologists and endoscopists. Specific Comments 1. It is very important to make sure that this only includes patients with pseudocysts. As you know we have learned over the years that pancreatic necrosis is very common with significant pancreatitis in that most collections, in fact, result from necrosis. Thus, it may be very difficult to completely exclude that necrosis could have been present. I would agree that abscesses are more likely to be excluded radiographically.

Thank you for your comments. We agree that the definition of pseudocyst may not be the same in every study and it has changed over the years. Amendments have been made in the text.

2. Do we know that transpapillary stenting was not used or if so should those patients be handled separately?

Thank you for your comment. These patients were excluded from the study.

3. You mention an adverse event rate of 67% in one study of percutaneous drainage. It would be important to know what the adverse events were and if we know that fistulas were created.

Thank you for your comment. The types of adverse events were described in table 4. Intra-abdominal infections occurred in 45.5% of the patients and pancreatic fistulas are included in this group of patients. Bleeding occurred in 9.1% of the patients.

4. When discussing EUS vs EGD drainage, you did mention the one study with two patients having significant bleeding. What were the overall complications for the EGD group as compared to the EUS group?

Thank you for your comment. The outcomes of EGD vs EUS guided drainage were summarized in table 6. The overall adverse events rates were similar between the two groups. For the EGD group, the adverse events rate was 10% – 18.9% whilst in the EUS group, the rate was between 0 – 19.6%.

5. Under Discussion you mention whether surgical drainage is preferred over percutaneous drainage. I assume there have been no comparative studies. The limited comparative data would suggest that EUS is preferred but as you mentioned may not be available at all centers. Nevertheless, the issue of percutaneous drainage for a simple pseudocyst needs to be better explored.

Thank you for your comments. The comparison of the outcomes of surgical and percutaneous drainage is summarized in table 4. Our conclusion that surgical drainage is preferred over percutaneous drainage is based on the results of these studies.

6. Methods – Provide definitions of outcome variables being compared in the different studies i.e. treatment success, recurrence rates, re-intervention and adverse events.

Thank you for your comments. Amendments have been made in the text.

7. Tables – Include countries of publication in Table 1. Please add duration of follow-up for each study in Tables 4,5,6. Table 5: the size of PFC and duration of hospitalization are given in median and IQR in the RT by Varadarajulu et al, and not mean (IQR), please correct. Table 6: Explanation of alpha is given in the footnote but no alpha is listed in the table as superscript. Please remove alpha from the footnote.

Thank you for your comments. Amendments have been made in the text.

Reviewer 5

It is an interesting systematic review but the authors included both recent and very old studies (since 1980). The authors should emphasize that classification of pancreatic lesions has changed during the last years (new Atlanta classification). Some pancreatic lesions originally characterized as pseudocysts are walled off pancreatic necrosis and the management would be different in these cases

Thank you for your comments. We agree that some of the older studies may have classified walled off pancreatic necrosis as pseudocysts. Amendments have been made in the text

Reviewer 6

This manuscript attempts to review the available literature regarding various modalities of drainage for pancreatic pseudocysts. Unfortunately, due to the small amount of high-quality studies available for review, analysis in the form of a meta-analysis could not be performed. The study thus is presented in a descriptive form (much like a review), yet the studies contained are quite old. Only plastic stents are used and most of the surgical studies use open techniques. For a topic like this, with a flood of recent publications regarding metallic stents and minimally invasive approaches (step-up, combined approach), I think expanding the study to include more current studies would go a long way towards making this study clinically relevant. In its current form it is already somewhat outdated

Thank you for your comments. We agree that some of the included studies were from the older era. However, the studies included were according to a stringent criterion and only comparative studies were included. Thus, conclusions could only be drawn from the data available. Hence our conclusions that large randomized studies with current definitions of pseudocysts and longer-term follow-up are needed to assess the efficacy of the various modalities.