

Dear Editor,

We thank the reviewers for their courteous and constructive comments. We paid attention to all suggestions and every single comment addressed and the manuscript has been improved according to the comments of the reviewers. Added text is highlighted in yellow. Deleted text is crossed out using the Track Changes function.

Reviewer's code: 03474653

- **Which type of study is this. Review;**

This is a review.

- **There is no clear hypothesis**

In agreement with the reviewer's comment we have added the following paragraph in the introduction section: We assumed that selective use of ERCP and sphincterotomy combined with interval cholecystectomy and concurrent pseudocyst management, if required, is the best option for treating patients after recovering from an acute episode of severe biliary pancreatitis.

We have deleted the last sentence from the introduction as irrelevant: A management algorithm has been developed for patients surviving severe biliary pancreatitis according to the currently published data in the literature.

- **and there is no methods, no material.**

This is a very important point and we have added the following section titled Material-Methods:

A pertinent literature search was performed concerning the management of patients after recovering from an acute episode of severe biliary pancreatitis. The electronic databases MEDLINE, PubMed, Embase, Cochrane Library and Google scholar were used to search for relevant articles published in the literature from 1976 to 2016, using the following terms and/or combinations in their titles, abstracts, or keyword lists: acute pancreatitis,

biliary pancreatitis, severe acute pancreatitis, pancreatic pseudocysts, index cholecystectomy, interval cholecystectomy, percutaneous pseudocyst drainage, endoscopic pseudocyst drainage, surgical pseudocyst management. The above-mentioned terms were used in “[MESH]” (PubMed and Cochrane Library), where applicable; otherwise, they were combined using “AND/OR” and asterisks.

The following exclusion criteria were initially applied to all articles identified: publication of abstract only, case reports, and mean or median follow-up of six months. Inclusion criteria were: observational cohort studies, randomized trials, reviews, meta-analyses, systematic reviews and Cochrane Database Systematic Reviews, studies available in full text and published in the English language. Further references from the selected articles were reviewed manually to supplement the electronic search for additional relevant articles. The following variables concerning studies that address the management of patients with acute severe biliary pancreatitis were recorded: authors, journal and year of publication, country of origin, trial duration and participant demographics. Data concerning follow-up evaluation, ratios and percentages of morbidity, mortality, biliary events, recurrent pancreatitis, sepsis and other complications according to each treatment option were recorded in a database (Microsoft Excel spreadsheet, Microsoft Corporation).

- **Conclusion to little for such an extensive material.**

In our opinion all key points of the present review have been stressed in the conclusion section.

- **In core tip there are two different types of typography.**

This has been corrected.

- **Missing abbreviations in introduction about IAP/APA.**

The missing abbreviation IAP/APA has been added: International Association of Pancreatology/American Pancreatic Association

- **In introduction direct after Reference nr 9 comes ENREF 6 that makes no conclusion with the rest of the text.**

The reviewer's remark is correct, so ENREF 6 has been deleted from the text.

Reviewer's code: 03000523

- **This review article is very consist and informative. It is supported by literature and based uppod authors experience. The special value is algorithm for final treatment of biliary pancreatitis.**

We thank the reviewer for the very kind comments.

Reviewer's code: 03475309

- **General remarks: The article is easy to read. -The subject is important, and some controversies still remain concerning the definitive treatment.**

We appreciate the comments of the Reviewer.

- **The general layout is good, but the article should be better structured to facilitate the reading.**

We agree with the reviewer and have added a section titled Material-Methods were we have included the background data as a paragraph.

- **English should be carefully checked for vocabulary and grammar errors (words missing, numbers starting a sentence, ...) throughout the manuscript.**

English language has been checked by an English native speaker, English teacher and member of an official English language editor's network of Cambridge Massachusetts (CAEN) (CAEN@yahoogroups.com), and has been improved.

- **Abstract:-The abstract is clear**

We thank the reviewer.

- **Introduction:-Authors should define precisely acute severe pancreatitis**

The following sentence has been added to the Introduction: Severe acute pancreatitis is defined by the presence of organ failure persisting beyond 48 hours.

- **Background data: -This part seems a bit redundant compared to the introduction. I would try to combine the 2 parts**

This is a very important comment for the structure of the manuscript. In this respect after the addition of Material-Methods section according to the comments, we have included the Background data in this section, as more suitable.

- **Core part of the text: Where are the methods? It should be stated how the search was performed.**

This is another comment of importance that has already been addressed by adding a section titled Material-Methods.

- **Please specify in the manuscript when open cholecystectomy should be performed instead of laparoscopic cholecystectomy**

We have added in the section cholecystectomy under fit for surgery the following:

Open cholecystectomy has a limited role; it can be performed along with debridement of necrotizing pancreatitis, and, in cases where a pancreatic pseudocyst is present, after unsuccessful percutaneous or endoscopic approaches, and in failed laparoscopy.

We have also deleted the following as inappropriate: ...but in some cases open cholecystectomy is still performed.

- **How do you define a patient fit for surgery?**

In the section background data, we have added the following:

Patients are generally considered fit for surgery according to their physiological fitness and functional capacity to cope with the above-mentioned procedures/interventions. There is a wide variety of prediction models referred to in the literature and used in different centers.

- **In the figure the rate of biliary events, recurrent pancreatitis and mortality is higher for interval cholecystectomy compared to index cholecystectomy, but in the text it is mentioned that guidelines recommend interval cholecystectomy in case of severe acute pancreatitis in fit for surgery patients. How do you explain this?**

This is a comment of great importance: We initially added two white-coloured square panels to index cholecystectomy in order to provide a more detailed information about the outcomes of this management option which was a bit confusing.

Accordingly, we combined the results presented in these two panels in a single one. This way the reader has the easily digestible information that index cholecystectomy has a complication rate of 44% and sepsis in 47% of cases.

Thank you again for reviewing our manuscript. Looking forward listening from you.

Kind Regards,

Georgia Dedemadi MD, PhD, FACS