

November 25<sup>th</sup>, 2019  
Athens, Greece

To the Editorial Board of “*World Journal of Gastrointestinal Surgery*”

We are submitting for consideration our revised manuscript (#52022) entitled: “*Acute Esophageal Necrosis :a Systematic review and Pooled analysis*”. We would like to thank the reviewers and the Editor of the Journal, for taking the time and effort to assess the initial version of our manuscript so meticulously. Our research group took into account all of your recommendations and we modified our manuscript accordingly. Detailed replies to the reviewers’ comments are provided below:

**Reviewer #1:**

**Overall impression:** “*I think that this paper is interesting and the results of this study is one of the important clinical analysis of the rare entity.*”

**Authors’ reply:** Thank you for appreciating our work and for suggesting ways to further improve it.

**Comment 1.1:** “*The authors had not reveal the complications in detail. Could you describe the contents and percentage of the complications?*”

**Authors’ reply:** Thank you for your remarks. As you suggested we added in the discussion section the list and percentages of complications.

**Comment 1.2:** “. *Sub-analysis separating cases before and after 2006 showed that frequency of surgical or endoscopic intervention was significantly increased, but mortality rate was similar. Could you consider the issue?*”

**Authors’ reply:** Thank you for your comment. We noted that cases of AEN after 2006 seem to be more severe than earlier years, likely due to patients having more comorbidities. Therefore, these cases demanded aggressive surgical or endoscopic intervention. Interestingly enough though, this more aggressive approach was not associated with increased mortality rates.

**Reviewer #2:**

**Overall impression:** “This manuscript is a systemic review with well design and preparation. It should be interested by our readers and can be accepted for publication.”

**Authors’ reply:** Thank you for appreciating our work.

**Reviewer #3**

**Overall impression:** “*Well conducted meta analysis and adequate statistical analysis of a rare condition (perhaps mild cases are not identified). although a rare condition it makes a good recall for thoracic surgeons and gastrointestinal surgeons*”

**Authors’ reply:** Thank you for appreciating our work.

**Reviewer #4**

**Overall impression:** “*Acute Esophageal Necrosis: a Systematic Review and Pooled Analysis In this study, the authors aimed to systematically review and synthesize all available data on demographics, clinical features, outcomes and the management of this medical condition. 114 patients with Acute Esophageal Necrosis (AEN) were included in the review. They found that gastrointestinal symptoms on presentation and need for surgical or endoscopic treatment have been associated with increased odds of complications. The authors have concluded that although the frequency of surgical and endoscopic intervention has increased in recent years, outcomes have remained the same. Therefore, further investigations are needed to better understand how to best treat this potentially lethal disease. This manuscript is well written; also the figure and the tables are all appropriate.*”

**Authors’ reply:** Thank you for appreciating our work.

**Reviewer #5**

**Overall impression:** “Well written manuscript”

**Authors' reply:** Thank you for appreciating our work and for suggesting ways to further improve it.

**Comment 5.1:** what is the purpose of this study?

**Authors' reply:** Thank you for taking the time to review our manuscript. The aim of this study was to systematically review and synthesize all available data on demographics, clinical features, outcomes and the management of patients with acute esophageal necrosis so as the present work can serve as a useful guide to clinicians contemplating how to best treat this rare condition.

**Comment 5.2:** (doi: 10.1159/000175414) and ( doi: 10.12659/AJCR.890713) I suggest both of these uptodate studies for the references.

**Authors' reply:** Thank you for your comment. These two studies are very interesting but not relevant to our topic. One is a report on a patient with a Dieulafoy lesion and the other one is a report on a patient with a phytobezoar. Therefore, we believe that there is no benefit for the readership to include them in our review.

### **Reviewer #6**

**Overall impression:** «Dear Authors, Thank you for sharing your hard worked article entitled "Acute Esophageal Necrosis: a Systematic Review and Pooled Analysis»

**Authors' reply:** Thank you for appreciating our work and for suggesting ways to further improve it.

**Comment 6.1:** It needs some little correction in spelling and punctuations

**Authors' reply:** Thank you for your remark. We carefully reviewed our manuscript several times and made the appropriate corrections.

**Comment 6.2 :** *I would like to read your inclusion and exclusion criteria.*

**Authors' reply:** Thank you for your thoughtful remark. As you suggested, we added a paragraph to the methods section with our inclusion and exclusion criteria

**Comment 6.3:** *Tables should be shorter*

**Authors' reply:** Thank you for your comment. As you suggested table 1 was divided in two separate tables.

**Comment 6.4:** *I would also like to read most encountered reasons of Acute Esophageal Necrosis in numbers or percentage and the reasons of choosing different treatment modalities in your included articles, if possible. Sincerely*

**Authors' reply:** Thank you for your remark. We recorded the symptoms at presentation in emergency room and the comorbidities of patients with AEN. Unfortunately we cannot define the exact reasons of AEN, since the majority of studies describes black esophagus as a result of each patient's comorbidities in total.

With regards to choosing different treatment modalities most authors supported a conservative approach by correcting the underlying disease, intravenous hydration, establishing supportive parenteral alimentation, and intravenous PPIs together with sucralfate. In cases of suspected esophageal perforation, prompt esophagectomy with decortication, surgical drainage and lavage of mediastinal collection was performed. In case of strictures or stenosis endoscopic treatment was performed. All the aforementioned points are being addressed in the results and discussion section of the manuscript.

## **Reviewer #7**

**Overall impression:** *“This is a comprehensive review of Acute Esophageal Necrosis, including isolated clinical cases and (few) series published. The description of clinical presentation, associated diseases, evolution, mortality has not changed through the years. However the authors showed a significant difference in treatment when separating cases/series published before or after 2006, with more surgical and endoscopic treatment in the later cases”*

**Authors’ reply:** Thank you for appreciating our work and for suggesting ways to further improve it.

**Comment 7.1:** It would be useful to describe (shortly, with the aid of a table) the endoscopic treatments performed, as this is a rare condition and endoscopic treatment rarer still.

**Authors’ reply:** Thank you for your comment. As you suggested we added a table that describes the endoscopic treatments performed

Thank you for taking the time to critically review our manuscript. We hope that by editing our manuscript based on the thoughtful suggestions made by the reviewer’s, our work will be deemed appropriate for publications to the *World Journal of Gastrointestinal Surgery*. We look forward to hearing from you and we would be pleased to answer any further questions and/or comments you may have.

Sincerely yours,

Theochari Nikoletta, MD  
Society of Junior Doctors, Athens, Greece