

Dear Dr.Ma,

Thank you very much for your decision letter and advice on our manuscript entitled “Endoscopic treatment for acute appendicitis with coexistent acute pancreatitis: a case report”. We also thank the reviewers for the constructive comments and suggestions. We have revised the manuscript accordingly, and all amendments are indicated by red font in the revised manuscript. In addition, our point-by-point responses to the comments are listed below this letter.

This revised manuscript has been edited and proofread by *Medjaden* Bioscience Limited.

We hope that our revised manuscript is now acceptable for publication in your journal and look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Wenjuan Ding

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1

Specific Comments

One wonders though if there could be potential complications given the insufflation of air (possibly CO<sub>2</sub> would be better) in such a case.

Response: Thank you for your query. The carbon dioxide or air is used for insufflation mainly during the passage of the colonoscope from the anal canal into the colon up to the appendix. During ERAT, we use saline rather than gas to expose the operating area. In addition, in order to ensure patient safety and comfort, all the operations were performed by experienced endoscopic surgeons, who used the

minimum amount of gas for insufflation, and the gas was exhausted out of the intestinal tract as much as possible while withdrawing the colonoscopy after the procedure. We chose carbon dioxide because it is easier to absorb, reducing the likelihood of bloating and exacerbating acute pancreatitis. Air injection is also possible in the absence of carbon dioxide.

1 do you have a CT scan showing the appendicitis.

Response: Thank you for your query. We did not perform CT abdomen in both the patients. The diagnosis of acute appendicitis was made based on abdominal color ultrasound in both patients.

2 your case and tidal show coexistent acute pancreatitis. While this patient had acute pancreatitis, I assume that the impetus for such an endoscopic technique would not necessarily be acute appendicitis but some critically ill patient where surgery may not be appropriate. Perhaps a title revision might better.

Response: Thank you for your advice. Indeed, ERAT technology is not only suitable for patients with acute appendicitis coexisting with acute pancreatitis, but also a good choice for some critically ill patients who do not want to undergo appendectomy. In the title of our manuscript we have mentioned endoscopic treatment of acute appendicitis combined with acute pancreatitis, because both the cases discussed in this article had acute pancreatitis. In the future, we will be treating other critically ill patients having acute appendicitis with ERAT.

3 the case report and discussion are much too lengthy and should be significantly reduced which will not influence the case whatsoever.

Response: Thank you for your suggestion. We have made some appropriate deletions in the manuscript.

4 while the infusion of an antibiotic sounds reasonable, for a potentially local infection where debridement is what may be needed, I wonder if it really is necessary.

I assume that systemic antibiotics would be given anyway.

Response: Thank you for your comment. Intravenous antibiotics are necessary, and were given to both the patients. ERAT is an invasive procedure with the risk of appendiceal mucosal injury and perforation. Moreover, patients with acute pancreatitis have intestinal dysbiosis, and mucosal edema. Hence, to prevent ERAT-related secondary infection, local antibiotic irrigation was given.

5 it appears that this technique has only been reported from one center in China. Do you know if this is excepted by surgeons at your institution or worldwide? In many cases, we know that antibiotics alone will settle the case until further definitive surgical therapy may be undertaken.

Response: Thank you for your comment. As mentioned in the discussion section of our manuscript, the appendix is involved in the body's immune system, secretes various digestive enzymes and regulates the balance of intestinal flora. Therefore, conservative treatment of appendicitis with antibiotics is being increasingly adopted worldwide. However, medical therapy has been associated with high risk of long-term recurrence rate. Hence, in order to avoid surgery and increase the success rate of medical therapy, the technique of ERAT ha been developed.

ERAT technology was first reported by Chinese Professor Bingrong Liu in 2012, and subsequently a series of studies have been conducted. Its effectiveness and safety have been recognized by physicians and surgeons, and it has gradually been widely carried out in various hospitals in China. In our hospital, there was a study in which surgeons participated with us. We compared the efficacy and complications of ERAT and surgical resection (including laparotomy or laparoscopy), proving that ERAT is effective and safe in the treatment of acute non-perforated appendicitis.

Reviewer #2:

An interesting case report of a new method. However, it should be stated whether the second patient (44-year-old woman) continued to receive antibiotics after the procedure?

Response: Thank you for your query. The second patient continued to receive antibiotics after surgery, which has been added in the revised manuscript.