

Responses to reviewer's comments

Thank you for reviewing my manuscript. I greatly appreciate your helpful and insightful comments and suggestions.

I will address each reviewer's comment individually.

<Comment>

This interesting study is focused on clinical, pathological and radiological characterization of an uncommon but not much rare disease as appendiceal diverticulitis. Some points need to be clarified: - Methods: Authors stated that they "carefully examined the resected specimens in order to distinguish appendiceal diverticulitis from acute appendicitis". As this is a retrospective study, it is unclear if the fixed specimen was re-evaluated in all cases. - Statistical analysis: please check the normal distribution of values of numerical variables before using the mean and the t-test for statistical comparison (if not normally distributed, the median, range and non-parametric tests should be adopted) - Results: was surgically approach (open vs. laparoscopic) similar in the two groups? - Discussion: CT scan is not a first level exam for the diagnosis of acute appendicitis, as it is generally performed in more advanced or clinically doubtful cases. This study, in the evaluation of potential radiological differences in CT imaging, includes retrospectively a group of patients who performed CT scan. As such, a selection bias may have occurred, and should be included in the Discussion as a potential limitation.

<Answer>

*As this is a retrospective study, it is unclear if the fixed specimen was re-evaluated in all cases.

⇒ As suggested by the reviewer, the specimen was not re-evaluated in this study. However, since the pathologist in our institute has been interested in the diagnosis of appendiceal diverticulitis, he has manipulated and examined the specimens very carefully in all cases.

I revised my manuscript to say:

"The pathologist in our institute originally prepared the specimens very carefully, and thoroughly examined microscopically to detect diverticula. Appendiceal diverticulitis was diagnosed as inflammation of one of the

diverticula, with no or slight inflammation of the appendiceal wall^[11].”

*Please check the normal distribution of values of numerical variables before using the mean and the t-test for statistical comparison (if not normally distributed, the median, range and non-parametric tests should be adopted)

⇒ As suggested by the reviewer, non-parametric tests (Wilcoxon signed-rank test and Fisher’s exact test)have been adopted in the statistics.

*Was surgically approach (open vs. laparoscopic) similar in the two groups? -
Discuss

⇒ In all cases, open appendectomy was performed.

I have added “Open appendectomy was performed in all cases.” in the Results section.

*This study, in the evaluation of potential radiological differences in CT imaging, includes retrospectively a group of patients who performed CT scan. As such, a selection bias may have occurred, and should be included in the Discussion as a potential limitation.

⇒As suggested by the reviewer, there may be a selection bias between the groups who performed CT scans and who did not. Therefore, I have added the following sentence in the Discussion section.

“This study has several limitations, because it. First, ours was a retrospective study. there may be a selection bias between the groups who performed CT scans and who did not.To confirm the exact incidence of appendiceal diverticulitis and differences of CT findings between acute appendicitis and appendiceal diverticulitis, a prospective evaluation is necessary.”

<Comment>

1.) In the Introduction part the Phillips criteria are mentioned. An explanation of the classification is needed. 2.) In the DISCUSSION part it is said: ...” It is

very important for both pathologists and surgeons to consider the possibility of appendiceal diverticulitis and to examine the specimen carefully.”... The question is why it is so important. Is there a therapeutically consequence. 3.) The Conclusion is not significant. The question is there a therapeutically consequence, like a conservative therapy in cases of a sigma diverticulitis. Is an improvement imaging (procedures) constructive (e.g. use of MRI) in patients with such symptoms to select appendiceal diverticulitis from appendicitis patients. Is a differentiation only from scientific interest or is there the possibility to differ patients in patients with a mild diverticulitis (conservative treatment) from those with a severe diverticulitis and appendicitis (surgical treatment).

<Answer>

*In the Introduction part the Phillips criteria are mentioned. An explanation of the classification is needed.

⇒ To avoid the confusion to the readers, we deleted the description about the Phillips criteria.

*In the DISCUSSION part it is said: ...” It is very important for both pathologists and surgeons to consider the possibility of appendiceal diverticulitis and to examine the specimen carefully.”... The question is why it is so important. Is there a therapeutically consequence

In order to diagnose appendiceal diverticultis accurately, pathologists and surgeons should manipulate the resected specimens appropriately considering the possibility of appendiceal diverticulitis. After confirming accurate diagnosis, we can investigate the preoperative imaging diagnosis and therapeutic strategy such as conservative antibiotic therapy, open surgery, and laparoscopic surgery.

*The Conclusion is not significant. The question is there a therapeutically consequence, like a conservative therapy in cases of a sigma diverticulitis. Is an improvement imaging (procedures) constructive (e.g. use of MRI) in patients with such symptoms to select appendiceal diverticulitis from appendicitis patients. Is a differentiation only from scientific interest or is there the possibility to differ patients in patients with a mild diverticulitis (conservative

treatment) from those with a severe diverticulitis and appendicitis (surgical treatment).

⇒ I revised the Discussion part of the manuscript as follows.

“This study has several limitations, because it was a retrospective study. there may be a selection bias between the groups who performed CT scans and who did not. To confirm the exact incidence of appendiceal diverticulitis and differences of CT findings between acute appendicitis and appendiceal diverticulitis, a prospective evaluation is necessary. Despite these limitations, we believe that appendiceal diverticulitis can be diagnosed preoperatively with a combination of clinical features and suggestive findings on CT. If we are able to diagnose appendiceal diverticulitis accurately, we will be able to further investigate whether conservative antibiotic therapy or surgery is desirable for appendiceal diverticulitis in the future.”

<Comment>

In this study the authors found appendiceal diverticulitis, until now considered a rare finding, to be present in unexpected percentage in patients with symptoms of acute appendicitis. Although this conclusion may be noteworthy, it is doubtful that the management and outcome of patients suffering this condition may be influenced: it appears that an early diagnosis of appendiceal diverticulitis does not affect time and surgical choice and this issue should be at least mentioned in the discussion. One limit of the study is to be a retrospective one and, considering the incidence of about 10% of appendiceal diverticulitis among those operated for acute appendicitis, a prospective evaluation could be interesting to confirm such elevated percentage. Some topics may be more deeply addressed: ? Is the presence of an appendiceal diverticulum consequent to the same anatomic derangement (i.e. vasa recta) of the colon diverticula? It is probable, considering that in the study only false diverticula were found, but it should be discussed. ? The distinction in diverticula of the distal, middle and proximal third does not seem influential in such a short organ like appendicitis. I would avoid it ? All the CT scans are in a coronal space. Why a transversal plane is not showed? ? The length of surgery (40 min vs 50 min!) and the blood

loss can be affected by several factors and I doubt that they could have any relevance to the presence of an appendiceal diverticulum. Do the authors have any particular explanation for this? ? It would be very interesting to have photographs of some specimens with appendiceal diverticula, an important documentation in such types of papers. ? Is the longer duration of symptoms before consequent to less severe symptoms during the course of the disease? It should be specified. ? Can the authors give any explanation about the discrepancy between lower white blood cells count and the higher CRP in patients with diverticulitis? In conclusion, while the study seems relatively relevant for the incidence and the diagnosis of appendiceal diverticula, it could be accepted only after several revisions.

<Answer>

*Although this conclusion may be noteworthy, it is doubtful that the management and outcome of patients suffering this condition may be influenced: it appears that an early diagnosis of appendiceal diverticulitis does not affect time and surgical choice and this issue should be at least mentioned in the discussion.

⇒ Unfortunately, it is not known whether the preoperative diagnosis of appendiceal diverticulitis will alter the management of these patients. I have revised the Discussion part of my manuscript, adding “Despite these limitations, we believe that appendiceal diverticulitis can be diagnosed preoperatively with a combination of clinical features and suggestive findings on CT. If we are able to diagnose appendiceal diverticulitis accurately, we will be able to further investigate whether conservative antibiotic therapy or surgery is desirable for appendiceal diverticultis in the future.”

*One limit of the study is to be a retrospective one and, considering the incidence of about 10% of appendiceal diverticulitis among those operated for acute appendicitis, a prospective evaluation could be interesting to confirm such elevated percentage.

⇒ As suugested by the reviewer, this study has several limitations because of the retrospective one. Therefore, I have added sentences in the discussion section as follows:

“ This study has several limitations, because it was a retrospective study. there

may be a selection bias between the groups who performed CT scans and who did not. To confirm the exact incidence of appendiceal diverticulitis and differences of CT findings between acute appendicitis and appendiceal diverticulitis, a prospective evaluation is necessary.

*Is the presence of an appendiceal diverticula consequent to the same anatomic derangement (i.e. vasa recta) of the colon diverticula? It is probable, considering that in the study only false diverticula were found, but it should be discussed.

⇒ As suggested by the reviewer, It is interesting that the same anatomic derangement occurs in colon diverticula and in appendiceal diverticula.

I have revised the manuscript as follows.

“Most appendiceal diverticula were false diverticula, formed by herniation of the mucosa and submucosa through a defect in the muscular layer. This is similar to the anatomical derangement seen in diverticula of the colon.”

*The distinction in diverticula of the distal, middle and proximal third does not seem influential in such a short organ like appendicitis. I would avoid it

⇒ I have deleted the statement distinguishing the location of the diverticula.

*All the CT scans are in a coronal space. Why a transversal plane is not showed

⇒ I have added the transversal plane for each case.

The length of surgery (40 min vs 50 min!) and the blood loss can be affected by several factors and I doubt that they could have any relevance to the presence of an appendiceal diverticulum. Do the authors have any particular explanation for this

⇒ In appendiceal diverticulitis group, pararectal incision and drainage procedure are often necessary because of the higher rate of perforation and localized abscess. As such, this may affect surgical time and intraoperative blood loss.

I revised my manuscript, adding “Appendiceal diverticulitis is often associated

with localized abscess formation and perforation, often making surgery more difficult with increased surgical time and intraoperative blood loss compared to appendicitis surgery” in the Discussion section.

Can the authors give any explanation about the discrepancy between lower white blood cells count and the higher CRP in patients with diverticulitis

⇒ The lower white blood cells count and the higher CRP is suggestive of a longer duration of inflammation before admission. I added the explanation for this comment in the Discussion section as follows.

“The WBC level was decreased and the CRP level was increased in patients with appendiceal diverticulitis compared to those with acute appendicitis, suggesting that patients with appendiceal diverticulitis had a longer duration of inflammation at admission.”

<Comment>

This study have been undertaken to describe the CT findings of appendiceal diverticulitis and to determine if appendiceal diverticulitis can be differentiated from usual acute appendicitis using computed tomography. Results have been demonstrated that in patients who had undergone appendectomy, 9.7% had appendiceal diverticulitis. Patients with appendiceal diverticulitis had different clinical features and CT findings from patients with acute appendicitis. 1. In the discussion section the authors have been stated that “ . Second, our results revealed several clinical characteristics that may assist in the diagnosis of appendiceal diverticulitis, such as older age, longer duration of symptoms, higher rate of perforation, and higher incidence of localized abscess ” However these findings previously reported by other investigators. These are not new findings. Therefore the statement should be revised and these findings should be discussed. 2. Language needs minor revisions.

⇒ As suggeseted by the reviewer, It is true that several clinical features were previously reported by other investigators. However, these findings are very important in that our appendiceal diverticulitis patients had the same features

as the appendiceal diverticulitis patients reported in previous papers even though the incidence of appendiceal diverticulitis is much higher in our study. It is a kind of indirect confirmation of high incidence of appendiceal diverticulitis. Therefore, I have added "The clinical features of appendiceal diverticulitis in our study are quite similar to those in previous reports, providing further evidence that the incidence of appendiceal diverticulitis is higher than previously reported" in the Discussion section.