

Peer Review File

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**Reviewer A**

Article aimed at describing a risk score for complicated acute appendicitis and applying it to predict the outcome of exclusive medical treatment for acute uncomplicated appendicitis. Very well written article robust methodology, testing and validation cohort in the operated appendicitis population and a test application cohort to verify the success or failure of proprietary medical treatment in an acute appendicitis population. The paper is well written and interesting, some modifications could improve the manuscript.

**Comment 1:** The title must be changed, which does not reflect the case and does not reflect the predictive nature of complicated or uncomplicated acute appendicitis (as finally shown in the mini abstract).

**Reply:** We agreed with the suggestion of expert, and the title has already changed into “A risk score system for predicting complicated appendicitis and aid decision-making for antibiotic therapy in acute appendicitis”.

**Comment 2:** In the abstract, the authors state that antibiotic therapy is a feasible option for uncomplicated appendicitis - Are the CT scanners with intravenous injection or not. I would rather say: exclusive antibiotic therapy is a feasible option.

**Reply:** We thank the reviewer for the suggestion, and we have modified our text as advised. (see page 1, line 11)

**Changes in the text:** Exclusive antibiotic therapy is a feasible treatment option for uncomplicated appendicitis.

**Comment 3:** A CT slide of what a peri appendiceal fat stranding is could be useful.

**Reply:** We agreed with the reviewers and found that peri appendiceal fat stranding was a strong predictor of complicated appendicitis in this study.

**Comment 4:** In the methods section, the authors should tell us if the recruitment is prospective or retrospective.

**Reply:** We thank the reviewer for the suggestion to add more details of recruitment protocol, which we have modified our text as advised (see page 7, line 133) in revised manuscript.

**Changes in the text:** This study was a retrospective study, and data on patients' medical history, physical examinations and laboratory results were collected retrospectively by a case manager on a structured case record form.

**Comment 5:** In the methods section, the authors should give a reference for the antibiotic treatment. Did the authors take this schema from a randomized control trial?

**Reply 5:** We thank the reviewer for the suggestion to add reference for the antibiotic treatment, and we add two references in the revised manuscript. We mainly refer to the relevant system reviews of antibiotic treatment of appendicitis and the actual situation of the patient to formulate the antibiotic treatment schema.

**Comment 6:** It is not clear how the authors choose the weight for each variable of the nomogram, please explain.

**Reply 6:** Firstly, we found that age, duration of abdominal pain, shifting pain in the right lower quadrant, vomiting, peritonitis, TEMP, WBC count, CRP level, NEUT count, NEUT%, LY count, LY%, PLT count, ALB level, the NLR, appendix diameter, pelvic inflammation and PFS were associated with complicated appendicitis by univariate analysis. Secondly, multivariate Logistic regression results showed that PFS, NLR and CRP were independent risk factors for complicated appendicitis. Finally, the nomogram model was constructed using the rms package in R software and the risk score was calculated by nomogramEx package. See details in the article: 3.2 Nomogram construction and predictive performance (page:11, line183-196); 2.4 Statistical analysis page7-8:154-161.

**Changes in the text:** The nomogram model was transformed into a clinically applicable scoring system called the nomogram risk score by nomogramEx package. Page8, line:161.

**Comment 7:** How he makes the choice in this population of nearly 2000 patients for medical treatment or surgical treatment.

**Reply 7:** In our center, all patients were recommended for surgical treatment, and the final treatment schedule was determined according to the patient's wishes.

**Comment 8:** In the results section, among the 169 patients who had an antibiotic treatment, 23.7% underwent surgical drainage with or without appendectomy. The authors should give details on the indication for drainage without appendectomy in a non-complicated appendicitis whereas, as explain in the methods section, the first evaluation was performed 3 days after the beginning of the treatment. It is not clear.

**Reply 8:** In the Antibiotic therapy cohort, after 3 days of treatment, routine blood and CRP tests were performed. If the tests were normal, no further treatment was

administered; otherwise, the infusion was continued to reduce inflammation until the tests returned with normal results. Imaging examinations were immediately reviewed if symptoms and signs worsened during treatment (see page 6, line115-119).

### **Reviewer B**

The authors present a great study on appendicitis, with well described methods.

However, some points need to be clarified:

**Comment 1:** The nomogram used to predict uncomplicated appendicitis is not clearly described. If the entire nomogram is the figure 2, so it only includes PFS, CRP, and NLR. In this situation, the nomogram is based on biological and CT features, and no clinical aspect is used.

**Reply:** We thank the reviewer for the suggestion and the manuscript was revised. Firstly, we found that age, duration of abdominal pain, shifting pain in the right lower quadrant, vomiting, peritonitis, TEMP, WBC count, CRP level, NEUT count, NEUT%, LY count, LY%, PLT count, ALB level, the NLR, appendix diameter, pelvic inflammation and PFS were associated with complicated appendicitis by univariate analysis. Secondly, multivariate Logistic regression results showed that PFS, NLR and CRP were independent risk factors for complicated appendicitis. Finally, the nomogram model was constructed using the rms package in R software and the risk score was calculated by nomogramEx package. See details in the article: 3.2 Nomogram construction and predictive performance (page:11, line183-196); 2.4 Statistical analysis page7-8:154-161.

**Changes in the text:** We found that the proposed risk score system based on biological and CT features.....(see page 2, line 39; page 11, line 240; page 15, line 332 ).

**Comment 2:** Bowel obstruction is reported in the introduction as one of the complications of acute appendicitis. The occurrence of bowel obstruction in the series is not reported.

**Reply:** Thanks for the question raised by the reviewer. In our study, a total of 9 patients developed Th intestinal obstruction was occurred in nine patients (1.67%, 9/543), which was lower than reported in the literature, which may be related to the short follow-up time. Considering the duration of follow-up and the purpose of the study, the incidence of intestinal obstruction was not reported.

**Comment 3:** As a remark: The definition of complicated appendicitis is controversial. The authors have correctly stated this limitation in the discussion. The regional peritonitis could also be evaluated, but is also subjective.

**Comment 4:** The medical treatment can be quite aggressive. The authors do not state how the type of antibiotic therapy is chosen.

**Reply:** The conventional antibiotic treatment is the second or third generation cephalosporin + metronidazole or ornidazole. If the abdominal CT and laboratory tests indicate a more serious condition, the more aggressive antibiotic regimen will be selected (see page 5-6, line 111-114).

**Changes in the text:** The conventional antibiotic treatment is the second or third generation cephalosporin + metronidazole or ornidazole. If the abdominal CT and laboratory tests indicate a more serious condition, the more aggressive antibiotic regimen will be selected.

**Comment 5:** The efficacy of antibiotic therapy should be evaluated in patients receiving the same modality of medical treatment.

**Reply:** Thanks for the question raised by the reviewer. In this study, we found that the use of cephalosporin was associated with the success of antibiotic treatment (Table 4). The failure rate of cephalosporin or not were 19.3% (27/140) and 44.8% (13/29),  $P=0.007$ , respectively. However, the multivariate analysis showed no statistical significance (see Table 5).

**Comment 6:** The advantages of some antibiotics treatments over surgery can be questioned (duration of the treatment, the long-term effects, the selection of germs). Especially for uncomplicated appendicitis, with lower rate of postoperative complications.

**Reply:** We very much agree with the comments of reviewers. In our center, all patients were recommended for surgical treatment, and the final treatment schedule was determined according to the patient's conditions and wishes.