Author’s response to reviews

Title: Trends in Diagnostic Approaches for Pediatric Appendicitis: Nationwide Population-Based Study

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Version: 1 Date: 27 Jan 2017

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Reply to Editors and Reviewers

The authors thank the editors and the reviewers for the comprehensive review and valuable comments in our manuscript. We have revised the manuscript based on the reviewer’s suggestions. The revised and added contents in the revised manuscript are underlined.

Reply to reviewer’s queries

(1) Reply to reviewer 1

Reviewer #1: I would like to thank the authors for submitting this article for publication. The article is well written, and highlights utilization of diagnostic imaging over a 9-year period and trends in non-perforated and perforated appendicitis in children. The major flaw of this study is the lack of clinical and demographic information which is key to the incidence of the main outcome- perforated appendicitis. Even though this was addressed in the discussion as a limitation, it is still very relevant to the evidence presented by the authors for publication. I have outlined my concerns in the points below.
1. Results section; Table 1:

Q1- How were the age groups determined? is there any rationale behind selecting 3 age groups vs 2, or for the ages used for each group? is there historical literature which informed this categorization? categorizing data into smaller groups increases the likelihood of finding a significant association purely by chance. was there any statistical correction used to adjust for this? this was not stated in the methods.

Answer: Thank you for your question. There was no historical literature which informed this age categorization. Previous reports mentioned that even with advances in ultrasound and computed tomography, perforation rates in children under 6 years of age were reported to be 54%~74% over the last 3 decades (stated in the introduction section). we hypothesize that there is possible correlation of age factors in the perforation of pediatric appendicitis, the study evaluate the correlation between age and perforation in pediatric appendicitis by categorizing the patients into three age groups. The results of the study confirmed our hypothesis. We added the above description in the Methods section (underlined at line 99-100, page 6).

Q2 do you have any data on socio-economic status, access to healthcare/insurance information, duration of symptoms, presenting complaint/physical signs? this important information was not provided in the baseline characteristics table.

Answer: Thank you for your valuable opinions. The database (the Collaboration Center for Health Information Application) in the study did not provide the socio-economic status, duration of symptoms, and presenting complaint/physical signs. Most medical expenses are covered by national health insurance in our country, therefore socio-economic factor is relatively less relevant in the current study. We added description in the Discussion section (underlined at line 210-219, page 12)

2. Results section, line 142-145: higher rates of perforated appendices were detected among patients between 7 and 12 years old and < 6 years old, compared to those aged 13-18 years.

The trend seen with higher incidence of perforation in the younger age groups is not surprising, given that younger children are less able to express symptoms, can have atypical signs and may have a longer duration of symptoms prior to presentation. unfortunately this important information- duration of symptoms is unavailable and is likely a major confounder that was not adjusted for in this study.

Answer: Thank you for your valuable question. We fully agree with your point of view about the hypothesis of higher perforation rate in younger age group and the duration of symptoms is a major confounder in this study. The database of the study did not provide the information of the duration of symptoms. The added description was shown in the Discussion section (underlined at line 210-219, page 12)
3. Results section, line 139-145: The authors highlight a significantly increased odds of perforation if you were diagnosed by CT (OR 2.744; 95% CI 2.55,2.95; p<0.001) or by US and CT (OR 5.062; 95% CI 3.14, 8.17; p<0.001) compared to patients without radiologic evaluation. Only age and gender were adjusted for in this analysis. Important clinical information such as duration of symptoms and latency period (lag time from clinical suspicion to definitive diagnosis by US or CT) were not available nor adjusted and may be major confounders in this analysis.

Answer: Thank you for your valuable question. We agree that the duration of symptoms and the latency period of imaging studies (US or CT) are two major confounders in this study. The database of the study did not provide the information of clinical symptoms (including the duration of symptoms), the time from clinical suspicion to definitive diagnosis by US or CT can’t be adjusted and analyzed. Future studies collaborating with other medical centers are expected in order to obtain more detailed clinical data for further analysis. We added description was shown in the Discussion section (underlined at line 220-221, page 12).

4. Results section, line 129-130: the incidence of perforated appendicitis cases remained relatively stable at 0.024%~0.023% from 2003 to 2012 - it is interesting that the increased utility of US and CT did not affect the outcome of perforated appendicitis over the study period, but the incidence of non perforated appendicitis reduced. what do the authors think is responsible for the stable perforated appendicitis rates? this was not addressed in the discussion section.

Answer: Thank you for your question. The increased utility of US and CT did not affect the outcome of perforated appendicitis over the study period, but the incidence of non perforated appendicitis reduced. The reason may be that those patients with suspicious appendicitis without US or CT confirmation may underwent negative appendectomies. If those patients received either or both study, the negative appendectomies may be avoided. We added the description in the Discussion (underlined at line 186-189 of page 11).

5. Results section, line 135 - 137: The percentage of patients proceeding to appendectomy without evaluation of US and CT gradually decreased from 97% in 2003 to 79% in 2012- what is the hypothesis for the increase in diagnostic imaging utilization over the study period? change in national guidelines? increased availability of imaging services at health centers? improved healthcare access for the population in general? this was not addressed in the discussion section.

Answer: Thank you for your valuable opinions. It is a trend to use US or CT examination to assist the diagnosis of appendicitis in children in these decades. In our country, majority of the hospital or medical center use US and/or CT to diagnose pediatric appendicitis. We added description in the discussion section (underlined at line 172-175 of page 10).

6. Discussion section, line 179: the authors infer that latency from clinical suspicion to confirmation of diagnosis by CT or US may increase the risk of appendiceal perforation- while this may hold true, this information was not collected so it cannot be determine if this indeed is the case. in addition, other potential confounding variables such as duration of symptoms and
clinical signs were not adjusted for in the analysis so the incidence of appendiceal perforation may not be solely due to a prolonged latency period.

Answer: Thank you for your kind suggestion. We not yet able to collect the exact data of waiting time for the US or CT examinations, but both examinations require scheduling and waiting time, that should hold true in most circumstances. We added description in the Discussion section (underlined at line 195-199, page) and also added further description in the Methods section based on the other reviewer’s suggestion (underlined at line 107-114, page 7).

(2) Reply to reviewer 2

The authors investigated benefits of different methods for diagnosis of pediatric appendicitis in Taiwan on a large patient’s sample.

Overall very nice study.

Although the study is well designed and written, there are some objections that needs to be corrected before possible publication:

1. Methodology - Please include a chapter with hypothesis, primary and secondary outcome measurements.

Answer: Thank you for your valuable opinion to improve our manuscript, we added the description of the measures of primary and secondary outcome in the Method section (underlined at line 107-114, page 7).

2. Results - What was the rate of negative appendectomies in this study? Please include graph with rates of negative appendectomies during study period. That might be one of important findings and possible explanation of previous findings. Probably at line the number of negative appendectomies nowadays is lower than before 10 years.

Answer: We agree with your good point of view. Unfortunately, the clinical information about negative appendectomy is not available from the database of the study. This is beyond the scope of current study because negative appendectomy has no suitable ICD-9 to match; a future longitudinal study is needed to clarify such relationship. We added description of the above information you highlighted (underlined at line 221-225, page 12)

3. Discussion - The authors found that the incidence of non-perforated appendicitis significantly decreased over the study time course and the rate of perforations remained relatively stable at 0.024 %~0.023% from 2003 to 2012. This is one of the main findings and there is no explanation for this in discussion. Please discuss what was possible reason for decreased incidence of non-perforated appendectomies were. Is it because of higher percentage of using of imaging studies?

Answer: Thank you for your question. We added description in the Discussion section (underlined at line 186-189, page 11).