Author’s response to reviews

Title: Unenhanced multidetector computed tomography findings in acute central pulmonary embolism

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Author’s response to reviews:

Editorial Office

Dr. Frank G Zöllner
BMC Medical Imaging
RE: Manuscript ID: BMIM-D-18-00028

Dear Editor, BMC Medical Imaging

Thank you for your reviewing our manuscript entitled “Unenhanced multidetector computed tomography findings in acute central pulmonary embolism”, and for the valuable reviewer comments. We have read the comments carefully, and revised the manuscript based on their suggestions. All changes to the text are indicated in “track-changes” and our list of responses is below.

We are very grateful for the opportunity to submit a revised manuscript, and we hope with these changes you find our revised manuscript acceptable for publication in your journal.

Looking forward to your next correspondence.

With best regards,
Response Letter:

Technical Comments: Formatting Changes:

1. Please rename "Introduction" as "Background" in the article section.

*Response: We have renamed the section to “Background” accordingly.

Reviewer reports:

Ernest Ekpo, Ph.D (Reviewer 1): General comments: This resubmitted paper sought to assess the diagnostic performance of non-enhanced MDCT for pulmonary embolism. A major limitation is the sample size. The regression analyses do not well capture the aims of the work, and the discussion needs some work.

Abstract:

Background: good

2. Methods: last sentence change "predict" to a more suitable word. "Predict" in this sentence means there is no PE yet, but "MDCT shows that there will be PE in the future"

*Response: Thanks you for pointing out this inappropriate word. We have changed the word from “predict” to “detect” in the revised manuscript.

3. Results: The second and third sentences need to be revised to enhance clarity. E.g. MDCT had a sensitivity of 71.9% and specificity... when there was high attenuation embolus in the PA... How was the Wells scores assigned?

*Response: We have rephrased the sentences to highlight the finding of the overall performance of MDCT. The Wells scores were calculated using data extracted from medical records by
previously described methods prior to the imaging analysis [ref 20], and we have indicated this in the “Methods” section of the revised abstract.

4. Why report performance for emboli in PA alone MDCT? It would be better to report the sensitivity and specificity of MDCT for each of the features of PE defined in the methods or present the overall performance of MDCT regardless of the features. Last sentence in the results requires a revision.

*Response: Thank you for the suggestion, in the revised abstract, we have added the sensitivity and specificity of MDCT for each of the features. The performance of MDCT regardless of the feature (given any one or more positive findings on unenhanced MDCT) were also added to the revised Table 3. In addition, the typo of the last sentence has also been revised.

5. Line 42: This is not a prediction study, it is a diagnostic performance study. Please change the word "predicting" to a more appropriate word

*Response: Thank you for pointing out this inappropiate word. We have changed the word from “predicting” to “detecting”.

6. Introduction: A better rationale is needed. What are the limitations of these few studies that necessitate further studies? What is the relevance of identifying the most sensitive MDCT criteria for the diagnosis of PE on MDCT?

*Response: In order to better layout the rationale, we have revised Introduction of the manuscript, and describe it below.

Currently, the diagnostic strategy of pulmonary embolism (PE) mainly evaluates the hemodynamic status first, and then predicts the possibility of PE by the clinical risk assessment system (Wells score or Geneva score). Wells score and revised Geneva score can be used to rule-out the non-PE patients, but cannot be used for definitive PE diagnosis. After confirmation of PE or ruling out non-PE patients using hemodynamic and clinical risk assessment test, the suspected PE patients may perform radiological assessment using multi-detector contrast-enhanced computed tomography angiography (CTPA), which is the gold standard for the imaging diagnosis of PE. However, excessive use of CTPA may result in excessive radiation exposure. Therefore, unenhanced multi-detector CT (MDCT) has been used as an alternative approach to quickly obtain images for PE diagnosis. Previous published studies focused on high-attenuation emboli in pulmonary arteries, but did not compared the other unenhanced MDCT features, i.e., main PA dilatation > 33.2 mm, and peripheral wedge-shaped consolidation individually or assessed as a whole. In this study, we evaluated the diagnostic performance of unenhanced MDCT in a multi-component strategy.
7. What is the essence of comparing MDCT to Wells score when you have clearly established that Wells Score is not a good tool for the diagnosis of PE?

*Response: In clinical situations when gold standard CTPA is inaccessible or contraindicated, Wells score may be the sole or one of the few tools at hand to assess the probability of pulmonary embolism. Hence, we compared unenhanced MDCT findings to Wells score to show the likely clinical benefit of unenhanced MDCT in this setting.

Methods:

8. The sample size is very small

*Response: Thank you for the comment. We agree that the current sample size is not very large, but this study was designed to demonstrate the performance of unenhanced MDCT for diagnosing PE compared to gold standard CTPA. Although the patient numbers are not very large, the results of this study did prove unenhanced MDCT is an alternative for the diagnosis of PE. We acknowledge further studies with larger sample size is necessary, and have included this in the limitations section of the revised manuscript.

9. P4lines 82 is redundant. There is no relevance in stating the capacity of the hospital.

*Response: In the revised manuscript, we have removed these irrelevant information accordingly. Page 5, Methods section, Patient subsection.

10. I am not quite sure how regression analyses fit these data.

*Response: We adopted the regression analyses to evaluate the association of findings on unenhanced MDCT with diagnosis of PE. Furthermore, as Wells score is used generally before radiological assessments for PE, and the multivariate analyses showed the associations found between MDCT findings and diagnosis of PE were independent of Wells score and patient characteristics. We have revised the “Statistical analysis” section by elaborating the reason for performing regression analyses.

11. Regression analysis examines which of the independent factors contribute to the dependent variable. Using the word predict PE, sounds like MDCT features contribute or are predictors of PE.

*Response: Thanks again for pointing this out. We have changed the word from “predict” to “detect”.
12. Again, it is unclear what the multivariate analyses were for. Is it to establish how age and sex predict Wells Score? If so, are they determinants of Wells Score? The ORs aren't relevant. I would suggest a simple diagnostic performance study focusing on sensitivity, specificity, PPV, PNP, PLR (Positive likelihood ratio), NLR (negative likelihood ratio).

*Response: In this study, regression analyses was used to evaluate the association of findings on unenhanced MDCT with diagnosis of PE in order to select the most relevant finding for entering the ROC analysis. We would like to point out that diagnostic performance results of sensitivity, specificity, PPV, PNP, were present in Table 3. In the revised Table 3, PLR and NLR are added as suggested by the reviewer.

Results:

13. P7Line153-q54: Rephrase, the p-value reported shows no significant difference between ages of individuals with and without a PE

*Response: Thank you. We have rephrased the sentence accordingly in the revised manuscript. Please refer to Results section, Paragraph 1, Sentence 2.

14. P8line 175: provide the exact cut of point and describe what it means.

*Response: We have defined the optimal cut-off point as “the number of findings on unenhanced MDCT ≥ 1”. This means the performance of MDCT for a diagnosis of PE given any one or more positive findings on unenhanced MDCT regardless of the features, the sensitivity was 96.9% (95% CI: 83.8%, 99.9%) and specificity was 71.9% (95% CI: 53.3%, 86.3%). Please see the revised “Results” section, Paragraph 4.

15. P8L181: See previous comment. Why are you comparing MDCT to a method (Wells Score) that you have acknowledged to have significant limitations? Again, saying that AUC represents "predictability" is incorrect. AUC is a global measure of performance of the tool, which in this case is the ability of MDCT to detect PE, not predict PE. Detection and prediction are two different things. For the purpose of this study detection is a better term. Detection is ability to identify the presence of PE; Prediction is the ability to forecast PE

*Response: As previously described, we compared unenhanced MDCT with Wells score as the latter may be one of the few available tools for the physician to rely on when CTPA is not accessible or appropriate to diagnose pulmonary embolism.

The word “predict” has been changed to “detect” in the “Results” section as in other parts of the revised manuscript.

Discussion:
16. This needs to be thoroughly reworked. This section mainly provides a quantitative summary of the results and compares their findings to other studies. There is no discussion about the qualitative meaning of these results, what this has added to the existing literature, the implications of the findings and their relevance to patient, and this should influence policy and practice.

*Response: Thanks for the referee’s comments. In response to this and the following comment, we have emphasized more on the qualitative aspects of our findings in the 2nd paragraph of “Discussion”.

17. P9185-187: provide a qualitative summary of the results instead of restating the quantitative results

*Response: In the revised 2nd paragraph of Discussion section, we have highlighted the qualitative aspects of our findings and the clinical relevance it may bring to current practice. Nevertheless, the present study is a retrospective study, and further confirmation is required to advocate for implementation of the multi-component unenhanced MDCT strategy.

18. References: There are a few factual statements that should be supported with the appropriate references.

*Response: Thank you for the comment. We have rewritten parts of the introduction and discussion paragraphs in this revision, and at the same time reviewed the supporting references cited. If there are oversight, please direct us specifically to where the supporting citations are required.

Tables: Fine

Figures: Fine

Klaus Irion, MD, FRCR (Reviewer 2): The authors present a manuscript on non-enhanced CT scan of the chest for the diagnosis of acute central pulmonary thromboembolism.

The authors defined acute central embolism as a clot in the main right or left pulmonary artery.

The paper is well written and the topic is interesting. The presence of enlargement of the pulmonary artery and increased attenuation of the pulmonary artery in the non-enhanced scan have shown a specificity of 100% for pulmonary thromboembolism, with a modest sensitivity (72%). As per the authors, the AUC was much larger than that of a Wells score.
The ethics committee approved the study and the consent was waived (retrospective analysis). The authors informed that their CTPA protocol include a pre-contrast phase, an arterial phase and a venous phase scan.

The figures are appropriate.

The references are pertinent to the study.

19. I would suggest minor changes to the conclusion, as per below:

"Non-enhanced MDCT has shown better performance than Well's score for confirming acute thrombi in the main right or left pulmonary arteries, but cannot rule out pulmonary thromboembolism."

*Response: Thank you for this valuable suggestion. In the revised manuscript, we have incorporated the suggested change to the conclusion section.*