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Name of journal: World Journal of Radiology

Manuscript NO: 38129

Title: Magnetic Resonance Angiography for the Primary Diagnosis of Pulmonary Embolism : A Review from the International Workshop for Pulmonary Functional Imaging

Reviewer 1 Comments

Comment 1: I also suggest to add the discussion regarding weakness of MRA and CE-MRA.

Our response:

We added the following to the discussion:

Weaknesses of MRA (Added this to the discussion per Reviewer number 1 comment number 1)

There are limitations for the use of MRA for the primary diagnosis of pulmonary embolism. First, this modality should not be used for unstable patients. Second, patients with allergies to gadolinium based contrast material should only be imaged if there is no access to MDCT or Ventilation Perfusion scanning, and only then after premedication with steroids for 24 hours and Benadryl. Third, small children or adults that are unable to hold their breath, or hold still, for the 13-20 second MRA are poor candidates for this exam. Fourth, readers experienced with the interpretation of MRA for pulmonary embolism are needed to ensure that the correct diagnosis is reached in these exams. Fifth, up to date MRI hardware (high performance gradients and multicoils) and software (rapid k-space sampling and accelerated image acquisition) are needed to allow for the acquisition of 3D MRA exams with nearly isotropic voxels. There is noise associated with the rapid switching of the gradient coils that may bother some patients if there is not adequate hearing protection (Reviewer 1 comment 2).

Comment 2: It is often difficult for some elderly patients that I treated to experience the noise produced by MR. Is there any evidence?

Our response:

There is noise associated with the rapid switching of the gradient coils that may bother some patients if there is not adequate hearing protection (Reviewer 1 comment 2).

May 25, 2018

Fang-Fang Ji

Science Editor, Editorial Office

Baishideng Publishing Group Inc

Dear Fang-Fang Ji,

Thank you for your recent letter (email) of May 24, 2018 regarding Review Manuscript 38129.

Each comment from your letter is numbered and immediately below each numbered comment is our response and its location in the revised manuscript.

Comments:

1. In the abstract, the authors mention that outcomes data on V/Q scan show they are effective alternatives. V/Q scans are not the major focus of the manuscript, and discussion of these tests is primarily to show how they compared to CTA or CE-MRA. I don't believe there is any discussion of patient outcomes regarding V/Q scan in the manuscript. Therefore, I would recommend removing this mention from the abstract.

Our response- We have removed V/Q scanning from the abstract.

2. In the introduction, the authors provide appropriate use ratings for different imaging modalities according to professional society guidelines. I would recommend providing a definition for these ratings. For instance, is 2/10 good or bad?

Our response page 8- We have added the following sentence in the introduction to clarify this issue: "(where 10/10 is the highest value for appropriateness)"

3. In the discussion of the PLOPED study, the authors mention a high rate of technically inadequate studies. Is this thought to be an issue with the centers or the imaging modality itself?

Our response page 12: "The low rate of technical adequacy was likely related to the site-specific training and volumes for this multicenter trial where the sites that did the most subjects had better overall technical performance."

4. On page 8, the authors discuss a trial of acenocoumarol in VTE. This is an extremely old trial in a small number of patients, and I think the authors' interpretation are somewhat flawed. We commonly treated VTE with oral anticoagulants, and heparin is not absolutely necessary. I recommend using more contemporary trials or perhaps eliminating this discussion altogether, as it somewhat deviates from the point of the manuscript.

Our response: We have deleted this section of the discussion on treatment using acenocoumarol and the associated reference.

5. On page 9, the authors mention that CE-MRA is useful for follow up scans on PE. Follow up scans are not routinely performed and not recommended in guidelines. Therefore, I'm not sure this can be considered a strength of CE-MRA.

Our response: We respectfully disagree with this reviewer comment. There are frequent cases in our multi-institutional experience where known VTE patients under treatment or having just finished treatment get reimaged with CTA or MRA to determine if new PE are present causing new chest pain. We have left this statement in. Most of the authors of this work are Fleischner Society members with more than 30 years of experience in this area. This is a review and reflects our opinion in this matter.

6. On page 10, the authors mention a much lower inadequate study rate in a University of Wisconsin study compared to PIOPED. The criteria for an inadequate study in the retrospective study are very different from that of PIOPED, and I think this should be acknowledged in the discussion.

Our response page 15: "This improvement in technical success likely reflects the maturation of CE-MRA methodology since the time of the PIOPED III scans nearly a decade ago (2006-2008). In addition, this improvement may be related to the fact that lack of visualization of the subsegmental pulmonary arteries was not a criterion for determining the presence of a limited examination. Thus, our criteria for an inadequate study are less strict than those that were used for PIOPED III. This may account for some of the differences in reported technical adequacy for these two studies."

7. I concede CE-MRA can be useful in patients with renal insufficiency and contrast allergies. However, I'm not sure why it should be considered at all in patients with a low-to-intermediate pretest probability and negative D-dimer. The guidelines the authors cite state this would be an inappropriate test. CE-MRA is much less available

than CTA and is more costly. Awaiting such a study would typically lead to a longer emergency room or hospital stay. Importantly, it's not clear why such patients need contrast-enhanced imaging at all. I do not think the authors make it clear why CE-MRA is appropriate in this specific patient population. I think this discussion should be expanded. Alternatively, the authors could focus on other patient groups where this imaging would be useful.

Our response on page 28: CE-MRA can be considered as an alternative to other testing modalities that are available, not a complete replacement. We have expanded the discussion as follows. "While CE-MRA is a similar cost to CTA at our institution, some extra considerations need to be weighed before ordering CE-MRA. First, this is not a widely available method and each institution will have to determine their expertise at performing this in a clinical setting before it can be ordered in a patient. Second, careful patient selection is critical for a successful test. Those patients that are short of breath are not good CE-MRA candidates. Third, the wait times for CE-MRA are longer than CTA at our institution as CTA is so much faster to perform. Fourth, in a low to intermediate risk population it may be appropriate not to image this group, if the clinical decision rules have a low pretest probability of PE."


We hope that these responses meet with your approval for publication.

Sincerely yours,

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