Dear Editor,

# Re:Point-of-care ultrasound for critically-ill patients: A mini-review of key diagnostic features and protocols

We are grateful for the review and responses. Please find enclosed the point-bypoint replies, in black font. We have amended the paper according to the reviewers' comments and we hope it improves the quality of the content.

Yours faithfully Yie Hui <u>Lau</u> Kay Choong <u>See</u>

Reviewer 1 (03342506): Scientific Quality: Grade B (Very good) Language Quality: Grade B (Minor language polishing) Conclusion: Minor revision Reviewer comments: In this mini-review the authors review current diagnostic modalities of point of care ultrasound particularly highlighting thoracic ultrasound in the form of cardiac and lung ultrasound. They also outline multiple ultrasound protocols for evaluation of various common pathologies seen in critically ill patients. For the highlighted modalities, they review sensitivities, specificities, various other statistical considerations, utility, and limitations. Understanding the space constraints of mini-review the following suggestions should be considered prior to acceptance for publication in the journal

1) While the thoracic (lung and heart) ultrasound is important, most emergency physicians and many critical care physicians use POCUS to examine abdomen (i.e. FAST exam) looking for free fluid, hydronephrosis, focus of infection). Its unclear why this was omitted.

We have included FAST and outlined possible findings in abdominal ultrasound in the text, and examples in Figure 3.

2) The introduction includes a reference to point of care ultrasound filling a void in order to reduce diagnostic uncertainty. There is not but likely should be some reference to how point of care ultrasound can increase diagnostic uncertainty and potentially even harm in the wrong hands.

The reference has been added and the caution about potential harm is included in the revised manuscript.

3) The tables nicely organize the applications of lung and cardiac ultrasound and then the associated protocols. Some of the protocols and modalities are included with statistical data (sensitivity, specificity, AUROC, etc.) while others are not. It is not clear why. Some consistency may be helpful here in addition to fulfilling the goals of the mini-review as outlined in the authors' abstract and introduction.

We have revised the statistical data of the tables to be more consistent.

4) Basic critical care echocardiography: • The authors mention 4 echocardiographic views but do not outline what those 4 views are. It might be worthwhile to emphasize that the majority of findings in this category require advanced skill and image acquisition that might require all 4 of those views and even then would require interpretation with caution. Wall motion abnormalities and hypokinesis are not mentioned in this introduction section but are mentioned and explored under certain pathologies

We have outlined the 4 views in the first paragraph of this section, listed wall motion abnormalities, and the emphasis that skill is required to complete the assessment.

• Pericardial effusion – Sensitivity/specificity do not reference which view or window.

We included the views for the sensitivity/specificity is described in the reference. The authors might also consider discussing how limited views may influence such sensitivity and specificity depending upon the amount of fluid present.

We included this under "Limitations"

- Tamponade IVC evaluation may be limited by PPV/mechanical ventilation. This may be a worthwhile limitation to emphasize especially if the cited references do so. Expanded on, with references added
- RV strain Diameter and longitudinal measurements should specify where measurements should begin and end.

We have included the measurements, with references.

Moreover, RV strain is somewhat unusual term, in basic CCUS RV function and in particular RV size are more often used then the term "RV strain".

We have edited "RV strain" to "right ventricular dilatation and dysfunction". Limitations might include a mention (and appropriate reference) of the difficulty in obtaining adequate RV views in critically ill patients.

Included under "limitations"

- LV dysfunction Many studies have demonstrated that even trainees with limited education regarding assessment of LV function are able to estimate mild, moderate, and severe reductions in LVEF. (example: J Am Soc Echocardiogr 2011;24:1319-24). Included under "clinical utility" with reference.
- IVC diameter It may be prudent to discuss that accuracy of measurement depends upon the angle of insonation (given the cylindrical nature of the structure being evaluated).

Included, under "Limitations"

- 5) Lung ultrasound: A line A-pattern in diagnosis and exclusion of pulmonary embolism is misleading as currently discussed. It may be worthwhile to outline this in regards to large pulmonary embolism but certainly not all pulmonary emboli. Included discussion about how it may be different for smaller, peripheral pulmonary emboli under "Limitations"
- Pneumothorax Given the table includes a portion outlining "during M-mode" it might be helpful to include a subheader for "during b-mode" as well.

## Edited accordingly

• Occult pneumothorax – It might be worthwhile to outline or clarify "absent lung sliding plus the A-line sign".

### Explanation included in the "features" column

• B-profile – Currently the authors to not further clarify that false-positive "comet tails" may be present but not fully obliterate A-lines. Furthermore, there is currently no reference to false positives at all and no discussion of pathology other than acute pulmonary edema that can contribute to a B-line pattern.

Updated accordingly to include other differentials

- Consolidation The authors do not discuss atelectasis as a potential false positive. Included in the revised manuscript
- Pleural effusion Similar to the section on pericardial effusion, this portion would likely benefit from further discussion of how ultrasound can characterize a pleural effusion (septations, debris, homogeneous vs. heterogeneous, etc.) It may also be worthwhile to discuss false positives and limitations given the potential procedural complications that can arise pericardial effusion, elevated hemidiaphragm, in appropriate diaphragm visualization and mistaking effusion for subdiaphragmatic ascites, loculated effusions may be missed or misjudged with inadequate scanning. Included under "Clinical Utility" and "Limitations"
- 6) POCUS protocols This table seems overly ambitious and the result is ultimately confusing. This information may be better evaluated and outlined if the authors chose more specific comparators and discussed why the particular protocols were chosen for review. Furthermore, there are many protocols (as referenced in Tavares et al. DOI 10.2147/OAEM.S199137 that are not included or discussed. The protocols do not seem to be listed in a particular order.

We have organised the protocols based on the types of modalities used, and they are further arranged in alphabetical order.

• BLUE protocol is missing the year described.

The year has been included.

PLAPS acronym is used but not defined in the table description or elsewhere in manuscript.

Added to the table legend.

- FALLS protocol bullet point #3 of limitations is confusing. The protocol is also listed twice in the protocols table. Revised.
- SESAME Would have the authors clarify if there are proposed or suspected limitations to the limited view of the femoral vein (as isolated lower femoral vein or "V-point" evaluation does not evaluate for VTE as extensively as other VTE protocols do. Highlighted the difference and included in the discussion and cited justification for this in the "limitations column"
- VExUS does not have the year described outlined.

#### Amended.

It may be worthwhile to discuss the limitations or benefits in cirrhotics (given the extent of hepatic and portal vein evaluation).

Included limitations and references.

It may also be worth discussing that this modality involves difficult/complex image acquisition and measurements.

Included.

- ASE protocol is referenced later in the manuscript but not included in this table. Included.
- 7) Future directions and research: The authors nicely outline the drawbacks of attempting to study the impact of POCUS on critically ill patients especially in reference to an evasive and markedly confounded outcome such as mortality. Their discussion of AI in POCUS is provocative, interesting, and limitations are outlined. They appropriate emphasize the need for comprehensive evaluation and formal confirmation of any abnormalities found during POCUS.
- On POCUS utility in cardiac arrest, the authors might also discuss and possibly provide further references on the use of POCUS in elucidating the underlying etiology of shock or arrest (tamponade, RV failure, thrombus-in-transit, etc.). Included in text, with references
- The authors may want to consider how institutions or societies might work toward protocolization of POCUS in intensive care unit while considering infrastructure and local resources in the process of choosing (especially considering the wide array of protocols and the fact that they will never see head-to-head study or standardization of included devices, etc.)

#### Included a this in the discussion section.

• Hand-held POCUS as an extension of physical exam (i.e. stethoscope) is becoming more popular. It would be worthwhile to have a separate paragraph discussing the role, pitfalls and future opportunities, particularly if POCUS is integrated with structured assessments such as ACLS, ATLS, CERTAIN

# Included in text, with pitfalls and opportunities, with references

Reviewer 2 (02446627): Scientific Quality: Grade B (Very good) Language Quality: Grade A (Priority publishing) Conclusion: Minor revision Dear Authors: I like to thank the authors for addressing this important and the current issue. The POCUS is now replacing the stethoscope in the ICU. This review addresses and serve as a quick review for the findings and the sensitivity and specificity of the findings. The tables are very informative and can serve as a source for quick revision. Would suggest following edits Add the references to certain place as marked in the manuscript Add a separate column in the table and on the side of the findings put and image with the arrow showing that findings. That will be an excellent edition to the manuscript

- Included POCUS features and images separately in Figures 1,2 and 3

Editor Comments: 1 Scientific quality: The manuscript review current diagnostic modalities of point of care ultrasound particularly highlighting thoracic ultrasound in the form of cardiac and lung ultrasound. The topic is within the scope of the WJCCM. Scientific Quality: Grade B (Very good), Grade B (Very good) Language Quality: Grade A (Priority publishing), Grade B (Minor language polishing) Conclusion: Minor revision, Minor revision (1) Classification: Grade B (2) Summary of the Peer-Review Report: The review was conducted by 2 reviewers. Detailed comments of the reviewers are mentioned above 3) Format: There are three tables

and No figures. (4) References: A total of 49 references are cited, including 21 reference published in the last 3 years.

This is been expanded to include more references relevant to the revisions made. (5) Self-cited references: There is one self-citation; The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper selfcitations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated. Reference 22 needs to be corrected. (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorial office@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Grade A (Priority publishing), Grade B (Minor language polishing). No language editing certificate was provided, as the authors are native English speakers. 3 Academic norms and rules: The authors did not provide the Biostatistics Review Certificate (not needed), the STROBE Statement are not not needed, the Institutional Review Board Approval Form is not needed, as the manuscript is a minireview. Written informed consent is not needed. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJCCM. 5 Issues raised: (1) The authors should follow the recommendations of the reviewers. (2) reference 22 need to be corrected 6 Re-Review: Required. 7 Recommendation: Minor revision with conditional acceptance.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good) Reference 22 (now 33) has been corrected