Reviewer’s report

Title: Lung Ultrasound Guided Fluid Management Protocol for the Critically Ill Patient: study protocol for a multi-centre randomized controlled trial

Version: 0 Date: 30 Jan 2019

Reviewer: Robin McKinney

Reviewer’s report:

SUMMARY. - Grigoras et al submitted to TRIALS a manuscript detailing the research protocol of a randomized controlled trial entitled " Lung Ultrasound Guided Fluid Management Protocol for the Critically Ill Patient: study protocol for a multi-centre randomized controlled trial". The problem addressed by this trial is the fluid overload frequently seen in patients admitted to the ICU after fluid resuscitation. They plan to use lung ultrasound to assess volume status and guide fluid resuscitation or fluid removal with diuretics based off of the results of the lung ultrasound. Their hypothesis is that lung ultrasound guided fluid management will lead to lower mortality than standard care. This is a clinically significant outcome. Trial status: patient enrollment in the trial started in November 2017 and is expected to end in October 2019.

MAJOR COMPULSARY REVISIONS

ABSTRACT (< 350 words). - The list of keywords must be moved to the end of the manuscript.

METHODs

The objectives paragraph should be stated in the introduction. The objectives of the study should not be stated in the methods section. The procedure that will be performed should be laid out in a step by step fashion.

The settings section: The rationale for the sites chosen does not need to be stated.

What will the composition of the fluids used for resuscitation be? Crystalloid? Colloid? Blood products? If the composition of the fluids is left to the discretion of the treating physician in both arms of the study this should be stated. Or if they are controlled please elaborate on this.

Sample size calculation:

Last sentence starting "In our opinion…" is not needed.

Strengths and Limitations of study
Given the risk of protocol non-compliance will you analyze the data on an intention to treat basis?

* I agree with the investigators that this RCT cannot be blinded. Did they take any measures to prevent bias related to an unblinded intervention?

* End Points and Main Outcome Measures. - When is a patient considered to have completed the study? What is the end point for each individual patient?

MINOR ESSENTIAL REVISIONS (not for publication)

Study Interventions: You do not state what time of day the follow up LUS will be performed. Will they be performed at set times, or at set intervals from the first ultra sound?

Keywords. - Three to 10 key words chosen according to the list of Medical Subject Headings (MeSH) provided by the Index Medicus must be added. Please, add, "randomized controlled trial".

References.

The references must be formatted according to the editorial standards of the journal TRIALS.

* In the body text, references must be reported with plain text and between brackets; thus, they must look like [1-3] rather than [1] [2].

* The list of authors must be ended by a colon ( : ) rather than a period ( . ) (all references).

* The title must be printed in bold characters.

* The name of the journal must be in italics (all references).

* No dot at the end of a journal name (all references).

* Put a comma after year of publication (example: 1999, 200:149-170).

* Volume must be printed in bold characters.

* Delete number of issue (many references).

CONCLUSION.

I worry that assessing the fluid status of ICU patients once a day will not be sufficient to categorize and evaluate patients sufficiently given that fluid resuscitation and volume status can
rapidly change over 24 hours in the ICU. A patient found to be fluid neutral by ultrasound can quickly progress to fluid overload prior to the next ultrasound. Conversely, a patient started on diuretic therapy could be quickly progress to intravascular depletion if they have a robust response to diuretics.

* The study is relevant: objective assessment of fluid status in ICU patients is needed and of utmost importance.

* The research question is clear: can LUS improve outcomes by monitoring fluid status in the ICU.

* The design of the study has flaws as enumerated above and acknowledged by the authors themselves. The heterogeneity of the patient population enrolled may make detecting a difference between the two groups difficult as will individual physician non-compliance with the protocol.

I believe that this manuscript is almost ready to be published. It can be considered for publication if the editors of the journal Trial considers that this paper is of interest for his readership.

**Level of interest**
Please indicate how interesting you found the manuscript:

An article of importance in its field

**Quality of written English**
Please indicate the quality of language in the manuscript:

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All images and figures within the manuscript should be genuine i.e. without evidence of manipulation. No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. If you have concerns about the veracity of the figures you should choose the first option below.

**Statistical review**
Is it essential that this manuscript is seen by an expert statistician? If so, please give your reasons in your report.

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