ARTICLE DETAILS

TITLE (PROVISIONAL)  Developing a magnetic-assisted-POCUS guided bronroscope among patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomized controlled study

AUTHORS  Tian, Yuan; Fei, Yuda; Bing, Bai; Cui, Xulei; Zhang, Yuelun; Wang, Chunrong; Chunhua, Yu; Huang, Yuguang

GENERAL COMMENTS

I’ve read with interest the manuscript entitled “Developing a magnetic-assisted-POCUS guided bronchoscopy among patients with suspected difficult endotracheal intubation: protocol for a randomized controlled study”. The manuscript is well written and interesting. I only have two questions.

Section of Study interventions

Line 44-45 Why is to ensure end-tidal carbon dioxide is more than 93% during preoxygenation? Is it PetCO2? Or to ensure SpO2 more than 93%?

Line 55-56 When is topical airway anesthesia and sedation required? When is general anesthesia required? What are the criteria for different types of anesthesia method? And will it affect the outcomes?

REVIEWER  Ajit Kumar
AIIMS Rishikesh

REVIEW RETURNED  19-Feb-2023

GENERAL COMMENTS

Introduction: Well written
Study design: Properly plan and methodologically
Discussion: Adequate

REVIEWER  Scott Segal
Wake Forest School of Medicine, Anesthesiology

REVIEW RETURNED  20-Mar-2023

GENERAL COMMENTS

The authors propose a randomized trial of MGPOCUS vs. conventional fiberoptic intubation (FOI) in suspected difficult airway. I have several thoughts on the proposal:
1. Sample size calculation. I am unclear on how it was done, and more details should be presented. First, where does 50 seconds at baseline come from, and where does 22 seconds for the targeted margin for superiority arise from? What are the standard deviations associated with these estimates? These are needed to calculate the sample size (and that assumes that the times to first pass success are normally distributed and that parametric stats are used). Please clarify and provide supporting details.

2. Technique. I think it needs to be presented in more detail for the inexperienced reader. The Johnson paper (ref 24) describes a technique in which a needle is passively redirected by the magnet. Is that happening here? Please explain if so. If not, is the needle just used to help visualize the bronchoscope? (BTW, this is the preferred term, not “bronchoscopy”, when referring to the instrument instead of the technique of using it).

3. Justification for MGPOCUS. The authors hope that this modification will improve success in instances in which ordinary FOI is unsuccessful. In my experience, and consistent with the literature, I wonder if midline errors, as illustrated in Figures 2 and 3, are really the reasons for failures. My sense is that it is far more commonly secretions, blood, or masses, rather than midline errors. Please address, with support from the literature if possible, the causes of difficult/failed FOI and why MGPOCUS is likely to help.

4. Ethics. I do not doubt the authors’ genuine adherence to ethical research techniques and do not think they would not get informed consent from subjects. But I still worry about this study. They are randomizing patients they feel need an awake intubation. Difficult intubation occurs in 5-10% of patients, and need for awake techniques in ~1%. So some 30,000+ subjects will be approached to get the required sample. And I am concerned that patients with “tricky” airways, but not necessarily requiring awake FOI, would be asked to consent for the study, when a less uncomfortable technique such as videolaryngoscopy, might suffice instead. Please explain what the specific indications for awake intubation will be and how they will ensure that there is not undue pressure to enroll subjects with less challenging airways.

VERSION 1 – AUTHOR RESPONSE

Dear Dr. Phillips, Dr. Cheng, Dr. Kumar, Dr. Segal, and all concerned,

Thank you for your email and the opportunity to submit a major revision of our manuscript to BMJ Open. We appreciate the constructive feedback provided by the reviewers and editors.

We have carefully reviewed all of the peer review comments and have made the following changes to address them:

- We have revised the title of our manuscript to include the setting, as requested.
- We have removed the discussion section, as it is not part of the journal formatting requirements for protocol articles.
- We have marked any entries in our SPIRIT checklist that are not suitable for our study as N/A.
- We have provided an example of the participant consent form as a supplemental material file, as per item #32 of the SPIRIT checklist.
- We have updated the trial registry with our data-sharing plan to comply with the BMJ Open data-sharing policy.
- We have corrected the clerical error of pulse oximetry saturation in the section of study interventions Lines 44-45.
We have clarified that we will enroll only in bronchoscope intubation after induction and that all the cases will accept institutional standard general anesthesia, as described in “study interventions”.

Based on the fact that this study was conducted to confirm the differences between the two groups, the epidemiologist recalculated a sample size of 49 cases per group based on the pre-experimental results. We have provided supporting details for our sample size calculation, including the standard deviations associated with the estimates. Please refer to “Data management and statistics - sample size calculation” of the revised manuscript for this information.

We have explained the technique in more detail for the inexperienced reader, including the fact that the needle is used to help visualize the bronchoscope, as described in “MGPOCUS-assisted bronchoscope-guided ETI”.

We agree with Dr. Segal, a common reason for FOI failure is that secretions, blood, or masses (1,2) that make it difficult to view the tracheal entrance, thus losing their way. So is the trachea concealed by secretions or masses, or being outside the bronchoscopic field of view? How can we tell if we are on the right way and obstructed, or if we are going in the wrong direction? MGPOCUS provides an assisted view to help making judgement by locating the relative position of the trachea and bronchoscope from the outside. We supposed, that the bronchoscope is moving in the right direction when the bilateral vocal cord midline, the tracheal opening, coincides with the magnetic navigation needle. We hope that this will provide a clearer understanding of our rationale for using this technique. (1.Touré T, et al. Patient factors associated with difficult flexible bronchoscopic intubation under general anesthesia: a prospective observational study. Can J Anaesth. 2020 Jun ; 2.Law, J Adam et al. Canadian Airway Focus Group updated consensus-based recommendations for management of the difficult airway: part 2. Planning and implementing safe management of the patient with an anticipated difficult airway. CJA 2021): 1405-1436. doi:10.1007/s12630-021-02008-z)

The issue of specific indications for awake or post-induction intubation was not the focus of discussion in this study. Because the trial has not yet begun, and given the potential impact of different situation of intubation on outcomes and ethical issues, we have changed the protocol to enroll only post-induction bronchoscopic intubation. The primary anesthesia team will have no undue pressure to recruit subjects with various challenging airways as they are independent of the study.

### VERSION 2 – REVIEW

| REVIEWER           | Qinghao Cheng  
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<td>Department of Anesthesiology, Emergency General Hospital, Beijing, 100028, China</td>
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<td>REVIEW RETURNED</td>
<td>13-Apr-2023</td>
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### GENERAL COMMENTS

I've read the revision of “Developing a magnetic-assisted-POCUS guided bronchoscopy among patients with suspected difficult endotracheal intubation: protocol for a randomized controlled study”. At present, I have no other questions or doubts, and I wish the study a smooth and good result.

| REVIEWER           | Scott Segal  
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### GENERAL COMMENTS

Thank you for submitting this revised research proposal. Many of the reviewers’ initial questions have been addressed. I do continue to have several thoughts that should be addressed.

1. The abstract and the power analysis do not agree on the sample size. In the abstract you note N=350 but in the methods/SS calculation you note 54 subjects per group would be recruited, for
2. Description of the MGPOCUS bronchoscope and technique for bronchoscopy. It is improved, but I'm still unclear as to whether the magnet actually moves the bronchoscope or whether the needle is there only for visualization purposes. In the referenced work, it appears that the external magnet actually moved the needle during nerve blocks. In this case, I believe you are using a magnetic detector to sense the magnetized needle affixed to the bronchoscope, so that it is a visualization aid, not a passive repositioning device. I think a rewrite of this important text in the section "MGPOCUS-assisted bronchoscope-guided ETI" in the Study Interventions section is still indicated to make it very clear.

3. Can you cite the preliminary study from which the first attempt numbers of 28 ± 22 and 50 ± 41 seconds come from? If it is unpublished data, please be explicit about this fact; give the N of subjects used to derive these numbers; and show how you calculated the sample sizes, given the difference in expected SDs. I cannot recapitulate your calculation of 49 subjects per group at alpha .05 and beta 0.9 using standard formulas, whether I used the larger SD of the usual treatment group of 41, or the average of the two groups of 31.

4. I am absolutely sensitive to the fact that the authors are likely not writing in their first language, but there are numerous places in the manuscript where standard written English is not being used, and some sentences that are unclear enough that I cannot follow the meaning the authors intend. So with respect, please consider the service of an English language scientific editor to assist you.

VERSION 2 – AUTHOR RESPONSE

Dear Dr. Segal, Dr. Cheng, Dr. Phillips, and all concerned,

Thank you for your email and for the opportunity to submit a minor revision of our manuscript to BMJ Open. We appreciate the constructive feedback provided by the reviewers and editors.

In response to reviewer's comments:

1. Regarding the comment on the sample size, we apologize for the inconsistency between the abstract and the methods/SS calculation. The correct sample size is 54 subjects per group, for a total of 108. We have made the necessary correction in the revised manuscript.

2. Regarding the MGPOCUS bronchoscope and technique for bronchoscopy, we have revised the text in the "MGPOCUS-assisted bronchoscope-guided ETI" section of the study interventions to make it clear that the needle is used only for visualization purposes and that the magnet does not move the bronchoscope.

3. The preliminary study from which the first attempt numbers of 28 ± 22 and 50 ± 41 seconds come is unpublished data from our hospital. We apologize for not being explicit about this fact in our manuscript. There were 13 and 16 subjects in the control and experimental groups, respectively, to obtain these numbers, and we have included this information in the revised manuscript. We have also shown how we calculated the sample sizes, given the difference in expected SDs, according to the model of test for two means of Pass software, in the supplement materials.
4. We appreciate your concerns about the clarity of our English writing. We have carefully reviewed the manuscript and have made revisions to improve the clarity of our writing. However, we understand that there may still be areas that are unclear. In light of this, we will consider the service of an English language scientific editor to assist us.

VERSION 3 – REVIEW

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<th>GENERAL COMMENTS</th>
<th>The authors have continued to improve this manuscript. I have a few additional requests from the authors:</th>
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<td>1. Explain why the needle needs to be magnetized. Now that you have clarified that it is not magnetized so that a magnet can move the needle (and thus the bronchoscope) please tell the reader why the needle is magnetized. We do ultrasound-guided nerve blocks with echogenic but not magnetized needles all the time. Why the magnet?</td>
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<td>2. Please add the N to the sample size calculation in the paragraph presenting the unpublished data.</td>
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<td>3. The manuscript is still definitely in need of the services of an English language editor to make it more readable.</td>
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VERSION 3 – AUTHOR RESPONSE

Dear Dr. Segal, Dr. Cheng, Dr. Phillips, BMJ Open Editorial Office, and all concerned,

Thank you for your feedback and for the opportunity to revise our manuscript. We appreciate the constructive feedback provided by Dr. Segal.

In response to your comments:
1. Regarding the reason the needle needs to be magnetized, we have revised the introduction. We have explained that the characteristics of ultrasound limit intratracheal imaging, and the application of magnetic assistance makes up for this deficiency.
2. We provided the N to the sample size calculation in the data management and statistics paragraph.
3. We appreciate your concerns regarding the clarity of our writing in English. We have used a language editing service to improve the language. However, we understand that there still may be unclear areas. In light of this, we would be happy to choose the organization that the editors or reviewers designate.
4. We have modified the main documents to include five bullet points on the “strengths and limitations of this study”.

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