Developing a magnetic POCUS-guided bronchoscope for patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomised controlled study

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

ABSTRACT

Introduction Endotracheal intubation (ETI) is a crucial but risky procedure, especially among patients suspected of difficult endotracheal intubation (DTI). Bronchoscope, as an improved technique commonly used in DTI, might encounter visualisation difficulties. The magnetic point-of-care ultrasound (MGPOCUS) provides a novel visualisation from the outside and enables estimation of the relative position and trajectory of the bronchoscope. The purpose of the study was to evaluate the efficiency of MGPOCUS-guided bronchoscopy, including the time required for successful ETI, the first attempt and overall success rate, the number of attempts, complications, and satisfaction with the visualization of the procedures.

Methods and analysis The study is a randomised, parallel-group, single-blinded, single-centre study. Participants (n=108) will be recruited by the primary anaesthesiologist and randomised to groups of ETI with bronchoscope or MGPOCUS-guided bronchoscope. The primary outcome is the time taken to the first-attempt success ETI. Secondary outcomes include procedure time, the first-attempt and overall success, complications, and satisfaction of visualisation. Cox regression with Bonferroni correction and linear mixed regression will be used to analyse the outcomes.

Ethics and dissemination The trial protocol was approved by the ethics committees at the Peking Union Medical College Hospital (Institutional Review Board #ZS-3428). Findings will be disseminated through conference presentations and peer-reviewed journals.

Trial registration number NCT05647174

INTRODUCTION

Endotracheal intubation (ETI), although crucial as a fundamental method to secure the airway, is the leading cause of death or vegetative state among healthy participants undergoing elective surgery. It has consistently been seen that difficult endotracheal intubation (DTI) majorly contributes to adverse events. Though the advent of the flexible bronchoscope has brought revolutionary innovations for DTI, it is still worrisome, as the closed-claims analysis of USA has shown. Most often, intubation by flexible bronchoscope is performed via the oral route. The procedure can be tricky or delayed because of difficulty in visualisation. Visibility impaired by blood or secretions is supposed to predict difficult bronchoscope intubation. Dealing methods, such as clearance of secretions, keeping the tip in the midline or withdrawing until the location can be identified, remain widely varied in rapidity and uncertainty about maintaining the proper orientation. Active research to improve visualisation and movement confirms that this issue continues to challenge physicians.

Point-of-care ultrasound (POCUS) has broadened the horizons for airway management since it allows visualisation of the upper airway from the outside. The American Heart Association has updated the Guideline...
for Adult Advanced Cardiovascular Life Support and recommends the use of ultrasound as a confirmation method for tracheal intubation. Several studies provide promising results about the high pooled sensitivity (about 98%) and specificity (about 97%) of POCUS in confirming ETI. Real-time POCUS further extends to assist ETI. Notably, POCUS provides a view independent of laryngoscopy or bronchoscopy, making it possible to combine the outside with the inside visualisation.

Although ultrasound has shown advantages in evaluating soft tissues on the surface of the airway, it is difficult to display the inside of the air-filled airway. The progress of magnetically assisted ultrasound in the regional block and vascular catheterisation suggests that it can be used to visualise the relative position of the targets in the case of poor ultrasonography. The magnetic POCUS (MGPOCUS) technology collects magnetic signals and calculates the trajectory modelled by corresponding software. It enables the possibility of estimating the relative position and the advanced trajectory, guiding the bronchoscope when encountering difficulty in laryngeal exposure. To date, there has been little conclusive evidence to seek the application of an MGPOCUS-guided bronchoscope in anticipated difficult intubation.

The study is designed to estimate the application of MGPOCUS-guided bronchoscope within anticipated DTI on the procedure time for successful ETI, the first attempt and overall success rate, the number of attempts, complications, and the visual satisfaction of procedures. Compared with the flexible bronchoscope alone, we seek to estimate the significance of combined visualisation with the MGPOCUS-guided bronchoscope.

METHODS AND ANALYSIS

Study design and setting
This is a randomised, parallel-group, single-blinded, single-centre study. The study will be conducted in the anaesthesia department and operating room of the Chinese Academy of Medical Sciences, Peking Union Medical College Hospital (Beijing, China), a tertiary academic hospital with an annual operation census of above 80000 participants. The protocol is structured based on the Standard Protocol Items for Randomised Trials Statement: defining standard protocol items for a clinical study.

Participant recruitment
After assessing the eligibility and obtaining informed consent (see online supplemental file 1), the primary anaesthesiologist will recruit the participants while performing preoperative evaluations. The research team will confirm the eligibility.

Inclusion criteria
Participants will be eligible for inclusion if they meet all of the following criteria:

- Aged between 18 years and 85 years.
- Requiring ETI and without known indicators for awake tracheal intubation.
- Anticipated DTI meets one or more positive findings in the airway evaluation, including history, examination and appropriate investigations of anatomy (Table 1).
- The primary anaesthesia team, independent of the study team, considers bronchoscope intubation after induction to be the first choice.
- Signed written informed consent.

Table 1 Airway assessment

<table>
<thead>
<tr>
<th>Specific predictors</th>
<th>Positive findings</th>
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<tr>
<td>Morbid obesity</td>
<td>Body mass index ≥40</td>
</tr>
<tr>
<td>Adverse dentition</td>
<td>Presence</td>
</tr>
<tr>
<td>Prior difficulty in endotracheal intubation</td>
<td>Presence</td>
</tr>
<tr>
<td>Mouth opening</td>
<td>&lt;4 cm</td>
</tr>
<tr>
<td>Head and upper neck extension</td>
<td>&lt;30° from neutral</td>
</tr>
<tr>
<td>Mandibular protrusion (lip bite test)</td>
<td>Limited mandibular protrusion</td>
</tr>
<tr>
<td>Modified Mallampati class</td>
<td>III or IV</td>
</tr>
<tr>
<td>Thyromental distance</td>
<td>&lt;6 cm</td>
</tr>
<tr>
<td>Sternomental distance</td>
<td>&lt;12 cm</td>
</tr>
<tr>
<td>Neck circumference</td>
<td>&gt;40 cm</td>
</tr>
</tbody>
</table>

- High risk of aspiration.
- Current pregnancy.

Exclusion criteria
Participants will be excluded if they meet at least one of the following criteria:

- Anterior neck lesions (masses, lacerations or subcutaneous emphysema).
- A history of neck operation or tracheotomy.
- Allergies to ultrasound coupling gel.
- At risk of pulmonary or cardiovascular complications during intubation with a flexible bronchoscope, including severe hypoxaemia, severe pulmonary hypertension, and unstable or intense obstructive airway disease.
- High risk of bleeding during bronchoscope intubation, including anticoagulants or coagulopathy, renal insufficiency, and superior vena cava syndrome.
- High risk of aspiration.

Randomisation and concealment
Participants will be randomised in a 1:1 ratio to an intervention group (MGPOCUS-guided bronchoscope) or a control group (bronchoscope). A random number sequence will be generated by the ‘if’ package of R software by delegated research staff and uploaded to our institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co, Beijing, China). The primary care anaesthesiologist will
be informed of the database account information before performing ETI to guarantee allocation concealment.

**Blinding**

Trial participants and data analysts will be blinded to the assignment of interventions. Blinding of the investigator is generally impossible, yet evaluating outcomes is objective.

**Study interventions**

This study compares two interventions of performing DTI, a novel MGPOCUS-guided bronchoscope and a standard bronchoscope. Participants in each group will accept common perioperative interventions, including the essential monitoring of physiological parameters, sufficient preoxygenation institutional standard general anaesthesia, and confirmation of ETI position by capnography. Critical monitoring will be performed before, during and after ETI, with at least echocardiography, non-invasive blood pressure and pulse oximetry saturation of more than 93%.

ETI in both groups will be performed by a senior anaesthesiologist with more than 5 years of experience in flexible bronchoscope. MGPOCUS-guided bronchoscope intubation will be performed in collaboration with a senior anaesthesiologist with more than 5 years of experience in POCUS and who has fulfilled more than 50 cases of ultrasound-guided airway management. An additional experienced airway manager will stand by in the operating room.

Institutional standard general anaesthesia will include propofol 1.5–2.5 mg/kg, fentanyl 25–100 mcg/kg, lidocaine 0.5–1.5 mg/kg, midazolam 1–2 mg and rocuronium 0.6–1.2 mg/kg. The position of the tracheal tube will be confirmed by capnography with at least four consistent waves and bilateral auscultation of breath sounds.

**Bronchoscope-guided ETI**

After clear suctioning of oropharyngeal secretions, the tip of a bronchoscope will be put through the middle of the incisors. The bronchoscope will be appropriately oriented and flexed to move along the oral midline and achieve a satisfactory view of airway structures. Once the epiglottis and glottis are located, the tip of the bronchoscope will be advanced through the glottis to the level above the carina, followed by the advancement of a tracheal tube already loaded. According to the operators’ will, approaches can be used to improve visualisation, including jaw thrust, pulling tongue forward, cervical extension when not contraindicated, and bronchoscope withdrawal.

**MGPOCUS-assisted bronchoscope-guided ETI**

The system of MGPOCUS was derived and adapted from a previously described model used in vascular catheterisation. The system is only used for visualisation of the needle fixed on the bronchoscope, not moving the bronchoscope. It consists of an ultrasonic machine (Piloter US scanner, Wisonic, Shenzhen, Guangdong, China), a 4–15 MHz linear transducer with integrated ultrasonic and magnetic sensing capabilities (Wisonic, Shenzhen, Guangdong, China), a magnetising box (Wisonic, Shenzhen, Guangdong, China), and a magnetised metal needle fixed near the tip of the bronchoscope (Figure 1).

The MGPOCUS system uses several display features to enable the three-dimensional positioning of the bronchoscope tip to be displayed in a two-dimensional ultrasonic image. Figure 2 shows an example of how the trajectory of the magnetising needle fixed on a bronchoscope is displayed when it does or does not overlap with the ultrasound beam. Specifically, the trajectory of a magnetised bronchoscope is indicated by a solid line when it is within the ultrasonic beam. Otherwise, its trajectory is shown as a dashed line when positioned anterior or posterior to the ultrasound beam.

While there is clear suctioning of oropharyngeal secretions, the transducer is positioned transversely at the patient’s thyroid cartilage level. Moving the transducer cephalad or caudal, a view of the vocal folds is visualised as an isosceles triangle with a central tracheal shadow (Figure 3). The line connecting the vocal cords’ anterior and posterior commissure is marked as the midline of the ultrasonography. The midline is maintained, and directed cephalad to visualise the tongue and epiglottis. The second provider will perform intubation with a bronchoscope, as described above. When the view of the bronchoscope is unclear, MGPOCUS can provide an assisted view to locate the relative position of the bronchoscope and the vocal folds. Suppose the two lines locating the bilateral vocal cord midline and the bronchoscope do not partially overlap. In that case, the performer will adjust the direction of advancement according to the...
magnetised bronchoscope’s relative position to the vocal cords’ midline. Once the solid line displaying the magnetised bronchoscope is within the trachea, the preloaded tracheal tube will be advanced. Once the solid line is displayed posterolateral to the airway, the bronchoscope will be withdrawn and adjusted according to the MGPOCUS image. Similar to adjusting the direction of the needle to achieve the puncture target, the magnetised needle on the bronchoscope is guided to the trachea according to the ultrasonography with magnetic signals.

**Discontinuing interventions**

Desaturation below 90% will be considered a failed attempt of ETI. If desaturation is encountered, face mask ventilation will be performed with 100% oxygen for 2 min, and the attempt will be repeated. The procedure will be considered a failure with more than two attempts or 600 s, and the airway manager will proceed with the following strategy or technique. If emergencies arise, such as oxygen desaturation or haemodynamic instability, challenging to correct, the primary anaesthesia team will determine whether to continue or terminate the trial.

**Outcomes**

Baseline assessments will be collected during the preoperative evaluation, including demographic characteristics (age, sex, height, weight, body mass index, American Society of Anesthesiologists physical status score, procedure performer) and airway assessment (table 1).

The primary outcome is the time for successful ETI at the first attempt. Time will be recorded in real time from the first bronchoscopic passage through the teeth to the tube getting placed properly. The first-attempt success is successful ETI with no more than 180 s and without re-insertion of the bronchoscope through the teeth. Successful ETI is confirmed by capnography with at least four consistent waves.

The secondary outcomes are to detect the procedure time, the first attempt and overall success, the number of attempts, complications, and satisfaction with visualisation. Complications will be recorded, including desaturation, obvious trauma, bloody secretions, postextubation hoarseness and sore throat. The 5-point Likert Scale assesses satisfaction with visualisation.

**Data management and statistics**

**Sample size calculation**

Based on our preliminary study (unpublished data), it is supposed that MGPOCUS-assisted bronchoscope-guided ETI will achieve first-attempt success in $28\pm22$ s (N 16) and bronchoscope-guided ETI in $50\pm41$ s (N 13). Hence, it is estimated that a sample size of 98 subjects will achieve a power of 90% (type II error 0.1) to detect a statistically significant difference between the two groups with a
two-sided type I error of 0.05. Assuming the potentially skewed distribution of the time of first-attempt success would lead to 10% statistical power loss, 54 subjects will be recruited in each group.

Data collection and protection
All data will be collected on the institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Beijing, China) by an investigator independently. Data entry and processing will be performed before unblinding of investigators. The database will be centralised and managed by the leading researchers. A unique research identification data (ID) code will be used to ensure confidentiality and anonymity. The ID will be used to identify participants and the allocation. The recorded data in the study will not be linked to the participant’s personal information. The data will be transferred securely and stored confidentially on password-protected computers that the researchers can only access by General Data Protection Regulation.

Data statistics plan
Demographic characteristics and airway assessment variables will be presented using descriptive statistics for the overall sample. Continuous data will be described using mean (SD) or median (IQR), depending on the distribution of the data. Categorical data will be described using numbers and proportions.

For the primary outcome, the time taken to the first-attempt success will be analysed using a Cox proportional hazards model with the Bonferroni correction as a multiplicity adjustment that treats failed ETI at the first attempt as censored. For secondary outcomes, procedure time for successful ETI will be analysed using a linear mixed model that treats ETI success or failure as the outcome and procedure performer as a random effect. The first attempt and overall success will be analysed using mixed-effects logistic regression. Any two-sided value of p<0.05 will be considered statistically significant. Statistical analyses will be performed on R software V.3.5.1 (R Foundation for Statistical Computing).

Termination of the study
An independent statistician will conduct the interim analysis of the primary outcome when 50% of participants have been enrolled. The results will be reported to the independent data and safety monitoring committee and discussed with the steering committee. The Peto approach will be used to terminate the study when the intervention group greatly benefits from the control group using symmetrical stopping boundaries at p<0.001. The study will be stopped when futility of the independent data and the potential stopping for futility will be discussed with the steering committee, in this case, it will be discussed with the steering committee.

Data monitoring
A steering committee will manage the study. Screening and recruitment will be reviewed at monthly meetings. An independent data and safety monitoring committee will meet every 3 months to ensure patient safety and data quality.

Safety
The independent data and safety monitoring committee will supervise the progress of the study by examining safety variables monthly. Adverse events are defined as ‘any undesirable experience occurring to a subject during the study, whether or not considered related to the intervention’. Any potential adverse events must be monitored, recorded and discussed with the independent data and safety monitoring committee.

Patient and public involvement
The study protocol was developed in collaboration with anaesthesiologists with extensive experience managing difficult airways or POCUS. Their feedback and expectations regarding research questions and outcome measures were applied for adjustment. Because of the absence of experimental knowledge and subjective feeling, participants were not involved in design, conduct, reporting, or dissemination plans of the research.

Ethics approval and study registration
Ethical approval has been granted by the respective ethics committees at the Peking Union Medical College Hospital (Institutional Review Board #ZS-3428), and written informed consent will be obtained from all participants. The study was registered online (clinicaltrials.gov; NCT05647174; Sponsor; date of registration: 12 March 2022).

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Contributors All authors contributed to the conception and design of the study protocol. YT drafted the manuscript. YF, BB and CW acquired and analysed data. YZ interpreted data and methodologically revised the manuscript. XC, YC and YH reviewed and revised the manuscript critically. All authors have read, provided feedback on and approved the final version of the manuscript.

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Competing interests None declared.

Patient and public involvement The public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES
Participant Consent Form

Project: Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation

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Date: Mar, 2022

Background information

General anesthesia tracheal intubation is the primary anesthetic method to ensure the completion of surgery and patient safety. Detection of unintended tracheal intubation is an important step in this method and is an important factor in reducing anesthetic accidents and ensuring postoperative regression. Real-time ultrasound is a rapid, non-invasive detection method that potentially benefits patients with difficult intubation.

In our study, patients willing to participate in this study and at risk for difficult intubation were randomly assigned to either the ultrasound-assisted laryngoscopic view or the laryngoscopic view group, and the location of tracheal intubation was detected using noninvasive cervical ultrasound-assisted intubation with laryngoscopic view or laryngoscopic view at the same time as tracheal intubation to assess the difference in the effectiveness of the two methods. In order to obtain data related to the application of ultrasound-assisted methods for detecting the position of intubation in patients with difficult intubation.

Our study can provide more valuable evidence for clinical decision making in the refinement of airway management in patients with difficult tracheal intubation. Your participation will make an important contribution to obtaining such evidence, allowing other patients to benefit from your contribution.

Who should not participate in the study?

There are strict inclusion and exclusion criteria for this study. Any patient who does not meet the inclusion criteria should not participate in this study, in addition to 1) patients who are participating in other clinical studies; 2) those who are considered by the investigators to be unsuitable for clinical studies for other reasons.

What will I need to do if I participate in the study?

1. Before you are enrolled in the study, your doctor will ask questions, record your
general condition, and assess whether you are at risk for difficult intubation. It will be
determined that you are an eligible inclusion, that you are volunteering for the study,
and you will be asked to sign an informed consent form.
2. If you volunteer to participate in the study, we will perform a standard or
ultrasound-assisted protocol for you, depending on the randomization group, and
record the monitoring results.

Possible benefits of participating in the study.
If you participate in the study, the results of the study will have important implications
for clinical decision making in all general anesthesia tracheal intubation populations
and will provide you with the following improved support for evaluation and consultation
during your anesthesia. This includes:
1. better assessment measures: including more detailed and improved airway
assessment. There are no tests outside of the current treatment routine, which will not
increase the cost of your treatment, and if additional tests are incurred as a result of
the study itself, they will be free of charge to you.
2. Specialized visits and consultations: The visits and consultations of this project will
be conducted by specially trained personnel, so that you can receive timely and
comprehensive consultations on the contents related to general anesthesia tracheal
intubation, and your relevant questions will be answered and dealt with in a timely
manner.

Possible risks, adverse reactions and discomfort, inconvenience of participating
in the study.
This project uses laryngoscopic visualization alone and ultrasound-assisted
laryngoscopic visualization; laryngoscopic visualization is a routine clinical method
and ultrasound-assisted method is a non-invasive method, so participation in this
project itself will not increase your risk.
You will be required to participate in airway evaluations during the study, and these
will take up some of your time and may also cause you problems or inconvenience.
If you experience any discomfort after the clinical study, including during the study,
or if there are any new changes in your condition, or any unforeseen circumstances,
whether or not related to the study, you should promptly notify your physician, who
will make a determination and provide appropriate medical treatment.

Related Costs and Compensation
There are no additional anesthetic risks or costs associated with either of the methods
involved in this study, and the patient is responsible for the costs associated with
routine anesthetic management. Treatments and examinations required for your
concurrent medical conditions will also not be covered free of charge. However, if
additional tests are performed as a result of the program itself, they will be free of
charge to you.
The intervention methods involved in this study are non-invasive and routine, and will
not cause damage to the patient, so there is no compensation involved in this project.
Is personal information confidential?
Your medical records (study charts/CRFs, labs, etc.) will be kept intact at the hospital you visit. Your doctor will record the results of laboratory tests and other examinations in your medical record. The investigator, ethics committee and drug regulatory authorities will be given access to your medical records. Records of all your personal information, including name, phone number, email, and address, will not appear in electronic databases, and any public reports of the results of this study will not disclose your personal identity and information. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law.

How can I get more information?
You can ask any questions about this study at any time and get the appropriate answers. For inquiries (investigator contact): 17611356059; and you have the right to ask questions about your rights or related risks, inquiries (ethics review committee contact): 69156874

Your physician will promptly notify you of any important new information during the study that may affect your willingness to continue to participate in the study. You can voluntarily choose to participate in the study and withdraw from the study Participation in the study is entirely at your discretion. You may refuse to participate in the study or withdraw from the study at any time during the study, and this will not affect the relationship between you and your physician, nor will it affect your medical treatment or any other loss of benefits.

Your physician or investigator may discontinue your participation in this study at any time during the study for reasons of your best interest.

If you withdraw from this study for any reason, you may also be asked to undergo laboratory tests and physical examinations if your doctor deems it clinically necessary.

What should I do now?
It is up to you (and your family) to decide whether to participate in this study. Please ask your doctor as many questions as possible before you make a decision to participate in the study.

Thank you for reading the above materials. If you decide to participate in this program, please tell your doctor and he/she will make all the arrangements for you to participate in the study. Please keep this information with you.

Statement of Consent
I have read the above description of this study and have had the opportunity to discuss and ask questions about this study with my doctor. All of the questions I have asked have been answered to my satisfaction.
I am aware of the possible risks and benefits of participating in this study. I understand that participation in this study is voluntary, I acknowledge that I have had sufficient time to consider it, and I understand that I can ask my doctor for more information at any time.
I may withdraw from this study at any time without discrimination or reprisal, and without my medical treatment or rights being affected in any way.

I am equally aware that if I withdraw from the study in the middle of the study, especially if I withdraw for medication reasons, it would be very beneficial to the study as a whole for me to inform my physician of any changes in my condition and to complete the appropriate physical and physical examinations.

If I need to take any other medication due to a change in my condition, I will consult my doctor beforehand or tell him/her truthfully afterwards.

I give my consent to the drug regulatory authority, ethics committee or sponsor's representative to access my study data.

I will be provided with a signed and dated copy of the informed consent form.

Finally, I have decided to give my consent to participate in this study and I promise to follow medical advice as far as possible.

Subject's name

Subject's signature

Date

If the patient has appointed a legal proxy (if applicable, and signed a proxy agreement):

Name of legal attorney (in block letters)

Signature of legal attorney

Date

I confirm that the details of this study, including their rights and possible benefits and risks, have been explained to the patient and that they have been given a copy of the signed informed consent form.

Name of investigator

Signature

Date