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Ventilator settings for fibreoptic bronchoscopy during mechanical ventilation: a study protocol for a pragmatic randomised double-blind controlled trial VentSetFib

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ABSTRACT

Introduction Fibreoptic bronchoscopy (FOB) is a challenging procedure during mechanical ventilation (MV) as it considerably reduces the endotracheal tube's internal diameter, causing a drastic increase in respiratory resistance, which may compromise the delivery of ventilatory assistance. According to respiratory physiology principles applied to MV, the reduction of inspiratory flow and tidal volume is likely to reduce airway pressure during the inspiratory phase when respiratory resistances increase. Based on this assumption, we propose new ventilator settings aimed at reducing airway pressure during FOB. This study represents the first investigation to test special ventilator settings in order to facilitate FOB during MV.

Methods and analysis This is a single-centre randomised double-blind controlled trial, in which intubated patients undergoing an FOB will be assigned (1/1) either to receive the new ventilatory strategy or to stay on the ventilator settings previously selected by the attending physician. The intervention group will be applied the specific ventilator settings (inspiratory flow ≤25 L/min, tidal volume=5 mL/Kg, 1 s≤inspiratory time≤1.3 s, respiratory frequency=16 c/min, positive end-expiratory pressure=5 cm H_2O). The primary endpoint will be the reduction of the occurrence of a serious adverse event (inability to deliver ventilatory support, significant arterial desaturation or haemodynamics instability) during FOB, prompting the interruption of the procedure. The primary endpoint will be validated a posteriori by an external adjudication committee. The sample size was estimated at a minimum of 42 patients to demonstrate a 50% reduction in the occurrence of such a serious adverse event with a power of 90% and an alpha risk of 0.05 (χ^2 test). Considering the possibility of technical problems in 10% of cases, 46 patients will be included.

Ethics and dissemination The study has been approved by the national ethics committee for the protection of the individuals (ID number: 2024-A00747-40). Written informed consent will be obtained from all patients. The results will be submitted for publication in peer-reviewed journals.

Trial registration number NCT06562725.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study is designed as a randomised double-blind controlled trial, including critically ill patients on mechanical ventilation allocated (1:1) to receive either the specific ventilator settings aiming to reduce airway pressure to facilitate fibreoptic bronchoscopy (FOB) or conventional ventilator settings chosen by the attending practitioner.
⇒ The primary endpoint—reduction of the occurrence of a serious adverse event prompting FOB interruption—will be validated a posteriori by an external adjudication committee not aware of the patient's allocation.
⇒ Data entry and coding as well as statistical analysis will be performed without knowing group allocation.
⇒ The secondary endpoints will explore the ventilatory, respiratory and haemodynamic consequences of FOB depending on the ventilator settings attributed according to randomisation.

INTRODUCTION

Background and rationale

Fibreoptic bronchoscopy (FOB) is a frequent diagnostic and therapeutic intervention for intubated critically ill patients under mechanical ventilation (MV). During MV, FOB can become a challenging, potentially dangerous procedure as it considerably reduces the endotracheal tube's internal diameter, causing a drastic increase in respiratory resistances, which may compromise the delivery of ventilatory assistance.[1 2] Poiseuille's law of physics states that resistance to laminar airflow is directly proportional to the length of an airway and inversely proportional to the fourth power of the airway radius.[3] For example, the introduction of a 5.7 mm outward diameter flexible bronchoscope into an 8 mm internal diameter endotracheal tube increases the airway resistances to flow

by 11 times.[4] It prevents complete lung emptying at expiration and causes significant gas trapping. FOB can thus cause high levels of auto-positive end-expiratory pressure (auto-PEEP) that have been measured up to 35 cm H_2O.[5] Once the bronchoscope has been introduced into the endotracheal tube, peak airway pressure at insufflation can reach the maximal inspiratory pressure alarm, preventing the tidal volume (VT) from being delivered.[6] Potentially severe cardiovascular consequences have also been described, especially in older individuals (>60 years) undergoing FOB.[7]

The equation of motion tells us that the airway opening pressure results from the product of the airway resistances times the inspiratory flow set on the ventilator.[8] According to these respiratory physiology principles applied to MV, decreasing inspiratory flow and VT will likely reduce airway pressure during the inspiratory phase when respiratory resistances increase. Based on this assumption, we propose new ventilator settings aimed at reducing airway pressure during FOB.

Objectives

This study represents the first investigation to test special ventilator settings to facilitate FOB during invasive MV and, above all, to ensure that ventilatory assistance is actually delivered to the critically ill patient during the procedure.

Primary objective: to reduce the occurrence of any adverse events (ventilatory, respiratory or cardiocirculatory event) that can compromise the FOB or prevent the delivery of ventilatory assistance during the procedure.

Secondary objective: to reduce the occurrence of a specific adverse event, either a ventilatory, a respiratory or a circulatory one.

METHOD AND ANALYSIS

Study design

This is a single-centre, prospective, double-blind, controlled study, randomised in two parallel groups. As shown in figure 1, the patients will be randomised in a 1:1 ratio to receive either the conventional ventilator settings chosen by the attending intensivist (control group) or the specific ventilator settings aimed at reducing the peak airway pressure to facilitate FOB (experimental group).

Study setting

The candidates will be recruited among the critically ill intubated patients of the 15-bed intensive care unit (ICU) of the Arras Hospital, a French tertiary hospital.

Eligibility criteria

Inclusion criteria include:

- Adult patient>18 years old.
- Acute respiratory failure treated by invasive MV.
- Sedated patient with low Richmond Agitation and Sedation Scale (RASS <–3).[9]
- FOB indicated for diagnosis, treatment or to guide percutaneous tracheostomy procedure.
- Written informed consent obtained from either the patient or his/her representative.

Exclusion criteria include:

- Presence of an absolute contraindication to FOB (respiratory arrest, severe acute respiratory distress syndrome, refractory shock, uncontrolled heart rhythm).
- Non-intubated patients, patients under non-invasive ventilation.
- Severe patient-ventilator dysynchronies or patients in respiratory distress despite appropriate sedation.

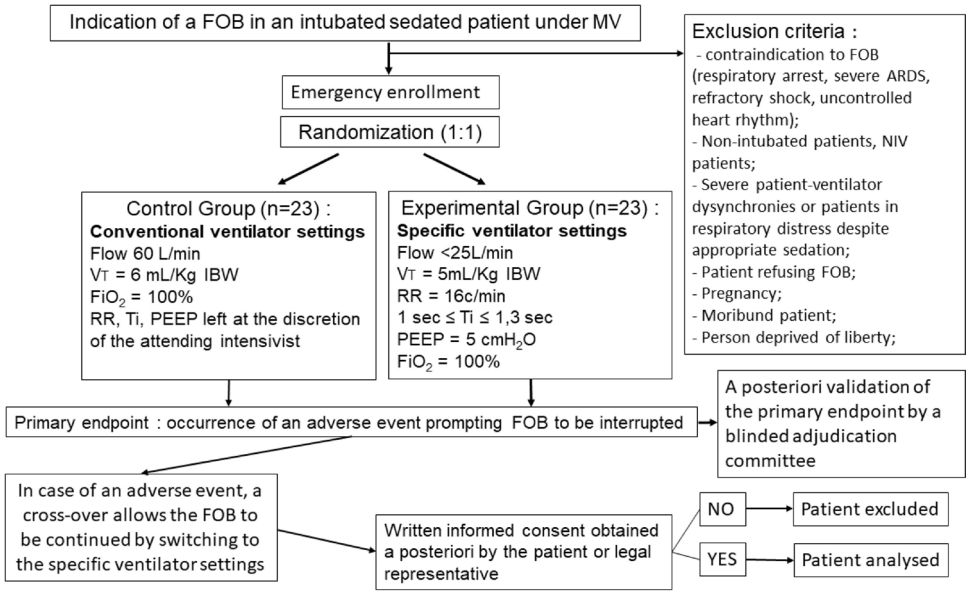

Figure 1 Flow chart over the study procedure. ARDS, acute respiratory distress syndrome; FOB, fibreoptic bronchoscopy; IBW, ideal body weight; MV, mechanical ventilation; NIV, non-invasive ventilation; PEEP, positive end-expiratory pressure; RR, respiratory rate; Ti, inspiratory time; VT, tidal volume.

- Patient refusing FOB.
- Pregnancy.
- Moribund patient.
- Person deprived of liberty.

Intervention

The patients of the two groups will be ventilated in constant flow assist control ventilation. All of them will be sedated (for a RASS <−3) and intubated for a critical illness requiring invasive MV support. FOB will be indicated for atelectasis, haemoptysis, bronchial suction, broncho-alveolar lavage, endotracheal tube replacement or to guide a percutaneous tracheostomy. The procedure will be performed using a 5.6 mm outward diameter single-use flexible video bronchoscope (Bronchoflex Vortex, The Surgical Company, Axess Vision Technology, France). The ventilator settings attributed according to the randomisation will be started 30 min before performing the FOB to ensure a safety period on the allocated ventilator settings. The patients will be pre-oxygenated at FiO_2 of 100% 5 min before the start of the intervention and during the entire duration of the intervention. In both groups, the high-pressure alarm will be set to its maximum (Pmax=105 cm H_2O) to facilitate the delivering of the VT in case of increased respiratory resistances.

The two groups are designed as follows:

- Experimental group: specific settings of the ventilator in preset flow (assist control ventilation) with lengthening of the insufflation time (1 s≤Ti≤1.3 s), decreased inspiratory flow ≤25 L/min, decreased VT to 5 mL/kg ideal body weight, decreased respiratory rate to 16 breaths/min and decreased PEEP to 5 cm H_2O.
- Control group: conventional ventilator settings at preset flow (assist control ventilation) with inspiratory flow 60 L/min and VT 6 mL/kg IBW; respiratory frequency, Ti, and PEEP left to the discretion of the attending practitioner.

Outcomes

Primary outcome

The primary endpoint is the occurrence of a serious adverse event requiring early termination of the procedure within the first 5 min. Serious adverse events are defined as follows:

- Ventilatory event: inability to continue MV with a decrease in minute ventilation >50% of its initial value or non-delivery of the VT caused by the peak airway pressure reaching the maximum alarm pressure.
- Respiratory event: occurrence of an episode of significant arterial oxygen desaturation defined by a SaO_2 <90% during the FOB or a drop in SaO_2 >4% compared with its initial value.
- Cardiocirculatory event: tachycardia with increase in heart rate >40 breaths/min, appearance of a cardiac arrhythmia or circulatory instability with a drop in mean arterial pressure >20% compared with its initial value.

Secondary outcomes

The secondary endpoints are:

- Avoiding a significant decrease in minute ventilation (>50% of its initial value) during the FOB.
- Avoiding a significant decrease in the PaO_2/FiO_2 ratio (>50) during the FOB compared with its initial value.
- Avoiding a significant increase in $PaCO_2$ (>5 mm Hg) during the FOB compared with its initial value.
- Avoiding a significant decrease in episodes of tachycardia, cardiac arrhythmia or circulatory instability occurring during the FOB.

Statistical power and sample size

The study's main objective is to show that using specific ventilator settings facilitates the feasibility of FOB during MV. Considering that FOB will not be safely feasible in 60% of cases with conventional ventilator settings because of the occurrence of serious adverse events, a total sample size of at least 42 patients is needed to detect an absolute risk reduction of 50% in the occurrence of a serious adverse event during FOB between the conventional ventilator settings and the specific ventilator settings with a power of 90% and an alpha risk of 0.05 using a two-sided two-sample test of proportions (Fisher's exact test). Considering the possibility of encountering technical problems in approximately 10% of cases, the number of subjects needed to be included is therefore increased to 46 patients in total or 23 patients in each of the two groups.

Between-group comparisons for continuous variables will be assessed using Student's t-test or Wilcoxon rank-sum test, as appropriate. Analysis of categorical data will be performed using the χ^2 test or Fisher's exact test. Statistical analysis for the primary outcome will be performed using the χ^2 test. The statistician will be kept blinded from the patients group allocation, which will be designated by a letter in the data spreadsheet.

Collected parameters

Data collection will include the main anthropometric parameters, the endotracheal tube internal diameter, the dose of sedation and analgesia, the patient's past medical history, especially smoking habits, chronic obstructive pulmonary disease or any chronic respiratory disease, the cause of the acute respiratory failure episode requiring endotracheal intubation, the patient's severity at admission assessed by the Sequential Acute Physiologic Score 2,[10] and the reason for the FOB procedure. The main respiratory mechanics parameters will be collected from the ventilator, including inspiratory flow, VT, respiratory rate, inspiratory time, minute ventilation, peak airway pressure, plateau pressure, total PEEP, allowing the calculation of static respiratory compliance and airways resistance before and during FOB. Arterial blood gas samples will be taken before FOB and at 5 min from the onset of FOB. Haemodynamic parameters such as heart rate, systolic and diastolic arterial pressure will also be collected before and during the FOB procedure.

Data management

Participants' names and dates of birth will be removed from the data sheets to preserve their anonymity. The correspondence table linking patients to their inclusion number will be kept under lock and key in the clinical research department. All computerised data will be identified through the inclusion number only.

A clinical research associate not involved in the study will perform data entry and coding. Likewise, data will be analysed without knowing group allocation.

Randomisation and blinding

Randomisation will be centralised and carried out using a randomisation table provided by the study sponsor based on blocks of size 6, balanced (1:1) between the two arms. Patient allocation will be revealed by consecutively opening a sealed numbered envelope kept in the research department.

Of course, the intubated, sedated, critically ill candidate for an FOB will be blinded to the group allocation at the time of inclusion and randomisation.

The primary endpoint—occurrence of a severe adverse event prompting the FOB to be interrupted—will be validated a posteriori by an adjudication committee also blinded from the group allocation. This adjudication committee will comprise two intensivists and one ICU nurse, not involved in the randomisation, not in charge of the included patients and all capable of reading the ventilator curves. Pictures of the ventilator screen and the patient's ICU monitor will be taken before and during the FOB procedure. The pictures will be taken with a digital camera and kept on a storage card in the research department. Restricted meetings of the adjudication committee will be held at regular intervals to study the primary endpoint of the included participants based on the pictures taken at the time of the FOB.

Crossover

In order not to prevent the FOB from being carried out, a switch to the specific ventilator settings will be allowed in any case of adverse events compromising the pursuit of the procedure with the randomisation settings. For instance, if the ventilatory assistance cannot be safely delivered with the conventional ventilator settings, the patient can be switched to the specific ventilator settings to allow the FOB to be continued. This condition of the protocol will ensure that the patient's inclusion in the study does not harm the patient's clinical management by preventing the FOB from being done. The number of patients who will have to be switched to the specific ventilator settings will be analysed, and their meaningful parameters of respiratory mechanics will be compared before and after the change in the ventilator settings. Only the patients with adverse events blindly validated by the external adjudication committee will be taken into account in the analysis.

Patient and public involvement

For now, patients and the public are not expected to be involved in the design, or conduct, or reporting, or dissemination plans of this research.

ETHICS AND DISSEMINATION

Consent or assent

The study has been approved by an independent ethics committee (Comité de protection des personnes Centre Ouest Angers) with the ID-RCB 2024-A00747-40 (online supplemental file 1). The Arras Hospital is the sponsor of the trial.

Patients will be included after their eligibility has been checked and if exclusion criteria are ruled out. The patient—whenever possible—or next-of-kin will receive clear and loyal information from the investigator regarding the study as soon as possible. Given that patients will be intubated and sedated at the time of inclusion and that the procedure is considered as an emergency one, signed informed consent will be sought a posteriori.

Confidentiality

Data will be handled according to the French law Jardé. The data will be collected in an anonymised password-protected Excel database. All original records will be archived at the research department of Arras for 5 years. The clean database file will be kept for 5 years.

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Contributors All authors have read the manuscript and declare no potential competing interest, no prior publication or concurrent submission and no copyright constraints. ML conceived the research question, contributed to the development of the trial protocol and wrote the first draft and final version of the manuscript. JM provided substantial contributions to the conception and design of the study, estimated the sample size and wrote the statistical analysis plan. MG, C-EL, AB, HC and CA contributed to the development of the Trial Protocol and provided critical inputs to the article and approved the final version. ML acted as guarantor.

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Competing interests None declared.

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