BMJ Open

Effect of endotracheal tube plus stylet versus endotracheal tube alone on successful first-attempt tracheal intubation among critically ill patients: the multicentre randomised STYLETO study protocol

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To cite: Jaber S, Rolle A, Jung B, *et al*. Effect of endotracheal tube plus stylet versus endotracheal tube alone on successful first-attempt tracheal intubation among critically ill patients: the multicentre randomised STYLETO study protocol. *BMJ Open* 2020;**10**:e036718. doi:10.1136/bmjopen-2019-036718

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2019-036718).

Received 30 December 2019
Revised 08 April 2020
Accepted 19 July 2020

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ABSTRACT

Introduction Tracheal intubation is one of the most daily practiced procedures performed in intensive care unit (ICU). It is associated with severe life-threatening complications, which can lead to intubation-related cardiac arrest. Using a preshaped endotracheal tube plus stylet may have potential advantages over endotracheal tube without stylet. The stylet is a rigid but malleable introducer which fits inside the endotracheal tube and allows for manipulation of the tube shape; to facilitate passage of the tube through the laryngeal inlet. However, some complications from stylets have been reported including mucosal bleeding, perforation of the trachea or oesophagus and sore throat. The use of a stylet for first-attempt intubation has never been assessed in ICU and benefit remains to be established.

Methods and analysis The endotracheal tube plus stylet to increase first-attempt success during orotracheal intubation compared with endotracheal tube alone in ICU patients (STYLETO) trial is an investigator-initiated, multicentre, stratified, parallel-group unblinded trial with an electronic system-based randomisation. Patients will be randomly assigned to undergo the initial intubation attempt with endotracheal tube alone (ie,without stylet, control group) or endotracheal tube + stylet (experimental group). The primary outcome is the proportion of patients with successful first-attempt orotracheal intubation. The single, prespecified, secondary outcome is the incidence of complications related to intubation, in the hour following intubation. Other outcomes analysed will include safety, exploratory procedural and clinical outcomes.

Ethics and dissemination The study project has been approved by the appropriate ethics committee 'Comité-de-Protection-des-Personnes Nord-Ouest3-19.04.26.65808 Cat2 RECHMPL19_0216/STYLETO2019-A01180-57'". Informed consent is required. The results will be submitted for publication in a peer-reviewed journal and presented at one or more scientific conferences. If combined use of endotracheal tube plus stylet facilitates tracheal intubation of ICU patients compared with endotracheal tube alone, its use will become standard practice, thereby decreasing first-attempt intubation failure rates and, potentially, the frequency of intubation-related complications.

Trial registration details ClinicalTrials.gov Identifier: NCT04079387; Pre-results.

Strengths and limitations of this study

- ► This ongoing pragmatic trial will provide the first comparison of clinical outcomes between endotracheal tube plus stylet and endotracheal tube alone to facilitate tracheal intubation of critically ill adults.
- ► The broad inclusion criteria and the high number of participating intensivecare units will increase generalisability and the large size will provide the opportunity to examine subgroups of interest.
- ► All intubation performed around the clock (nights and weekend) will be included.
- ► The nature of the study intervention does not allow blinding.

INTRODUCTION

Background and rationale

This manuscript was written in accordance with the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines.[1]

Patients admitted to intensive care units (ICU) often require respiratory support. Tracheal intubation is one of the most frequent procedures performed in ICU.[2 3] It may be associated with life-threatening complications in up to one half of the cases,[4 5] the ultimate complication being cardiac arrest related to intubation in 2.7% of the cases.[6] Difficult intubation, defined by more than two intubation attempts, is associated with

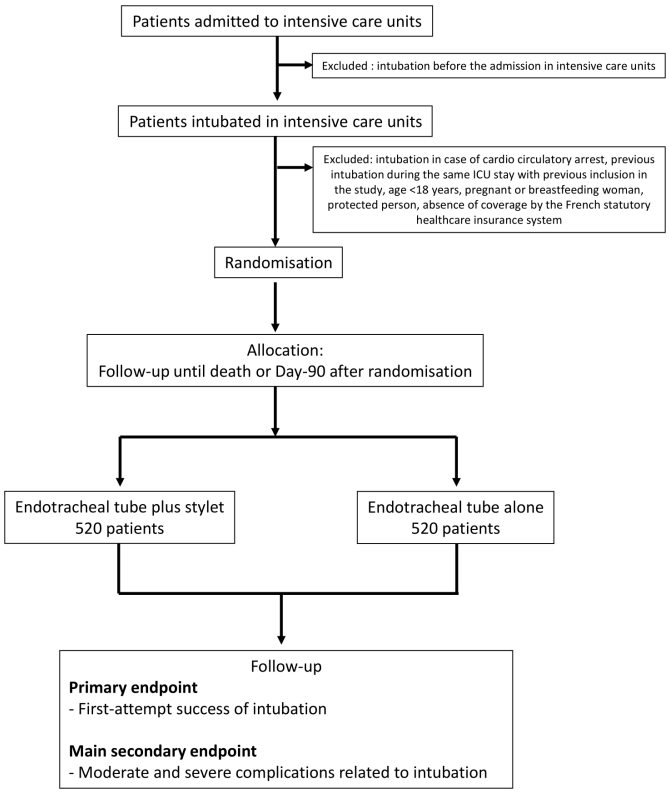

Figure 1 CONSORT diagram of the STYLETO trial. ICU, intensive care unit.

life-threatening complications.[4 5 7–10] To prevent and limit the incidence of complications related to intubation, intubation algorithms have been developed,[7 8] and risk factors for difficult intubation in ICU have been identified that constitute the MACOCHA score (Mallampati score III or IV, obstructive sleep Apnoea syndrome, reduced mobility of Cervical spine, limited mouth Opening <3 cm, Coma, severe Hypoxaemia (<80%) and non-Anaesthesiologist status).[5]

Devices aiming to facilitate tracheal intubation in ICU have been recently assessed. In 2018, a large multicentre study[2] reported first-attempt intubation success rates using direct laryngoscopy of 70% and videolaryngoscopy of 67%. In 2019, a multicentre randomised trial,[11] assessing whether positive-pressure ventilation with a bag-mask device (bag-mask ventilation) during tracheal intubation of critically ill adults prevents hypoxaemia, reported a first-attempt success rate of 81%. Other authors reported an overall first-attempt intubation success rate of 74%.[5] The 20% to 40% first-attempt failure rates throughout studies highlight the opportunity to improve the safety and efficiency of this critical procedure. Using a preshaped endotracheal tube plus stylet may have potential advantages over endotracheal tube alone without stylet. The stylet is a rigid but malleable introducer which fits inside the endotracheal tube and allows for manipulation of the tube shape; usually into a hockey stick shape, to facilitate passage of the tube through the laryngeal inlet. The stylet also provides additional rigidity to the tube which may aid in tube passage. The stylet can help to increase success of intubation in operating rooms, although the available literature is poor.[12]

However, some complications from intubating stylets have been reported including mucosal bleeding, perforation of the trachea or oesophagus and sore throat.[13 14] In 2018, one study has compared the use of a bougie to the use of the endotracheal tube plus stylet in the emergency department.[10] However, in ICU, the systematic use of a stylet is still debated and recent recommendations[15 16] do not recommend to use or not to use such devices for first-attempt intubation.

The routine utilisation of a stylet for first-attempt intubation using direct laryngoscopy in ICU has never been assessed and benefit remains to be established.

We hypothesise that adding a stylet to the endotracheal tube will facilitate higher first-attempt intubation success compared with endotracheal tube alone (ie, without stylet) in ICU patients needing mechanical ventilation.

Objectives

Primary objective

To determine whether endotracheal tube plus stylet increases first-attempt success during intubation procedure over endotracheal tube alone in ICU patients needing mechanical ventilation.

Secondary objectives

To compare in both groups, the incidence of complications related to intubation and other secondary outcomes.

The main hypothesis is that endotracheal tube plus stylet increases first-attempt success during intubation procedure over endotracheal tube alone in ICU patients needing mechanical ventilation.

Trial design

The endotracheal tube plus stylet to increase first-attempt success during endotracheal tube alone in ICU patients (STYLETO) trial is an investigator-initiated, multicentre, stratified, parallel-group unblinded trial with an electronic system–based randomisation. Patients will be randomly assigned to undergo the initial intubation attempt with endotracheal tube alone (ie, without stylet, control group) or endotracheal tube + stylet (experimental group).

CONSORT diagram

Figure 1 shows the CONSORT diagram of the STYLETO trial.

METHODS: PARTICIPANTS, INTERVENTIONS AND OUTCOMES

Study setting

The STYLETO study will take place in 35 ICUs, in France.

Eligibility criteria

Inclusion criteria

Patients must be present in the ICU, adult (age ≥18 years), covered by public health insurance, with written informed consent from the patient or proxy (if present)

before inclusion or once possible when patient has been included in a context of emergency and require mechanical ventilation through an endotracheal tube.

Exclusion criteria

Patients fulfilling one or more of the following criteria will not be included: intubation in case of cardio circulatory arrest, previous intubation during the same ICU stay with previous inclusion in the study, age <18 years, pregnant or breastfeeding woman, protected person, refusal of study participation or to pursue the study by the patient, absence of coverage by the French statutory healthcare insurance system.

Outcomes

Primary outcome

Primary outcome variable is the proportion of patients with successful first-attempt endotracheal intubation, which is defined based on a normal-appearing waveform of the partial pressure of end-tidal exhaled carbon dioxide curve over four or more breathing cycles.[2]

In case of absence of end-tidal exhaled carbon dioxide (dysfunction or cardiac arrest during intubation), the first-attempt success was defined using pulmonary auscultation: auscultation for bilateral breath sounds and absence of stomach inflation.

The criterion 'first-attempt intubation success' was chosen because directly related to the potential benefits of using a stylet and associated with complications related to intubation.[17]

Main secondary outcome

The single, prespecified, secondary outcome is the incidence of complications related to intubation[4 5] in the hour following intubation (severe: severe hypoxaemia defined by lowest saturation <80%, severe cardiovascular collapse, defined as systolic blood pressure less than 65 mm Hg recorded at least once or less than 90 mm Hg lasting 30 min despite 500 to 1000 mL of fluid loading (crystalloids solutions) or requiring introduction or increasing doses by more than 30% of vasoactive support, cardiac arrest, death during intubation; moderate: difficult intubation, severe ventricular or supraventricular arrhythmia requiring intervention, oesophageal intubation, agitation, pulmonary aspiration, dental injuries).

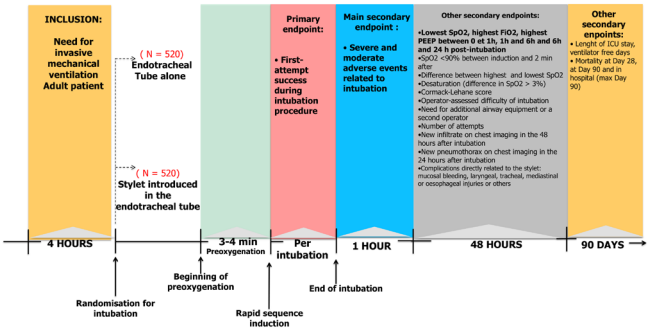

Figure 2 Study design of the STYLETO trial. FiO2,fraction of inspired oxygen; h, hours; ICU, intensive care unit; PEEP, positiveend-expiratory pressure; SpO2, peripheral oxygen saturation.

Main safety outcomes

The main safety outcomes will be the lowest peripheral oxygen saturation (SpO2), highest fraction of inspired oxygen (FiO2) and highest positive end-expiratory pressure (PEEP) in the time period of 6 to 24 hours post-intubation.[11] The complications that could be directly related to the stylet use will also be recorded during the first intubation attempt: mucosal bleeding, laryngeal, tracheal, mediastinal or oesophageal injuries or others.[10 13]

Exploratory procedural and safety outcomes

A separate analysis of severe and moderate complications related to intubation[4 5] and of each of its components will be performed.

The other exploratory procedural and safety outcomes will be the incidence of lowest SpO2 less than 90% from induction to 2 min after intubation;[11] change in SpO2 from SpO2 at induction to lowest SpO2;[11] desaturation, defined as a change in SpO2 of more than 3% from induction to 2 min after intubation;[11] Cormack-Lehane grade of glottic view;[11] operator-assessed difficulty of intubation;[11] need for additional airway equipment or a second operator;[11] number of laryngoscopy attempts;[11] lowest SpO2, highest FiO2 and highest PEEP from 0 to 1 hours and 1 to 6 hours after intubation;[11] new infiltrate on chest imaging in the 48 hours after intubation;[11] new pneumothorax on chest imaging in the 24 hours after intubation,[11] new pneumomediastinum on chest imaging in the 24 hours after intubation.[11] New infiltrate, pneumothorax or pneumomediastinum on chest imaging will be determined by the referent local ICU investigator.

Exploratory clinical outcomes

The exploratory clinical outcomes will be: ICU length of stay, ICU-free days, invasive ventilator-free days, mortality rate on day 28, in hospital (until day 90) and day 90 mortality.[11 18]

Interventions

Patients eligible for inclusion will be randomly assigned to the experimental group (endotracheal tube plus stylet) or to the control group (endotracheal tube alone, figure 2, online supplemental figure S1). First laryngoscopy for first-attempt will be performed with a standard Macintosh laryngoscope. The experimental group consists in intubating the trachea with an endotracheal tube plus stylet with a 'straight-to-cuff' shape and a bend angle of 25° to 35°.[19] The control group consists in intubating the trachea with an endotracheal tube alone (ie, without stylet). The type of blade (plastic or metal, size 3 or 4) for standard laryngoscopy and the type of endotracheal tube will be left to the operator discretion according to standard recommendations.[20]

The availability of equipment for management of a difficult airway will be checked.[21] The difficulty of intubation will be assessed using the MACOCHA score.[5] The Montpellier intubation protocol[8 22] will be strongly advised to be followed for each procedure. In brief, before intubation will be performed: fluid loading in absence of cardiogenic oedema and early introduction of vasopressors, preoxygenation with non-invasive ventilation and high-flow nasal cannula oxygen for apnoeic oxygenation in the case of acute respiratory failure,[18 23 24] preparation of sedation by the nursing team and the presence of two operators. During the intubation period, recommended induction will be rapid sequence induction using short-acting hypnotics (etomidate or ketamine or propofol in case of haemodynamic stability), and a rapid onset muscle relaxant (succinylcholine or rocuronium in case of hyperkalaemia), with application of cricoid pressure (Sellick manoeuvre). After the intubation will be performed: verification of the tube's position by capnography, initiation of long-term sedation as soon as possible (to avoid agitation) and low pressure (low tidal volume, low PEEP and low rate, with a protective mechanical ventilation and a recruitment manoeuvre following intubation after haemodynamic stabilisation.[25 26] At any time, vasopressors are recommended in the event of severe haemodynamic collapse.

During the procedure, after preoxygenation, the patient will be ventilated in case of desaturation to less than 90%. In case of inadequate ventilation and unsuccessful intubation, emergency non-invasive airway ventilation (supraglottic airway) will be used. In cases of intubation failure, the intubation algorithm of each unit will be followed.[7]

Participant timeline

The participant timeline is described in table 1.

Sample size

The primary outcome is the first-attempt success during intubation procedure. For this study, 2×485 patients are needed to detect a 10% difference in the first-attempt success rate during intubation procedure (from 70% without stylet to 80% with stylet, difference judged clinically important,[2 10] at a two-sided α level of 0.05 and a statistical power of 95%).[4 27 28] To take into account withdrawn consent after randomisation, inclusions not meeting the inclusion criteria or improvement or death before intubation, 1040 patients will be included: 520 patients in each group.

Recruitment

Patients are expected to be included during a 1.5-year inclusion period starting October 2019. Among the 35 participants centre, each one would include 4 to 10 patients per month during the 8 months study period.

March 2019 to September 2019: Protocol, approvals from ethics committee and trial tool development (case report form, randomisation system).

October 2019 to May 2020: Inclusion of patients.

September 2020: Cleaning and closure of the database. Data analyses, writing of the manuscript and submission for publication.

METHODS: ASSIGNMENT OF INTERVENTIONS

Allocation and sequence generation

Randomisation will be managed by the clinical research unit of Montpellier University Hospital with Capture System software (Ennov Clinical, randomisation module). The randomisation will be centralised and available online. It will be stratified on centre,[5 15] balanced with a 1:1 ratio and blocks of variable sizes.

Blinding

Given the nature of the devices, a blinded design is not possible for the investigator and associate investigator. The methodologist will be blinded to the group.

METHODS: DATA COLLECTION, MANAGEMENT AND ANALYSIS

Data collection and management

Data will be collected and recorded on electronic case report forms by trained local research coordinators or physicians. Methodology will be similar than the methodology used in a previous published paper, showing

Table 1 Participant timeline

	Inclusion	Intubation + 5 min + 60 min	48 hours after intubation	Discharge from ICU	Day 28	Day 90
Informed consent	X					
Eligibility: check inclusion and exclusion criteria	X					
Randomisation	X					
Filling of case report forms	X	X	X	X	X	X
Outcomes		X	X		X	X

ICU, intensive care unit.

that intubation procedure is a challenging issue in ICU because strongly associated with cardiac arrest related to intubation occurrence.[6] Patients will receive standard ICU monitoring consisting of ECG analysis, SpO2 and a non-invasive blood pressure cuff. Prior to tracheal intubation, the nurse will set the time intervals on the non-invasive blood pressure cuff monitoring and electronic medical record in the patient's room to run every minute until 15 min after successful intubation.

The following data will be collected and registered before intubation: demographic and epidemiological data: age, sex, weight, height, date and hour of intubation, on-call procedure, severity scores (Simplified Acute Physiologic Score (SAPS) II at admission, Sequential Organ Failure Assessment score on the day of the procedure), type of admission, reason of ICU admission, indication of intubation and comorbidities. The following parameters will be recorded during the 4 hours before intubation: arterial pressure and lowest saturation, arterial blood gases with calculated arterial oxygen tension to FiO2 ratio (PaO2/FiO2) ratio if performed, delay between the time where the intubation is decided and its realisation (defining real emergency (endotracheal intubation required without delay), relative emergency (endotracheal intubation required within 1 hour), deferred emergency (endotracheal intubation required in more than 1 hour)), presence of vasopressor drugs, prior non-invasive ventilation or high-flow nasal cannula oxygen use, existence of predictive criteria of difficult intubation evaluated by the MACOCHA score.[5]

During preoxygenation, the following data will be recorded: the length of preoxygenation, the vital parameters (SpO2 at the beginning and at the end of the preoxygenation, the type of preoxygenation).

During the intubation procedure, the following parameters will be collected : doses of hypnotic and neuromuscular blocker used, SpO2 at the beginning and at the end, lowest SpO2, lowest and highest arterial pressure and heart rate, total duration of the intubation procedure, number of operators, number of attempts, Cormack grade, traction force on the laryngoscope, Sellick manoeuvre, difficult intubation (more than two attempts), modified Intubation Difficulty Scale score[29] and occurrence of complications related to intubation. The compliance with the Montpellier intubation protocol[8] will be recorded.

After the intubation procedure (until 1 hour after): arterial blood gases with calculated PaO2/FiO2 ratio if performed at 5 min and 30 min and ventilatory settings will be recorded. Moderate and severe complications occurring and nature, number of operators and their training, will be collected.[11]

From postoperative day 1 to hospital discharge will be assessed: ventilatory settings (lowest SpO2, highest PEEP and highest FiO2 at 1 hour, 6 hours and 24 hours), chest X-ray at 24 hours and 48 hours to identify pneumothorax or new pulmonary infiltrate, morbi-mortality by the length of mechanical ventilation, the length of stay in ICU and the mortality at day 28.

Statistical methods

Statistical analysis

The statistical analysis will incorporate all the elements required by the CONSORT statement for non-pharmacological interventions. Statistical analysis will be performed in an intention to-treat population, including all the randomised patients except patients who withdraw their consent, do not meet the inclusion criteria or improve before intubation and were not intubated. All analyses will be conducted by the medical statistical department of the Montpellier University Hospital using statistical software (SAS, V.9.4; SAS Institute; Cary, North Carolina, USA, and R, V.3.6.2). A two-sided p value of less than 0.05 will be considered to indicate statistical significance.

Description of the patient groups at baseline

The baseline features of the overall population and of each group will be described. Categorical variables will be reported as frequencies and percentages and continuous variables as either means with SDs or medians with IQRs.

Primary analysis

Unadjusted test of intervention effect. Uncorrected χ^2 test will be used for primary outcome analysis. Endotracheal tube plus stylet group will be compared with endotracheal tube alone.

Secondary analyses

We will conduct the following prespecified secondary analyses:

(1) Secondary, safety and exploratory Outcomes.

We will perform unadjusted, intention-to-treat analyses comparing patients in the endotracheal tube plus stylet group to the endotracheal tube alone group with regard to each of the prespecified secondary and exploratory outcomes.

Continuous outcomes will be compared with the Student's t-test or Mann-Whitney rank-sum test according to the conditions of application and categorical variables with the χ^2 test or the Fisher's exact test, according to the conditions of application. For repeated data, a mixed linear model will be used, including the subject as a random variable.

(2) Per-protocol analysis.

We will perform a per-protocol analysis comparing patients in the endotracheal tube plus stylet group to the endotracheal tube alone group (regardless of group assignment).

(3) Effect modification (subgroup analyses).

We will examine whether prespecified baseline variables modify the effect of study group on the primary outcome. We will evaluate for effect modification by fitting a logistic regression model for the primary outcome of first-attempt success. Independent variables will include study group assignment, the potential effect modifier variable of interest and the interaction between the two (eg, study group*SpO2 at induction). Significance will be determined by the p value

for the interaction term, with values less than 0.10 considered suggestive of a potential interaction and values less than 0.05 considered to confirm an interaction. Subgroups derived from categorical variables will be displayed as a forest plot. Continuous variables will be analysed using cubic splines with 3 to 5 knots. If the presentation of data requires it, dichotomisation of continuous variables for inclusion in a forest plot will be performed.

Prespecified subgroups that may modify the effect of adding a stylet for tracheal intubation include:[11]

1. SpO2 at induction (continuous variable).[11]
2. Highest FiO2 received in the 6 hours prior to intubation (continuous variable).[11]
3. Receipt of non-invasive ventilation in the 6 hours prior to intubation (yes/no).[11]
4. Indication for intubation (acute respiratory failure, not acute respiratory failure).[11]
5. Neuromuscular blocking agent (depolarising, non-depolarising, none).[11]
6. SAPS II score at enrolment (continuous variable).[11]
7. Body mass index (continuous variable).[30 31]
8. Operator's prior number of tracheal intubations (continuous variable).[11]
9. Operator training (critical care medicine, anaesthesia)[11] and experience.[2 5]
10. Obesity (yes/no).[32 33]
11. Difficult intubation (yes/no).[5]

(4) Multivariable modelling to account for confounding.

A logistic regression will be used for the analysis of the main criteria with OR of first-attempt success calculation, before and after adjustment on confounding variables despite the randomisation. Covariates will be defined as binary variables and continuous variables dichotomised according to their median tested in the model, and will be selected in a backward selection procedure if p<0·15 in the univariate analysis and then presented as adjusted ORs with 95% CIs.

A centre effect will be checked using a mixed effect logistic model, considering the centre both as a random and then a fixed variable. Interactions between variables and time will be tested.

Handling of missing data

Based on prior trials in similar settings, we anticipate less than 5% missing data for the primary outcome. For the primary analysis, missing data will not be imputed.

Corrections for multiple testing

We have prespecified a single primary analysis of a single primary outcome. For the exploratory outcomes, a False Discovery Rate method[34] will be used.

METHODS: MONITORING

Data monitoring

Before the start of patient recruitment, all physicians and other healthcare workers in the ICUs will attend formal training sessions on the study protocol and data collection.

The physicians and a clinical research nurse and/or clinical research assistant are in charge of daily patient screening and inclusion, ensuring compliance with the study protocol and collecting the study data, with blinded assessment.

Harms

The trial may be temporarily stopped for an individual patient, at the discretion of the attending physician, in case of major serious adverse events suspected to be associated with the technique of intubation used.

ETHICS AND DISSEMINATION

Research ethics approval

This research involving humans will be conducted in compliance with French 'Loi n°2012–300 du 5 mars 2012 relative aux recherches impliquant la personne humaine (Loi Jardé), 'Loi N°78–17 du 6 janvier 1978 modifiée relative à l'Informatique, aux fichiers et aux Libertés'.

This study will be conducted in accordance with Good Clinical Practice, as defined by the International Conference on Harmonisation.

The study project has been approved by the ethics committee 'Comité de Protection des Personnes Nord Ouest 3 19.04.26.65808 Cat 2 RECHMPL19_0216 / STYLETO 2019-A01180-57'. The STYLETO study is conducted in accordance with the declaration of Helsinki and is registered on at http://www.clinicaltrials.gov (NCT04079387).

Consent or assent

Three methods of consent will be used, as required by the institutional review board in accordance with the 2013 Declaration of Helsinki. If possible, the patient will be included after written informed consent. However, the patient often cannot understand information given because of underlying disease. These patients will be included after written informed consent is provided by next of kin or an emergency procedure (investigator signature) if next of kin is not present. When available, after recovery, patients will be retrospectively asked for written consent to continue the trial. Informed consent material is available in online supplemental file 2.

Patient and public involvement

The development of the research question and outcome measures was not informed by patients' priorities, experience and preferences. Patients were not involved in the design, recruitment and conduct of the study. The burden of the intervention was not assessed by patients themselves. The results will be available for study participants on demand. No systematic disseminating of the results for study participants was planned.

Confidentiality

Data will be handled according to French law. All original records will be archived at trial sites for 15 years. The clean database file will be anonymised and kept for 15 years.

Declaration of interest

The study is an investigator-initiated trial. Study promotion is performed by Montpellier University Hospital, Montpellier, France. There is no industry support or involvement in the trial.

Dissemination policy

Findings will be published in peer-reviewed journals and presented at local, national and international meetings and conferences to publicise and explain the research to clinicians, commissioners and service users. All investigators will have access to the final data set. Participant-level data sets will be made accessible on a controlled access basis.

DISCUSSION

To the best of our knowledge, the STYLETO trial is the first pragmatic randomised controlled trial powered to investigate if adding a stylet to the endotracheal tube increases first-attempt success during the intubation procedure in ICU.

Intubation in ICU is associated with severe complications,[4 5] the ultimate being the occurrence of intubation-related cardiac arrest.[6] Intubation-related cardiac arrest was found to be an independent risk factor for day 28 mortality.[6] Optimising intubation procedure is, therefore, of particular importance, to reduce morbi-mortality in ICU.[7] However, although many efforts have been made to improve the security of intubation procedure in ICU,[8] the devices used for intubating the trachea have been poorly studied. Use of a stylet allows to pre-shape the endotracheal tube, adds rigidity to the endotracheal tube and could help to improve the ability to catheterise the trachea.[35]

The primary endpoint of the trial is the first-attempt success during intubation procedure. The first-attempt success rate in ICU is ranged between 60% and 80% depending on the setting, the population, the level of expertise of operators and the device used.[2 5 18] Increasing first-attempt success could decrease the apnoea period length which can last several minutes, especially when the intubation is difficult. Increased length of apnoea before successful intubation and ventilation is associated with increased occurrence of hypoxaemia.[7] The first-attempt success is of paramount importance in preventing the development of subsequent complications including intubation-related cardiac arrest.[6] The first-attempt success rate is one of the most used main criteria when evaluating devices used for intubation procedure in emergency settings.[2 10] The criterion 'first-attempt intubation success' was chosen because directly related to the potential benefits of using a stylet and associated with complications related to intubation. In a large, multicentre database retrospective analysis of complications related to 1844 intubation in the ICU,[36] we recently reported that first-attempt success was associated with fewer complications related to intubation than first-attempt failure. The time to successful intubation is also important but was less likely to be affected by the use of a stylet. Moreover, since we collect and report on most complications related to intubation, either severe or moderate, it may still be possible to determine the effects of stylet on other complications associated with intubation. If this trial demonstrates superiority of the endotracheal tube with stylet, intubation without a stylet might decrease significantly worldwide.

Strengths of the study are that all intubation performed around the clock (nights and weekend) will be included. The randomised design of the study, combined to a sufficient power (95%) with large sample size, will allow to conclude to the usefulness of a stylet. Moreover, as it is a pragmatic and multicentre study, the external validity of the study will be high. Limitations of the study are the non-blinded design, even if it will likely not influence the operator, given the vital character of the intubation procedure. We chose not to allow videolaryngoscopy for the first-attempt of intubation, to avoid confounding factors regarding the association between stylet use and first-attempt success.[2 37 38] Besides, according to recent data showing the results of an online nationwide survey in 180 French ICUs,[39] the videolaryngoscopy was used for the first attempt in only 8 (4%) ICUs. Therefore, the external validity of our study will be higher focussing on Macintosh direct laryngoscopy for first-attempt success.

In conclusion, the STYLETO trial is an investigator initiated pragmatic randomised controlled trial powered to test the hypothesis that adding a stylet to the endotracheal tube in comparison to the endotracheal tube alone allows to increase first-attempt success and decrease intubation-related complications during the intubation procedure using a Macintosh direct laryngoscopy blade of ICU patients requiring mechanical ventilation.

Trial status

The trial is started and actively enrolling since October 2019.

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Contributors ADJ drafted the manuscript together with SJ. SJ designed the study together with ADJ, HB, DG and CC. NM and ADJ wrote the statistical analysis plan and estimated the sample size. All authors (ADJ, AR, BJ, GC, HB, DG, CC, NM, SJ) revised the manuscript for important intellectual content and read and approved the final version of the manuscript.

Funding The study is an investigator-initiated trial. Study promoter is Montpellier University Hospital, Montpellier, France.

Competing interests SJ reports receiving consulting fees from Drager, Fisher & Paykel and Xenios.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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