« ASSESMENT OF THE SELLICK MANEUVER IN RAPID SEQUENCE INDUCTION OF GENERAL ANESTHESIA»

PHRC IRIS

BIOMEDICAL RESEARCH PROTOCOL

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This version corresponds to the protocol version and its appendix sent to the CPP and appropriate authorities concerning ethical approval and authorization to perform a biomedical research .

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SYNOPSIS

1. GENERAL INFORMATION

1.1 Summary

Introduction: Pulmonary aspiration occurs during general anesthesia because of the loss of the reflexes protecting airways. Its incidence is low during elective surgery, when preoperative fasting rules have been applied and in the absence of risk factors for regurgitation of gastric contents. In emergency conditions, non-compliance with preoperative fasting rules and delayed gastric emptying markedly increase the risk of pulmonary aspiration.[5] In this context, a rapid sequence induction of anesthesia is recommended to minimize the risk of aspiration, combining the use of a short acting hypnotic and a muscle relaxant associated with the application of a the Sellick maneuver). The goal of the Sellick maneuver is to compress the esophagus between the cricoid cartilage and the fifth cervical vertebra. This maneuver is recommended although its efficacy has been poorly documented, and thus remains controversial.

Hypothesis: The aim of this study is to assess the Sellick maneuver during rapid sequence induction in adults (pregnant women excluded) by comparing the incidence of pulmonary aspiration whether the maneuver is applied or sham, in a noninferiority trial.

Primary end point: Incidence of pulmonary aspiration in the operating room, as detected either at the glottis level during laryngoscopy or by tracheal aspiration just after tracheal intubation.

Secondary end points : Cormack et Lehane grade to assess the laryngeal exposure, incidence of difficult tracheal intubation, incidence of impossible tracheal intubation, effects of Sellick maneuver interruption on these 3 criteria, incidence of pneumonia during the first 24 hours, traumatic complications related to Sellick maneuver (esophageal and cricoid cartilage ruptures), mortality at hospital discharge or 28 days.

Methods: Multicenter, randomized, double-blind study. The two groups only differ by the application of the Sellick maneuver or a sham procedure.

Number of patients: Noninferiority trial. The number of patients to be included is estimated at 1,750 per group, a total of 3,500.

Inclusion criteria: Any patient requiring a rapid sequence induction of general anesthesia. Written informed consent obtained from the patient or a close relative/surrogate. In case of emergency conditions and if such a person was absent, the patient was randomized according to the specifications of emergency consent authorized by the ethical committee and the patient was asked to give his/her consent for the continuation of the trial when his/her condition allowed.

Exclusion criteria : Patients <18 years-old, pregnancy, contraindication of the Sellick maneuver or succinylcholine administration, clinical signs of pneumonia during the pre-

anesthesia visit, severe pulmonary contusion, upper respiratory tract abnormalities, patients requiring an alternative technique for tracheal intubation, consciousness abnormalities, decision to use a plastic blade for laryngoscopy, decision to use rocuronium for rapid induction sequence, inclusion in another randomized trial, lack of national health care insurance.

Conclusion: The application of the Sellick manoeuver during rapid sequence induction of anesthesia is aimed to reduce the risk of pulmonary aspiration of gastric content. If, when the Sellick maneuver is not performed, the risk of pulmonary aspiration is not increased, it would be possible to avoid it and thus to not expose patients to its related adverse effects and known complications.

2. SCIENTIFIC RATIONALE AND GENERAL DESCRIPTION OF THE RESEARCH

2.1 State of knowledge

Loss of consciousness induced by general anesthesia is associated with loss of reflexes that protect the airway and thus is associated with an increased risk of gastric content regurgitation and pulmonary aspiration. Therefore, anesthesia of a patient with a full stomach presents a risk of pulmonary aspiration.

The incidence of anesthesia-induced pulmonary aspiration is variable. It is absent in case of loco-regional anesthesia. The incidence is very low in elective surgery when preoperative fasting rules have been followed and in the absence of risk factors for regurgitation of gastric contents (esophageal reflux, hiatus hernia, gastroparesia, previous gastric surgery, pregnancy etc.…)[1] and markedly increases in emergency surgery performed under general anesthesia.[2,3] In emergency conditions, delayed gastric emptying associated with conditions cited above (ileus), non-compliance with preoperative fasting rules, pain, anxiety, and use of opioids are considered as risk factors that markedly increase the risk of pulmonary aspiration.[1] To limit this risk, loco-regional anesthesia should be preferred if feasible.[2] In the other cases, the anesthesia technique should reduce the delay between the loss of consciousness and the cuff inflation of the tracheal tube to limit the risk of pulmonary aspiration. To fulfill this objective, induction of anesthesia should be performed using a rapid sequence induction using short acting anesthetic drugs.[4]

To reduce the risk of pulmonary aspiration the rapid sequence induction of anesthesia comprises the application of the Sellick maneuver.[4] During this maneuver, the esophagus is manually compressed and thus occluded between the cricoid cartilage and the fifth cervical vertebra.[5,6] However, the Sellick maneuver described more than 40 years ago, remains controversial.[7,8] It has not been demonstrated that the esophageal occlusion is complete in all cases and even that it is an efficacious measure to protect against regurgitation.[9-11] In addition, this maneuver may even facilitate regurgitation if inappropriately applied,[12,13] and may induce difficulties in intubating the trachea or compromise mask ventilation.[14-18]

Thus, the aim of the study is to assess the interest of the Sellick maneuver during rapid sequence induction of anesthesia in adults (pregnancy excluded) by comparing the incidence of pulmonary aspiration whether this maneuver is real or sham.

2.2 Literature review and prerequisites

2.2.1 Pulmonary aspiration and anesthesia

The incidence of anesthesia-induced pulmonary aspiration has been poorly documented, as well as that of aspiration-induced pneumonia, some of them being not appropriately diagnosed.[19] Pulmonary aspiration is absent during loco-regional anesthesia without sedation,[2] but occurs during general anesthesia because of the loss of airway protective reflexes as consciousness is impaired due to anesthetic agents used. Pulmonary aspiration occurs mainly during induction of anesthesia but may also occur during anesthesia recovery. Their incidence and consequences are variables. In a study conducted in 172,334 patients who underwent 215,488 general anesthetics, the incidence was estimated 1/3886 (0.03%) during elective surgery. In emergency surgery, the incidence was reported as 1/885 (0.1%) with a higher incidence in the most severe patients (ASA 4: 1/343; 0.3%).[2] In another study including 185,385 anesthesia, the incidence of aspiration-related pneumonia was 1/2131 (0.1%) and an emergency condition was noted in half the cases.[3] Moreover, the incidence of pulmonary aspiration is increased in case of difficult tracheal intubation.[20] The consequences of pulmonary aspiration are also highly variable.[19] In the Warner et al. study,[2] 2/3 of the patients had no clinical signs, and 1/3 required prolonged mechanical ventilation. In the Olsson et al. study,[3] a radiological diagnosis of the pneumonia was performed in 47% of cases and 17% of patients required prolonged mechanical ventilation. However, several very severe cases have been reported and the severity of the disease depends on the volume and characteristic of inhaled gastric content.[19] In a more recent study assessing the complications observed after 3,423 tracheal intubations performed in emergency conditions in an academic hospital, the incidence of pulmonary aspiration was 2,8%.[21]

2.2.2 Prevention of the risk of aspiration

In a patient with a full stomach or having some regurgitation risk factors, several techniques are possible to prevent the occurrence of pulmonary aspiration and aspiration-induced pneumonia:

- to administer an anti-acid oral drug to diminished the acidity of the gastric content ;
- to promote gastric emptying either by administering drugs which accelerate gastric emptying or by aspiration of the gastric content using a nasogastric tube;
- induction of anesthesia should be performed using a rapid induction sequence which comprise a careful preoxygenation procedure, the administration of a short-acting anesthetic drug and a short-acting muscular relaxant, and the Sellick maneuver .[4]

2.2.3 The Sellick maneuver

Described more than 40 years ago, the maneuver aims to occlude the esophagus by manually compressing it between the cricoid cartilage and the 5th cervical vertebra.[5] The initial description was performed in human cadavers and the efficacy of the maneuver was reported in a short series of 26 patients at high risk of pulmonary aspiration: in 23 patients no regurgitation of the gastric contents was observed whereas in the remaining 3 patients this occurred after the release of the cricoid pressure. Although its efficacy has been poorly documented, the Sellick maneuver has become a recommended procedure. Later, the maneuver has been described in more details. A pressure between 20 and 40 Newtons should be applied on the cricoid cartilage, downward,[22] as soon as the consciousness is lost, until inflation of the cuff of the tracheal tube.[4] The pressure should be released in case of active vomiting to avoid esophageal rupture.[22-24] The Sellick maneuver is contraindicated in case of cervical spine trauma,[25] laryngeal trauma, and foreign bodies in the trachea or the esophagus.[26] Although widely recommended, the Sellick maneuver remains controversial.[8]

Several reasons can explain this controversy:

- Anatomical studies have shown that the esophagus is not centrally placed between the cricoid cartilage and the vertebra and thus a complete occlusion cannot be obtained in all cases during the Sellick maneuver.[9-11]
- The Sellick maneuver seems to be easy to apply but the pressure level to be used is difficult to verify and thus this maneuver is not always appropriately performed.[27-31]
- A too low pressure may facilitate regurgitation because it could induce a release of the lower esophageal sphincter.[12,13,32,33]
- Some cases of regurgitation and pulmonary aspiration have been reported despite the application of the Sellick maneuver.[34-36]
- The Sellick maneuver may compromise tracheal intubation,[17,18,37-39] insertion of a laryngeal mask, [14,15,40] and mask ventilation.[41]
- Lastly, the Sellick maneuver may induce severe complications such as esophageal rupture or fracture of the cricoid cartilage.[22-24,42-44]

2.3 Summary of the known risks and foreseeable risks to the research subjects

2.3.1 Risks associated to anesthesia with rapid sequence induction

- Risk of pulmonary aspiration because of fasting noncompliance and/or emergency conditions in a patient with a full stomach and/or risk of regurgitation as described above. The pulmonary aspiration risk is estimated between 0.5 and 3 % according to previous studies. The hypothesis is that the risk of pulmonary aspiration is not increased when the

Sellick maneuver is not performed. However, the aim of this study is to demonstrate that the risk of pulmonary aspiration when the Sellick maneuver is not performed, is not greater.

2.3.2 Risk associated with the Sellick maneuver

Risks related to the Sellick maneuver:

- increased risk of pulmonary aspiration ;
- difficult laryngeal exposure during tracheal intubation;
- difficult mask ventilation if required ;
- risk of cricoid cartilage fracture ;
- risk of esophageal rupture;

Risk associated to the sham procedure:

- Increased risk of pulmonary aspiration ;

3. RESEARCH OBJECTIVES

3.1. Tested hypothesis :

We test the noninferiority hypothesis that the incidence of pulmonary aspiration in adult patients requiring a rapid induction sequence is not increased when the Sellick maneuver is not performed (Sham group) as compared to its application (Sellick group).

3.2. Primary objective :

The primary end point is to demonstrate that the incidence of pulmonary aspiration is not increased when the Sellick maneuver is not performed during a rapid induction sequence. Pulmonary aspiration is detected in the operating room just after tracheal intubation either at the glottis level during laryngoscopy or by tracheal aspiration just after tracheal intubation.

3.3. Secondary objectives :

- Laryngeal exposure during tracheal intubation assessed using Cormack and Lehane grade.[45]
- Difficult tracheal intubation as defined by the SFAR Consensus : tracheal intubation requiring more than 2 attempts and/or requiring an alternative technique (despite optimization of the head position and external laryngeal manipulation).[46]

- Impossible tracheal intubation impossible defined par intubation failure requiring awakening of the patients after use of alternative techniques and/or requiring cricothyroidomy or tracheotomy.
- Mask ventilation requirement.
- Interruption of the Sellick maneuver as requested by the tracheal intubation operator ;
- Consequences of Sellick maneuver interruption assessed by the Cormack and Lehane grade.
- Traumatic complications related to the Sellick maneuver : esophageal rupture and cricoid cartilage fracture. Because these complications are rare and highly symptomatic, no specific examination is required.
- Incidence of aspiration pneumonia within the first 24h. The diagnosis is retained when pulmonary aspiration is observed in the operating room and new radiological infiltrates is observed.[2] A chest X-ray is performed in the recovery room only in case of : 1) pulmonary aspiration observed in the operating room (cf. above), 2) any clinical sign enabling to suspect aspiration pneumonia. A new Chest-X ray should be performed at 24 hours in the previous cited cases even if the initial chest X ray is normal. Aspiration pneumonia is considered as severe when at least one of the following item is present : 1) decrease in oxygen saturation when breathing room air greater than 10% compared to the value before anesthesia; 2) PaO_2/FiO_2 less than 300;[2] 3) requirement of mechanical ventilation (invasive or not) and 4) prolonged hospital duration.
- Mortality at Day 28 or at hospital discharge if it occurs before Day 28. It seems reasonable to capture all mortality events when pulmonary aspiration occurs (primary end point).

4. RESEARCH DESIGN

4.1. Type of the study

This is a multicenter, randomized, double-blind, noninferiority study comparing a group of patients requiring anesthesia and a rapid induction sequence without the Sellick maneuver (Sham group) with a group of patients requiring anesthesia and a rapid induction sequence with a Sellick maneuver (Sellick group).

4.2. Precise statement of the primary end point and, where applicable, secondary end points.

4.2.1. Primary end point

The primary end point is the presence or absence of bronchial inhalation diagnosed in the operating room with the presence of gastric fluid in the vocal cords or in the tracheal aspiration immediately after intubation.

4.2.2. Secondary end point

- Cormack and Lehane grade (Appendix 1)
- Number of difficult tracheal intubations
- Number of impossible tracheal intubations
- Number of oxygen desaturations (< 92%)
- Number of face mask ventilations required
- The need to interrupt the Sellick maneuver in both arms of the study and the reasons for the interruption.*****
- Effects of the Sellick maneuver release on tracheal intubation conditions assessed by the Cormack and Lehane grade
- Morbidity related to the application of the Sellick maneuver in the Sellick group. This is evaluated by looking for known complications of the maneuver such as an esophageal rupture occurring during vomiting efforts or a fracture of the cricoid cartilage.
- Incidence of inhalation pneumonia within H24.
- Mortality on Day 28 or on discharge from hospital if prior to Day 28.

4.3. Description of the research methodology, including a schematic presentation specifying the planned visits and examinations.

4.3.1. Patient follow-up

4.3.1.1. Checking inclusion and non-inclusion criteria

During the pre-anesthetic evaluation of patients, the anesthetic strategy is decided. Also, inclusion and non-inclusion criteria are verified at this stage. This pre-anesthetic evaluation will be carried out as part of the emergency department on the day of surgery. In other situations, verification of inclusion criteria will be done during the anesthesia consultation at least 48 hours prior to surgery.

4.3.1.2.Information and informed consent of the patients

Information and informed consent is collected before inclusion.

Within the framework of scheduled surgery, in the presence of a regurgitation risk factor, recognized during an anesthesia consultation (at least 48 hours before the surgery), the information is delivered and written informed consent is obtained during this same consultation or during the pre-anesthetic visit carried out the day before the operation.

As part of an emergency procedure, information is provided and informed consent is obtained during the pre-anesthetic evaluation on the day of surgery. If the patient is unable to sign the consent, the explanation of the study and collection of the consent of a relative, family member or designated trustworthy person is done. In this case, consent is obtained from the patient, after being informed as soon as the patient's state of health permits. An emergency inclusion procedure may be performed by the investigating physician in charge of the patient, after consultation with an independent physician. In this case, as soon as a family member, relative or designated trusted person has been contacted, the information is issued and consent is requested. As soon as possible, the patient is informed and his/her written informed consent is obtained for the eventual continuation of the research.

4.3.1.3. Follow -up

Any randomized patient is evaluated up to Day 28 or until discharge from the hospital if prior to Day 28.

4.4 Description of the measures taken to reduce and avoid bias, including in particular :

4.4.1. Recruitment

This study is aimed to include as much as possible all eligible patients to guaranty that the included population actually reflects the population requiring rapid induction sequence. The inclusion criteria are simple and the exclusion criteria only comprised rare contraindications of the Sellick maneuver or the rapid induction sequence (cf above) and preexisting pneumonia of consciousness abnormalities which may make the primary end point difficult to assess. Patients will be recruited in 10 academic centers (Department of anesthesiology and critical care, Groupe Hospitalier Pitié - Salpêtrière – Paris, Department of anesthesiology and critical care, Hôpital Beaujon – Clichy, Department of anesthesiology and critical care, hôpital Bicêtre – Le Kremlin Bicêtre, Department of anesthesiology, hôpital Avicenne – Bobigny, Department of anesthesiology and critical care, Hôpital Bichat - Paris, Department of anesthesiology, CHU de Rouen – Rouen, Department of anesthesiology and

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4.4.2. Randomization

It will be a centralized randomization (Randoweb®) managed by the URC Pitié-Salpêtrière. Each investigator will be able to access the randomization site using a personal password. The randomization arms are the following: effective application (Sellick group) or feinting of the Sellick maneuver (Sham group). This randomization is carried out on the day of surgery before entering the operating room. The randomization list will be generated by blocks in a 1:1 ratio and will be stratified by center. Within each block, the number of patients in Sham group will be equal to the number of patients in the Sellick group. The size of the blocks will be defined by the person in charge of randomization, and will only be communicated to the DRCD Quality Assurance department.

4.4.3. Blinding methods

In order to carry out this double-blind study, in the experimental group, the Sellick maneuver is simulated so that the person performing the orotracheal intubation does not know which arm the patient is in.

4.5. Research participation and total expected research time

Each patient's participation period is a maximum of 28 days. The inclusion period is 24 months, so the study is planned to last 25 months.

4.6. Summary table of the chronology of the research and examinations conducted

In case of scheduled surgery:

	Pre-anesthesia consultation At least 48h before	Pre-anesthesia visit day of surgery	Day 0 = Day of surgery	Day 1	Day 2 to Day 28
Protocol presentation	**X**	**X**			
Submission of the information note and consent form	**X**	**X**			
Inclusion and exclusion criteria verification	**X**				
Signature of consent form	**X**	**X**			
Past medical history	**X**				
Clinical examination	**X**				
Randomization			**X**		
Rapid sequence induction			**X**		
Bacteriological sampling			**(x)**	**(x)**	
Chest X-ray			**(x)**	**(x)**	
Adverse and serious adverse events recording			**X**	**x**	**x**

X : performed according to routine care
(x) : if necessary

In case of emergency surgery :

	Day 0 = Pre-anesthesia visit = Day of surgery	Day 1	Day 2 to Day 28
Protocol presentation	**X**		
Submission of the information note and consent form	**X**		
Inclusion and exclusion criteria verification	**X**		
Signature of consent form	**X**		
Past medical history	**X**		
Clinical examination	**X**		
Randomization	**X**		
Rapid sequence induction	**X**		
Bacteriological sampling	**(x)**	**(x)**	
Chest X-ray	**(x)**	**(x)**	
Adverse and serious adverse events recording	**X**	**x**	**x**

X : performed according to routine care
(x) : if necessary

4.7. Description of final or temporary stop rules

The decision to discontinue the study will be taken by the Independent Monitoring Committee. The convening of an extraordinary meeting may take place at the request of the principal investigator or methodologist, in the event of serious adverse events or results that might call into question the existence of the protocol.

The following will also be considered grounds for discontinuing the study:

4.7.1. In case of insufficient recruitment:

a) if one year after the official research start date, no inclusion has been made, the DRCD will decide on the premature termination of the research.

b) if at 30% of the time allowed for inclusion of subjects in the study, fixed from the date of the first inclusion, less than 15% of the subjects have been included, an analysis of the causes will be carried out and corrective actions taken (motivation of the centers, addition of additional centers, modification of the criteria on the population to be included).

c) lastly, if less than 30% of the patients have been included, at 50% of the expected duration of the inclusions defined as above, the DRCD is likely to decide, after obtaining the assent of

the independent Supervisory Committee, whether the inclusions should be definitively discontinued, or even whether the research should be terminated prematurely.

4.7.2. In the event of serious adverse events in excess.

The study will be interrupted if the serious adverse events (SAE) are doubled.

4.7.3. Other specifically monitored events

The study may be interrupted in the event of a doubling of these specific events. The increase in the number of severe pneumonia, *i. e.* requiring mechanical ventilation or lengthening the length of hospitalization, increased incidence of impossible intubation and excess mortality at Day 28 or upon discharge from hospital, will be criteria for premature discontinuation of the study.

5. INCLUSION AND EXCLUSION OF PATIENTS

5.1. Criteria for inclusion of patients

1. All adult patients requiring emergency general anesthesia or presenting regurgitation risk factors, for whom a rapid sequence induction should be performed.

2. Obtaining the consent of the patient or a trusted person/family member. In an emergency situation and in the absence of a close relative/trustworthy person, the patient may be randomized on the advice of an independent physician. Consent to continue the research will be sought as soon as the patient's condition permits.

5.2 Criteria for non inclusion of patients

1. Patients under 18 years of age

2. Pregnant women (interrogation diagnosis)

3. Patients with contraindications to the Sellick maneuver:

- spinal cord injury - cervical spinal cord injury;
- laryngeal trauma ;
- intra-tracheal foreign body ;
- esophageal foreign body ;

4. Patients with contraindications to succinylcholine:

- hyperkalemia or risk of hyperkalemia;
- allergy;
- -previous history of malignant hyperthermia;
- myopathy;
- extensive burns > 24 hours;
- paraplegia/tetraplegia/denervation > 24h;
- plasma pseudocholinesterase deficiency;
- injury to the eye.

5. Patients with signs suggestive of pneumonia during preanesthetic evaluation

6. Patients with severe pulmonary contusion

7. Patients with upper airway morphological abnormalities

8. Patients requiring an alternative technique to direct laryngoscopy.

9. Patient with consciousness disorders

10. Decision to use a disposable plastic laryngoscope blade

11. Decision to use rocuronium

12. Patient not affiliated the national health care insurance (beneficiary or entitled).

6. TREATMENT OF PATIENTS INCLUDED IN THE STUDY

Patients requiring general anesthesia in the emergency room –except those with expected difficult tracheal intubation- benefit from an anesthesia protocol that meets the recommendations for Good Clinical Practice.[4] Neutralization of gastric acidity can be achieved by taking effervescent cimetidine 20 minutes prior to induction, left to the discretion of the anesthesiologist. After careful pre-oxygenation (4 vital capacities in case of emergency conditions or until an expired oxygen fraction (FeO2) > 90% is obtained), induction of anesthesia is achieved by intravenous administration of a fast-acting hypnotic adapted to the

patient's hemodynamic state (propofol (1.5 to 2.5 mg/kg), thiopental (3 to 5 mg/kg), etomidate (0.2 to 0.4 mg/kg), ketamine (2 to 3 mg/kg) and a muscle relaxant with short duration of action: succinylcholine at the dosage of 1 mg/kg. Tracheal intubation is then performed using a MacIntosh laryngoscope with metallic blade.[47] The correct position of the tracheal tube is confirmed by the presence of a capnogram (3 cycles). The Sellick maneuver is maintained from loss of consciousness until the balloon of the tracheal tube is inflated and the correct intratracheal position has been verified. The efficacy of the Sellick maneuver to prevent pulmonary aspiration being the primary end point, patient groups differ only in the actual or feigned performance of the maneuver.

6.1. Control group : the Sellick maneuver

Thus, in the Sellick arm of the study, the Sellick maneuver is applied, as initially described by Sellick et al.[5] To do so, after having identified the cricoid cartilage, the operator exerts a pressure equivalent to 30 Newtons (~3 kg) with the first 3 fingers of his dominant hand. The pressure is applied using the thumb and middle finger, positioned at 10 and 2 o' clock respectively. The index finger is positioned on the cricoid cartilage to control the direction of compression. The Sellick maneuver is taught to all anesthesiologists in training and performed daily. However, specific training to carry out the Sellick maneuver is planned before the inclusion of the first patient in each center. This training will include a manikin to clarify the position of the operator's fingers and a pressure training session according to an ergonomic, reproducible model: the obstructed syringe model described by Flucker et al.[48] This model reproduces the 10 and 30 Newton pressures recommended in the Sellick maneuver by reducing the piston of a 50 ml syringe filled with air and blocked to 40 and 33 ml respectively. This training will be repeated on a monthly basis throughout the study.

6.2. Experimental group : The feigned Sellick maneuver

In the experimental arm, the Sellick maneuver is feigned; the operator who has to perform it is the only one who knows which arm of the study the patient is in. Thus, he/she positions his/her fingers as described in the Sellick arm (see above) without exerting pressure on the cricoid cartilage.

In both arms, the Sellick maneuver, whether actual or feigned, can be released at the request of the person performing tracheal intubation, particularly to improve intubation conditions or in case of active vomiting. On the other hand, it must be maintained if ventilation with the face mask is required.

6.3. Induction of anesthesia

The induction of anesthesia is carried out by at least two individuals, one of them performing the Sellick maneuver, whether actual or feigned. In order to maintain the blind person regardless of intubation conditions, the person performing the Sellick maneuver, whether feigned or actual, will not be able to replace the operator in case of difficult tracheal intubation, so it is not possible to interchange the functions of the person who intubates and the person performing the Sellick maneuver.

In order to optimize the tracheal intubation conditions of patients, student anesthesia nurses and anesthesia fellow with less than one year of seniority will not be able to intubate patients participating in the study. However, they will be able to perform the Sellick manoeuver after training, as described above.

Sellick's manoeuver can only be carried out by medical or paramedical personnel trained in anesthesia (nurse anesthetist, student nurse anesthetist, senior anesthesiologist, junior anesthesiologist).

If the patient is carrying a nasogastric tube, after suctioning the stomach contents, the nasogastric tube is removed or left in place during induction, depending on the choice of the operator.

The methods of induction of anesthesia meet the requirements of induction in rapid sequence. The choice of hypnotic agent is left to the anesthesiologist. The muscle relaxant used for induction is succinylcholine at the dosage of 1 mg/kg. Anesthesia is induced after pre-oxygenation using a facial mask, using a fraction inhaled in 100% oxygen to obtain an exhaled oxygen fraction greater than 90%. The Sellick maneuver, whether effective or feigned, is released in the event of active vomiting or difficulty in exposing the glottis.

The Sellick maneuver, whether effective or feigned, is maintained in case of the need for facial mask ventilation unless ventilation is also difficult and potentially hampered by cricoid compression.

6.4. Data collection

All data of patients meeting the inclusion criteria and hospitalized during the study, are collected anonymously. For eligible patients not included in the study, the reason for non-inclusion is recorded.

Data on patients included in the study are collected by investigators and clinical research technicians under the supervision of a clinical research associate on paper observation books. Each notebook contains the center number, the inclusion number and the patient's initials.

Any randomized patient is evaluated up to Day 28 or until discharge from the hospital if prior to Day 28. Data are collected anonymously.

Demographic data **(**sex, age and type of surgery), as well as morphological data (size, weight), the duration of the preoperative fasting period, elements that increase the risk of regurgitation (gastroparesis, gastroesophageal reflux disease, hiatal hernia, previous gastric surgery, functional or organic ileus, nausea, vomiting, obesity, pain), variables relevant to airway management (Mallampati score (see Appendix 3), mouth opening and thyromental distances, dentition, macroglossia, prior difficult tracheal intubation, cervical spine mobility, retrognathy) are indicated from the preanesthetic consultation file. The other data are reported in the operating room, recovery room and hospital ward.

Pulmonary aspiration as well as procedural complications are listed in the operating room, aspiration pneumonias are collected up to the 24th hour. Overall mortality (all causes combined) is estimated at Day 28 or on discharge from the hospital if prior to Day28.

In the operating room:

Data concerning the conduct of anesthesia:

- drug used for anesthetic induction (hypnotic, opioid, curare): type, dosage, mode of administration.

Data concerning possible inhalation;

- observation during the procedure of regurgitation with gastric content in the vocal cords;
- detection of gastric content in the tracheal aspiration immediately after intubation of the trachea;
- data concerning the realization of Sellick maneuver, whether actual or feigned;
- quality of the operator performing the Sellick manoeuver;

- the need to interrupt the Sellick maneuver due to active vomiting;
- the need to interrupt Sellick maneuver because of difficulties in exposing the glottis;
- effect of Sellick maneuver release on tracheal intubation conditions (Cormack and Lehane grade);
- upper airway management data ;
- quality of the tracheal intubation operator;
- duration of the procedure to intubate the trachea (delay between the insertion of the laryngoscope blade and verified intubation of the trachea, i. e. inflation of the balloon of the tracheal tube and presence of 3 capnograms).
- Cormack and Lehane grade;
- oxygen desaturation (SpO2 < 92%) ;
- duration of oxygen desaturation ;
- necessity of face mask ventilation;
- traumatic complications (dental damage, bleeding).

In the recovery room:

- traumatic complications related to the execution of the Sellick maneuver
- Chest X-ray in case of suspected pulmonary aspiration

In the hospital ward:

- search for early pneumonia up to 24 hours.
- chest X-ray in case of suspected pulmonary aspiration bronchial inhalation if the X-ray performed in the recovery room is normal.

Status at Day 28 or at discharge from hospital if prior to Day 28

- Status: living or deceased: the date of death will be collected if applicable

7. SAFETY EVALUATION

7.1. Description of safety evaluation parameters

- **Adverse event**

Any harmful manifestation occurring in a person who is suitable for biomedical research, whether or not this manifestation is related to any experimental element of the research and whether or not it is related to the acts performed or the products used.

- **Adverse effect**

Any harmful and unwanted reaction to any experimental element of the research and what is being done or products used.

- **Serious adverse event or effect**

Any adverse event or effect that results in death, endangers the life of the person being searched for, requires hospitalization or prolonged hospitalization, results in significant or lasting disability or incapacity, or results in birth defects or birth defects.

- **Unexpected adverse effect**

Any undesirable effect whose nature, severity or evolution does not agree with the information contained in the standards recognized by the authorities.

- **New Facts**

Any new safety data, which may lead to a reassessment of the report on the benefits and risks of the research or which may be sufficient to consider changes in the documents relating to the research, the conduct of the research and, where appropriate, in the use of the product.

7.2. Methods and timetables for measuring, collecting and analysing safety evaluation parameters

7.2.1. Steering committee

Role:

It will be composed of the principal investigators of the project, the biostatistician in charge of the project, representatives of the promoter and the URC nominated for this research. It will define the general organization and conduct of the research and coordinate the information. It will initially determine the methodology and decide during the course of research on what to do in unforeseen cases, monitor the progress of the research, particularly with regard to tolerance and adverse events

Composition:

It will be made up of the main investigators of the project (Aurélie Birenbaum, François Lenfant, Olivier Langeron, Bruno Riou), the methodologist in charge of the project representing the URC (Marie Laure Tanguy), and a member of the Ile de France Clinical Research Delegation (DRCD) nominated for this trial.

7.2.2 Independent oversight committee

Nil

7.2.3 Independent Committee for the Evaluation of Critical Events

Roles

The committee will:

- validate, independently of the investigators and in a homogeneous manner, without knowing the treatments administered or the procedure followed, the clinical, biological, endoscopic, ultrasound, anatomopathological, etc... evaluation criteria necessary to validate the primary end point and

- have an advisory and decision-making function when the sponsor engages the sponsor on medical issues such as tolerance and adverse events. It may decide to discontinue the study if a serious adverse event occurs.

Composition

This committee will be composed of external experts, including at least one methodologist or biostatistician. We propose Prof. Paul Landais (biostatistician, CHU Carrémeau, Nîmes, France), Prof. Alexandre Duguet (pulmonologist and intensivist, Hôpital Pitié Salpêtrière, Paris, France), Dr. Bernard Vigué (anesthesiologist, Hôpital Bicêtre, Kremlin Bicêtre, France).

7.3. Procedures for registration and reporting adverse events

7.3.1. Non severe adverse events (AE):

Any undesirable events - not serious as defined above - observed during the research and its aftermath should be reported in the observation book in the section provided for this purpose.

Only one event must be reported per item. The event may correspond to a symptom, diagnosis or additional test result deemed significant. All clinical or para-clinical elements that best describe the corresponding event must be reported.

7.3.2. Serious adverse events (SAE) :

The research-validated SAE reporting form is included in the annexed protocol. The same applies to the classification grid for serious and non-severe AE. This grid has been developed to assist the investigator in managing AE (*i. e.*, to help the investigator differentiate between events according to their severity and expected nature). The grid is elaborated and validated by all the actors involved in the research (i. e.: the Head of the Clinical Research Unit, the Principal Investigator of the research, the Project Manager of the study, the Medical Coordinator of the DRCD and the Head of Pharmacovigilance of the DRCD). It may evolve as the research progresses, depending on the statements received by the sponsor.

The investigator is required to immediately notify the sponsor AP-HP (Assistance Publique-Hôpitaux de Paris) of all serious adverse events except those identified in the schedule as not requiring immediate notification.

The investigator completes the SAE report form (from the research observation book) and sends it to the DRCD by fax to 01 44 84 17 99 within 48 hours (after an immediate telephone call to 01 44 84 17 23 in the event of death or life-threatening threats, if possible).

For each SAE, the investigator will have to give an opinion on the causal link between the event and any experimental element of the research, whether the acts performed or the products used.

Obtaining information relating to the description and assessment of an AE may not be possible within the time limit for initial reporting.

Also, the clinical progress as well as the results of any clinical assessments, diagnostic and/or laboratory examinations, or any other information allowing an adequate analysis of the causal link will be reported:

- on the initial SAE declaration if they are immediately available ;
- at a later date and as soon as possible, by faxing a new completed SAE declaration (and indicating that it is a declared SAE tracking and the tracking number).

All statements made by investigators must identify each subject participating in the research by a unique code number assigned to each subject.

In the event of a notified death of a subject participating in the research, the investigator will provide the sponsor with all additional information requested (hospitalization report, autopsy results, etc.).

Any new developments in the research or in the context of the research, arising from literature data or ongoing research, should be notified to the sponsor.

Reporting of serious adverse events to health authorities

This will be carried out by the DRCD's Pharmacovigilance Centre, after evaluation of the seriousness of the AE, the causal link with the experimental element of the research, whether the acts performed or the products used, and the unexpected nature of the adverse effects. All suspected serious unexpected SAE will be reported by the sponsor to the competent authorities within the legal timeframe.

Any safety data or new developments which could significantly modify the assessment of the benefits and risks of the experimental element of the research (and whether they concern acts performed or products used) or the research, or which could lead to changes in the conduct of the research, will be transmitted by the sponsor to the competent authorities, the Committee for the Protection of Individuals and the investigators of the research.

Like, for example:

(a) any clinically significant increase in the frequency of onset of an expected serious adverse reaction;

b) suspected unexpected SAE in participants who have completed the trial and are reported by the investigator to the sponsor, as well as any follow-up reports;

(c) any new developments concerning the conduct of the clinical trial, where such developments are likely to affect the safety of the participants. For example: a SAE that is likely to be related to the investigation and diagnostic procedures of the trial and that could affect the conduct of the trial, a significant risk for the trial population, such as a lack of efficacy of the experimental element used to treat a life-threatening disease, significant safety results from a recently completed animal study (such as a carcinogenicity study), early stopping or temporary interruption for safety reasons.

7.4. Modalities and duration of follow-up of individuals patients following the occurrence of an adverse event

Any patient with an AE should be monitored until it is resolved or stabilized. If the event is not serious, the evolution will be noted on the corresponding page of the observation book in the section provided for this purpose. If the event is serious, a follow-up SAE will be sent to the DRCD.

8. STATISTICAL ANALYSIS

The statistical analyses will be carried out under the responsibility of the biostatistics and data management division of the URC Pitié-Salpêtrière-Charles-Foix using SAS 9.2 software (SAS Institute, Cary, NC).

8.1. Description of statistical methods envisaged, comprising timetable of planned interim analysis.

8.1.1. Descriptive analyses

Patient characteristics will be described in each of the two groups. Quantitative variables will be described by their mean, standard deviation, median and interquartile range. Qualitative variables will be described by frequency and percentage.

8.1.2. Analysis of the primary end point

The objective is to demonstrate the noninferiority of the group in which the Sellick maneuver is feigned (sham) on the incidence of pulmonary aspiration. We will take a noninferiority margin equal to 50% of the incidence observed in the group with effective Sellick maneuver (Sellick group).

The Wald method will estimate a 95% one-sided confidence interval for the excess risk induced by the absence of Sellick maneuver (Sham group). If the limit of the interval is

less than 50% of the incidence of pulmonary aspiration in the Sellick group, then the noninferiority of the Sham group will be validated.

8.1.3. Analysis of secondary end points

The conditions of tracheal intubation, characterized by the Cormack and Lehane grade, will be compared between the Sham group and the Sellick group by Student's t test. The rate of face mask ventilation will be compared using the Chi-square test.

A Chi-square test will also be used to compare morbidity, defined by the occurrence of the following complications: esophageal rupture occurring during vomiting efforts or a fracture of the cricoid cartilage. Similarly, the incidence of H24 pneumonia, the number of difficult tracheal intubations, the number of impossible tracheal intubations and mortality at Day 28 or at hospital discharge occurs prior to Day 28, will be compared.

Multivariate models (mixed linear models or mixed logistic models depending on the type of variable) will be implemented in order to adjust the effect of the treatment group on clinical characteristics to inclusion (age, sex, etc.) and the center. Characteristics at inclusion will be analyzed as fixed effects, while the center will be considered a random effect.

8.2. Sample size estimation

The objective of the study is to demonstrate that if the Sellick maneuver is not performed (Sham group), the number of pulmonary aspirations will not be increased by 50%. It is estimated that the rate of pulmonary aspiration will be 2.8% in each of the two groups. Therefore, the objective will be to have a 95% unilateral confidence interval for excess risk (*i.e.* the difference between pulmonary aspiration rates) of which the limit will not exceed +0.014. With this assumption, and to obtain a power of 80%, then 1717 patients per group should be included (nQuery Advisor 7.0). This corresponds to a total of 3434 patients; for convenience, it was decided to recruit 3500 patients. The choice of t = 50% is based on the low incidence of pulmonary aspiration and on the acceptability of increasing the incidence of pulmonary aspiration to 4.2% in the Sham group if at the same time, tracheal intubation conditions are improved in the absence of effective Sellick maneuver. Difficult intubation in emergency situations is itself a risk of pulmonary aspiration, due to the prolongation of the procedure (increased time for airway protection) and the need for ventilation in the event of desaturation in patients with a full stomach. In addition, difficult tracheal intubation in emergency conditions may be associated with a risk of difficult ventilation in patients in whom facial mask ventilation could not be tested prior to injection of curare, due to the risk of pulmonary aspiration, with a major hypoxemic risk.

8.3. Expected number of patients in each research location with statistical justification.

The incidence of pulmonary aspiration during emergency intubation varies between 0.5% and 3% depending on the studies. A sample size of 3500 patients over 25 months is needed and therefore justifies this study being carried out in several centers. The recruitment capacities of the 10 investigative centers are sufficient to answer the question asked. (Table 1) In fact, considering that only 25% of eligible patients will actually be included, over a period of 2 years in the 10 research centers, the expected number of 3500 patients is largely reached.

Table 1: Estimated number of eligible patients and number of patients included expected.

INVESTIGATION CENTERS	NUMBER OF ELIGIBLE PATIENTS/ YEAR	EXPECTED NUMBER OF INCLUDED PATIENTS (25%) /YEAR	EXPECTED NUMBER OF INCLUDED PATIENTS OVER 2 YEARS
Amiens	1800	450	900
Avicenne	1440	360	720
Bichat	1200	300	600
Beaujon	1800	450	900
Bicêtre	1200	300	600
Bordeaux	400	100	200
Lille	1000	250	500
Nîmes	1500	375	750
Pitié-Salpêtrière	1600	400	800
Rouen	750	187	374
TOTAL	12690	3172	**6344**

8.4. Level of statistical significance expected

The noninferiority tests will be unilateral at the 5% level, the comparison tests will be bilateral at the 5% level.

8.5. Statistical criteria for stopping the research (to be described according to the medical context of the research).

Not applicable, no interim analysis is scheduled.

8.6. Method of accounting for missing, unused or invalid data.

For the primary end point, missing values for the primary end point should be rare given the short duration of follow-up. Nevertheless, the most unfavorable value is expected to be attributed to the noninferiority of the Sham group (*i.e.* pulmonary aspiration in the Sham group, absence of inhalation in the Sellick group, maximum bias hypothesis).

For categorical secondary end points, the missing data will be imputed by the most unfavorable value to the effect of the Sham group (maximum bias). For the quantitative secondary end points, the missing data will be imputed to the mean value of the opposite group, in order to reduce the alpha risk.

8.7. Management of changes to the original strategy analysis plan.

Any changes in the analytical strategy will be amended.

8.8. Choice of patients included in the analyses

The noninferiority analysis will be performed with the intention of treating for the Sham group and per protocol in the Sellick group, to ensure that the Sellick maneuver was correctly performed in this group. Comparison of the secondary end points will be performed in an intention-to-treat analysis.

9. RIGHT OF ACCESS TO SOURCE DATA AND DOCUMENTS

Persons having direct access, in accordance with the laws and regulations, in particular articles L. 1121-3 and R. 5121-13 of the French public health code (e. g. investigators, quality control officers, monitors, clinical research assistants, auditors and any persons involved in trials) shall take all necessary precautions to ensure the confidentiality of information relating to investigational medicinal products, trials, persons who are suitable for testing and, in particular, their identity and the results obtained. The data collected by these persons during quality controls or audits are then made anonymous.

10. QUALITY CONTROL

The research will be supervised according to the standard operating procedures of the sponsor. The conduct of the research in the investigation centers and the handling of the subjects will be carried out in accordance with the Helsinki Declaration and Good Clinical Practices.

10.1 Monitoring procedures

This research presents a C risk with a high level of monitoring. Clinical research assistant (CRA) representing the sponsor will conduct visits to the investigative centers at the timing that corresponds to the patient monitoring scheme, the inclusions in the various centers and the level of risk assigned to the research.

- Opening visit of each center: before inclusion, for a protocol implementation and acquaintance with the various biomedical research stakeholders.

- During subsequent visits, the notebooks will be reviewed as the research progresses by the CRA. The lead investigator at each center, as well as other investigators who include or track individuals involved in the research, are committed to receiving CRA at regular intervals.

During these site visits and in accordance with Good Clinical Practice, the following elements will be reviewed:

- adherence to the research protocol and procedures,

- verification of informed patient consent

- examination of the source documents and comparison with the data reported in the observation book as to accuracy, missing data, consistency of the data according to the rules laid down by the DRCD procedures.

- Closing visit: retrieval of observation books, balance sheet at the pharmacy, biomedical research documents, archiving.

10.2 Transcription of data into the case report form (CRF)

All information required by the protocol should be provided in the CRF and an explanation given by the investigator for each missing data. The data will have to be transferred to the CRF as they are obtained, whether clinical or paraclinical data. The data must be copied clearly and legibly in black ink into these CRF (this will facilitate duplication and computer input). The erroneous data detected on the CRF will be clearly crossed out and the new data will be copied to the CRF with the initials and date by the investigator's team member who made the correction.

The anonymity of the subjects will be ensured by a code number and initials of the person who is willing to search on all documents necessary for the search, or by deleting by appropriate means personal data on copies of source documents for research documentation.

The computerized data on a file will be declared to the CNIL according to the procedure adapted to the case.

11. LEGAL AND ETHICAL CONSIDERATIONS

The promoter is defined by Act 2004-806 of 9 August 2004. In this research, AP-HP is the sponsor and the Department of Clinical Research and Development (DRCD) carries out its regulatory missions.

11.1 Application to the ANSM authorization

In order to start the search, the AP-HP as sponsor must submit an application for ANSM authorization. The competent authority, as defined in Article L. 1123-12, pronounces itself with regard to the safety of persons who lend themselves to biomedical research, taking into account in particular the safety and quality of products used during research in accordance, where applicable, with the applicable standards, their condition of use and the safety of persons with regard to acts performed and methods used, as well as the procedures laid down for monitoring persons.

11.2 Request for the Ethical Committee decision

In accordance with article L. 1123-6 of the French Public Health Code, the research protocol must be submitted by the sponsor to an ethical committee (Comité de Protection des Personnes, CPP). The opinion of this committee shall be notified to the competent authority by the promoter before the start of the research.

11.3 Amendment

DRCD should be informed of any proposed protocol changes by the coordinating investigator. The amendments will have to be qualified as substantial or not. A substantial change is a change that can, in one way or another, modify the guarantees given to those who lend themselves to biomedical research (amendment of an inclusion criterion, extension of an inclusion period, participation of new centers, etc.).

After the start of the research, any substantial modification of the research at the initiative of the sponsor must obtain, prior to its implementation, a favorable opinion from the CPP and an authorization from the competent authority. In this case, if necessary, the CPP ensures that a new consent of the research participants is obtained.

In addition, any extension of research (deeply modifying the therapeutic regimen or the populations included, extending treatments and/or therapeutic acts not initially provided for in the protocol) must be considered as new research.

Substantial changes will require the sponsor to submit an application for authorization to the ANSM and/or a request for an opinion from the PPC.

11.4 CNIL declaration

The law provides that the declaration of the computerized file of personal data collected for research must be made before the actual start of the research.

A reference methodology specific to the processing of personal data carried out within the framework of biomedical research defined by law 2004-806 of August 9,2004, as it falls within the scope of articles L. 1121-1 and following of the French Public Health Code was established by the CNIL in January 2006. This methodology allows for a simplified reporting procedure when the nature of the data collected in the research is compatible with the list provided by the CNIL in its reference document.

When the protocol benefits from data quality control by a CRA representing the promoter and falls within the scope of the simplified CNIL procedure, the DRCD as promoter will ask the promoter to make a written commitment to comply with the simplified MR001 reference methodology.

11.5 Information note and informed consent

Written consent must be obtained from any person who is suitable for research prior to any act required for biomedical research.

Failing this, an emergency inclusion procedure may be carried out by the investigating physician in charge of the patient. As soon as possible, the relative and the patient will be informed and the patient's written consent will be obtained for the eventual continuation of the research.

There will be 3 types of consents:

- one for the patient if he/she is able to sign it at the time of inclusion
- one for the parent or close relative if present when the patient is unable to sign consent
- one for the patient when he wakes up to authorize further research

11.6 Final research report

The final research report will be written collaboratively by the coordinator and biostatistician for this research. This report will be submitted to each investigator for comment. Once a consensus has been reached, the final version should be endorsed by each investigator's signature and sent to the sponsor as soon as possible after the actual completion of the research. A report prepared in accordance with the Competent Authority's reference plan shall be forwarded to the Competent Authority and the PPC within one year of the completion of the research,

12. DATA PROCESSING AND STORAGE OF RESEARCH DOCUMENTS AND DATA

Research documents within the scope of the Biomedical Research Act must be archived by all parties for a period of 15 years after the end of the research. (See BPCs, Chapter 8: Essential documents). This indexed archive includes:

- copies of the ANSM authorization letter and the mandatory notice from the CPP;
- successive versions of the protocol (identified by version number and version date);
- correspondence letters with the promoter;
- signed consents of the subjects under sealed cover with the inclusion list or register in correspondence;
- the completed and validated observation book of each subject included;
- all specific annexes to the study;
- the final report of the study from the statistical analysis and quality control of the study (double sent to the sponsor);

- any audit certificates that may have been issued during the course of the research.

The database that gave rise to the statistical analysis must also be archived by the person in charge of the analysis (paper or computer support).

13. INSURANCE AND SCIENTIFIC COMMITMENT

13.1. Insurance

Assistance Publique - Hôpitaux de Paris is the promoter of this research. In accordance with the law on biomedical research, it has taken out insurance with HDI-GERLING for the entire duration of the research, guaranteeing its own civil liability as well as that of any intervener (physician or personnel involved in the research) (law n°2004-806, Art L. 1121-10 of the CSP).

Assistance Publique - Hôpitaux de Paris reserves the right to interrupt the research at any time for medical or administrative reasons. In this case, a notification will be given to the investigator.

13.2. Scientific commitment

Each investigator will undertake to respect the obligations of the law and to conduct the research in accordance with the Good Clinical Practice, respecting the terms of the Helsinki Declaration. To this end, a copy of the scientific commitment (DCDD-type document) dated and signed by each investigator in each clinical department of a participating center will be given to the sponsor's representative.

14. PUBLISHING RULES

Assistance Publique - Hopitaux de Paris owns the data and no use or transmission to a third party may be made without its prior consent.

Only one publication in an international journal is envisaged. Investigators will be divided into a short list (authors) and an exhaustive list of investigators listed in the appendix to the article. For authors, the following rules will apply. The first signatory of the publication will be Dr. Birenbaum, the second last signatory will be Dr. François Lenfant, and the last signatory will be Pr. Riou. The additional authors (1 per center) will be designated by each center, and the order will be determined by the number of patients included by each center. Only centers with more than 100 patients can claim to have an author on this list. An annex list of investigators will be drawn up, with each center being able to propose a maximum of 2

investigators in this list. Writing of the initial draft will be performed by Dr. Birenbaum. All selected authors will participate in the reading of the final manuscript. A scientific editorial steering committee is responsible for compliance with these rules and will resolve any disputes (Dr. Aurélie Birenbaum, Dr. François Lenfant, Pr. Bruno Riou).

Assistance Publique - Hôpitaux de Paris must be mentioned as the promoter of biomedical research and as financial support where appropriate. The words "Assistance Publique - Hôpitaux de Paris" must appear in the authors' addresses.

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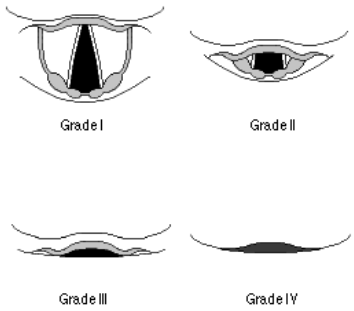
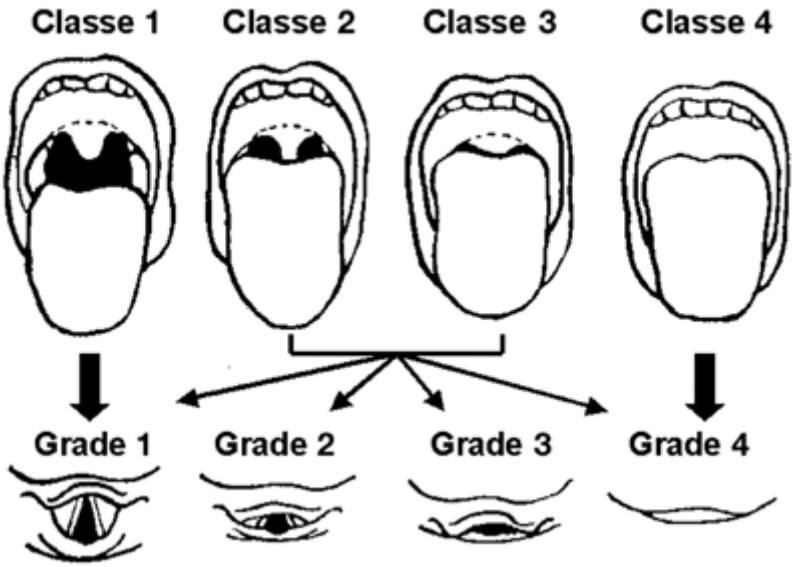
13. APPENDIX :

APPENDIX 1 : Cormack and Lehane grade



APPENDIX 2 : Mallampati score



APPENDIX 3 : Grid for Serious Adverse Events (SAE)

Undesirable Events Notification Grid for Biomedical Research Not Related to a Health Product
(Art. R. 1123-54 of French Public Health Code)

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

IRIS

Project Code : P120120
IDRCB 2013-A00624-41

Research Risk : **C**

CSI / DSMB : YES ☒ **NO** ☐

« IRIS, Assesment of the Sellick maneuver in rapid sequence induction of general anesthesia. Noninferiority trial »

TO NOT BE NOTIFIED TO THE PROMOTER Events listed in the protocol as not to be notified but which can be collected in the observation book (CRF)		**TO BE NOTIFIED TO PROMOTER WITHOUT DELAY** Send the SAE notification form by fax (01 44 84 17 99) and fulfill the CRF	
EVENTS THAT MAY BE SERIOUS BUT NOT RELATED TPO ACTS AND PROCEDURES ADDED BY THE RESEARCH	**EXPECTED NON SERIOUS ADVERSE EVENTS** Known to be related to research proceedings and procedures.	**EXPECTED SERIOUS ADVERSE EVENTS (SAE)**	**UNEXPECTED SERIOUS ADVERSE EEVENTS (USAE)**
Description: -Anything related to the natural and habitual evolution of the pathology: • hospitalisation programmed or not to monitor the pathology; • aggravation of the disease; • ARDS not related to aspiration pneumonia; • Severe sepsis not related to aspiration pneumonia; • Septic shock not related to aspiration pneumonia; • Reintubation not related to aspiration pneumonia; • Post-operative non-invasive ventilation not related to aspiration pneumonia; -Any SAE that may be related to the treatments prescribed as part of the care during the follow-up of the research.	Description Adverse reactions related to rapid sequence induction • dental breakage • vocal cord lesions	Description - SAE related to rapid induction sequence ● Pulmonary aspiration ● Aspiration pneumonia ● ARDS related to aspiration pneumonia ● Severe sepsis related to aspiration pneumonia ● Septic shock related to aspiration pneumonia - SAE related to Sellick Maneuver ● Cricoïd cartilage fracture ● Esophageal rupture - Other SAE ● Reintubation related to pulmonary aspiration ● Postoperative noninvasive ventilation related to pulmonary aspiration	Notify all events with one of the severity criteria noted below, except those identified in the protocol as not requiring notification: 1- Death 2- Life-threatening 3- Requires or prolongs hospitalization 4- Sustainable sequelae 5- Congenital abnormality or malformation 6- Event considered serious by the investigator (reason to be specified) WARNING: any discovery of PREGNANCY during biomedical research must be reported immediately to the sponsor and will be followed up until delivery.

Name, surname and signature of principal investigator :	Name, surname and signature of URC chief:	Name, surname and signature of project referent:	Name, surname and signature of safety chief :	Name, surname and signature of medical chief :