

## Invited Commentary

# Is 30 Newtons of Prevention Worth a Pound of a Cure?—Cricoid Pressure

Samuel A. Tisherman, MD; Megan G. Anders, MD; Samuel M. Galvagno Jr, DO, PhD, MS

**Aspiration** remains one of the most dreaded complications of endotracheal intubation. To mitigate the risk of aspiration in patients who are at high risk, rapid sequence induction (RSI) is used with an anesthetic and short-acting neuromuscular blocking agent. Cricoid pressure (the Sellick maneuver) has frequently been used for physically preventing aspiration.

Recognizing the lack of clinical trials that demonstrate clinically relevant beneficial outcomes, the use of cricoid pressure during RSI has been debated over the past decade.<sup>1-3</sup> Regarding efficacy, although cricoid pressure is often not performed appropriately (ie, applying 30 newtons of pressure in the proper location), most studies demonstrate that cricoid pressure may prevent gastric insufflation by occluding the esophagus and postcricoid hypopharynx.<sup>4,5</sup> However, other studies have suggested that cricoid pressure may displace the esophagus laterally or decrease lower esophageal sphincter pressure, thus increasing the risk of regurgitation.<sup>6</sup> In addition, cricoid pressure may worsen the laryngoscopic view, further providing equipoise for studying its effectiveness.

In this issue of *JAMA Surgery*, Birenbaum et al<sup>7</sup> developed a novel, rigorous, double-blind randomized clinical trial design to compare cricoid pressure with a sham procedure in patients at risk for aspiration who are undergoing RSI without bag-mask ventilation. A standardized approach to cricoid pressure application was implemented after an extensive training period. Anesthetic techniques were standardized. They demonstrated no increased risk of aspiration if cricoid pressure was withheld during RSI. Furthermore, the investigators

found that applying cricoid pressure actually impeded the view of the glottis and increased the time required to secure the airway, corroborating the work of others.

While the authors state that the noninferiority of withholding cricoid pressure could not be proven because of the overall lower-than-expected incidence of aspiration, no clinically significant increase in the risk of aspiration was observed. One could postulate that either the participants did not have as high a risk of aspiration as initially expected or other standard practices to prevent aspiration were sufficient to make the risk low. Nonetheless, this study is one of the strongest to date to demonstrate no benefit of cricoid pressure when used with RSI.

Outside of the operating room, the emergency medicine and critical care literatures have similarly found little net benefit from cricoid pressure. The recommendations for its use have been removed from most airway management guidelines.<sup>8</sup> In the operating room, using cricoid pressure has traditionally been endorsed based on limited evidence and “common sense.” The work by Birenbaum et al<sup>7</sup> represents an important advance in understanding the true lack of effectiveness of this technique, although some questions remain. Is cricoid pressure beneficial for pregnant patients or patients with multiple risk factors for aspiration? What about community hospitals, nonacademic centers, or outside the hospital? Is there a role for cricoid pressure during bag-mask ventilation to prevent gastric distention? With the rigor of the study by Birenbaum et al,<sup>7</sup> future studies of cricoid pressure should answer these questions. For now, it seems that 30 newtons of cricoid pressure is not worth a pound of a cure.

## ARTICLE INFORMATION

**Author Affiliations:** University of Maryland School of Medicine, Baltimore.

**Corresponding Author:** Samuel A. Tisherman, MD, Cowley Shock Trauma Center, University of Maryland School of Medicine, 22 S Greene St, Baltimore, MD 21201 (stisherman@umm.edu).

**Published Online:** October 17, 2018.  
doi:10.1001/jamasurg.2018.3590

**Conflict of Interest Disclosures:** None reported.

## REFERENCES

1. Salem MR, Khorasani A, Zeidan A, Crystal GJ. Cricoid pressure controversies: narrative review. *Anesthesiology*. 2017;126(4):738-752. doi:10.1097/ALN.0000000000001489
2. Algie CM, Mahar RK, Tan HB, Wilson G, Mahar PD, Wasiak J. Effectiveness and risks of

cricoid pressure during rapid sequence induction for endotracheal intubation. *Cochrane Database Syst Rev*. 2015;(11):CD011656.

3. Priebe HJ. Cricoid pressure: effective measure or ritual? *Anesthesiology*. 2018;128(1):233-234. doi:10.1097/ALN.0000000000001951
4. Zeidan AM, Salem MR, Mazoit JX, Abdullah MA, Ghattas T, Crystal GJ. The effectiveness of cricoid pressure for occluding the esophageal entrance in anesthetized and paralyzed patients: an experimental and observational glidescope study. *Anesth Analg*. 2014;118(3):580-586. doi:10.1213/ANE.0000000000000068
5. Rice MJ, Mancuso AA, Gibbs C, Morey TE, Gravenstein N, Deitte LA. Cricoid pressure results in compression of the postcricoid hypopharynx: the esophageal position is irrelevant. *Anesth Analg*. 2009;109(5):1546-1552. doi:10.1213/ane.0b013e3181b05404

6. Boet S, Duttchen K, Chan J, et al. Cricoid pressure provides incomplete esophageal occlusion associated with lateral deviation: a magnetic resonance imaging study. *J Emerg Med*. 2012;42(5):606-611. doi:10.1016/j.jemermed.2011.05.014



7. Birenbaum A, Hajage D, Roche S, et al. Effect of cricoid pressure compared with a sham procedure in the rapid sequence induction of anesthesia: the IRIS randomized clinical trial [published online October 17, 2018]. *JAMA Surg*. doi:10.1001/jamasurg.2018.3577

8. Mayglothling J, Duane TM, Gibbs M, et al; Eastern Association for the Surgery of Trauma. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73(5)(suppl 4):S333-S340. doi:10.1097/TA.0b013e31827018a5

# Effect of Cricoid Pressure Compared With a Sham Procedure in the Rapid Sequence Induction of Anesthesia

## The IRIS Randomized Clinical Trial

Aurélien Birenbaum, MD; David Hajage, MD, PhD; Sabine Roche, MD; Alexandre Ntomba, MD; Mathilde Eurin, MD; Philippe Cuvillon, MD, PhD; Aurélien Rohn, MD; Vincent Compere, MD, PhD; Dan Benhamou, MD; Matthieu Biais, MD, PhD; Remi Menut, MD; Sabiha Benachi, MD; François Lenfant, MD, PhD; **Bruno Riou, MD, PhD**

-  [Invited Commentary](#)
-  [Supplemental content](#)

**IMPORTANCE** The use of cricoid pressure (Sellick maneuver) during rapid sequence induction (RSI) of anesthesia remains controversial in the absence of a large randomized trial.

**OBJECTIVE** To test the hypothesis that the incidence of pulmonary aspiration is not increased when cricoid pressure is not performed.

**DESIGN, SETTING, AND PARTICIPANTS** Randomized, double-blind, noninferiority trial conducted in **10 academic centers**. Patients undergoing anesthesia with RSI were enrolled from February 2014 until February 2017 and followed up for 28 days or until hospital discharge (last follow-up, February 8, 2017).

**INTERVENTIONS** Patients were assigned to a cricoid pressure (Sellick group) or a sham procedure group.

**MAIN OUTCOMES AND MEASURES** Primary end point was the incidence of pulmonary aspiration (at the glottis level during laryngoscopy or by tracheal aspiration after intubation). It was hypothesized that the sham procedure would not be inferior to the cricoid pressure. The secondary end points were related to pulmonary aspiration, difficult tracheal intubation, and traumatic complications owing to the tracheal intubation or cricoid pressure.

**RESULTS** Of **3472** patients randomized, mean (SD) age was 51 (19) years and 1777 (51%) were men. The primary end point, **pulmonary aspiration**, occurred in 10 patients (**0.6%**) in the Sellick group and in 9 patients (**0.5%**) in the sham group. The upper limit of the 1-sided 95% CI of relative risk was 2.00, exceeding 1.50, failing to demonstrate noninferiority ( $P = .14$ ). The risk difference was  $-0.06\%$  (2-sided 95% CI,  $-0.57$  to  $0.42$ ) in the intent-to-treat population and  $-0.06\%$  (2-sided 95% CI,  $-0.56$  to  $0.43$ ) in the per protocol population. Secondary end points were **not significantly different** among the 2 groups (pneumonia, length of stay, and mortality), although the comparison of the **Cormack and Lehane grade** (Grades 3 and 4, 10% vs 5%;  $P < .001$ ) and the **longer intubation time** (Intubation time  $>30$  seconds, **47% vs 40%**;  $P < .001$ ) suggest an **increased difficulty of tracheal intubation** in the Sellick group.

**CONCLUSIONS AND RELEVANCE** This large randomized clinical trial performed in patients undergoing anesthesia with RSI failed to demonstrate the noninferiority of the sham procedure in preventing pulmonary aspiration. Further **studies are required in pregnant women and outside the operating room**.

**TRIAL REGISTRATION** ClinicalTrials.gov Identifier: **NCT02080754**

JAMA Surg. doi:10.1001/jamasurg.2018.3577  
Published online October 17, 2018.

**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:** Bruno Riou, MD, PhD, Service d'Accueil des Urgences, Hôpital Pitié-Salpêtrière, 47-83 boulevard de l'hôpital, 75013 Paris, France ([bruno.riou@aphp.fr](mailto:bruno.riou@aphp.fr)).

Induction of anesthesia induces a loss of protective upper airway reflexes and may be associated with pulmonary aspiration.<sup>1</sup> The incidence of anesthesia-induced pulmonary aspiration is very low (0.03%) in elective surgery<sup>2</sup> when preoperative fasting rules have been complied and in the absence of risk factors for regurgitation of gastric contents such as pregnancy or morbid obesity.<sup>3,4</sup> However, in emergency conditions, noncompliance with preoperative fasting rules and delayed gastric emptying markedly increase the risk of pulmonary aspiration.<sup>5</sup> In this context, a rapid sequence induction (RSI) of anesthesia is recommended to minimize the risk of aspiration, combining the use of a short-acting hypnotic and a muscle relaxant, mainly succinylcholine, associated with the application of a manual pressure to the cricoid cartilage (known as Sellick maneuver). The goal of the cricoid pressure is to compress the esophagus between the cricoid cartilage and the fifth cervical vertebra. The cricoid pressure was described more than 45 years ago<sup>6</sup> and is widely recommended, although its efficacy has been poorly documented.<sup>7</sup> Several studies have challenged its efficacy because occlusion of the esophagus is often incomplete,<sup>8</sup> and it could even facilitate the opening of the lower esophageal sphincter.<sup>9</sup> Moreover, the cricoid pressure may increase airway obstruction, compromising mask ventilation,<sup>10</sup> and/or alter the glottis vision increasing the rate of difficult tracheal intubation,<sup>7</sup> although this last point was not confirmed in a randomized study.<sup>11</sup> Lastly, although all anesthesiologists have been trained to perform the cricoid pressure, it is thought to be difficult to perform appropriately,<sup>7</sup> and some rare but severe traumatic injuries (esophageal or cricoid cartilage rupture) have been reported.<sup>12,13</sup> This multicenter, noninferiority randomized clinical trial was conducted to test the hypothesis that the incidence of pulmonary aspiration is not increased when cricoid pressure is not performed during a RSI of anesthesia.

## Methods

### Study Design

The IRIS (Sellick Interest in Rapid Sequence Induction) study was a multicenter, randomized, double-blind, noninferiority trial aiming to assess the cricoid pressure during RSI in adults by comparing the incidence of pulmonary aspiration whether this maneuver is applied or feigned. The protocol was registered in ClinicalTrials.gov and is available in Supplement 1. Recruitment began in February 2014 and ended (including follow-up) in February 2017. The study was approved by the Comité de Protection des Personnes Ile-de-France VI, Paris, France. Written informed consent was obtained from the patient or a close relative/surrogate in case of emergency conditions. Should such a person be 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. The reporting of this study followed the Consolidated Standards of Reporting Trials statement extended to noninferiority trials.<sup>14</sup>

### Key Points

**Question** Does the cricoid pressure prevent pulmonary aspiration in patients undergoing rapid sequence induction of anesthesia?

**Findings** In this randomized, noninferiority double-blind trial involving 3472 patients, the results failed to demonstrate the noninferiority of a sham procedure in preventing pulmonary aspiration compared with the cricoid pressure. Mortality, pneumonia, and length of stay did not differ significantly between groups, and differences in intubation time and laryngoscopic exposure suggest more difficulties in the Sellick group.

**Meaning** This large randomized trial failed to demonstrate the noninferiority of a sham procedure to prevent pulmonary aspiration during rapid sequence induction of anesthesia.

### Setting and Participants

Patients undergoing any type of surgery under general anesthesia requiring an RSI were eligible for enrollment. The inclusion criteria were patients 18 years and older with a full stomach (<6 hours fasting) or the presence of at least 1 risk factor for pulmonary aspiration (emergency conditions, body mass index >30 [calculated as weight in kilograms divided by height in meters squared], previous gastric surgery [sleeve, bypass, or gastrectomy], ileus, early [<48 hours] postpartum, diabetic gastroparesia, gastroesophageal reflux, hiatus hernia, preoperative nausea/vomiting, and pain).<sup>15,16</sup> The exclusion criteria were refusal of patient to participate, younger than 18 years, pregnancy, inclusion in another randomized trial, lack of national health care insurance, contraindication for the use of the cricoid pressure or succinylcholine, pneumonia or pulmonary contusion, upper respiratory tract abnormalities, consciousness disorders, and patients requiring an alternative technique to laryngoscopy.

We assessed the body mass index, Mallampati score,<sup>17</sup> mouth opening, and thyromental distance, enabling calculation of the risk of difficult tracheal intubation (post hoc).<sup>18</sup> The anesthesia and intubation procedures were standardized, following French guidelines.<sup>19</sup> When the patient had a nasogastric tube before anesthesia, the decision to remove it was left to the attending anesthesiologist as well as the decision to administer antacid before anesthesia. After preoxygenation (either until an expired oxygen fraction >90% had been obtained or following 4 forced vital capacity inspirations in emergency cases), anesthesia was induced using a rapid active hypnotic (propofol or thiopental or etomidate or ketamine) and succinylcholine (1 mg/kg), which provides excellent intubation conditions.<sup>20</sup> The choice of the hypnotic was left to the anesthesiologists. The use of rocuronium was not authorized. Tracheal intubation was performed in the sniffing position and using MacIntosh laryngoscope with a metallic blade because a plastic blade increases the rate of difficult tracheal intubation.<sup>21</sup> We measured the time to intubation (delay between insertion of the laryngoscope and inflation of the tracheal tube cuff). Correct positioning of the tracheal tube was confirmed by monitoring of end-tidal carbon dioxide. The decision to administer opioids was left to the anesthesiologist.

## Intervention

Patients were randomly allocated in a 1:1 ratio to 1 of the following 2 groups: Sellick group and sham group. In the Sellick group, an expected pressure equivalent to 30 N was applied with the first 3 fingers on the cricoid cartilage.<sup>22</sup> All operators had been trained to perform this maneuver, which is applied as a routine practice. However, a special training session was performed before the beginning of the study in each center using a mannequin and the syringe model.<sup>23</sup> This model enables reproduction of the recommended pressure using an obtruded 50-mL syringe and reducing its volume from 40 mL to 33 mL, this training being repeated each month. Only trained individuals were authorized to perform the cricoid pressure. In the sham group, the investigator did not apply any pressure. To ensure appropriate blinding of the rest of the team, an opaque cover was applied in both groups masking if the investigator applied pressure. To maintain appropriate blinding in case of difficult tracheal intubation, the unique unblinded investigator who applied the cricoid pressure could not replace the blind investigator who performed tracheal intubation. Among junior operators, only those with more than 1 year of training (2 years for nurse) were authorized to perform tracheal intubation.

The randomization list was computer generated, balanced by blocks of undisclosed size ( $n = 6$ ), and stratified on the center. Allocation concealment was achieved using a centralized, secure, interactive, web-response system accessible from each study center (Randoweb).<sup>24</sup>

## Study Outcomes

The primary end point was the incidence of pulmonary aspiration as detected either at visually the glottis level during laryngoscopy or by tracheal aspiration just after tracheal intubation. The secondary end points were related to pulmonary aspiration (frequency of suspected aspiration pneumonia within 24 hours requiring chest radiography and aspiration pneumonia when patients had both pulmonary aspiration and new infiltrates at the chest radiography; chest radiography was repeated within 24 hours if initially normal), difficult tracheal intubation (Cormack and Lehane grade, reflecting intubation conditions,<sup>25</sup> at intubation and if cricoid pressure was interrupted,<sup>22</sup> frequency of difficult and impossible intubation, the need of mask ventilation, oxygen desaturation [ $<92\%$ ], and cricoid pressure interruption) and traumatic complications owing to the tracheal intubation or cricoid pressure (esophageal rupture and cricoid cartilage fracture). Pneumonia was considered as severe when at least 1 of the following items was present: decrease in oxygen saturation greater than 10% compared with the value before anesthesia; ratio of partial pressure arterial oxygen to fraction of inspired oxygen less than 300; requirement of mechanical ventilation (invasive or not); and prolonged hospital stay. Difficult tracheal intubation was defined as that requiring more than 2 attempts and/or any alternative technique (except gum elastic bougie).<sup>18,26</sup> We recorded mortality at day 28 or at hospital discharge, admission to intensive care unit (ICU), lengths of hospital and ICU stays, and any adverse events declared, even if not associated with the intervention. Adverse events included the fol-

lowing categorical end points: pulmonary aspiration, aspiration pneumonia, difficult and impossible tracheal intubation, traumatic complications, postoperative reintubation, admission into ICU, and mortality; serious adverse events included the following end points: severe aspiration pneumonia, impossible tracheal intubation, postoperative reintubation, admission into ICU, and mortality.

## Statistical Analysis

Because of the wide range of pulmonary aspiration rate reported, we chose the estimate reported by Martin et al<sup>5</sup>: 2.8%. The population included patients requiring tracheal intubation in emergency conditions in an academic center performed by an anesthesiology team but not in an operating room<sup>5</sup> and was thought to be closed to that expected in our study. The sham procedure was considered noninferior to the cricoid pressure if the incidence of pulmonary aspiration was not more than 50% higher (relative risk of 1.5). A difference of less than 50% was considered clinically negligible because aspiration is a rare event that may occur despite the use of the cricoid pressure and also because the pressure itself is associated with adverse effects.<sup>7</sup> The sample size was calculated at 1717 patients per study arm, for a total of 3434 ( $\alpha = 0.05$ ;  $\beta = 0.20$ ) (NQuery Advisor 7.0, Statistical Solutions Ltd).<sup>27</sup> Taking into account an incidence of consent withdrawal of 1.5%, our total target sample size comprised 3500 patients.

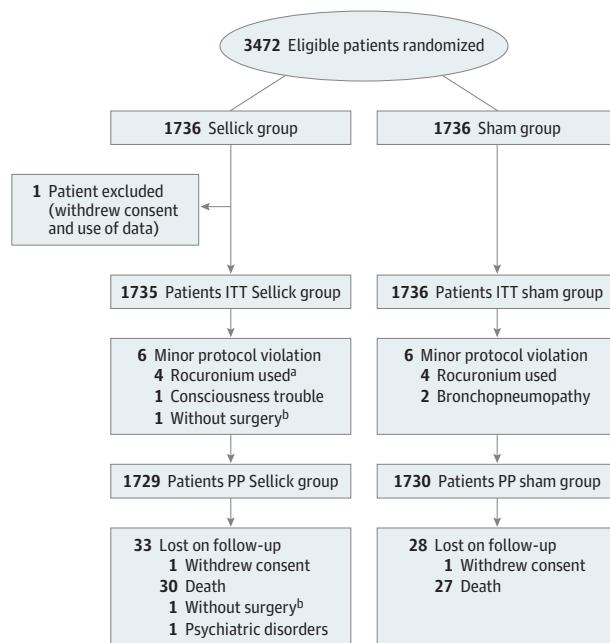
Characteristics of the intention-to-treat (ITT) population were expressed as number (percentage) for qualitative variables, and mean (SD) or median (interquartile range [IQR]) for quantitative variables, depending on their distribution. The analysis of the primary end point was performed based primarily on the per protocol (PP) population and repeated on the ITT population. The PP population was defined as patients without protocol violation. Noninferiority was assessed on the upper limit of the 1-sided 95% CI of the relative risk of aspiration (sham group/Sellick group). Because of the low event rate, a bias-corrected and accelerated bootstrap CI was computed using 10 000 resamples.<sup>28</sup> If the upper limit of the CI was lower than 1.5, the noninferiority hypothesis would be accepted. The 2-sided (precision) 95% CI was also reported. We also calculated the risk difference (post hoc) and its 2-sided 95% CI, as recommended.<sup>14</sup> The secondary end points were compared with a superiority hypothesis on the ITT population and using available data. Qualitative variables were compared using the Pearson  $\chi^2$  test, Fisher exact test, or Cochran-Armitage test for trend, and continuous variables were compared using the Wilcoxon rank sum test. No interim analysis was planned. All superiority tests were 2-sided, and  $P$  values of less than .05 were considered significant. Statistical analysis was performed using R software, version 3.4.1 (R Programming).

## Results

Twelve centers were invited to participate and 2 declined. The 10 participating centers recruited 3472 patients (Figure 1;



Figure 1. Flow of Participants Through the Study



ITT indicates intention to treat; PP, per protocol.

<sup>a</sup> Including 1 patient with allergy to succinylcholine.

<sup>b</sup> This refers to the same patient.

eTable 1 in Supplement 2). One patient was excluded because he withdrew consent and data use. No major protocol violation occurred, and minor violations were observed in 12 (0.3%), including use of rocuronium instead of succinylcholine ( $n = 8$ ), preexisting signs of pneumonia ( $n = 2$ ), preexisting disturbed consciousness ( $n = 1$ ), and lack of surgery ( $n = 1$ ). Two patients withdrew consent. Therefore, 1735 patients in the Sellick group and 1736 in the sham group were analyzed on an ITT basis; 1729 patients in the Sellick group and 1730 in the sham group were analyzed on a PP analysis.

The baseline characteristics of the 2 groups were well balanced (Table 1). Patients underwent mainly abdominal surgery ( $n = 2116$ ; 61%), endoscopy ( $n = 484$ ; 14%), orthopedic surgery ( $n = 462$ ; 13%), head and neck surgery ( $n = 123$ ; 4%), and cardiothoracic surgery ( $n = 68$ ; 2%) (198 missing values).

Concerning the primary end point, no missing value was observed. In the ITT population, pulmonary aspiration occurred in 10 patients (0.6%) in the Sellick group and in 9 patients (0.5%) in the sham group (relative risk, 0.90; 95% CI, 0.33-2.38) (Figure 2). In the PP analysis, pulmonary aspiration occurred in 10 patients (0.6%) in the Sellick group and in 9 patients (0.5%) in the sham group (relative risk, 0.90; 2-sided 95% CI, 0.33-2.38). In both the ITT and PP populations, the upper limit of the 1-sided 95% CI (1.99 and 2.00, respectively) exceeded the noninferiority margin of 1.5, thus noninferiority was not demonstrated ( $P = .14$  in both analysis). The risk difference was  $-0.06\%$  (2-sided 95% CI,  $-0.57$  to  $0.42$ ) in the ITT population and  $-0.06\%$  (2-sided 95% CI,  $-0.56$  to  $0.43$ )

in the PP population. The same results were obtained in the subgroups of patients without nasogastric tube ( $n = 3032$ ) and those requiring emergency surgery ( $n = 2286$ ) (data not shown; post hoc analysis).

The incidence of difficult tracheal intubation was higher in the Sellick group but did not reach statistical significance, although the comparison of the Cormack and Lehane grade and the longer intubation time suggest an increased difficulty of tracheal intubation in the Sellick group (Table 2). The incidence of interruption of the cricoid pressure was more frequent in the Sellick group as well as the improvement in the Cormack and Lehane grade after its release (Table 2). All traumatic complications were related to tracheal intubation, and there was no significant difference between groups.

There was no significant difference concerning the extubation procedure (Table 2). Extubation was performed mostly in the operating room ( $n = 2610$ ; 77%) and less frequently in the recovery room ( $n = 750$ ; 23%). Most patients ( $n = 1703$ ; 90%) who received a nondepolarizing muscular relaxant during surgery and were extubated postoperatively underwent either train-of-4 measurement to assess neuromuscular blockade and/or reversal of neuromuscular blockade.<sup>29</sup> When considering other secondary end points, no significant difference was observed between the Sellick and the sham group, including the incidence of adverse events (Table 3; eTable 2 in the Supplement).

## Discussion

This large, randomized double-blind trial in patients undergoing anesthesia with RSI failed to demonstrate the noninferiority ( $\delta = 50\%$ ) of the sham procedure as compared with the cricoid pressure in preventing pulmonary aspiration. We also observed a low incidence of pulmonary aspiration (0.5%), and we did not observe any significant secondary end points except those suggesting a more difficult tracheal intubation in the Sellick group.

Although the cricoid pressure has been used in clinical practice for decades and is recommended by most countries during RSI, it remains controversial, including its effectiveness in preventing pulmonary aspiration as well its deleterious effects such as airway-related complications (interference with laryngeal exposure, difficult tracheal intubation, and mask ventilation)<sup>7</sup> and rare traumatic complications.<sup>12,13</sup> Some paradoxical effects, potentially favoring aspiration, have been reported such as opening of the lower esophageal sphincter.<sup>9</sup> Moreover, application of an appropriate pressure to the cricoid cartilage may not be simple, and many studies have focused on its appropriate application and training, and 47% to 63% of operators may improperly apply cricoid pressure.<sup>7</sup> The lack of a large randomized trial explains these controversies. In a systematic review, Algie et al<sup>30</sup> identified only 1 small randomized trial ( $n = 40$ )<sup>31</sup> and concluded that there is no relevant information available from randomized trials with respect to the application of cricoid pressure during RSI.

Table 1. Main Baseline Characteristics<sup>a</sup>

Variable	No. (%)		
	Sellick Group (n = 1735)	Sham Group (n = 1736)	Total (N = 3471)
Age, mean (SD), y	51 (20)	51 (19)	51 (19)
Men	893 (51)	884 (51)	1777 (51)
BMI, mean (SD)	26.4 (6.8)	26.7 (7.2)	26.6 (7.0)
Regurgitation risk factors			
Emergency condition	1150 (66)	1137 (65)	2287 (66)
Nonfasting	169 (10)	169 (10)	338 (10)
Gastroesophageal reflux	351 (20)	328 (19)	679 (20)
Hiatal hernia	110 (6)	116 (7)	226 (7)
Diabetic gastroparesis	63 (4)	85 (5)	148 (4)
Ileus	559 (32)	540 (31)	1099 (32)
Nausea and/or vomiting	399 (23)	391 (23)	790 (23)
Obesity (BMI >30)	212 (12)	261 (15)	473 (14)
Pain	399 (23)	372 (21)	771 (22)
Postpartum (<48 h)	3 (0.2)	0	3 (0.1)
Previous gastric surgery <sup>b</sup>	87 (5)	88 (5)	175 (5)
Others	158 (9)	141 (8)	299 (9)
Factors, No. (IQR)	2 (1-3)	2 (1-3)	2 (1-3)
Difficult intubation risk factors			
Mouth opening, mean (SD), mm	46 (10)	47 (10)	47 (10)
Missing values, No.	40	40	80
Thyromental distance, mean (SD), mm	81 (18)	81 (18)	81 (18)
Missing values, No.	44	46	90
Mallampati score			
1	778 (45)	786 (46)	1564 (46)
2	749 (44)	698 (41)	1447 (42)
3	172 (10)	211 (12)	383 (11)
4	15 (0.9)	16 (0.9)	31 (0.9)
Missing values, No.	21	25	46
Receding mandible	90 (5)	79 (5)	169 (5)
Missing values, No.	19	19	38
Difficult intubation risk			
Low risk	1082 (65)	1091 (66)	2173 (63)
Intermediate risk	571 (34)	563 (34)	1134 (34)
High risk	16 (1)	8 (0.5)	24 (0.7)
Missing values, No.	66	74	140
Nasogastric tube aspiration before	256 (15)	246 (14)	502 (14)
Nasogastric tube in place	218 (13)	221 (13)	439 (13)
Missing values, No.	3	4	7
Antacid medication	206 (12)	203 (12)	409 (12)
Missing values, No.	4	5	9
Anesthetic induction			
Propofol	1546 (89)	1560 (90)	3106 (90)
Ketamine	161 (9)	165 (9)	326 (9)
Etomidate	154 (9)	139 (8)	293 (8)
Thiopental	32 (2)	42 (2)	74 (2)

(continued)

Table 1. Main Baseline Characteristics<sup>a</sup> (continued)

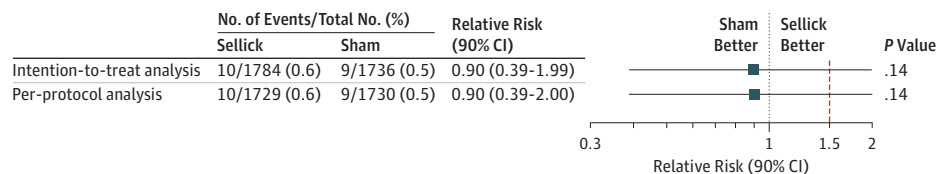
Variable	No. (%)		
	Sellick Group (n = 1735)	Sham Group (n = 1736)	Total (N = 3471)
Combined administration	158 (9)	166 (10)	324 (9)
Missing values, No.	1	0	1
Opioid administration	497 (29)	544 (31)	1041 (30)
Missing values, No.	1	1	1
Dose of succinylcholine, mg (SD)	81 (20)	81 (22)	81 (21)
Missing values, No.	4	5	9
Nondepolarizing muscular relaxant	972 (56)	998 (58)	1970 (57)
Missing values, No.	0	5	5

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range.

<sup>a</sup> No significant difference between groups.

<sup>b</sup> This includes sleeve, bypass, and gastrectomy.

Figure 2. Comparison of the Incidence of Pulmonary Aspiration (Primary End Point) Between the Sellick Group and the Sham Group



The points represent the estimates of relative risk (sham group/Sellick group), and the horizontal bars represent the associated 2-sided 90% CI. The upper limits are identical to those of the 1-sided 95% CI used in this study for

establishing noninferiority. Clinical noninferiority of the sham procedure would be accepted if the upper limit of these intervals fell below the predefined noninferiority margin represented in red dotted line.

Our primary end point was the occurrence of pulmonary aspiration either during laryngoscopy or tracheal aspiration. This end point is thought to directly assess the efficiency of the cricoid pressure and minimize lost on follow-up because it is recorded immediately after tracheal intubation. This end point is probably less sensitive than those using a biomarker<sup>32</sup> but has the advantage of excluding aspirations that could occur intraoperatively or postoperatively and that cannot be prevented by the cricoid pressure. This study failed to demonstrate noninferiority because the incidence of aspiration was overestimated (2.8% expected vs 0.5% observed). We do not think that this was related to the inclusion of patients with a too-low risk of regurgitation because our study population reflects that in which RSI remains recommended, and most of our patients fulfilled at least 2 criteria or more for high risk of aspiration (Table 1). Several differences may explain this lower incidence of pulmonary aspiration in our study compared with that of Martin et al<sup>5</sup> such as operating room vs nonoperating room setting (ie, more compliance with RSI recommendations), more frequent use of succinylcholine (99% vs 60%) and propofol (90% vs 18%), and less frequent cardiac arrests (0% vs 45%). When looking at other secondary end points (mortality, pneumonia, adverse effects, and length of stay) no indication was noted in favor of the cricoid pressure.

The cricoid pressure has been accused of leading to difficult tracheal intubation or even difficult mask ventilation.<sup>7,11</sup> Our study confirmed that it adversely interferes with dura-

tion of intubation and laryngeal exposure but without significant increase in the incidence of difficult tracheal intubation (Table 2). This result is in agreement with that obtained in a randomized study.<sup>11</sup> The main reason is that the cricoid pressure is usually interrupted when facing unexpected difficult tracheal intubation. Together with the lack of significant difference in traumatic complications, this result suggests that the interference of the cricoid pressure with airway control has previously been overestimated.

Our study has several strengths. To maximize the effectiveness of the cricoid pressure, we standardized anesthesia, tracheal intubation, and cricoid pressure procedures, which are considered essential in such a trial.<sup>7</sup> We repeatedly trained the operators, using a simple simulation device,<sup>23</sup> although all operators were already trained and frequently used the technique. We also carefully assessed residual neuromuscular blockade and swallowing reflex because postoperative aspiration may have influenced secondary end points (pneumonia, length of stay, and mortality). We did not standardize the use of gastric tubes, but excluding patients with a gastric tube did not change our results.

### Limitations

Our study has several limitations. We excluded pregnant women and children, and thus, our results may not apply to obstetric and pediatric populations. This is important because pulmonary aspiration still remains a cause of maternal death.<sup>3</sup> Fur-

Table 2. Tracheal Intubation and Extubation

	No. (%)		
Variable	Sellick Group (n = 1735)	Sham Group (n = 1736)	P Value
Tracheal intubation			
Intubation time, median (IQR), s	27 (19-40)	23 (15-37)	<.001
Intubation time >30 s	792 (47)	677 (40)	<.001
Missing values, No.	42	49	NA
Operator			
Senior anesthesiologist	184 (11)	162 (9)	.33
Junior anesthesiologist	439 (25)	465 (27)	
Senior nurse anesthetist	990 (57)	970 (56)	
Junior nurse anesthetists	109 (6)	125 (7)	
Missing values, No.	13	14	NA
Use of a bougie	536 (21)	546 (21)	.63
Missing values, No.	1	0	NA
No. of attempts			
1	1585 (92)	1589 (92)	.19
2	119 (7)	126 (7)	
>2	28 (2)	18 (1)	
Missing values, No.	3	3	NA
More than 1 operator	70 (4)	82 (5)	.32
Missing values, No.	5	4	NA
Cormack and Lehane grade			
1	1285 (74)	1381 (80)	<.001
2	270 (16)	256 (15)	
3	133 (8)	76 (4)	
4	42 (2)	17 (1)	
Missing values, No.	5	6	NA
Interruption of the cricoid pressure	246 (14)	86 (5)	<.001
Missing values, No.	5	5	NA
Improvement in Cormack and Lehane Grade after cricoid pressure interruption	152 (62)	28 (33)	<.001
Missing values, No.	1	1	.55
Vomiting	6 (0.3)	4 (0.2)	
Missing values, No.	1	0	
Difficult tracheal intubation	72 (4)	51 (3)	.05
More than 2 attempts	51	39	
Other technique used	31	21	
Missing values, No.	1	0	
Impossible tracheal intubation	0	1	NA
Missing values, No.	1	0	>.99
Mask ventilation required	23 (1)	20 (1)	NA
Missing values, No.	2	0	.64
Oxygen desaturation (<92%)	67 (4)	66 (4)	NA
Missing values, No.	4	0	.92
Tracheal extubation			
Postoperative extubation	1676 (97)	1687 (97)	.42
Missing values, No.	3	1	NA
Patients with NDMR and extubated	930 (54)	962 (55)	.29
Missing values, No.	1	0	NA

(continued)



Table 2. Tracheal Intubation and Extubation (continued)

Variable	No. (%)		P Value
	Sellick Group (n = 1735)	Sham Group (n = 1736)	
Train-of-4 measurement <sup>a</sup>	817 (88)	835 (87)	.45
Train-of-4, median (IQR), % <sup>a</sup>	97 (91-100)	97 (91-100)	.86
Missing values, No.	3	2	NA
Reversal agent administered <sup>a</sup>	515 (56)	464 (56)	.78
Missing values, No.	3	1	NA
Swallowing reflex present	1659 (99)	1667 (99)	.84
Missing values, No.	62	56	NA
Postoperative dyspnea	9 (0.5)	11 (0.6)	.66
Missing values, No.	51	47	NA
Postoperative oxygen desaturation (<92%)	60 (4)	62 (4)	.88
Missing values, No.	68	51	NA
Postoperative NIV	2 (0.1)	5 (0.3)	.45
Missing values, No.	51	45	NA
Postoperative tracheal reintubation	2 (0.1)	2 (0.1)	>.99
Missing values, No.	50	45	NA
Traumatic complication	17 (1)	9 (0.5)	.11
Missing values, No.	3	0	NA

Abbreviations: IQR, interquartile range; NA, not applicable; NDMR, nondepolarizing muscular relaxant; NIV, noninvasive ventilation.

<sup>a</sup> Results are provided for patients with NMDR and extubated.

Table 3. Secondary End Points

Variable	No. (%)		Mean Difference, % (95% CI) <sup>a</sup>	P Value
	Sellick Group (n = 1735)	Sham Group (n = 1736)		
Mortality	30 (2)	27 (2)	-0.2 (-1.0 to 0.7)	.69
Suspected pneumonia within 24 h	15 (0.9)	10 (0.6)	-0.3 (-0.8 to 0.3)	.31
Aspiration pneumonia	4 (0.2)	4 (0.2)	0 (-0.3 to 0.3)	>.99
Severe pneumonia	2 (0.1)	2 (0.1)	0 (-0.2 to 0.2)	>.99
Length of hospital stay, median (IQR), d	3 (1-9)	4 (1-9)	0.3 (-0.2 to 0.8)	.89
Length of hospital stay >28 d	91 (5)	93 (5)	0.1 (-1.4 to 1.6)	.89
Admission into ICU	181 (10)	201 (12)	1.1 (-0.9 to 3.2)	.28
Length of ICU stay, median (IQR), d	5 (2-11)	5 (2-10)	-0.4 (-1.9 to 1.1)	.58
Adverse events <sup>b</sup>	276 (16)	256 (15)	-1.2 (-3.6 to 1.2)	.34
Serious adverse events <sup>c</sup>	200 (12)	211 (12)	0.6 (-1.5 to 2.8)	.57

Abbreviations: ICU, intensive care unit; IQR, interquartile range.

<sup>a</sup> Mean difference is calculated as Sellick group minus sham group.

<sup>b</sup> Systematically included the following categorical end points: pulmonary aspiration, aspiration pneumonia, difficult and impossible tracheal intubation, traumatic complications, postoperative reintubation, admission into ICU, and

mortality, which were present in 83% of patients with adverse events.

<sup>c</sup> Systematically included the following categorical end points: severe aspiration pneumonia, impossible tracheal intubation, postoperative reintubation, admission into ICU, and mortality, which were present in 83% of patients with serious adverse events.

ther randomized trials are needed in these specific populations, and our study may help to obtained better ethical acceptance of such randomized studies.<sup>7</sup> Our results may not apply to emergency conditions outside the operating room in which sedation and tracheal intubation conditions are worse, and pulmonary aspiration may have occurred before RSI.<sup>33</sup> Our study population may have comprised patients with heterogeneous risk factors for pulmonary aspiration but there is no evidence-based indication for the exact weight of these factors.<sup>15</sup> Very low levels of aspiration could have also been clinically unnoticed. Finally, our study took place in urban academic centers and might not be generalizable in other settings.

## Conclusions

In what is, to our knowledge, the first large randomized trial performed in patients undergoing anesthesia with RSI, we failed to demonstrate the noninferiority ( $\delta = 50\%$ ) of a sham procedure as compared with the cricoid pressure in preventing pulmonary aspiration. We did not observe any significant difference in pneumonia, length of stay, and mortality. Further randomized studies are required in pregnant women and in emergency conditions outside the operating room, both conditions not studied here.

## ARTICLE INFORMATION

**Accepted for Publication:** July 8, 2018.

**Published Online:** October 17, 2018.

doi:10.1001/jamasurg.2018.3577

**Author Affiliations:** Department of Anesthesiology and Critical Care, Hôpital Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France (Birenbaum, Roche); Sorbonne Université, Department of Biostatistics Public Health and Medical Information, Hôpital Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France (Hajage); Université Jules Verne, Department of Anesthesiology and Critical Care, CHI Amiens-Picardie, Amiens, France (Ntoubu); Department of Anesthesiology and Critical Care, Hôpital Beaujon, Assistance Publique-Hôpitaux de Paris, Clichy, France (Eurin); Université de Montpellier, Department of Anesthesiology and Critical Care, Hôpital Carémieu, Nîmes, France (Cuvillon); Department of Anesthesiology and Critical Care, Centre Hospitalier Universitaire Régional de Lille, Lille, France (Rohn); Université de Haute-Normandie, Department of Anesthesiology and Critical Care, Hôpital, Rouen, France (Compere); Université Paris-Sud, Department of Anesthesiology and Critical Care, Hôpital Bicêtre, Assistance Publique-Hôpitaux de Paris, Le Kremlin-Bicêtre, France (Benhamou); Université Victor Segalen, Department of Anesthesiology and Critical Care, Hôpital Pellegrin, Bordeaux, France (Biais); Université Toulouse 3-Paul Sabatier, Department of Anesthesiology and Intensive Care, University Hospital of Toulouse, Toulouse, France (Menut); Department of Anesthesiology and Critical Care, Hôpital Avicenne, Assistance Publique-Hôpitaux de Paris, Bobigny, France (Benachi); Department of Anesthesiology, Centre Hospitalier Simone Veil, Cannes, France (Lenfant); Sorbonne Université, UMR Inserm, Institut hospitalo-universitaire ICAN, Department of Emergency Medicine and Surgery, Hôpital Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France (Riou).

**Author Contributions:** Drs Birenbaum and Riou had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Concept and design:** Birenbaum, Lenfant, Riou.

**Acquisition, analysis, or interpretation of data:** Birenbaum, Hajage, Roche, Ntoubu, Eurin, Cuvillon, Rohn, Compère, Benhamou, Biais, Menut, Benachi, Riou.

**Drafting of the manuscript:** Birenbaum, Hajage, Lenfant, Riou.

**Critical revision of the manuscript for important intellectual content:** All authors.

**Statistical analysis:** Hajage.

**Obtained funding:** Birenbaum, Riou.

**Administrative, technical, or material support:** Hajage.

**Supervision:** Birenbaum, Hajage, Riou.

**Conflict of Interest Disclosures:** Dr Biais reported personal fees from Maquet Critical Care and from Edwards Lifesciences outside the submitted work. No other disclosures were reported.

**Funding/Support:** The Sellick Interest in Rapid sequence Induction study was funded by the French Ministry of Health (Programme Hospitalier

de Recherche Clinique National, P120120) and sponsored by Assistance Publique-Hôpitaux de Paris.

**Role of the Funder/Sponsor:** The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Additional Contributions:** We thank the IRIS investigators who played a substantial role in the study: Mathieu Raux, MD, PhD, Olivier Langeron, MD, PhD, Sorbonne Université, Hôpital Pitié-Salpêtrière, APHP, Paris France; Audrey Solis, MD, Sadek Beloucif, MD, PhD, Université Paris 13, Hôpital Avicenne, APHP, Bobigny, France; Thomas Geerearts, MD, PhD, Université de Toulouse, CHU Rangueil, Toulouse, France; Laurent Varin, MD, Hôpital Bicêtre, APHP, Le Kremlin-Bicêtre, France; Emmanuel Lorne, MD, PhD, Hervé Dupont, MD, PhD, Université Jules Vernes, CHU Amiens-Picardie, Amiens, France; Catherine Paugam-Burtz, MD, PhD, Lynda Lagha, Université Paris-Diderot, Hôpital Beaujon, APHP, Clichy, France; Laurent Stecken, MD, Cédric Carrié, MD, CHU Pellegrin, Bordeaux, France; Sébastien Bertran, MD, Sylvie Simon, Hôpital Caremeau, Nîmes, France; Delphine Garrigue, MD, Benoît Tavernier, MD, PhD, Université de Lille, CHRU de Lille, Lille, France; and Pauline Garel, Jérôme Moriceau, CHU de Rouen, Rouen, France. Alexandre Lafourcade, MSc, and David Hajage, MD, PhD (Clinic Research Unit-URC, Hôpital Pitié-Salpêtrière, APHP, Paris France), provided statistical analysis; Mostafa Hajji, Mohamed-Ouamrane Slimi, Jessica Palmyre, and Florence Tubach, MD, PhD (Clinic Research Unit-URC, Hôpital Pitié-Salpêtrière, APHP, Paris France), provided administrative support, and the Data and Safety Monitoring Board consisted of Alexandre Duguet, MD, PhD (Sorbonne Université, Hôpital Pitié-Salpêtrière APHP, Paris, France), Paul Landais, MD, PhD (Université de Montpellier, Hôpital Carémieu, Nîmes, France), and Bernard Vigué, MD, (Hôpital Bicêtre, APHP, Le Kremlin-Bicêtre, France). We thank David Baker, DM, FRCA, (Emeritus Consultant Anesthesiologist, Department of Anesthesiology and Critical Care, Hôpital Necker-Enfants Malades, APHP, Paris, France) for reviewing the article. No compensation was received from a funding source.

## REFERENCES

- Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary aspiration during the perioperative period. *Anesthesiology*. 1993;78(1):56-62.
- Olsson GL, Hallen B, Hambraeus-Jonzon K. Aspiration during anaesthesia: a computer-aided study of 185,358 anaesthetics. *Acta Anaesthesiol Scand*. 1986;30(1):84-92.
- Thomas TA, Cooper GM. *Why Mothers Die 2000-2002: The Sixth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom*. London: RCOG; 2001:137-138.
- Langeron O, Birenbaum A, Le Saché F, Raux M. Airway management in obese patient. *Minerva Anesthesiol*. 2014;80(3):382-392.
- Martin LD, Mhyre JM, Shanks AM, Tremper KK, Khetarpal S. 3,423 emergency tracheal intubations

at a university hospital: airway outcomes and complications. *Anesthesiology*. 2011;114(1):42-48.

6. Sellick BA. Cricoid pressure to control regurgitation of stomach contents during induction of anaesthesia. *Lancet*. 1961;2(7199):404-406.

7. Salem MR, Khorasani A, Zeidan A, Crystal GJ. Cricoid pressure controversies: narrative review. *Anesthesiology*. 2017;126(4):738-752.

8. Smith KJ, Dobranowski J, Yip G, Dauphin A, Choi PT. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology*. 2003;99(1):60-64.

9. Tournadre JP, Chassard D, Berrada KR, Boulétreau P. Cricoid cartilage pressure decreases lower esophageal sphincter tone. *Anesthesiology*. 1997;86(1):7-9.

10. Shorten GD, Alfille PH, Gliklich RE. Airway obstruction following application of cricoid pressure. *J Clin Anesth*. 1991;3(5):403-405.

11. Turgeon AF, Nicole PC, Trépanier CA, Marcoux S, Lessard MR. Cricoid pressure does not increase the rate of failed intubation by direct laryngoscopy in adults. *Anesthesiology*. 2005;102(2):315-319.

12. Ralph SJ, Wareham CA. Rupture of the oesophagus during cricoid pressure. *Anaesthesia*. 1991;46(1):40-41.

13. Heath KJ, Palmer M, Fletcher SJ. Fracture of the cricoid cartilage after Sellick's manoeuvre. *Br J Anaesth*. 1996;76(6):877-878.

14. Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJW, CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *JAMA*. 2006;295(10):1152-1160.

15. American Society of Anesthesiologists Committee. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2011;114(3):495-511.

16. Mahajan V, Hashmi J, Singh R, Samra T, Aneja S. Comparative evaluation of gastric pH and volume in morbidly obese and lean patients undergoing elective surgery and effect of aspiration prophylaxis. *J Clin Anesth*. 2015;27(5):396-400.

17. Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J*. 1985;32(4):429-434.

18. Langeron O, Cuvillon P, Ibanez-Estève C, Lenfant F, Riou B, Le Manach Y. Prediction of difficult tracheal intubation: time for a paradigm change. *Anesthesiology*. 2012;117(6):1223-1233.

19. Molliex S, Berset JC, Billard V, et al; Société Française d'Anesthésie et de Réanimation. [Airway management in adult anesthesia except with the exception of difficult intubation. Recommendations of the jury. Short text--2000]. *Ann Fr Anesth Reanim*. 2003;22(8):745-749.

20. Tran DT, Newton EK, Mount VA, Lee JS, Wells GA, Perry JJ. Rocuronium versus succinylcholine for rapid sequence induction intubation. *Cochrane Database Syst Rev*. 2015;10(10):CD002788.
21. Amour J, Marmion F, Birenbaum A, et al. Comparison of plastic single-use and metal reusable laryngoscope blades for orotracheal intubation during rapid sequence induction of anesthesia. *Anesthesiology*. 2006;104(1):60-64.
22. Herman NL, Carter B, Van Decar TK. Cricoid pressure: teaching the recommended level. *Anesth Analg*. 1996;83(4):859-863.
23. Flucker CJ, Hart E, Weisz M, Griffiths R, Ruth M. The 50-millilitre syringe as an inexpensive training aid in the application of cricoid pressure. *Eur J Anaesthesiol*. 2000;17(7):443-447.
24. Morice V. RandoWeb, an online randomization tool for clinical trials. *Comput Methods Programs Biomed*. 2012;107(2):308-314.
25. Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. *Anaesthesia*. 1984;39(11):1105-1111.
26. Langeron O, Masso E, Huraux C, et al. Prediction of difficult mask ventilation. *Anesthesiology*. 2000;92(5):1229-1236.
27. Blackwelder WC. "Proving the null hypothesis" in clinical trials. *Control Clin Trials*. 1982;3(4):345-353.
28. Efron B, Tibshirani RJ. *An Introduction to the Bootstrap*. New York: Chapman & Hall; 1993.
29. Baillard C, Gehan G, Reboul-Marty J, Larmignat P, Samama CM, Cupa M. Residual curarization in the recovery room after vecuronium. *Br J Anaesth*. 2000;84(3):394-395.
30. Algie CM, Mahar RK, Tan HB, Wilson G, Mahar PD, Wasiak J. Effectiveness and risks of cricoid pressure during rapid sequence induction for endotracheal intubation. *Cochrane Database Syst Rev*. 2015;18(11):CD011656.
31. Mills P, Poole T, Curran J. Cricoid pressure and the pressor response to tracheal intubation. *Anaesthesia*. 1988;43(9):788-791.
32. Bohman JK, Kashyap R, Lee A, et al. A pilot randomized clinical trial assessing the effect of cricoid pressure on risk of aspiration. *Clin Respir J*. 2018;12(1):175-182.
33. Higgs A, McGrath BA, Goddard C, et al; Difficult Airway Society; Intensive Care Society; Faculty of Intensive Care Medicine; Royal College of Anaesthetists. Guidelines for the management of tracheal intubation in critically ill adults. *Br J Anaesth*. 2018;120(2):323-352.