Cleveland Clinic

Study protocol

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Comparison of McGrath Videolaryngoscopy and Direct Laryngoscopy for Rapid Sequence Intubation: *an international, multicenter randomized trial*

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BACKGROUND

Securing the airway is a fundamental priority in the treatment of critically ill or injured patients. In the regular OR setting, direct laryngoscopy is the primary method for performing endotracheal intubation. But even in experienced hands, along with regular training and practice, successful endotracheal intubation sometimes requires additional tools to assist endotracheal intubation.[1-3] Airway complications are rare but may lead to severe complications, such as brain damage and even death[4]. Set aside the “cannot ventilate and cannot intubation” scenario, difficult intubation has been associated with significant patient morbidity. For example, repeated intubation attempts are associated with respiratory and hemodynamic complications, including hypoxemia, cardiac arrest, regurgitation, aspiration, and airway trauma — along with bradycardia and cardiac arrest in emergency settings[5] [6].

Rapid Sequence Intubation (RSI) is indicated when patients are not fully conscious or are otherwise at increased risk of gastric regurgitation and aspiration.[7] The main objective of this technique is to minimize the time interval between loss of protective airway reflexes and tracheal intubation with a cuffed endotracheal tube. The period between induction of general anesthesia and securing the airway is most critical since aspiration of gastric content is then most likely.[8] However, rapid sequence induction is associated with, hemodynamic instability and oxygen desaturation.[9-11] It‘s therefore crucial to minimize the number of intubations attempts and the time to intubation, as both prolonged time to intubation and multiple intubation attempts significantly attribute to perioperative morbidity and mortality.

Videolaryngoscopes were introduced into clinical practice approximately two decades ago and have gained wide acceptance in the elective OR setting.[12] Videolaryngoscopes can facilitate endotracheal intubation by improving visualization of the larynx, thereby facilitating direct observation of the tracheal tube during passage through the vocal cords.[13-17] Consequently, videolaryngoscopy may decrease intubation difficulties and ultimately increase first-attempt and overall intubation success rate.[13-17] However,

available literature is heterogeneous in study design, patient characteristics, and intubation provider experience.

Several trials demonstrated that videolaryngoscopes improve vocal cord visualization, but not first-pass intubation success.[18,19] Interestingly, in a trial with ICU patients, videolaryngoscopy did not improve first-attempt intubation success and was associated with severe complications including death, cardiac arrest, cardiovascular collapse and hypoxemia.[19] In contrast, other trials reported improved glottis visualization, improved first-pass success[16] and no difference in rate of complications compared with direct laryngoscopy.[20] In a recent Cochrane review of more than seven thousand patients with and without difficult airways, videolaryngoscopy was associated with fewer complications (e.g., laryngeal or airway trauma, postoperative hoarseness, hypoxia), fewer failed intubations, and no increase in the time required for intubation.[21] The extent to which videolaryngoscopes might facilitate intubation in patients undergo RSI is unclear.

The McGrath (Medtronic, Minneapolis, MN) is an FDA-approved and commercially available videolaryngoscope that includes a Macintosh blade and a camera which provides an indirect view of the glottis. The McGrath has been tested in a variety of settings[22-24] and consistently provides better glottis visualization than direct laryngoscopy in patients with difficult airways.[25,26] However, its suitability in the context of RSI has yet to be formally evaluated, and whether results from previous trials apply to these patients remains unknown.

Objectives and Hypothesis

Our goal is to compare conventional direct laryngoscopy using a Macintosh blade with the McGrath videolaryngoscope for rapid sequence endotracheal intubation. Specifically, we propose to test the ***primary hypothesis*** that videolaryngoscopy improves visualization of the vocal cords, defined using the modified Cormack and Lehane classification (primary outcome), versus direct laryngoscopy.

We will also test the ***secondary hypotheses*** that McGrath videolaryngoscopy decreases number of intubation attempts and the number of intubation failures. We hypothesize that the McGrath videolaryngoscopy reduces both, the number of intubation attempts and the number of intubation failures.

We will also assess the following ***exploratory outcomes***:

1. Ease of intubation;
2. Glottis opening score (POGO) score;
3. Duration of intubation.

We will also assess the following ***safety outcomes***:

1. Incidence of cut lips, airway injury, or dental injury;
2. Incidence of postoperative coughing;
3. Incidence or severity of postoperative sore throat;
4. Incidence or severity of postoperative hoarseness.

METHODS

Design

We propose a patient-blind multi-center randomized trial that will be coordinated by the Department of Outcomes Research at the Cleveland Clinic, Main Campus.

Patients

We will enroll up to 800 (including 25 – 50 pilot) consenting adults, with American Society of Anesthesiologists (ASA) physical status 1-3, who are scheduled for elective non-cardiac surgery requiring endotracheal intubation with rapid sequence induction for general anesthesia. Written informed consent will be obtained. Participating study centers will be:

- Cleveland Clinic, Main Campus, Cleveland OH
- Tabriz University of Medical Sciences, Tabriz, Iran
- The University of Health Science, Konya City Hospital, Konya, Turkey
- The University of Health Science, Bakırköy Dr. Sadi Konuk Education, and Research Hospital, Istanbul, Turkey

Inclusion criteria

1. Age between 18 and 99 years;
2. American Society of Anesthesiologists (ASA) physical status 1-3;
3. Elective surgery requiring oral endotracheal intubation for general anesthesia;
4. Any clinical indication for rapid sequence induction as determined by the attending anesthesiologist;
5. Anticipated extubation in the operating room.

Exclusion criteria

1. Refusal of participation by attending anesthesiologist;
2. Indicated fiberoptic awake intubation

3. Body Mass index (BMI) > 45 kg/m^2.

Protocol

In the preoperative period, airway details for participating patients will be recorded by a research coordinator or anesthesia provider. Patients will be positioned supine and in a standardized ramped position on the OR table. Patients will be pre-medicated with midazolam, as clinically appropriate. All patients will be pre-oxygenated until the fraction of expired oxygen exceeds 80%.

Rapid sequence induction will be induced as preferred by the attending anesthesiologist, usually with a combination of lidocaine 1 mg/kg, propofol 2-5 mg/kg, fentanyl 1-3 µg/kg, and succinylcholine 1.5 mg/kg or rocuronium 1.0 mg/kg. Complete muscle relaxation will be confirmed by absence of palpable twitches in response to supra-maximal train-of-four stimulation of the ulnar nerve at the wrist.

Patients will be randomized 1:1 before induction, stratified for primary anesthesia providers (*experienced* – specialist, attending *vs. unexperienced* – trainees) to:

- Direct laryngoscopy using an appropriately sized Macintosh blade (usually size 3 or 4);
- McGrath videolaryngoscope in an appropriate size (usually blade size 3 or 4).

Randomization will be based on computer-generated codes accessed from the Redcap system.

Intubations will be performed with a regular endotracheal tube of adequate diameter, usually 7.0 mm to 8.0 mm. Endotracheal tubes will be equipped with a hockey-stick-shaped stylette, which will be prepared by the anesthesiologist in advance. The McGrath or the Macintosh blade will be introduced into oral cavity according to manufacturer recommendations and clinical practice. Minor airway manipulation procedures including BURP or Sellick maneuvers will be allowed to improve

visualization of the vocal cords. If initial intubation attempts fail, the endotracheal tube will be removed. Minor adjustments of patient's position and/or tube stylette will be used as clinically appropriate. Up to two intubation attempts will be made as necessary. Further airway management will follow clinical assessment of the anesthesiologist. The anesthesiologist will be permitted to terminate study participation and switch to an alternative method.

Once intubation is achieved, the endotracheal tube will be connected to the anesthesia circuit, and the endotracheal cuff pressure will be measured placed between 25 and 30 cm H_2O.

Mechanical ventilation with O_2 and air will be adjusted to maintain end-tidal PCO_2 between 32 and 35 mmHg as clinically necessary. Maintenance of general anesthesia will be provided, as clinically indicated.

At the end of the surgical procedure, patients will be extubated and transferred to the post anesthesia care unit (PACU). Patients will then be assessed for postoperative complications 2 hours following extubation, or at PACU discharge.

Measurements

Demographic and morphometric characteristics will be collected from electronic medical records.

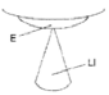
1. Age
2. Sex
3. Race
4. BMI
5. ASA status
6. Airway examination
    a. History of obstructive sleep apnea (yes/no)
    b. History of snoring (yes/no)

c. History of CPAP (yes/no)
d. History of difficult airway (yes/no)
e. Mobility of cervical spine (0, 15, 30, and 45 degrees)
f. Mouth opening (cm)
g. Inter-incisor gap (cm)
h. Mandibular protrusion test (Class A, B, C)
i. Thyro-mental distance (cm)
j. Thyro-mental height (cm)
k. Sterno-mental distance (cm)
l. Neck circumference (cm)
m. Upper lip bite test (Class I, II, III)
n. Mallampati score (1/2/3/4)
o. Teeth status (Edentulous, missing frontal teeth or full dentition)

Outcomes

Primary outcome:

Best glottis visualization, defined as visualization according to the modified Cormack and Lehane classification[27]

Original Cormack and Lehane system	1 Full view of the glottis	2 Partial view of the glottis or arytenoids		3 Only epiglottis visible	4 Neither glottis nor epiglottis visible
View at laryngoscopy					
Modified system	1 As for original Cormack and Lehane above	2a Partial view of the glottis	2b Arytenoids or posterior part of the vocal cords only just visible	3 As for original Cormack and Lehane above	4 As for original Cormack and Lehane above

Secondary Outcomes:

- Intubation attempts, defined as introducing the endotracheal tube into oral cavity to perform endotracheal intubation (1, 2, 3, etc.)

- Intubation failure, defined as
    - Failure to intubate within 3 intubation attempts
    - Need to switch intubators or intubation device
    - Need to stop study per anesthesiologist's discretion

Exploratory outcomes:

- Portion of glottis opening score (POGO) score, defined as estimation of the glottis, which is visible during laryngoscopy (0, 25, 50, 75, 100%)[28,29]

- Time to intubation, defined as the time between the laryngoscope introduced into oral cavity and cuff inflation (RSI definition) and to the first appearance of end-tidal CO_2.

- Ease of intubation, defined as subjective evaluation of the anesthesiologist after finishing the intubation procedure: (1) very easy; (2) easy; (3) moderate; (4) difficult; and, (5) impossible.[30,31]

Safety outcomes:

- Any apparent airway or dental injury including bleeding, airway trauma, dental fracture, aspiration, or bronchospasm.

- Incidence and severity of postoperative cough, assessed 2 hours after extubation in the PACU, and defined as continuous throat pain and rated as mild (less than a common cold), moderate (similar to a common cold), or severe (more than a common cold).[30,31]

- Incidence and severity of postoperative sore throat, assessed after 2 hours of extubation in the PACU, defined as an acoustic quality that was different from the previous voice quality of the patients and rated as mild (less than a common cold), moderate (similar to a common cold), or severe (more than a common cold).[30,31]

- Incidence and severity of postoperative hoarseness, assessed after 2 hours of extubation in the PACU, and rated as noticed by the patient only, apparent to an observer, or aphonia.[30,31]

Data analysis:

Statistical Analysis

We will assess the balance of two randomized groups (McGrath videolaryngoscopy vs. direct laryngoscopy) on **baseline and demographic characteristics** using the absolute standardized difference (ASD), defined as the absolute difference in means, mean ranks, or proportions divided by the pooled standard deviation. Any characteristics with ASD > maximum of 0.10 and $1.96\sqrt{(n_1 n_2)\mathrm{x}(n_1+n_2)}$ will be considered imbalanced and will be adjusted for in the primary and secondary analyses.

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All primary and secondary analyses will be completed using the modified intent-to-treat principle, thus including all randomized patients in whom intubation was attempted in the analyses. We will conservatively assign all missing outcome values as the highest possible score in the control group (direct laryngoscopy) and the lowest possible score in the treatment group (McGrath videolaryngoscopy) for all primary and secondary analyses.

Primary outcome:

Wilcoxon-Mann-Whitney test will be used to formally compare categorical outcome of glottis visualization (Cormack and Lehane classification) at the 5% significance level

between the two study groups; this test accounts for the ordinal nature of the outcome. If adjustment for imbalanced baseline covariates is required, we will attempt a proportion odds logistic regression model to compare randomized groups, reporting an odds ratio indicating the estimated odds of being better using videolaryngoscopy versus direct.

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If the proportional odds assumption does not hold after testing and also visualizing with further modeling, the outcome will be assessed using either an adjacent logit analysis or by combining categories and using chi-square test or binary logistic regression, as appropriate. The distribution of patients in each glottis visualization class will be reported for each randomized group.

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Secondary outcomes:

Randomized groups will be compared on the secondary outcome of Intubation failure (yes/no) via chi-square test and the associations reported using relative risk [97.5% confidence interval (CI)]. Randomized groups will be compared on the count of number of intubation attempts using either Wilcoxon-Mann-Whitney test or negative binomial regression, as appropriate. A Bonferroni correction will be applied and a significance criterion of 0.05/2=0.025 to control the overall Type I error at 5% level for two secondary hypotheses.

The exploratory and safety outcomes will be reported by study groups without formal statistical testing of the difference.

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Interim analyses to assess efficacy and futility will be conducted at each 25% of the maximum planned enrollment. We will use a gamma spending function with gamma parameter= -4 for efficacy and -1 for futility.

Sample size considerations. Sample size is based on the primary outcome of glottis visualization (Cormack and Lehane classification) and the Wilcoxon-Mann-Whitney test. From the literature we assume a distribution of scores for the Direct Laryngoscopy group such that the proportion of patients in categories 1, 2a, 2b, 3 and 4 are 0.50, 0.30, 0.15, 0.04, 0.01, and that for the videolaryngoscopy the proportions are improved to 0.65, 0.25, 0.07, 0.02, 0.01. We would thus need a total of 384 patients to detect this difference or larger with 90% power at the 0.05 significance level. Incorporating a maximum of 3 interim analyses and a final analysis with the above-detailed spending functions will require a maximum of N=438 patients. Simulations indicate that if the specified difference is a good estimate of the true effect, the expected sample size is about 78% of the maximum sample size, or N=342. In such a case, the study will have a very good chance of crossing an efficacy boundary at interim looks 2 or 3.

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Because our estimates of laryngeal view are uncertain, we plan to enroll a maximum of 800 patients in case the treatment effect is somewhat less than anticipated.

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Pilot patients: We will enroll 5-10 pilot patients prior to the start of the study at each study center to familiarize the study team with the protocol and identify any systematic issues that might result in protocol modifications. Pilot patients will be randomized either to McGrath videolaryngoscopy or direct laryngoscopy group in the same manner as it is planned for the study. Pilot patients will not be included in the statistical analysis.

Funding:

This study is an investigator-initiated study.

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