



Comparison of McGrath Videolaryngoscopy and Direct Laryngoscopy for intubation in patients with Morbid Obesity

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Summary of changes (version 2)

- Exact timing of randomization was defined: After confirming adequate bag mask manual ventilation, patients will be randomized 1:1 and stratified for BMI $>50 \text{ kg/m}^2$ (*Materials and Methods, page 7*)
- In cases of intubation failure, further airway management will be determined by the attending anesthesiologists. No airway device or technique will be proposed and rescue airway device/ technique will be documented (*Materials and Methods, page 7*)
- Once the patient is intubated, the endotracheal cuff pressure will be measured once. (*Materials and Methods, page 7*)
- Patients will be assessed for postoperative complications 2 hours after extubation, or at PACU discharge, whatever happens earlier (not follow up at wards) (*Materials and Methods, page 8*)
- Some measurements during Airway examination (*Materials and Methods, page 8*), have been changed:
 - Mobility of cervical spine (0, 15, 30, and 45 degrees)
 - Mandibular protrusion test (Class A, B, C)
 - Teeth status: Edentulous, frontal teeth missing, or full dentures

Background

Advanced airway management is often required for patients who need general anesthesia. Several supraglottic airway devices have been introduced into clinical practice during the last few decades, and are currently used on a regular base. However, endotracheal intubation (ETT) provides the best airway for mechanical ventilation and best prevents aspiration.

Airway complications are rare but may lead to severe complications, such as brain damage and even death¹. 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^{2 3}.

Obese patients present an airway challenge due to their unique anatomy, and are prone to early desaturation. Obese patients may also have comorbidities (e.g., diabetes) and increased intra-abdominal pressure, which places them at higher risk of aspiration. Obese patients are thus generally intubated quickly to reduce the risk of aspiration. There is data suggesting that obesity is a significant predictor of difficult laryngoscopy⁴ and intubation⁵. As the incidence of obesity continues to rise, it will become increasingly relevant for clinicians to decide on the best airway management devices for these patients.

Direct laryngoscopy (DL) has been the traditional method to insert an ETT. DL generally requires a direct “line of sight” to visualize the glottis and insert an ETT. While obesity per se is not a difficult airway, obesity carries risk factors that can lead to difficult mask ventilation and/or difficult intubation due to a combination of:

1. extra pre-tracheal soft tissue⁴,
2. thoracic fat pads and large breasts interference with the standard DL handle⁶,
3. limited neck mobility from laryngeal and cervical glycosylation from diabetes⁷.

Videolaryngoscopes were introduced approximately two decades ago and have gained wide acceptance because they improve glottis visualization which may improve first-pass intubation success rate and decrease complications. There is continued debate whether videolaryngoscopy

is superior to DL on parameters including first time intubation success rates, complications from intubation, and clinical benefits. Several trials demonstrated that videolaryngoscopes improved vocal cord visualization, but not first-pass intubation success^{8,9}. 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 hypoxemia⁹. In contrast, other trials show improved glottis visualization, improved first-pass success,¹⁰ and no difference in rate of complications compared with DL¹¹. 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 intubation¹².

Available literature is heterogeneous in study design, patient characteristics, and intubation provider experience. The extent to which videolaryngoscopes might facilitate intubation in obese patients thus remains unclear. Existing literature focused on obesity in the BMI range from 35-40 kg/m².^{13,14} There is a paucity of data comparing DL and videolaryngoscopes extremely obese patients, specifically those having a BMI ≥ 40 kg/m².

The McGrath (Medtronic, Minneapolis, MN) is an FDA-approved and commercial 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 settings¹⁵⁻¹⁷ and consistently provides better glottis visualization than DL in patients with difficult airways^{18,19}. However, intubation in morbidly obese patients (BMI ≥ 40 kg/m²) can be challenging and whether results from previous trials apply to these patients remains unknown.

Objectives and Hypotheses

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

We will also test the secondary hypotheses that McGrath videolaryngoscopy:

- 1) Does not increase number of intubation attempts
- 2) Does not increase the number of intubation failures.

We will also assess the following exploratory outcomes:

1. Ease 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.

Materials and Methods

Study Design

We propose a patient-blind randomized trial that will be conducted at the Cleveland Clinic, Main Campus.

Methods

We will enroll up to 136 *adult patients*, with American Society of Anesthesiologists (ASA) physical status of 1-3, who are scheduled for elective non-cardiac surgery requiring endotracheal intubation for general anesthesia. Informed consent will be obtained in the pre-anesthesia evaluation clinic. Intubators will be experienced anesthesia providers with sufficient experience, defined by having performed at least 75 with direct laryngoscopy and 75 with the McGrath system.

Inclusion criteria

- Elective surgery requiring oral endotracheal intubation for general anesthesia;
- Anticipated extubation in the operating room;
- American Society of Anesthesiologists (ASA) physical status 1-3;
- Age between 18 and 99 years;
- Body Mass index $\geq 40 \text{ kg/m}^2$.

Exclusion criteria

- Refusal of participation by attending anesthesiologist;
- Indicated rapid sequence induction for any reason including, but not limited to high risk of aspiration
- Indicated fiberoptic awake intubation.

Protocol

In the preoperative period, patient's airway data will be recorded by a research coordinator or anesthesia provider (**Table 1**). Patients will be positioned supine and in a standardized ramped

position on the OR table. Patients will be pre-medicated with midazolam 0-2 mg IV, as clinically appropriate. All patients will be pre-oxygenated until the fraction of expired oxygen exceeds 80%. General anesthesia 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 rocuronium 0.6-1.2 mg/kg or succinylcholine 1.5 mg/kg.

Manual bag-mask ventilation will be initiated, with no restriction on the use of oral airways, nasal airways, laryngeal masks. 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. After confirming adequate bag mask manual ventilation, patients will be randomized 1:1, stratified for BMI >50 kg/m², to:

- Direct laryngoscopy using an appropriately sized Macintosh blade (usually size 3 or 4);
- McGrath videolaryngoscopy 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 7.5 mm or 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 fails, the endotracheal tube will be removed and manual bag mask ventilation will resume. Minor adjustments of patient's position and/or tube stylette are allowed as clinically appropriate. Up to three intubation attempts will be made as necessary.

Further airway management will be determined by the attending anesthesiologists and not further airway device/ technique is proposed by this study protocol. Any further airway technique and device will be documented.

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 H₂O.

Mechanical ventilation with O₂ and air will be adjusted to maintain end-tidal PCO₂ between 32 and 35 mmHg as clinically necessary. The endotracheal tube cuff will be measured once. 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

Table 1. Demographic and morphometric characteristics will be collected from electronic medical records.

1. Age
2. Gender
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. Sterno-mental distance (cm)
 - k. Neck circumference (cm)
 - l. Upper lip bite test (Class I, II, III)

- m. Mallampati score (1/2/3/4)
- n. Teeth status: Edentulous, frontal teeth missing or full dentition.

Primary outcome:

- Best glottis visualization, defined as visualization according to the modified Cormack and Lehane classification²⁰

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, more than 3)
- Intubation failure, defined as
 - Grade IV visualization
 - 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%)^{21,22}

- Time to intubation, defined as the time between the endotracheal tube introduced into oral cavity and first appearance of end-tidal CO₂.
- Ease of intubation, defined as subjective evaluation of the anesthesiologist after finishing the intubation procedure (1) very easy, (2) easy, (3) moderate, (4) difficult, (5) impossible^{23,24}

Safety outcomes:

- Any obvious airway and teeth injury including bleeding, airway trauma, dental fracture, aspiration, or bronchospasm.
- Incidence and severity of postoperative cough, assessed 2 hours after extubation or at discharge from PACU (whatever happens earlier), 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).^{23,24}
- Incidence and severity of postoperative sore throat, assessed 2 hours after extubation or at discharge from PACU (whatever happens earlier), 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).^{23,24}
- Incidence and severity of postoperative hoarseness, assessed 2 hours after extubation or at discharge from PACU (whatever happens earlier), and rated as noticed by the patient only, apparent to an observer, or aphonia.^{23,24}

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 > 0.2 will be considered imbalanced and will be adjusted for in the primary and secondary analyses.

All primary and secondary analyses will be completed using the intent-to-treat principle, thus including all randomized patients in the analyses. We will conservatively assign all missing evaluations 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 outcomes:

Mann–Whitney U test will be used to formally compare categorical outcome of glottis visualization (Cormack and Lehane classification) at 5% significance level between the two study groups; the suggested test accounts for the ordinal nature of the outcome. A proportion of patients by glottis visualization classes will be reported for each randomized group.

Secondary outcomes:

The following secondary categorical variables will be compared between two study groups via Chi-square tests and corresponding odds ratio [97.5% confidence interval (CI)]:

1. incidence of intubation failures;
2. the proportion of patients requiring 1, 2, 3, and more than 3 intubation attempts

We will test if a McGrath videolaringoscopy is noninferior (i.e., not worse) than direct laryngoscopy on the listed below outcomes. We *a-priori* defined the noninferiority deltas for the outcomes:

1. incidence of intubation failures (noninferiority delta: 10% increase in intubation failures or 1.10 using odds ratio);
2. intubation attempts (noninferiority delta: 1.10 using odds ratio);

Noninferiority of McGrath videolaringoscopy versus direct laryngoscopy will be claimed for an outcome at the 0.025 significance level if the upper limit of 97.5% CI is below the corresponding noninferiority delta.

A Bonferroni correction for multiple testing will be applied and a significance criterion of $0.05/2=0.025$ will be used for secondary hypotheses testing correspondently to control the overall Type I error at 5% level for secondary hypotheses.

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

Sample size consideration

Sample size consideration is based on primary outcome glottis visualization grade. We assume that about 75% of the patients would have Grade 1 visualization by Cormack and Lehane classification with direct laryngoscopy. Thus, **65 patients per group (N=130 total)** would provide about 90% to identify a 20% increase in proportion of Grade 1 visualization (up to 95% of the patients) in the McGrath videolaryngoscopy group at the 5% alpha significance level. Other scenarios with different assumptions are presented in the Table below. (The situation described above is scenario #5).

Scenario #	Alpha	Computed N per Group			N per Group
		Ref Proportion	Proportion Diff	Actual Power	
1	0.05	0.70	0.15	0.90	161
2	0.05	0.70	0.20	0.90	82
3	0.05	0.73	0.15	0.90	145
4	0.05	0.73	0.20	0.90	73
5	0.05	0.75	0.20	0.90	65

Pilot patients

We will enroll 4-6 pilot patients prior to the start of the study 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. Therefore, we are planning to enroll a total of 136 patients to the study.

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