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Assessment of Airway in Patients with Acromegaly Undergoing Surgery: Predicting Successful Tracheal Intubation

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Abstract

Background In the field of anesthesia, acromegaly is considered a cause of difficult tracheal intubation and airway management. There is a high probability of unanticipated difficult intubation in acromegalic patients despite a lower percentage of patients being identified preoperatively as having a difficult airway. In this study, we carried out various airway assessment tests preoperatively and during induction of anesthesia to find out the predictors of easy tracheal intubation in patients with acromegaly.

Materials and Methods All patients of either sex, diagnosed as a case of acromegaly and scheduled to undergo pituitary surgery were enrolled over a period of 3 years. Various airway assessment tests were performed prior to surgery, which included modified Mallampati (MP) classification (sitting and supine), mouth opening (MO), upper lip bite test (ULBT), neck movement (NM), thyromental (TM) distance, thyrohyoid (TH) distance, sternomental (SM) distance, hyomental (HM) distance, length of upper incisors (IL), receding mandible (RM), any history of obstructive sleep apnea (OSA), mask ventilation (MV), Cormack-Lehane (CL) III and IV, and external laryngeal manipulation (ELM). Results were reported as odds ratios (95% confidence interval [CI]). The p-value < 0.05 was considered statistically significant.

Results A total of 42 patients were enrolled over a period of 3 years. The male-to-female ratio was 19:23 with a mean age of 37.95 years and mean weight of 72.7 kg. Out of 15 airway assessment parameters, only ULBT and CL grade showed significant results.

Conclusion We conclude that ULBT and CL grading are reliable predictors of easy intubation in patients with acromegaly undergoing surgery.

Keywords
► acromegaly
► airway
► intubation

Introduction

Patients with acromegaly present a challenge to anesthesiologists with regard to difficult tracheal intubation and airway management.[1] There is a high probability of unanticipated difficult intubation among patients suffering from acromegaly despite a lower percentage of patients identified preoperatively as having a difficult airway. The overall incidence of acromegaly is estimated to be three to four patients per million,[2] and the incidence of difficult intubation in these patients is four to five times more than in those without acromegaly.[3] The difficult intubation scenario can be managed by various methods ranging from awake fiberoptic-guided intubation to tracheostomy. In general, difficult tracheal intubation accounts for 17% of respiratory-related injuries resulting in significant morbidity and mortality.[4] In patients with acromegaly, inability to mask-ventilate or intubate can lead to 28% of all anesthesia-related deaths.[5] Therefore, the need and importance of airway assessment in patients with acromegaly cannot be overemphasized. Various airway assessment

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tests have to be used to assess difficult airway and tracheal intubation. In this study, we assessed various airway assessment tests predicting successful tracheal intubation as well as rate of complications such as multiple attempts (> 3) for intubation, failed tracheal intubation, and postoperative complications such as tracheal reintubation.

Materials and Methods

After taking the approval from institute ethics committee (IEC/NP-397/14.11.2014), we enrolled 45 patients of either sex, diagnosed as a case of acromegaly scheduled for pituitary surgery over a period of 3 years. The clinical diagnosis of acromegaly was made on the basis of growth hormone (GH) levels and magnetic resonance imaging (MRI) findings. Out of 45 patients, we excluded 3 patients who were either edentulous or had cervical spine disease (►**Fig. 1**). A written informed consent was obtained from all patients. All patients were evaluated preoperatively, by an independent observer (IK). Various airway assessment tests were done to assess the airway, which included modified Mallampati (MP) classification (sitting and supine positions), followed by mouth opening (MO), upper lip bite test (ULBT), thyromental (TM), thyrohyoid (TH), sternomental (SM), hyomental (HM) distance, length of upper incisors (IL), presence of receding mandible (RM), neck movement (NM), external laryngeal manipulation (ELM), and Cormack-Lehane (CL) grading (**Appendix A**). An associated history of obstructive sleep apnea (OSA) was also taken into account for assessing the difficult intubation, followed by OSA grading in patients with acromegaly posted for pituitary surgery (**Appendix B**). Methods of assessment of these tests are described in **Appendix C**.

General anesthesia was induced with fentanyl 2 µg/kg, propofol 2 mg/kg, and rocuronium 1 mg/kg intravenously. After 90 seconds of mask ventilation, laryngoscopy was performed by an anesthesiologist present in the operating theater in head extended position with an appropriately sized Macintosh blade (size 3 or 4) in all patients irrespective of the airway status. In situations of difficult tracheal intubation, that is, CL grades IIIb and IV, fiberoptic-guided intubation was done under general anesthesia. Following tracheal intubation, standard anesthesia protocol was followed for maintenance of anesthesia. At the end of surgery, neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg via intravenous route. Once the patient followed verbal command, and respiratory parameters were satisfactory, endotracheal tube was removed. All patients were shifted to neurosurgical intensive care unit (ICU) for observation and supportive management.

Statistical analysis was carried out using Stata 12.0 (College Station; Texas, United States). Data were presented as number percentage or mean ± SD (standard deviation) as appropriate. Chi-square test was used to assess the relationship between airway assessment parameters and ease of intubation. Logistic regression was used to find the odds associated with airway assessment parameters in relation to the ease of intubation. The results were reported as odds ratio (OR) (95% confidence interval [CI]). The **p**-value < 0.05 was considered statistically significant.

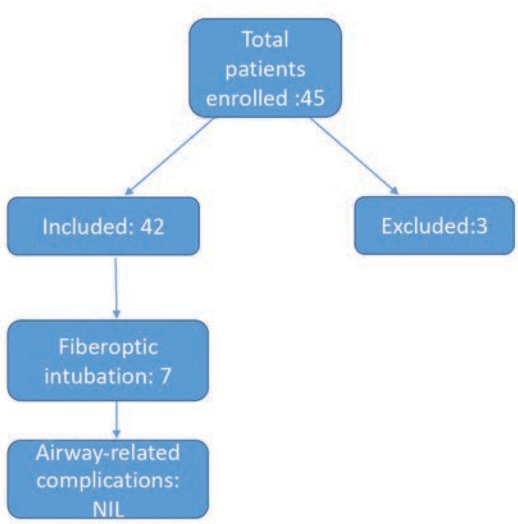

Fig. 1 Flowchart showing participation of patients.

Results

A total of 42 patients participated in this study conducted over a period of 3 years. ►**Table 1** shows the demographic characteristics of patients including sex, age, and weight. Various airway assessment parameters observed are summarized in ►**Fig. 2**. Out of 42 patients, only 7 patients required fiberoptic-guided intubation **(►Fig. 3)**. The calculated OR, 95% CI, and *p*-value of airway assessment tests are shown in ►**Table 2**. For NM, TM, RM, and OSA, OR could not be calculated.

Percentage of easy intubation based on criteria set by our study include MO > 3 FB in 83%, MP I and II (sitting and supine positions) in 64% and 52%, ULBT I and II in 90%, TM > 6 cm in 95%,TH > 2 FB in 93%, HM 4 to 6 cm or > 6 cm in 57%, SM > 12.5 cm in 83%, IL < 1.5 cm in 95%, easy MV in 64%, nonrequirement of ELM in 52%, and CL grades I and II were noted in 79% of patients. OSA was absent in 93% of patients. None of the patients had restricted NM and RM.

Discussion

Airway management in a patient can lead to temporary or permanent harm or even death. It has been observed that, even with proper evaluation, difficult airway was sometimes not picked up. The overall incidence of difficult intubation in general population has been described to be 5.8%; out of this 6.2% has been described for normal patients excluding obstetric and obese patients, 3.1% for obstetric patients, and

Table 1 Demographic characteristics

Male to female[a]	19:23
Age (y)[a]	37.95 (11.5)
Weight (kg)[a]	72.7 (10.3)

[a]Mean (standard deviation).

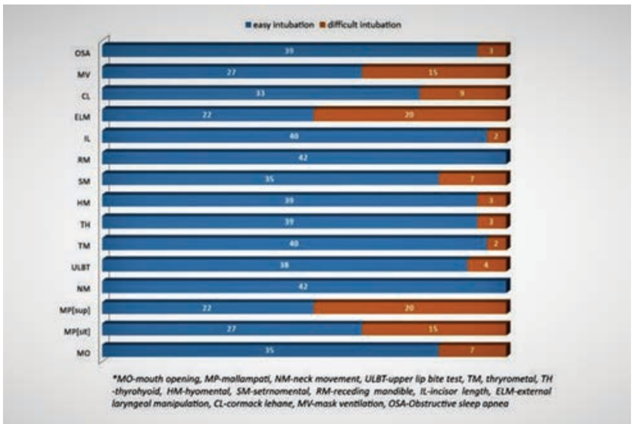

Fig. 2 Various airway assessment parameters. Y axis mentions the various airway assessment tests, expansions of which are mentioned in the figure.

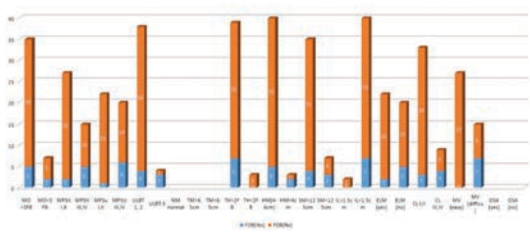

Fig. 3 Incidence of FOB-guided intubation in different airway assessment parameter groups. Y axis refers to number of patients already mentioned in the text.

Table 2 Odds ratios, 95% confidence intervals, and *p*-values for airway assessment parameters in patients with acromegaly

	OR (95% CI)	*p*-Value
MO	2.4 (0.36–15.9)	0.36
MP (sitting)	6.25 (1.03–37.6)	0.05
MP (supine)	8.99 (0.97–83.0)	0.05
ULBT	25.5 (2.12–307.2)	0.01
HM	13.6 (1.03–179.0)	0.05
SM	5.81 (0.93–35.9)	0.06
ELM	3.33 (0.57–19.5)	0.18
CL grade	8 (1.36–47.0)	0.02

Abbreviations: CI, confidence interval; CL, Cormack-Lehane; ELM, external laryngeal manipulation; HM, hyomental; MP, modified Mallampati; MO, mouth opening; OR, odds ratio; SM, sternomental; ULBT, upper lip bite test.

15.8% for obese patients.[6] Mallampati test is one of the most useful tests done to evaluate the airway preoperatively.[7,8] In contrary to our study in which we observed MP III and IV in 36% (sitting) and 48% of patients (supine), Ali et al noticed only 27% of patients with MP III and IV; however, they did not mention the position during the MP assessment.[9] There is a possibility of increased MP grading in the supine position due to inadequate visualization of oral structures that could justify the lower percentage of good-grade MP in our study. Our results show 6.25 times higher probability of difficult intubation with MP assessment in the sitting position and 8.9 times probability of difficult intubation with MP in the supine position in patients suffering from acromegaly. However, the result in relation to MP parameter assessment either in the sitting or supine position is of borderline significance. Both MP test and ULBT are less sensitive in patients suffering from acromegaly than in normal patients.[10] Aswar et al found that both MP and ULBT are poor predictors of difficult intubation when used as single preoperative bedside screening tests; however, MP is a better test at predicting difficult endotracheal intubation when compared with ULBT in normal patients.[11] Our study results show significant relationship between ULBT and difficult intubation with 25.5 times higher chances of difficult intubation in patients with acromegaly. Orofacial changes are found to be frequent in patients suffering from acromegaly. There is progressive development of lips, mandible, soft palate, uvula, and teeth that are rarely noticed because it happens over a period of time.[12] None of the previous studies have reported the relationship between MO and difficult intubation in patients with acromegaly. According to our study results, there are 2.4 times chances of difficult intubation in patients with MO < 3 FB; however, the result is of borderline significance. Another method to assess difficult airway is to measure TM distance that is measured from the thyroid notch to the tip of the jaw with the head extended. Ali et al noticed an increased TM distance in patients with a long duration of disease suffering from acromegaly, though increased TM distance was not associated with difficult laryngoscopy.[9] They also observed that their patients had a large TM distance (prognathism) with a mean of 8 cm. These values clearly exceed the values reported for patients without acromegaly.[13] In our study though we did not calculate the mean, 95% of patients had TM distance > 6 cm, and out of 95% patients, only 17.5% of patients had difficult intubation. Another study by Patil et al suggested that there was no difficulty in intubation in patients with a TM distance > 6.5 cm.[14] However, it has been observed that TM distance along with MP, preoperative assessment of anatomic abnormality, and cervical mobility provide a higher sensitivity and specificity in predicting difficult laryngoscopy.[15] Receding mandible refers to a smaller, shorter, and a backward retreated chin. It is also termed as *micrognathia*. It can occur because of many reasons that include congenital or acquired reasons. Acromegaly is usually associated with macrognathia because of excessive release of GH leading to enlargement of the jaw. Micrognathia may be an associated finding in syndromic patients (Turner syndrome, Pierre–Robin syndrome, trisomy 13, and trisomy 18). In our study none of the patients had receding mandible or micrognathia. Atlanto-occipital (A-O) gap is another major factor that limits the extension of the head on the neck. The longer the A-O gap, the more space is available for mobility of the head at that joint with good axis for laryngoscopy and intubation. Radiologically, there is reduced space between C1 and occiput.[16] Frerk et al observed that the atlantoaxial gap was not as good a predictor of difficulty intubation, which was contrary to the results obtained from the study conducted by Calder et al, which was done on patients with cervical spine disease.[17] In patients with acromegaly, atypical occipital condyles, in combination with the odontoid process hypoplasia and its slight inclination, are responsible for A-O and atlantoaxial instability. The gap between the occipital condyles and superior articular facets of the atlas indicate A-O dislocation.[18] Since in our study none of the patient had restricted neck movement, radiologic evaluation of A-O gap was not performed.

The effect of GH on skeletal tissue in patients suffering from acromegaly is well known. Normally the teeth (including incisors) grow continuously throughout life. When occlusion is normal, in this way they remain of a normal length. However, when occlusion is abnormal because of conditions that include mandibular prognathia that is common in patients with acromegaly, teeth may become greatly elongated because typical attrition of the incisors does not occur.[19] On literature search, none of the studies in past had observed an association between incisor length and difficult intubation in patients with acromegaly. However, our study result does not show any relationship between IL and difficult intubation.

The TH distance of > 2 FB between the hyoid bone and the thyroid cartilage can increase the chances of successful intubation. Till date no data are available on association between TH distance and difficult intubation in patients suffering from acromegaly. Our study result, though does not show any relationship between TH distance and difficult intubation. The mandibular space assessment is mainly suitable for adults and older children as a predictor of difficult airway. Huh et al observed that the HM distance and hyomental distance ratio (HMDR) defined as the ratio of the HMD at the extreme of head extension to that in the neutral position is significantly associated with difficult intubation.[20] In another study by Rao et al in which they found HMDR is a clinically reliable predictor of difficult intubation to certain extent because of its high specificity and negative predictive value.[21] Literature lacks studies on HM distance and its relationship with difficult intubation in patients with acromegaly. As per our study results, HM distances > 2 FB have 13.6 times higher chances of difficult intubation with borderline significance. Liaskou et al observed SM distance as a relatively poor single predictor of difficult laryngoscopy.[22] However, contrary to the above study, it has been observed that combination of modified MP and SM distance can be used as a good predictor of difficult intubation as it is simple and can be easily performed.[23,24] As per our study results, SM distance is not a good predictor of difficult intubation; however, there is 5.81 times probability of difficult intubation with SM distance < 12.5 cm.

Patients with acromegaly have increased ventilatory response to carbon dioxide and elevated GH level; both contribute to increased incidence of central sleep apnea.[25] Patients suffering from acromegaly with OSA have craniofacial structures different from patients without OSA. Patients with OSA have narrow posterior airway space, hyoid is displaced more caudally, and there is increased vertical dolichofacial growth, which make them candidates with difficult airway.[26] The literature shows the reported prevalence rate for sleep apnea in patients with acromegaly varies from 19 to 81%, depending on the methods and diagnosis criteria used.[27] Another study observed the presence of OSA in 37.5% of patients suffering from acromegaly.[28] As per our study results, OSA was absent in 93% of patients, showing comparatively low incidence of sleep apnea compared with other studies.

Patients suffering from acromegaly can have difficult MV because of various associated factors such as macroglossia, enlarged nasal bone, prognathism, and receding mandible. According to the study by Khan and Rasouli in which they had intubated 800 patients with acromegaly who underwent transsphenoidal surgery for pituitary tumors under general anesthesia during 1995 to 2008, difficult MV was observed in a significant number of patients.[29] Our study result shows insignificant relationship between MV and difficult intubation. External laryngeal manipulation (ELM) is used to get better laryngeal view during direct laryngoscopy. Studies have shown that the ELM done by the anesthetist makes the best laryngeal view for tracheal intubation.[30] Previous studies had observed that the application of external laryngeal pressure improves laryngeal visualization to CL grade II from CL grade III in patients suffering from acromegaly, but not always.[31] According to our study results, with application of ELM to improve the glottic view, there is 3.33 times probability of difficult intubation; however, it is found to be insignificant. As discussed above, the incidence of difficult intubation is higher in patients suffering from acromegaly compared with the normal population. Schmitt et al reported 26% incidence of difficult laryngoscopy grade (CL III); however, this percentage decreased to 10% with application of ELM. None of their patients had CL IV laryngoscopy grade.[31] In other three prospective studies, the reported incidence of CL grades III and IV is 17%, 6.1%, and 20%, respectively.[32] The percentage of CL grades I and II in our study is 79% that automatically calculates the percentage of CL grades III and IV to 21%, which is quite high compared with the above studies. The higher CL grade in our study could be due to the higher degree of acromegaly that may have led to difficult airway. Our study results suggest that with higher CL grading, there is eight times higher chances of difficult intubation, which is highly significant. None of the patients had complications associated with airway management.

Fiberoptic intubation can always be considered in patients with acromegaly.[33] In a case series of 32 patients suffering from acromegaly, Friedel et al observed the video laryngoscope-guided intubation in 21.9% of patients and fiberoptic-guided intubation in 12.5% of patients, which in total results in 34.4% of patients requiring advanced airway management devices for securing airway, which in comparison with our study results (17%) is almost double[28] (►**Fig. 1**). The lower percentage of advanced airway device use in our study compared with the study by Friedel et al could be due to a higher sample size compared with their study. Another factor could be the subjective variability in assessing the airway.

Few limitations of our study include (1) noncalculation of sample size as the major limitation and (2) dichotomized criteria of easy and difficult intubation that could have affected our results. We conclude that ULBT and CL grading are reliable predictors of easy intubation in patients with acromegaly undergoing surgery. Thyrohyoid distance, incisor length, and mask ventilation, however, were found to have no relationship with ease of intubation. Given the paucity of available data, further large studies are required to support the predictors of easy intubation in patients suffering from acromegaly.

Conflict of Interest
None declared.

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Appendix A Various airway assessment parameters categorized as easy and difficult

Tests	Easy intubation	Difficult intubation
1. Mouth opening	> 3 fingerbreadth	< 3 fingerbreadth
2. Modified Mallampati classification	Grade 1—soft palate, hard palate, faucial pillars, uvula Grade II—soft palate, hard palate, uvula	Grade III—uvula is obscured by base of tongue Grade IV—only hard palate is visible
3. Neck movement	Unrestricted	Restricted
4. Thyromental distance	> 6.5 cm or 6.0–6.5 cm	< 6.0 cm
5. Thyrohyoid distance	> 2.0 fingerbreadth	< 2.0 fingerbreadth
6. Hyomental distance	> 6.0 cm or 4.0–6.0 cm	< 4.0 cm
7. Sternomental distance	> 12.5 cm	< 12.5 cm
8. Upper lip bite test	Class 1: Lower incisors can bite upper lip above vermilion line Class 2: Lower incisors can bite upper lip below vermilion line	Class 3: can't bite the upper lip
9. Receding mandible	No	Yes
10. Length of upper incisor	< 1.5 cm	> 1.5 cm
11. History of OSA	No	Yes
12. OSA scoring	< 4	> 4
13. Mask ventilation	Easy	Difficult
14. External laryngeal manipulation	No	Yes
15. Cormack-Lehane grading	Grade I—glottic opening with vocal cords visible Grade II—posterior part of the vocal cords visible	Grade III—only epiglottis visible, but liftable Grade IV—epiglottis not visible

Abbreviation: OSA, obstructive sleep apnea.

Appendix B Obstructive sleep apnea grading

Identification and assessment of OSA: example
A. Clinical signs and symptoms suggesting the possibility of OSA 1. Predisposing physical characteristics a. BMI: 35 kg/m^2 (95th percentile for age and sex)[a] b. Neck circumference: 17 in (men) or 16 in (women) c. Craniofacial abnormalities affecting the airway d. Anatomical nasal obstruction e. Tonsils nearly touching or touching in the midline 2. History of apparent airway obstruction during sleep (two or more of the following are present; if patient lives alone or sleep is not observed by another person, only one of the following needs to be present: a. Snoring (loud enough to be heard through closed door) b. Frequent snoring c. Observed pauses in breathing during sleep d. Awake from sleep with choking sensation e. Frequent arousals from sleep f. Intermittent vocalization during sleep[a] g. Parental report of restless sleep, difficult breathing, or struggled respiratory efforts during sleep[a] 3. Somnolence (one or more of the following is present) a. Frequent somnolence or fatigue despite adequate "sleep" b. Falls asleep easily in a non-stimulating environment (e.g., watching TV, reading, riding in or driving a car) despite adequate "sleep" c. Parent or teacher comments that child appears sleepy during the day, is easily distracted, is overly aggressive, or has difficulty concentrating[a] d. Child is often difficult to arouse at usual awakening time[a]

continued

continued

If a patient has signs or symptoms in two or more of the above categories, there is a significant probability that he or she has OSA. The severity of OSA may be determined by sleep study (see below). If a sleep study is not available, such patients should be treated as though they have moderate sleep apnea unless one or more of the signs or symptoms above are severely abnormal (e.g., markedly increased BMI or neck circumference, respiratory pauses that are frightening to the observer, patient regularly falling asleep within minutes after being left unstimulated), in which case they should be treated as though they have severe sleep apnea. B. If a sleep study has been done, the results should be used to determine the perioperative anesthetic management of a patient. However, because sleep laboratories differ in their criteria for detecting episodes of apnea and hypopnea, the task force believes that the sleep laboratory's assessment (none, mild, moderate, or severe) should take precedence over the actual AHI (number of episodes of sleep disordered breathing per hour). If the overall severity is not indicated, it may be determined using the following table:		
Severity of OSA	Adult AHI	Pediatric AHI
None	0–5	0
Mild OSA	6–20	1–5
Moderate OSA	21–40	6–10
Severe OSA	40	10
Obstructive sleep apnea scoring system example		
Points A. Severity of sleep apnea based on sleep study (or clinical indicators if sleep study not available) Point score _____ (0–3)[b,c] Severity of OSA (Table 1) None 0 Mild 1 Moderate 2 Severe 3 B. Invasiveness of surgery and anesthesia Point score _____ (0–3) Type of surgery and anesthesia Superficial surgery under local or peripheral nerve block anesthesia without sedation 0 Superficial surgery with moderate sedation or general anesthesia 1 Peripheral surgery with spinal or epidural anesthesia (with no more than moderate sedation) 1 Peripheral surgery with general anesthesia 2 Airway surgery with moderate sedation 2 Major surgery, general anesthesia 3 Airway surgery, general anesthesia 3		
C. Requirement for postoperative opioids Point score _____ (0–3) Opioid requirement None 0 Low-dose oral opioids 1 High-dose oral opioids, parenteral or neuraxial opioids 3 D. Estimation of perioperative risk. Overall score—the score for A plus the greater of the score for either B or C Point score _____ (0–6)[d] A scoring system similar to this table may be used to estimate whether a patient is at an increased perioperative risk of complications from OSA. This example, which has not been clinically validated, is meant only as a guide, and clinical judgment should be used to assess the risk of an individual patient.		

Abbreviations: AHI, apnea–hypopnea index; BMI, body mass index; OSA, obstructive sleep apnea; TV, television.

[a]Elements in brackets refer to pediatric patients.

[b]One point may be subtracted if a patient has been on continuous positive airway pressure (CPAP) or noninvasive positive-pressure ventilation (NIPPV) before surgery and will be using his or her appliance consistently during the postoperative period.

[c]One point should be added if a patient with mild or moderate OSA also has a resting arterial carbon dioxide tension ($PaCO_2$) > 50 mm Hg.

[d]Patients with a score of 4 may be at increased perioperative risk from OSA; patients with a score of 5 or 6 may be at significantly increased perioperative risk from OSA.

Appendix C Methods of assessment of airway tests

Mallampati test: patient in sitting or supine position Head in neutral position No phonation Maximal tongue protrusion
Thyromental distance: distance from the mentum to the thyroid notch while the patient's neck is fully extended
Hyomental distance: distance between the mentum to the hyoid bone while the patient's neck is fully extended
Sternomental distance: distance from the upper border of the manubrium to the tip of the mentum while the patient's neck is fully extended
Neck moment: **Extension at atlanto-occipital joint**—patient is asked to hold the head erect facing directly to front -> maximal head extension -> angle traversed by occlusal surface of upper teeth is measured -> tells degree of extension **Flexion of cervical spine:** ask the patient to touch his manubrium sterni with his chin. If done, assures flexion of 25–35 degrees
Upper lip bite test: patient is asked to bite upper lip with lower incisors
Receding mandible: patient is asked to protrude lower incisors anterior to upper incisors