Anesthesiology
2000; 93:110-4

Difficult Intubation in Acromegalic Patients

Incidence and Predictability

Hubert Schmitt, M.D., Michael Buchfelder, M.D.,† Martin Radespiel-Tröger, M.D.,‡ Rudolf Fahlbusch, M.D.§*

Background: **Previous studies have suggested that the incidence of difficult intubation in acromegalic patients is higher than in normal patients. However, these studies were retrospective and did not include preoperative assessment of the airways. The aims of this study were to determine the incidence of difficult intubation and to assess the usefulness of preoperative tests in predicting difficult laryngoscopy.**

Methods: **One hundred twenty-eight consenting acromegalic patients requiring general anesthesia and tracheal intubation were studied. Preoperatively, Mallampati classification, thyromental distance, and head and neck movement were determined in each patient. After induction of anesthesia and muscle paralysis, laryngoscopic grade was assessed during direct laryngoscopy; Cormack and Lehane grade III or IV were classified as difficult. The association of individual airway assessment with laryngeal view was evaluated using the Fisher exact test. Predictors of difficult laryngoscopy were evaluated by calculating their sensitivity and specificity.**

Results: **Laryngoscopy was difficult (grade III) in 33 of 128 patients (26%). Application of external laryngeal pressure improved laryngeal visualization to grade II in 20 of these 33 patients. In the remaining 13 patients (10%), intubation was difficult (more than two attempts, blade change, use of gum-elastic bougie). Mallampati classes 3 and 4 were significantly related to laryngoscopy grade III (Fisher exact test, $P = 0.001$).**

Conclusions: **The incidence of difficult laryngoscopy and intubation in acromegalic patients is higher than in normal patients. Preoperative Mallampati scores of 3 and 4 were of value in predicting difficult laryngoscopy. Nevertheless, even this test will miss a significant number of patients with a difficult airway. (Key words: Anesthetic techniques; laryngoscopy; oropharyngeal classification.)**

MANAGEMENT of anesthesia for the patient with acromegaly requires careful attention to changes in the upper airway. Several case reports have documented the airway difficulties associated with acromegaly[1-3] and recommended specific management, ranging from awake fiberoptic intubation to routine tracheostomy in selected patients.[4-6] However, there are only few data available regarding the incidence of difficult intubation in acromegalic patients. Two published retrospective series documented an incidence of 12 and 30 per 100 patients, respectively,[7,8] but neither reported clinical signs for estimating the likelihood of difficult intubation in these patients.

Among many criteria tested as potential predictors for difficult intubation, three simple and easy-to-perform examinations—the modified Mallampati classification, measurement of the thyromental distance, and head and neck movement—have proven to predict a difficult airway with an acceptable accuracy.[9-11] We hypothesized that using these tests to assess typical acromegalic airway alterations such as enlargement of the tongue, hypertrophy of soft tissue, and mandibular prognathism may help to identify acromegalic patients at risk of a difficult airway. Therefore, we undertook this prospective study to ascertain the incidence of difficult laryngoscopy and intubation and to assess the usefulness of easy-to-perform preoperative tests.

Methods

Patients

The study was approved by our hospital's Ethics Committee, and written informed consent was obtained from all 128 patients. Between March 1994 and December 1998, all acromegalic patients (American Society of Anesthesiologists class I-III, 68 women, 60 men) scheduled for elective transsphenoidal resection of a growth hor-

* Assistant Professor, Department of Anesthesiology.

† Associate Professor, Department of Neurosurgery.

‡ Assistant Professor, Department of Medical Informatics, Biometry, and Epidemiology.

§ Professor and Chairman, Department of Neurosurgery.

Received from the Department of Anesthesiology, Friedrich-Alexander University, Erlangen-Nuremberg, Erlangen, Germany. Submitted for publication September 20, 1999. Accepted for publication February 14, 2000. Support was provided solely from departmental and/or institutional sources. Presented in part at the annual meeting of the American Society of Anesthesiologists, San Diego, California, October 18-22, 1997.

Address reprint requests to Dr. Schmitt: Department of Anesthesiology, Friedrich-Alexander University, Erlangen-Nuremberg, Krankenhausstrasse 12, D-91054 Erlangen, Germany. Address electronic mail to: hubert.schmitt@kfa.imed.uni-erlangen.de

mone secreting pituitary adenoma were investigated. The diagnosis of acromegaly was confirmed by clinical and endocrine reassessment (failure to suppress growth hormone to < 2 μg/l after an oral glucose load) as well as by magnetic resonance imaging showing the size and the extent of a pituitary adenoma just before surgery. All patients showed typical acromegalic features such as macroglossia, prognathism, or soft tissue swelling in various degrees. Cushing's traditional transnasal route for the transsphenoidal approach was used in all patients.

Study Protocol

Preoperative evaluation was performed in all patients using the following protocol. First, a modified Mallampati classification[12] was conducted in the sitting patient with the head in a neutral position without phonation. The view was graded as follows: class I = soft palate, fauces, uvula, and pillars visible; class II = soft palate, fauces, and uvula visible; class III = soft palate and base of the uvula visible; class IV = soft palate not visible at all. Second, the thyromental distance was measured with a ruler with the head fully extended and the mouth closed as straight distance between the thyroid notch and the bony point of the chin. The distance was rounded to the nearest 0.5 cm. Third, head and neck movement (full extension to full flexion) was estimated by visual assessment as described by Wilson *et al.*[11] and categorized as being $> 90° \pm 10°$ and $< 80°$. Finally, we questioned the patient for a history of difficult intubation and sleep apnea. Pretreatment with a long-acting somatostatin analog (octreotide acetate; Novartis Pharma, Nuremberg, Germany) was also documented.

All patients except those with sleep apnea were premedicated with a benzodiazepine (dikaliumclorazepat 0.2 mg/kg) in the evening and in the morning. Acromegalic patients with sleep apnea received no premedication. All patients underwent standard monitoring, including pulse oximetry (Sp_{O_2}), electrocardiogram, capnography, neuromuscular blockage, and noninvasive blood pressure. They were anesthetized according to a standardized regimen. After sufficient preoxygenation (Sp_{O_2} of 100% for at least 2 min) and pretreatment with a subparalyzing dose of atracurium, anesthesia was induced with propofol (1.5-2 mg/kg), sufentanil (10-20 μg), and succinylcholine (1.5 mg/kg). For mask ventilation, the patient's head position was optimized and, if necessary, an oropharyngeal airway was used. Between intubation attempts, Sp_{O_2} was not allowed to decrease to less than 90%. Difficult mask ventilation was defined as the inability to record a regular carbon dioxide waveform.

After loss of all four twitches from the train-of-four obtained by ulnar nerve stimulation at the wrist, initial laryngoscopy was performed using an appropriate Macintosh laryngoscope blade (size 3-5, Fa. Rüsch, Kernen, Germany). Laryngeal view was assessed under optimal conditions (appropriate blade size, optimal head and neck position) and classified according to the method of Cormack and Lehane.[13] External laryngeal pressure was applied by an assistant under instruction of the laryngoscopist in all patients with laryngeal view grades III and IV. If required a gum-elastic bougie was used. Intubation was defined as difficult with the following criteria: more than two attempts, change of blade, and use of a gum-elastic bougie. Preoperative airway assessment as well as tracheal intubation with laryngeal view grading were performed by one anesthetist (H.S.).

Statistical Analysis

Demographic data are reported as mean values with SD and range. Serum growth hormone levels were described using median and interquartile range. Laryngoscopic grades III and IV were defined as difficult. The two-tailed unpaired *t* test was used for comparison of unpaired samples with normally distributed data (age, weight, height, body mass index, thyromental distance) and homogenous variances. The Mann–Whitney U test was used for comparison of unpaired samples without assumption of normally distributed data (serum growth hormone). The association of individual airway assessments with laryngeal view was evaluated using the Fisher exact test. Two-tailed P values ≤ 0.05 were considered significant. Predictors of difficult laryngoscopy were evaluated by calculating their sensitivity, specificity, positive predictive value, and negative predictive value. The relative risk for difficult laryngoscopy was calculated by two-by-two tables.

Results

The study group consisted of 60 men and 68 women with a mean ± SD age of 46 ± 15 yr (range, 19-78 yr), height of 174 ± 11 cm (range, 150-205 cm), and weight of 85 ± 15 kg (range, 53-132 kg). The thyromental distance was 9.5 ± 1.5 cm (range, 6-14 cm), and median basal serum growth hormone measurement was 30 ng/ml (interquartile range, 47 ng/ml).

After induction of anesthesia, all patients could be ventilated *via* a face mask. In 85 patients, an oropharyngeal airway improved airway patency. To provide effective manual ventilation, a two-handed mask grip was necessary in 14 patients (for mandibular displacement and chin lift) requiring an assistant. The tracheas of all patients were successfully intubated using Macintosh blades size 3, 4, or 5 in 63, 61, and 4 patients, respectively.

In 33 of 128 patients (19 male, 14 female), laryngoscopy was classified as difficult (grade III). No patient had a grade IV view. In 20 of the 33 patients, application of external laryngeal pressure improved visualization to grade II and enabled tracheal intubation without difficulty. In the remaining 13 patients, the trachea was intubated after more than two laryngoscopies and required a change of blades and the use of a gum-elastic bougie. In 8 of these 13 patients, a very large epiglottis alone or together with hypertrophy of mucosal folds concealed the view at the glottic chink. Lifting the epiglottis with an appropriate laryngoscope blade and/or external laryngeal pressure improved the laryngoscopic view in 10 patients so that at least the arytenoids could be seen. Despite the application of laryngeal pressure in three acromegalic patients, only the epiglottis could be visualized; therefore, the endotracheal tube was inserted blindly. In the group with difficult laryngoscopy, MacIntosh blades size 3, 4, or 5 were used in 11, 20, and 2 patients, respectively.

Table 1 shows the patient characteristics of normal (grades I and II) and difficult (grade III) laryngoscopy. Comparison of several potential risk factors between these two groups yielded statistical significance for the concentration of growth hormone and Mallampati classes.

Table 2 shows the distribution of Mallampati classes. We defined the Mallampati classes 3 and 4 as predictors of difficult laryngoscopy. We found a significant association between Mallampati classes and difficult visualization of laryngeal structures (Fisher exact test, $P = 0.001$). The specificity and sensitivity of Mallampati class 3 and 4 together for predicting difficult laryngoscopy were 76% and 44%, respectively, positive predictive value was 32%, and negative predictive value was 84%. The presence of Mallampati classes 3 and 4 was found to be a predictor of laryngoscopy grade III (relative risk, 2.0; 95% confidence interval, 1.0-4.1).

Table 3 shows the distribution of head and neck mobility. Impaired neck extension (< 80°) was not significantly related to difficult laryngoscopy ($P = 0.37$, Fisher exact test; *post hoc* power = 16%; case number required for a power of 80%, n = 772).

The thyromental distance was not significantly different between patients with and without difficult laryngoscopy ($P = 0.12$, two-sided unpaired *t* test; table 1).

Difficult laryngoscopy was neither significantly related to somatostatin-analog pretreatment (n = 33; $P = 0.25$, Fisher exact test), nor to a history of difficult intubation (n = 1). Three patients had a history of sleep apnea evaluated by polysomnography. Of these, two presented a laryngoscopic view grade III and one a difficult intubation. All patients could be extubated after completion of surgery. Five patients (all in the difficult laryngoscopy group) complained about a sore throat the day after surgery.

Table 1. Patient Characteristics (Mean ± SD [Range]) and Serum Growth Hormone (Median [IQR]) in Relation to Laryngoscopic Grades

	Grades I and II (n = 95)	Grade III (n = 33)	Significance
Age (yr)	46 ± 16 [19–78]	47 ± 12 [27–74]	NS
Sex (m/f)	41/54	19/14	NS
Weight (kg)	86 ± 16 [60–132]	85 ± 15 [53–118]	NS
Height (cm)	174 ± 12 [152–205]	174 ± 11 [150–198]	NS
Thyromental distance (cm)	9.5 ± 1.5 [7–14]	9.0 ± 1.5 [6–13]	NS
Body mass index	28 ± 4 [21–46]	28 ± 3 [20–34]	NS
Serum growth hormone (ng/ml)	36 [45]	15 [31]	0.01*

* $P = 0.01$ (Mann–Whitney U test).
IQR = interquartile range; NS = not significant.

Table 2. Distribution of Laryngoscopic Grades in Relation to Mallampati Classes and Thyromental Distance

Laryngeal view (before external laryngeal pressure)	Mallampati Class* 1 (n = 9)	2 (n = 41)	3 (n = 65)	4 (n = 13)	Thyromental Distance (cm) (NS) (Mean ± SD)
I (n = 55)	7	18	29	1	10.0 ± 1.5
II (n = 40)	2	15	21	2	9.5 ± 1.5
III (n = 33)	0	8	15	10	9.0 ± 1.5

* Fisher exact test, $P = 0.001$.
NS = not significant.

Table 3. Distribution of Laryngoscopic Grades in Relation to Head and Neck Movement

Laryngeal View (Before External Laryngeal Pressure)	Head and Neck Mobility (NS)	
	Above 90° (n = 121)	Below 80° (n = 7)
I/II (n = 95)	91	4
III (n = 33)	30	3

NS = not significant (Fisher exact test, $P = 0.37$).

Discussion

Incidence of Difficult Intubation

The incidence of difficult intubation (10%) in our study (defined by more than two attempts, blade change, use of gum-elastic bougie) is as high as reported by Messick *et al.* (13%),[7] but lower than in the study by Müchler *et al.* (30%).[8] However, a comparison of our results to these retrospective reports has some limitations. First, Messick *et al.* and Müchler *et al.* did not exactly define the term "difficult intubation." Second, in our study, intubation was performed by only one anesthetist. Third, patients from studies in the past may have suffered from more severe acromegaly and may therefore have had a more difficult airway. Nevertheless, our results confirm the previous reported and clinically known high incidence of difficult intubation in acromegalic patients. Compared with published rates of difficult intubation of approximately 2–5% in large nonacromegalic populations,[14,15] the incidence in acromegalics is approximately four to five times higher.

In addition to difficult intubation, we found a high incidence (26%) of initial grade III view of the laryngeal structures with an inadequate exposure of the glottis. This incidence exceeds markedly the highest reported and well-documented rate of grades III and IV laryngoscopies in nonacromegalic patients (approximately 6%).[14] Our rate of initial difficult laryngoscopies is consistent with a recent report by Hakala *et al.*,[16] who found difficulties in seeing the vocal cords using a Macintosh laryngoscope in 5 of 15 acromegalic patients. In our patients, the known maneuver of application of external laryngeal pressure[11,17,18] decreased the rate of grade III to grade II laryngoscopies from 26% to 10% and also confirmed the benefit of this manipulation in acromegalic patients.

Prediction of Difficult Intubation

The second main aim of our study was the evaluation of several clinical criteria such as the Mallampati classes, thyromental distance, and head and neck movement, all potentially helpful in predicting difficult intubation in nonacromegalic patients. In context with data from nonacromegalic patients, we found Mallampati classes 3 and 4 to be of significant value in predicting difficult laryngoscopy in acromegalic patients. The prevalence of 10% of the Mallampati class 4 alone and of 61% of Mallampati classes 3 and 4 together exceed by far the highest reported rates for nonacromegalic patients.[9,10,14] These results are not unexpected because a large tongue, a typical acromegalic feature, is directly assessed by the Mallampati classification. For Mallampati classes 3 and 4 together, we found a specificity, sensitivity, and positive predictive value corresponding to published nonacromegalic data.[9,10,14,19] In contrast to these published data, we found a lower negative predictive value (approximately 80%) in acromegalic patients. This is clinically relevant, because it means that 20% of acromegalic patients assessed by the Mallampati classification as easy to intubate actually will have a difficult laryngoscopy. However, there is an important limitation in generalizing these results: The fact that the same investigator evaluated the Mallampati class and laryngoscopic view may have introduced a bias.

The rate of 5% of markedly reduced neck mobility is higher than in nonacromegalic patients.[11] Although this test gained no significance in our study, the low frequency of patients with impaired neck mobility does not permit concluding judgment of the validity of this test in acromegalics.

We did not find a relationship between difficult laryngoscopy or difficult intubation and thyromental distance in acromegalic patients. The large thyromental distance due to prognathism with a mean of 9 cm in our patients clearly exceeds the values reported for nonacromegalic patients.[10] Therefore, we assume this test introduced to recognize retrognathism may be not appropriate in acromegalic patients.

Interestingly, patients in the difficult laryngoscopy group had a lower growth hormone level than the patients in the "easy" group. It is known that the growth hormone levels are not related to the degree of acromegalic symptoms[20]; therefore, the validity of hormone levels in predicting a difficult airway remains unclear. In addition, no conclusion can be made regarding octreotide pretreatment and difficult laryngoscopy from our study because only one third of our patients were pretreated. However, there are data published that indicate octreotide treatment relieves patients of acromegalic symptoms.[21] A possible association between sleep apnea and difficult intubation was recently found by Hiremath *et al.*[22]

but cannot be derived from our results because we did not systemically investigate our patients for sleep apnea.

Acromegalic Features Influencing Intubation Performance

Many typical acromegalic features are suggested to cause a difficult airway in these patients. The most discussed changes are macroglossia, prognathism, enlargement and distortion of glottic structures with additional folds, and hypertrophy of laryngeal and pharyngeal soft tissue.[23,24] We cannot differentiate which of these factors contributed most to difficult laryngoscopy or intubation in our patients. A huge epiglottis, which was common in our patients, can completely conceal the view at the laryngeal aperture,[25] and additional folds may make interpretation of the laryngeal anatomy more difficult.[4] Furthermore, we believe hypertrophy of soft tissue (although we did not measure) is of enormous importance in acromegalic patients and is often underestimated. Soft tissue swelling affects all pharyngeal structures in a narrowing manner and, in our opinion, considerably influences intubation performance. Because of this, an increased effort is necessary to displace the enlarged tongue into the restricted submental space. Consequently, it will be difficult or impossible to bring the tracheal and pharyngeal axis into line. Limitations in head and neck mobility may contribute in addition to the acromegalic manifestations of difficult intubation performance in these patients.

In summary, this study indicates that the incidence of difficult laryngoscopy and intubation in acromegalic patients is higher than in normal patients and that the use of optimal external laryngeal pressure will improve the view at laryngeal structures. In addition, our results show that prediction of a difficult airway in acromegalic patients is not as accurate as one might wish. In our study, only the Mallampati test showed a moderate predictive validity. The fact that neck extension and thyromental distance was not related to difficult laryngoscopy may be because of the small number of patients with impaired neck mobility and the prevalence of prognathism with a relatively long thyromental distance, respectively. This study suggests that visualization of the larynx in acromegalic patients is complicated by typical features such as large tongue, large epiglottis, distortion of the larynx, enlargement of laryngeal structures, and soft tissue swelling.

The authors thank Dr. H. Mang, Department of Anesthesiology, for his assistance in reviewing the manuscript.

References

1. Kitahata LM: Airway difficulties associated with anaesthesia in acromegaly: Three case reports. Br J Anaesth 1971; 43:1187-90
2. Hassan SZ, Matz GJ, Lawrence AM, Collins PA: Laryngeal stenosis in acromegaly: A possible cause of airway difficulties associated with anesthesia. Anesth Analg 1976; 55:57-60
3. Burn JM: Airway difficulties associated with anaesthesia in acromegaly [letter]. Br J Anaesth 1972; 44:413-4
4. Ovassapian A, Doka JC, Romsa DE: Acromegaly: Use of fiberoptic laryngoscopy to avoid tracheostomy. ANESTHESIOLOGY 1981; 54:429-30
5. Young ML, Hanson CW: An alternative to tracheostomy following transsphenoidal hypophysectomy in a patient with acromegaly and sleep apnea. Anesth Analg 1993; 76:446-9
6. Southwick JP, Katz J: Unusual airway difficulty in the acromegalic patient: Indications for tracheostomy. ANESTHESIOLOGY 1979; 51:72-3
7. Messick JM Jr, Cucchiara RF, Faust RJ: Airway management in patients with acromegaly [letter]. ANESTHESIOLOGY 1982; 56:157
8. Müchler HC, Renz D, Lüdecke DK: Anesthetic Management of Acromegaly. Edited by Lüdecke DK, Tolis G. New York, Raven Press, 1987, pp 267-71
9. Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B, Freiberger D, Liu PL: A clinical sign to predict difficult tracheal intubation: A prospective study. Can Anaesth Soc J 1985; 32:429-34
10. Frerk CM: Predicting difficult intubation. Anaesthesia 1991; 46:1005-8
11. Wilson ME, Spiegelhalter D, Robertson JA, Lesser P: Predicting difficult intubation. Br J Anaesth 1988; 61:211-6
12. Samsoon GL, Young JR: Difficult tracheal intubation: A retrospective study. Anaesthesia 1987; 42:487-90
13. Cormack RS, Lehane J: Difficult tracheal intubation in obstetrics. Anaesthesia 1984; 39:1105-11
14. El-Ganzouri AR, McCarthy RJ, Tuman KJ, Tanck EN, Ivankovich AD: Preoperative airway assessment: Predictive value of a multivariate risk index. Anesth Analg 1996; 82:1197-204
15. Rose DK, Cohen MM: The airway: Problems and predictions in 18,500 patients. Can J Anaesth 1994; 41:372-83
16. Hakala P, Randell T, Valli H: Laryngoscopy and fibreoptic intubation in acromegalic patients. Br J Anaesth 1998; 80:345-7
17. Krantz MA, Poulos JG, Chaouki K, Adamek P: The laryngeal lift: A method to facilitate endotracheal intubation. J Clin Anesth 1993; 5:297-301
18. Benumof JL, Cooper SD: Quantitative improvement in laryngoscopic view by optimal external laryngeal manipulation. J Clin Anesth 1996; 8:136-40
19. Tse JC, Rimm EB, Hussain A: Predicting difficult endotracheal intubation in surgical patients scheduled for general anesthesia: A prospective blind study. Anesth Analg 1995; 81:254-8
20. Melmed S: Acromegaly. N Engl J Med 1990; 322:966-77
21. Lamberts SW, van der Lely AJ, de Herder WW, Hofland LJ: Octreotide. N Engl J Med 1996; 334:246-54
22. Hiremath AS, Hillman DR, James AL, Noffsinger WJ, Platt PR, Singer SL: Relationship between difficult tracheal intubation and obstructive sleep apnoea. Br J Anaesth 1998; 80:606-11
23. Jackson C: Acromegaly of the larynx. JAMA 1918; 71:1787-9
24. Bhatia ML, Misra SC, Prakash J: Laryngeal manifestations in acromegaly. J Laryngol Otol 1966; 80:412-7
25. Hotchkiss RS, Hall JR, Braun IF, Schisler JQ: An abnormal epiglottis as a cause of difficult intubation—airway assessment using magnetic resonance imaging. ANESTHESIOLOGY 1988; 68:140-2