

HYPERPARATHYROIDISM, HYPERCALCEMIA
AND DIFFICULT LARYNGOSCOPY: A
RETROSPECTIVE REVIEW

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Abstract

Background: The incidence of difficulty with intubation in the general population depends upon the definition used but results as high as 37% have been published. Endocrine disorders such as diabetes and hyperthyroidism have been linked to an increased incidence of difficult intubation via laryngoscopy. Hypercalcemia with resulting calcification has been demonstrated to result in neck pain, decreased cervical range of motion, and loss of skin and tendon compliance. We speculated that patients with hyperparathyroidism and resulting hypercalcemia would have an increased incidence of intubation difficulty via laryngoscopy.

Methods: We studied 382 patients presenting for parathyroidectomy in whom direct laryngoscopy was initially attempted compared to 262 patients presenting for abdominal surgery in whom laryngoscopy was initially attempted via retrospective chart review. Difficult laryngoscopy was defined as 3 or greater attempts at direct laryngoscopy or 2 attempts and the use of airway adjunct (Eschmann stylet), flexible fiberoptics, or an indirect laryngoscope (Pentax AWS or Airtraq). Awkward intubation was defined as requiring > 1 attempt at laryngoscopy, intubation requiring a change in laryngoscope blade, the use of an airway adjunct (Eschmann stylet), or a Cormack and Lehane's view on initial laryngoscopy > 2. Hypercalcemia was defined as serum $[Ca^{2+}] > 10.2$ mg/dl. Propensity score matching was done to create 88 matched patient sets. McNemar's test was used to evaluate intubation difficulties in patients presenting for parathyroidectomy. The relationship between difficult laryngoscopy and hypercalcemia in parathyroidectomy patients was assessed by simple logistic regression (unadjusted) and multiple logistic regression.

Results: There is no difference in the rate of difficult or awkward laryngoscopy or the rate at which laryngoscopy was abandoned in favor of another means of intubation between parathyroidectomy and abdominal surgery patients. Hypercalcemia also does not impact laryngoscopy difficulty.

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Conclusions: To our knowledge, this is the first manuscript evaluating the impact of parathyroidectomy surgery and hypercalcemia on ease of intubation via laryngoscopy. Despite the fact that patients presenting for parathyroidectomy have many potential etiologies of increased difficulty with laryngoscopy, they do not appear to be at increased risk of laryngoscopy problems. The same is true of those patients presenting with hypercalcemia.

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Introduction

Airway management and the threat of difficulty with intubation are paramount in the minds of all practicing anesthesiologists. The incidence of difficult intubation varies depending on the definition used but, despite the proliferation of airway management tools, still occurs between 0.1-37% of the time^{1,2}. Many papers and academic careers have been made attempting to discover the ideal method to predict difficulty with airway management but anesthesiologists can still find themselves dealing with the unexpected difficult airway. Patient factors found to be associated with difficulty with intubation via laryngoscopy include anatomical features and various disease processes.

Primary hyperparathyroidism results in hypercalcemia and occurs in 25/100,000 patients. Primary hyperparathyroidism is often asymptomatic but can present as cardiac arrhythmia, abdominal pain, nephrolithiasis, mental status changes, lethargy, fatigue,

muscle weakness, and depression. Other causes of hypercalcemia to consider include sarcoidosis, lithium intake, diuretic use, tamoxifen, milk alkali syndrome, vitamin D deficiency, increased calcium intake, adrenal insufficiency, and thyrotoxicosis^{3,4}. Other endocrine diseases such as diabetes have been implicated as contributing to difficulty with laryngoscopy by producing a stiff joint syndrome where joint mobility can be severely limited⁵.

Ectopic calcification is most often seen in the setting of a systemic mineral imbalance and can follow either a chemical or physical trauma. Scleroderma has been shown to result in cervical paraspinal calcinosis with resulting neck pain and decreased range of motion⁶. Skin and tendons are prone to developing ectopic calcifications in addition to visceral organs^{7,8}. Two case reports of extreme hypercalcemia document the effects of increased parathyroid hormone resulting in systemic calcification and bone reabsorption^{9,10}. While it is controversial if thyroidectomy is associated with an increased risk of difficult laryngoscopy, we hypothesized that patients presenting for parathyroidectomy might have an increased incidence of Difficult Laryngoscopy (DL)¹¹⁻¹³. Hyperparathyroidism and resulting hypercalcemia may cause a stiff-joint syndrome similar to that described with long-standing diabetes reflected as a higher incidence of DL and intubation than case-controls.

Methods

Following approval of the Institutional Review Board at the University of Wisconsin School of Medicine and Public Health, a retrospective chart-review of adults presenting for parathyroidectomy limited to the neck in whom direct laryngoscopy was initially attempted were compared to patients presenting for abdominal surgery requiring endotracheal intubation. 382 patients meeting inclusion criteria were evaluated in the parathyroidectomy group between 7/21/2006-5/20/2009. 262 patients meeting inclusion criteria were evaluated in the abdominal surgery group between 10/3/2007-5/20/2009. The airway examination was performed preoperatively by the staff anesthesiologist and consisted of mouth opening (good, moderate, poor), thyroid to chin distance (cm), neck extension (good,

moderate, poor), Mallampati Score, and dentition (absent, damaged, intact). Difficult laryngoscopy was defined as 3 or greater attempts at direct laryngoscopy or 2 attempts and the use of airway adjunct (Eschmann stylet), flexible fiberoptics, or an indirect laryngoscope (Pentax AWS or Airtraq). Awkward intubation was defined as requiring > 1 attempt at laryngoscopy, intubation requiring a change in laryngoscope blade, the use of an airway adjunct (Eschmann stylet), or a Cormack and Lehane's view on initial laryngoscopy > 2. Hypercalcemia was defined as serum $[Ca^{2+}] > 10.2$ mg/dl. To estimate treatment effects, we have used propensity score-matching methods¹⁴. This approach allows one to balance observed baseline covariates

in the parathyroidectomy and general anesthesia groups, much like in a randomized study. Propensity scores (probability to receive a parathyroidectomy, given observed baseline patient covariates) were obtained after adjusting for age, body mass index (BMI), thyroid-chin distance (cm), Mallampati score, neck extension status (well/moderate/poor), mouth opening status (wide/moderate/poor), dentition status (intact/not intact/dentures), diabetes status (yes/no). Parathyroidectomy and general anesthesia patients were matched on the logit of the propensity score based on a caliper of one standard deviation of the logit. The SAS macro %GMATCH written at the Division of Biostatistics at the Mayo Clinic and available at

Table 1
Patient baseline characteristics in original data

Variable	Group		P-value
	Parathyroidectomy	General	
Age (years)	58.7±13.6 (N=377)	51.9±17.6 (N=261)	< 0.0001*
Body mass index (BMI)	31.4±9.2 (N=341)	27.9±8.24 (N=226)	< 0.0001*
Thyroid-chin distance (cm)	4.0±1.6 (N=131)	3.4±1.3 (N=161)	0.0008*
Serum calcium (mg/dL)	10.5±0.9 (N=337)	NA	
Mallampati score			
1	105 (27.8%)	114 (43.7%)	0.436#
2	127 (33.7%)	108 (41.4%)	
3	22 (5.7%)	21 (8.0%)	
4	1 (0.4%)	0 (0%)	
Missing	122 (32.4%)	18 (6.9%)	
Neck extension			
Well	274 (72.7%)	205 (78.5%)	0.3078#
Moderate	33 (8.7%)	14 (5.4%)	
Poor	18 (4.8%)	11 (4.2%)	
Missing	52 (13.8%)	31 (11.9%)	
Mouth opening			
Wide	307 (81.4%)	228 (87.4%)	0.2703#
Moderate	18 (4.8%)	8 (3.1%)	
Poor	12 (3.2%)	5 (1.9%)	
Missing	40 (10.6%)	20 (7.6%)	
Dentition			
Intact	202 (53.6%)	191 (73.2%)	< 0.0001#
Not intact	74 (19.6%)	35 (13.4%)	
Dentures	52 (13.8%)	22 (8.4%)	
Missing	49 (13.0%)	13 (5.0%)	
Diabetes			
Yes	47 (12.5%)	28 (10.7%)	0.6003#
No	327 (86.7%)	233 (89.3%)	
Unknown	2 (0.5%)	0 (0%)	
Missing	1 (0.3%)	0 (0%)	

Reported are mean ± standard deviation, unless otherwise noted. P-values based on the two-sample t-test (*) and Fisher's exact test (#).

Table 2
Patient baseline characteristics in propensity score-matched data

Variable	Group		P-value
	Parathyroidectomy (N=88)	General (N=88)	
Age (years)	54.7±11.8	55.5±16.3	0.6811**
Body mass index (BMI)	30.4±7.6	30.1±9.6	0.8618**
Thyroid-chin distance (cm)	3.8±1.5	3.6±1.3	0.1208**
Serum calcium (mg/dL)	10.2±0.9	NA	NA
Mallampati score			
1	37 (42.0%)	38 (43.2%)	0.2031##
2	47 (53.4%)	41 (46.6%)	1.0000##
3	4 (4.6%)	9 (10.2%)	NA
4	0 (0%)	0 (0%)	NA
Neck extension			
Well	76 (86.4%)	75 (85.2%)	NA
Moderate	5 (5.7%)	7 (7.9%)	
Poor	7 (7.9%)	6 (6.8%)	
Mouth opening			
Wide	81 (92.1%)	82 (93.2%)	NA
Moderate	4 (4.5%)	3 (3.4%)	NA
Poor	3 (3.4%)	3 (3.4%)	NA
Dentition			
Intact	62 (70.4%)	62 (70.5%)	NA
Not intact	15 (17.1%)	14 (15.9%)	NA
Dentures	11 (12.5%)	12 (13.6%)	NA
Diabetes			
Yes	12 (13.6%)	13 (14.8%)	NA
No	76 (86.4%)	75 (85.2%)	

Reported are mean ± standard deviation, unless otherwise noted. P-values based on the paired t-test (**) and McNemar's test (##). When sample sizes were too small to provide reliable asymptotic results, no p-values were produced (NA).

mayoresearch.mayo.edu/research/biostat/sasmacros.cfm has been used to form pairs of parathyroidectomy and general anesthesia patients.

Given the paired nature of the propensity score-matched data, to compare laryngoscopy difficulty (yes/no), abandonment (yes/no) and awkwardness (yes/no) in the parathyroidectomy and general anesthesia patients we have used McNemar's test. The relationship between difficult laryngoscopy and hypercalcemia in parathyroidectomy patients was assessed by simple logistic regression (unadjusted) and multiple logistic regression (adjusted for age, BMI, thyroid-chin distance (cm), Mallampati score, neck extension status, mouth opening status, dentition

status, diabetes status).

Results

Baseline patient characteristics in the original sample are presented in Table 1 and indicate statistically significant imbalances in age, BMI, thyroid-chin distance (cm) and dentition status (p-values <0.0001, <0.0001, <0.0001 and 0.0008, respectively). However, after propensity-score matching, 88 parathyroidectomy/general anesthesia patient pairs have been created and patient baseline characteristics are shown in Table 2. As expected, baseline imbalances in age, BMI and thyroid-chin distance (cm) have been removed

Table 3
Outcomes in propensity score-matched data

	Parathyroidectomy group (N=88)	General group (N=88)		P-value
		Yes	No	
Procedure abandoned?	Yes	5	0	0.7266
	No	3	80	
Procedure awkward?	Yes	2	11	0.6476
	No	8	67	
Procedure difficult?	Yes	2	11	0.6476
	No	8	67	

P-values are based on McNemar's test for paired binary outcomes.

p-values 0.6811, 0.8618 and 0.1280, respectively). Balancing has been achieved in the other baseline characteristics, but formal testing is not available due to the small sample sizes. Rates of difficult laryngoscopy (DL) and rates at which laryngoscopy was abandoned in favor of another means of intubation, or was awkward are presented in Table 3 and demonstrate that there is no difference in the rates of DL between the parathyroidectomy and abdominal surgery patients (p-values 0.7266, 0.6476 and 0.6476, respectively). We have found no significant relationship between serum calcium on the rate of DL in parathyroidectomy patients. As such, the odds ratio (OR) (DL vs, non-DL) was estimated as 1.86 (p-value=0.348), with a 95% CI of (0.51, 6.79) in the unadjusted model. In the adjusted model, the estimated OR was 0.63 (p-value=0.722), with 95% CI (0.05, 8.31).

Discussion

Patients presenting for parathyroidectomy have many potential etiologies of increased difficulty with laryngoscopy. There is the potential for mass effect if there is a mass of adequate size in the parathyroid glands. There is also the possibility that chronic hypercalcemia could result in ectopic calcification of laryngeal and neck ligaments or skin tissue resulting in increased airway management difficulties.

Other endocrine disorders such as diabetes are one of the multitude of disease processes implicated in

increasing the risk of difficult laryngoscopy. Diabetes is thought to lead to an increased incidence of difficult intubation secondary to stiff joint syndrome. This rapidly progressive microvascular disease is thought to increase intubation difficulty via involvement of the atlanto-occipital joint. In a study by Hogan et al, diabetics presenting for kidney and pancreas transplant had a 32 and 40% incidence of difficult laryngoscopy respectively. Of the 122 patients studied, three patients aspirated on induction, three patients needed to be awakened and intubated via fiberoptic bronchoscopy, and two patients required emergency tracheostomy⁵. This was prior to the era of laryngeal mask and other supraglottic airway devices as well as newer optical intubation aids but does serve to highlight the impact that chronic endocrine disorders can have on intubation difficulty.

Many papers have been written discussing the overall incidence of difficult laryngoscopy. Rose and Cohen evaluated 18,500 patients and found that the incidence of difficult laryngoscopy was 1.8%. The risk factors that they reported for difficult laryngoscopy were male sex, age 40-59 yr, obesity, decreased mouth opening, shortened thyromental distance, poor visualization of the hypopharynx, and limited neck extension. Their definition of difficult intubation included encounters recorded as having been difficult and those requiring more than two attempts at laryngoscopy¹⁵. Burkle et al determined

that the incidence of difficult laryngoscopy in a large teaching hospital was 0.5% as determined by a scoring system¹⁶. Another study of 1171 patients found that minor difficulties with intubation occurred in 37% of cases and that 8% of cases had moderate to major difficulties with intubation².

The incidence of difficult airway management in other head and neck surgeries, such as thyroidectomy, has been extensively investigated. One study evaluated 2000 patients presenting for thyroidectomy and discovered that difficult intubation occurred 5.5% of the time and was associated with the presence of polynodal goiter and hyperthyroidism¹³. Another study of 320 patients presenting for thyroidectomy found that the rate of minor difficulties with intubation was 57.8% and that the rate of difficult intubation was 5.3%. They discovered that cancerous goiter was associated with a higher incidence of difficult laryngoscopy and speculated that this was secondary to cancerous invasion of laryngeal structures with resulting fibrosis. They speculated that this laryngeal fibrosis decreased the mobility of laryngeal structures during laryngoscopy and therefore increased intubation difficulty¹². A study of 324 patients presenting for thyroidectomy found that the rate of difficult intubation was 11.1% and was not related to presence of goiter. Goiter with alteration of airway structures and malignant thyroid were also not associated with an increased incidence of airway difficulties¹¹.

One problem with studies evaluating airway management difficulties is that they often use different definitions to define a difficult airway, experience of the operator, and the airway itself. The ASA has defined difficult laryngoscopy as being unable "to visualize any portion of the vocal cords with conventional laryngoscopy" and difficult intubation as "an airway that requires more than three attempts or more than ten minutes to secure by direct laryngoscopy"¹⁷. Rose and Cohen evaluated this problem and found that based on the definition of difficult intubation used (poor view on laryngoscopy vs greater or equal to three laryngoscopy attempts vs failure of intubation) the incidence ranged from 10.1 to 1.9 to 0.1%¹.

Some groups have suggested that intubation is not required for thyroid and parathyroid surgery. They have found that the laryngeal mask airway can be used

safely even in cases of deviated or narrow trachea. By utilizing a LMA, fiberoptic bronchoscopy, and nerve stimulation to evaluate vocal cord movement the recurrent laryngeal nerve can be easily identified and therefore protected¹⁸. We discovered that throughout the duration of our investigation the LMA was used safely in 85 patients with one patient requiring intubation secondary to poor seal and another secondary to laryngospasm which were then both easily managed with laryngoscopy and intubation. Taken together, this data may indicate that in certain populations, intubation for parathyroidectomy should not be the standard of care.

Another large push in the recent literature is to limit the number of direct laryngoscopy attempts in the setting of a difficult airway as repeated attempts are associated with hypoxemia, regurgitation, and esophageal intubation. The ASA Task Force on the Management of the Difficult Airway suggests that an alternate method of intubation (fiberoptic bronchoscopy, intubating LMA, etc) be considered when initial attempts at laryngoscopy are unsuccessful¹⁷. The theory is that repeated laryngoscopy attempts only result in increased tissue trauma with resulting swelling and bleeding that can eventually worsen the mask airway. Newer literature suggests that early use of an alternative airway device (fiberoptic bronchoscopy, LMA, etc) will result in decreased hypoxia and abdominal insufflation¹⁹⁻²². This may partially explain why our patients appear to have a higher incidence of difficult laryngoscopy as it was often the case that laryngoscopy was abandoned after only one attempt in favor of another means of intubation.

One limitation of our study is its retrospective nature and the fact that data was not recorded completely in all patients (i.e. the initial airway exam was not completed in a large number of patients). However, when intraoperative airway difficulties were encountered the documentation of the airway management event was very well recorded. We also have attempted to overcome the limitations of our retrospective analysis via the use of propensity scores and an elegant statistical analysis that has produced groups with similar characteristics. In addition, many of our intubations were performed by resident trainees but that was similar between the two groups. We have a

high rate of abandoning laryngoscopy in our study but this appears to be similar between the two groups and is likely an institution effect or merely a “sign of the times” where videolaryngoscopy, laryngeal mask airways, and fiberoptic bronchoscopy are being utilized with increasing frequency. We intentionally used a different definition of difficult intubation via laryngoscopy than that used by many other studies. Had we used Cormack score, we may have had a higher incidence of difficult intubation. The reality is that many patients

with high Cormack scores are still technically easy to intubate and a high Cormack score was built into our definition of awkward intubations. To our knowledge, this is the first manuscript evaluating the impact of parathyroidectomy surgery and hypercalcemia on ease of intubation via laryngoscopy. It appears at this point, despite sound clinical reasoning that these factors should increase the difficulty of intubation via laryngoscopy, that neither of these factors have a large impact.

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