ORIGINAL ARTICLE

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Positional Dyspnea and Tracheal Compression as Indications for Goiter Resection

Michael T. Stang, MD; Michaele J. Armstrong, PhD; Jennifer B. Ogilvie, MD; Linwah Yip, MD; Kelly L. McCoy, MD; Christopher N. Faber, MD; Sally E. Carty, MD

Hypotheses: Goiter is a surgically reversible cause of positional dyspnea (PD). Substernal tracheal compression (TC) predicts PD relief after thyroidectomy (Tx).

Design: Retrospective analysis of a prospective structured management algorithm.

Setting: Endocrine surgery academic center.

Methods: Before Tx, 1081 patients were queried about PD. Those patients with substernal goiter underwent computed tomography, and their degree of TC was estimated as greatest percent reduction of transverse tracheal diameter. For 197 patients with PD, TC, or both, surgical outcomes were examined with a mean follow-up of 12.6 months. After Tx, patients who carried the diagnosis of obstructive sleep apnea were referred for repeat sleep study evaluation.

Results: Positional dyspnea was reported by 188 of 1081 patients, and after Tx the PD improved or resolved in 82.4%. In the 151 patients with substernal goiter, TC was present on imaging in 97.2%; the mean (range) TC was 34% (5%-90%). Patients with TC had a high likelihood of PD (93.5%). After substernal goiter resection, PD improved in stepwise association with total resected thyroid gland weight. Improvement in PD was strongly predicted by both gland weight of 100 g or more ($P<.001$) and by TC of 35% or more ($P<.01$). After Tx, 59 of 77 snorers (76.6%) reported improvement in snoring, 77.1% of patients with obstructive sleep apnea reported improved PD, and 2 of 3 retested patients with obstructive sleep apnea demonstrated objective improvement in sleep study apnea-hypopnea index.

Conclusions: Resection of bulky goiter frequently improves PD, which in substernal goiter is highly associated with TC. Either PD or TC of 35% or more prompt Tx. Goiter should be considered when obstructive sleep apnea is diagnosed.

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Author Affiliations: Divisions of Endocrine Surgery (Drs Stang, Armstrong, Ogilvie, Yip, McCoy, and Carty) and Pulmonary, Allergy, and Critical Care Medicine (Dr Faber), University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania. Dr Ogilvie is now with the Division of Endocrine Surgery, New York University Langone Medical Center, New York.

THYROID SURGEONS ARE OFTEN asked to evaluate patients for consideration of goiter resection. Although many physicians recognize that symptoms such as dyspnea can improve after thyroidectomy (Tx) for goiter, the definition of such symptoms is unclear. Moreover, the indications for goiter resection remain uncertain, the definition of *goiter* itself remains controversial,[1] and the precise definition of *substernal extension* varies by expert.[2-6] The relation of goiter to obstructive sleep apnea (OSA) is unknown. With the hypothesis that thyromegaly is a reversible cause of dyspnea, we designed a unique structured management strategy, examined whether positional dyspnea (PD) improves after Tx, and looked for features that predict its improvement. Because during sleep the symptoms of airway obstruction and snoring can overlap, we also examined the hypothesis that Tx can be a surgically correctable cause of misdiagnosed OSA.

See Invited Critique at end of article

METHODS

STRUCTURED PROSPECTIVE MANAGEMENT ALGORITHM

All patients presenting for initial evaluation of thyroid disease by a single endocrine surgeon were prospectively queried specifically about breathing, supine breathing, swallowing, hoarseness, anterior neck pain, and history of OSA diagnosis. Positional dyspnea was de-

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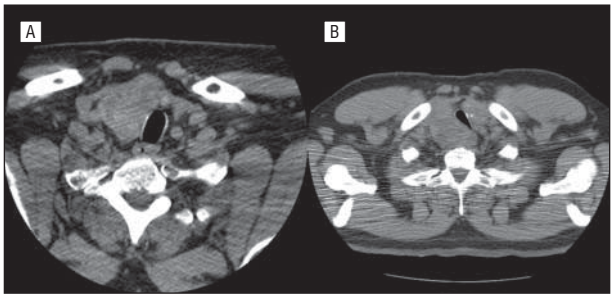

Figure 1. Representative illustrations of tracheal compression (TC) in substernal goiter. A, A moderate degree of intrathoracic TC (35%); B, A severe degree of intrathoracic TC (90%). The size of the intrathoracic thyroid tissue does not correlate well with the severe degree of TC.

fined by the report of trouble breathing at rest that was improved or ameliorated by position change.

Thyromegaly was defined as a clinical estimate of gland size at least 3 times normal. Patients who upon initial supine examination had cervical thyromegaly that extended caudally to the sternal notch underwent noncontrast neck computed tomography (CT). If the thyroid gland extended caudally past the sternal notch on CT or at surgery, the patient was considered to have substernal goiter (SG).

The extent of any tracheal compression (TC) on CT was quantified by the surgeon by direct review of cross-sectional images. Tracheal compression was measured at the longitudinal point of greatest percent reduction in transverse tracheal diameter (**Figure 1**).

Independently of any other indication, Tx was offered for TC of 20% or more. The following conditions were not considered to indicate Tx: thyroiditis, dysphagia, nonpositional or exertional dyspnea, tracheal deviation, cough, snoring, anterior neck pain, compressive sensation, or patient desire for surgery.

STUDY COHORT AND STATISTICAL ANALYSIS

For outcomes analysis we retrospectively reviewed the data of all 1081 consecutive patients who received 1129 thyroid operations from September 1, 2003, through June 30, 2009. This study was approved by the institutional review board of the University of Pittsburgh School of Medicine. Departmental records were also retrieved for the estimated number of new outpatients evaluated by the surgeon for thyroid disease. After excluding 1 case of anaplastic thyroid cancer, 1 case of thyroid lymphoma, and 48 cases of reoperative resection of an unenlarged thyroid lobe contralateral to a previous thyroid cancer (completion total Tx), we identified all patients who received Tx with PD, TC, or both and examined their demographic, radiologic, perioperative, and histologic data. We also compared the recorded indications for thyroid surgery with the recommendations of the 2009 American Thyroid Association guidelines for thyroid nodule and thyroid cancer management.[7] Follow-up data were retrieved from postoperative visits at 1 to 2 weeks and at 2½ months or more after Tx. Patients with OSA who reported improvement in PD or daytime somnolence were asked to undergo formal sleep study reevaluation; their postoperative changes in continuous positive airway pressure (CPAP) use and settings were assessed by self-report, and snoring was assessed by partner report. The mean (range) follow-up was 12.6 (2.6-85.1) months. The Fisher exact test was used to compare dichotomous variables and the *t* test to compare continuous variables. $P \leq .05$ was considered to be significant.

RESULTS

From September 1, 2003, through June 30, 2009, a total of 1738 new patients were evaluated for thyroid disease; among these, PD was reported in 188 (10.8%) and TC was identified in 139 (8.0%). The presence of PD was commonly expressed as "I have trouble breathing when I lay flat that gets better when I turn on my side" but also included "I can't breathe whenever I bend my neck forward to pray" and "I have trouble breathing when I raise my arms over my head." One patient presented with a Pemberton sign. Overall, Tx was performed in 1081 of the 1738 patients referred for surgical evaluation of thyroid disease.

The study cohort comprised 197 patients who underwent Tx in the setting of PD, TC, or both. The mean (range) age was 59 (18-89) years, and 79.2% were women. Unilateral thyromegaly was equally distributed with respect to laterality (32 left and 22 right). The extent of Tx was guided by the conditions present, with lobectomy and isthmusthectomy as the minimum operation; 54 patients had lobectomy and 143 patients had total Tx. In 3 cases, preoperative abnormal vocal fold function limited the extent of Tx to lobectomy. Papillary microcarcinoma (<1.0 cm) was the only histologic abnormality in 40 patients (20.3%), and differentiated thyroid cancer 1.0 cm or larger was found in 37 (18.8%), yielding an incidence of 39.1% for thyroid cancer. There was no operative mortality.

Substernal goiter was radiologically confirmed in 143 patients who had the condition suspected on examination, and another 8 were first identified to have SG at surgery; thus, a total of 151 of 197 patients (76.6%) had SG. On CT, SG extended caudally beyond the sternal notch in 65.7%, to the top of the aortic arch in 17.2%, caudal to the arch but above the carina in 15.6%, and to the level of the carina in 1.5% of patients. Patients whose SG extended caudally past the top of the arch on CT were evaluated preoperatively by the thoracic surgery team should chest exposure be required; however, Tx was accomplished via cervical incision in all 143 cases. During resection of large SG, we did not use morcelization or spoons. Tracheomalacia was not observed.

Figure 2 illustrates the interrelations of PD, TC, and SG. Positional dyspnea was reported by 188 of 197 patients (95.4%) and occurred without SG in 46 patients (23.4%). Regardless of the presence of PD, according to the 2009 American Thyroid Association guidelines, every PD patient also had at least 1 recognized indication for Tx.[7,8] Tracheal compression was present in 139 of 143 patients (97.2%) whose supine examination findings prompted CT imaging; the mean (range) degree of TC was 34.4% (5%-90%); the SD was 0.2% and the median was 30%. According to the 2009 American Thyroid Association guidelines, 130 of 139 TC patients had at least 1 recognized indication for Tx. Among TC patients, the rate of PD was high (130 of 139 [93.5%]). By contrast, in the 9 SG patients who had TC without reporting PD, the observed degree of TC was fairly mild (range, 5%-30%). When 134 SG patients underwent CT and reported PD, 130 (97.0%) were found to have TC.

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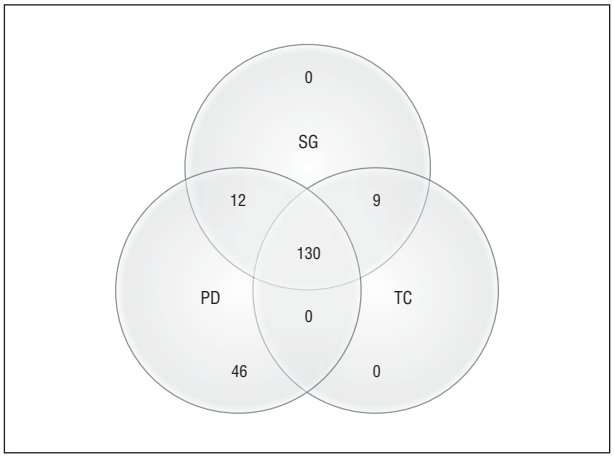

Figure 2. Venn diagram of the distributions of positional dyspnea (PD), substernal goiter (SG), and tracheal compression (TC) among 197 study patients.

After Tx, 155 of 188 PD patients (82.4%) reported the improvement or resolution of the symptom. In the 142 patients with both PD and SG (Figure 2), the response rate for surgical intervention was 88.0% (125 of 142), whereas in the 46 PD patients without SG, PD improved in 30 (65.2%). Body mass index and the presence of thyroid cancer did not predict postoperative PD improvement, but total resected thyroid gland weight was a strong predictor of PD response to surgery (**Figure 3**). After total Tx, resected total gland weights of 25 to 49 g, 50 to 74 g, and 75 to 100 g were respectively associated with stepwise PD improvement in 69.4%, 73.7%, and 85.7% of patients. After total Tx, a total resected gland weight of 100 g or more was associated with improvement or resolution in PD for 97.9% of patients (vs 60.0% for weight of ≤24 g; $P<.001$), and after lobectomy, a resected lobe weight of 75 g or more was associated with improved or resolved PD in 100% of patients. After SG resection, 125 of 151 patients (82.8%) experienced alleviation or resolution of PD; moreover, the likelihood of PD improvement or resolution after Tx varied stepwise with the degree of TC ($P<.01$) (**Figure 4**), and an inflection point was observed at TC of 35% or greater.

Obstructive sleep apnea had been formally diagnosed preoperatively in 35 of 197 patients (17.8%) who had PD, TC, or both. Tracheal compression was observed in 28 (90.3%) of the 31 patients with OSA who had CT imaging. The mean (range) degree of TC in patients with OSA was 34.8% (10%-90%), similar to that observed in study patients overall (34.4% [5%-90%]). After Tx, 77.1% of patients with OSA reported improvement or resolution of their PD. After Tx, 18 of 31 CPAP users (58.1%) reported they had decreased (n=4) or discontinued (n=14) their CPAP use. After Tx, 59 of 77 patients (76.6%) reported improvement or resolution of snoring. Noncompliance with repeat sleep study testing limited the objective reassessment of OSA, but 3 patients with OSA have undergone repeat formal sleep study after Tx to date. One patient had an equivalent apnea-hypopnea index. The second patient's apnea-hypopnea index improved from 53.8 to 28.9 after resection of a 31-g substernal gland associated with 40% TC. The third patient's apnea-hypopnea index normalized from 22.4 to 0.2 with resection of a 33-g substernal thyroid gland associated with 15% TC. Altogether, Tx performed in OSA patients with PD, TC, or both has been followed to date by self-reported symptom improvement and/or by documented physiologic improvement in 20 of 31 CPAP users (64.5%).

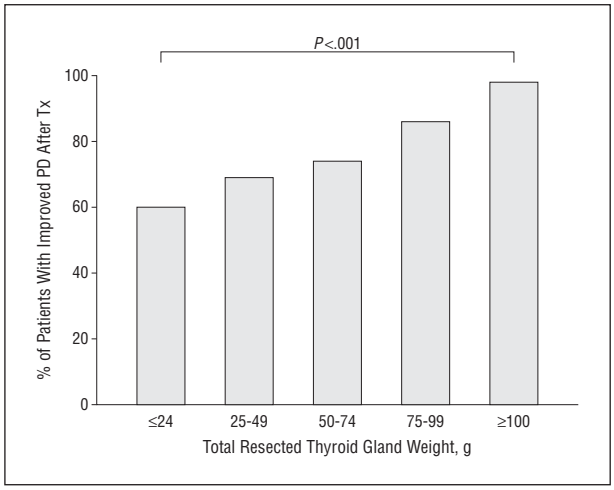

Figure 3. Improvement in positional dyspnea (PD) as a function of total resected thyroid gland weight. Tx indicates thyroidectomy. *P* values apply to comparison of categories linked by line.

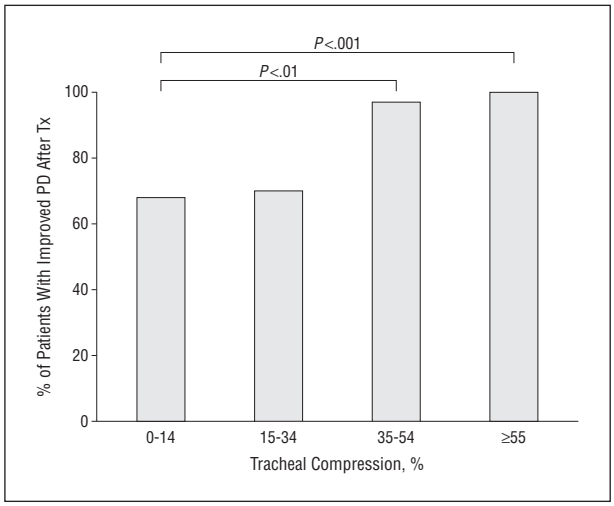

Figure 4. Postoperative improvement in positional dyspnea (PD) as a function of tracheal compression. Tx indicates thyroidectomy. *P* values apply to comparison of categories linked by line.

COMMENT

This investigation describes the outcomes of a unique intervention algorithm for patients with goiter. Aware that thyroid nodules occur in up to 70% of the adult population, unwilling to operate for goiter without clear indications, and interested in the surgical outcome for patients reporting PD, we initiated and evaluated a strategy of resection limited, in the absence of another recognized indication, to a specific radiologic criterion: SG with TC of 20% or more. Our study has limitations that in-

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clude retrospective data analysis, the subjective nature of PD and snoring symptomatology, a potential referral bias to surgery, inability to obtain CT imaging for all PD patients, and OSA patient noncompliance with CPAP use; after Tx we did not recommend self-directed CPAP changes, but patient recidivism could certainly contribute to the observation. Further limitations certainly included OSA patient reluctance for repeat sleep study evaluation after surgery, as well as lack of funding to facilitate such compliance and lack of insurer approval for repeat sleep study evaluation because goiter is not yet recognized as affecting obstructive sleep physiology.

Over decades, many discerning experts have thoughtfully contemplated and objectively tried to define *goiter* but without consensus. Autopsy studies in variable iodine-deficient populations describe a typical thyroid gland to be less than 25 g with an upper limit of 30 to 40 g,[9-11] whereas more contemporary data reflect a normal gland weight of 10 to 20 g in iodine-replete populations.[12,13] A recent definition of *goiter* is "a thyroid gland that is twice as large as a normal gland or greater than 40g."[1(p207)] The heterogeneity of definitions is compounded by the high vascularity of thyroid tissue in situ—that is, the gland is often considerably smaller and lighter after resection. Our findings do not define *goiter* but do provide a clinically useful yardstick because we can now inform patients that a resected thyroid gland weight of 25 g or more is 69% likely to relieve PD symptoms.

Goiter can occur in association with several symptoms, and in 1946 Pemberton[14] described the sign of facial suffusion, choking, stridor, and jugulovenous distension with both arms raised as indicative of mediastinal goiter. Goiter resection is now reported to improve dysphagia in several surgical series, including a recent randomized study,[15,16] but, although it may stand to reason that removal of a large paratracheal mass can improve breathing, to our knowledge, there are as yet no studies that systematically examine the effect of Tx on dyspnea. Meysman et al[17] reported a case series of 2 patients with goiter who exhibited postural differences in flow-volume loop studies. The postural differences improved dramatically in one patient who underwent Tx.[17] Our analysis reports that PD is common among patients referred for consideration of thyroid surgery (10.8%), is very likely to improve after Tx (82.4%), and improves in 97.9% of patients with a resected thyroid gland of 100 g or more. These findings are important in counseling patients. The results also suggest that PD can improve *without* significant thyromegaly because 60.0% of patients with a resected gland weight of less than 24 g reported PD relief; this finding may relate to the subjective nature of symptom reporting and/or the 3-dimensional projecting anatomy of some thyroid glands and nodules, and it warrants further investigation.

Regarding SG, Ríos et al[6] recently tabulated the inconsistent definitions that have been reported. Rather than a traditional definition, such as subclavicular and 50% intrathoracic, we chose to use a more quantifiable definition for SG (caudal extension to the supine sternal notch), but the important idea is expressed by Wang[3(p283)] that "substernal extension of a goiter into the unyielding thoracic inlet endows a generally benign neck mass with morbid potential," which is supported by the high incidences of PD and TC that we observed. Our SG definition may have served to underestimate SG prevalence because the sternal notch is typically more caudal than the top edge of the clavicle. Our results do not agree that SG resection is necessarily precarious because there was no mortality or need for thoracic access in SG resection even with extension to the carina, which is otherwise[18-20] reported to predict extracervical approach and poor outcome.

Neither the natural history nor correct medical management of substernal TC is fully understood. A study[21] from 1975 suggested that exertional dyspnea and a decrease in arterial oxygenation develops when upper airway compression limits the tracheal diameter to less than 8 mm. A 1983 surgical series[2] found symptoms of airway compression in 82% of patients with SG, whereas in a 1990 review article[22] 18% of patients with TC presenting for resection had acute airway problems. Tracheal compression was recently described by Shen et al[23] in relation to its potential for surgical complications. Our results demonstrate that TC associated with objectively defined SG is common in patients referred for thyroid surgery (8.0%); that TC is highly associated with PD (93.5%), which is likely to improve after Tx (82.8%); and that it is possible to have asymptomatic substernal TC. We further observed that in SG, the PD associated with TC improves or resolves as resected gland weight rises, and surgery for TC of 35% or more is likely to produce resolution of dyspnea (96.9%)—so likely that regardless of other indications or of a surgical rationale based on inability to perform cytologic biopsy of intrathoracic thyroid nodules, a 35% TC cutoff may usefully represent an objective criterion for SG resection. We caution physicians that both the presence of TC and the caudal extent of SG are not always described in a radiology report; therefore, the surgeon personally should perform direct image review.

The optimal extent of thyroid resection for goiter is also controversial. Although Yetkin et al[24] showed that after lobectomy a higher thyroid volume and multinodularity predicted recurrence of 3-mm nodules in the contralateral lobe, the clinical significance of contralateral micronodules is unclear, and a recent series with mean 10-year follow-up found that 89% of those who had unilateral resection did not require further thyroid surgery.[25] Conversely, a randomized study by Barczyński et al[26] compared total Tx with 2 types of bilateral subtotal goiter surgery and concluded that total Tx is the procedure of choice. In our selected study patients, thyroid resection was unilateral in 27.4%, but the optimal extent of goiter resection was not discernible except to note that 82.4% of those with PD reported improvement with the surgery performed.

Obstructive sleep apnea syndrome affects 5% of middle-aged people[27] with major symptoms that include snoring, nocturnal snorting and gasping, witnessed apnea, and daytime hypersomnolence.[28] The major risk factors are obesity, male sex, increasing age, and postmenopausal status in women in the absence of hormone replacement.[27,29] Patients with OSA experience impaired neurocognitive function,[30] have a higher risk for motor vehicle accidents, use health resources at a high rate,[31,32]

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and are at increased risk for hypertension, morbidity, cardiovascular mortality, and overall mortality.[27,28,33] Reiher and colleagues[34] recently reported a prospective study of 45 patients who completed a validated sleep apnea survey with improvements in sleep apnea symptoms and snoring after Tx. Here, despite the inability to systematically evaluate all patients with OSA postoperatively, we report the phenomenon of objective improvement in sleep study results after Tx for SG. This confirms the findings of a previous case series of 2 patients with OSA and goiter documenting sleep study improvement following thyroid surgery.[35]

The pathogenesis of upper airway obstruction in sleep apnea is not fully understood. Airway patency is thought to be maintained by a balance of anatomical and mechanical factors serving to collapse the airway vs pharyngeal muscular tone serving to dilate. Airway obstruction most often occurs at the oropharynx,[36] which is well above the level of the thyroid gland, and there is no evidence that goiter alters neural input to the pharyngeal dilator muscles. However, a possible mechanism for the benefit observed is restoration of a normal relationship of the trachea with the upper airway. In normal supine adults, the trachea moves caudally 0.4 to 1 cm during tidal breathing,[37] and this motion tenses the upper airway soft tissues (the so-called tracheal tug), serving to counter inspiratory upper airway collapse. Goiter may interfere with such caudal tracheal traction, and thus resection may restore pharyngeal tone to reduce inspiratory collapse of the upper airway. Loss of tracheal tug may not be attributable entirely to local anatomic distortion because goiter does reduce functional residual capacity,[38] and this reduction in end expiratory lung volume could also reduce caudal traction of the trachea on the upper airway. Thyromegaly is not yet known to be a cause of sleep-disordered breathing, yet with obese body habitus, the presence of goiter is not always easy to appreciate on examination or even by ultrasound. The prevalence of goiter among patients with OSA is unknown. Thus, without further investigation it is not possible to propose a clinical algorithm. Similarly, the other provocative finding of our study—that after Tx 76.6% of snorers reported improvement in snoring—calls for formal prospective study. Such an inquiry could include both preoperative and postoperative flow-volume analysis (not only for OSA response but also for goiter relation to PD) and longitudinal assessment of tracheal mechanical stability as a function of cross-sectional narrowing.[39]

In summary, we report the results of a structured surgical management strategy for patients with goiter. Results demonstrate that goiter resection is likely to improve symptomatic PD, that TC is a common finding in SG, and that for patients who have both PD and SG, either TC of 35% or more or a resected thyroid gland weight of 100 g or more predicts dyspnea relief after surgery. We thus suggest that both PD and TC of 35% or more indicate Tx. Pilot results also support further study of goiter as a correctable cause of snoring and misdiagnosed OSA.

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Correspondence: Michael T. Stang, MD, Division of Endocrine Surgery, University of Pittsburgh School of Medicine, 3471 5th Ave, Kauffman Bldg, Ste 101, Pittsburgh, PA 15213 (stangmt@upmc.edu).

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Study concept and design: Stang, Ogilvie, and Carty. *Acquisition of data:* Stang, Armstrong, Ogilvie, and Carty. *Analysis and interpretation of data:* Stang, Armstrong, Ogilvie, Yip, McCoy, Faber, and Carty. *Drafting of the manuscript:* Stang, Armstrong, Faber, and Carty. *Critical revision of the manuscript for important intellectual content:* Stang, Armstrong, Ogilvie, Yip, McCoy, Faber, and Carty. *Statistical analysis:* Stang and Armstrong. *Administrative, technical, and material support:* Stang, Armstrong, Yip, McCoy, and Carty. *Study supervision:* Ogilvie and Carty.
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INVITED CRITIQUE

ONLINE FIRST

"Doctor, My Thyroid Is Choking Me"

Common Sense and Scientific Inquiry

Using a structured algorithm to evaluate respiratory symptoms in patients presenting for surgical treatment of thyroid disease, Stang and colleagues[1] demonstrate that thyroidectomy ameliorates positional dyspnea and sleep apnea. Analysis of 197 patients with tracheal compression and/or positional dyspnea revealed that positional dyspnea improved in direct correlation to the resected gland weight. Those patients with obstructive sleep apnea experienced subjective improvement in snoring or dyspnea, but only a small number (3 patients) underwent postoperative polysomnography. Stang et al also observed a significant increase in the proportion of patients whose positional dyspnea improved when tracheal compression reached a threshold of at least 35%.

We applaud their systematic and careful inquiry into the relationship between respiratory compromise and thyroid enlargement. Using a validated questionnaire for sleep apnea, our group has similarly shown that thyroidectomy reduced snoring frequency and nuisance to others.[2] These studies provide data to support what many thyroid surgeons have always intuitively known. We have all met the poor patient subjected to repeated pulmonary function testing, sleep studies, bothersome constant positive airway pressure equipment, and an endless catalog of symptoms. Finally, an enlarged thyroid is "discovered," and the patient is referred for surgery.

Despite this seemingly obvious correlation, the exact anatomic or pathologic link between thyromegaly and respiratory symptoms remains elusive, as the authors outline in their discussion. As physicians, we are not satisfied to simply state the obvious: "The huge thyroid is choking the patient." A prospective evaluation of sleep apnea and thyroidectomy would certainly involve expensive preoperative and postoperative sleep studies or pulmonary function testing. We are not sure that is really necessary if we just trust our common sense and the well-done retrospective study reported in this article.

David Schneider, MD, MS
Herbert Chen, MD

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Author Affiliations: Department of Surgery, University of Wisconsin Medical School, Madison.
Correspondence: Dr Chen, Department of Surgery, H4/722 Clinical Science Center, University of Wisconsin Medical School, 600 Highland Ave, Madison, WI 53792 (chen@surgery.wisc.edu).
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