The Impact of Esophageal Compression on Goiter Symptoms before and after Thyroid Surgery

Filip Alsted Brinch^a Helle Døssing^a Nina Nguyen^b Steen Joop Bonnema^c
Laszlo Hegedüs^c Christian Godballe^a Jesper Roed Sorensen^{a, d}

^aDepartment of ORL Head & Neck Surgery and Audiology, Odense University Hospital, Odense, Denmark;

^bDepartment of Radiology, Odense University Hospital, Odense, Denmark; ^cDepartment of Endocrinology, Odense University Hospital, Odense, Denmark; ^dOPEN, Odense Patient Data Explorative Network, Odense University Hospital, Odense, Denmark

Keywords

Esophageal compression · Goiter · Thyroidectomy · ThyPRO · Quality of life · Dysphagia · Swallowing

Abstract

Introduction: Benign nodular goiter may be associated with swallowing difficulties, but insight into the associated pathophysiology is limited. The aim of this study was to investigate the effect of surgery on the degree of esophageal compression, and its correlation to swallowing difficulties. **Methods:** Esophageal compression and deviation were evaluated blindly on magnetic resonance imaging (MRI) of the neck, prior to and 6 months after thyroid surgery for symptomatic benign goiter. Goiter symptoms and swallowing difficulties were measured by the Goiter Symptom Scale of the Thyroid-Specific Patient-Reported Outcome (ThyPRO) questionnaire. Cohen's *d* was used for evaluating effect sizes (ES). **Results:** Sixty-four patients completed the study. Before surgery, median goiter volume was 57 (range 14–642) mL. The smallest cross-sectional area of the esophagus (SCAE) increased from a median of 95 (47–147) to 137 (72–286) mm² (ES = 1.31, *p* < 0.001). Median esophagus width increased from 15 (range 10–21) to 17 (range 12–24) mm (ES = 0.94, *p* < 0.001) after surgery, while no statistically significant change was ob-

served for the sagittal dimension (anterior-to-posterior), thus reflecting an increasingly ellipsoid esophageal shape. Median esophageal deviation decreased moderately after surgery from 4 (0–23) to 3 (0–10) mm (ES = 0.54, *p* = 0.005). The goiter symptom score improved considerably from (mean ± SD) 40 ± 21 to 10 ± 10 points (ES = 1.5, *p* < 0.001) after surgery, and the improvements were associated with improvements in SCAE (*p* = 0.03). **Conclusions:** In patients with goiter, thyroidectomy leads to substantial improvements in esophageal anatomy, as assessed by MRI, and this correlates with improved swallowing symptoms. This information is valuable in qualifying the dialogue with goiter patients, before deciding on the mode of therapy. Clinicaltrials.gov (NCT03072654).

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Introduction

Thyroid glands with nodular degeneration are common and, depending on definition and type of imaging, affect 20–76% of patients on a background of delicate in-

This study is registered at the Danish Data Protection Agency and www.clinicaltrials.gov (NCT03072654).

teractions between genetic and environmental factors [1–4]. Nodular goiter can lead to a wide range of symptoms including swallowing discomfort and respiratory disturbances, which can have a negative impact on quality of life (QoL) [1, 5, 6]. A clear correlation between goiter volume, tracheal compression, and relief from this compression following thyroidectomy is seen in patients with benign goiter [7], but little is known concerning the impact of goiter on the esophagus. In studies using patient-reported outcomes, 47–83% of patients referred for thyroidectomy report swallowing difficulties [8–14]. Uncomplicated thyroidectomy significantly improves both symptoms related to swallowing and QoL [5, 9, 15–18], but insights into the pathophysiology of this improvement are limited. Previous studies have found no significant correlations between disturbances in esophageal motility and size and symptoms of goiter, indicating that other measures than motility disturbances might be relevant for goiter symptoms at baseline and the pronounced relief after surgery [10, 19–21].

Esophageal compression and esophageal deviation on radiographic images are reported in 8–27% of patients with goiter [22, 23], and the ill-defined globus sensation seems to be linked to tracheo-esophageal deviation [24]. However, there is no clear definition of either esophageal compression or esophageal deviation, which impedes any attempt at interpreting alterations in these parameters following therapy.

The aim of this study was to investigate the degree of esophageal compression before and after thyroid surgery, and to correlate these findings with changes in goiter symptoms.

Materials and Methods

Participants

Patients with symptomatic benign nodular goiter scheduled for thyroid surgery were included in a prospective cohort study [7, 19]. The inclusion period was from 1 November 2014 to 30 April 2016. Patients were followed for 6 months, with the last visit on 2 March 2017.

Nodular goiter was defined as an ultrasonically confirmed, enlarged thyroid gland, with a volume of >18 mL for women and >25 mL for men, and containing at least 1 nodule [7]. Serum levels of total thyroxine (T_4) and total tri-iodothyronine (T_3) had to be within the normal range of 67–134 and 1.35–2.33 nmol/L, respectively, but both subclinical hypo- and hyperthyroid patients (serum thyrotropin > or < the reference range, respectively) were eligible for inclusion.

Exclusion criteria were: previous neck surgery, a suspected thyroid malignancy (such patients were managed by a fast track program [25]), an age <20 or >80 years, neuromuscular diseases in-

cluding diabetes mellitus, and an inadequate understanding of Danish. This study is a substudy of a larger cohort study investigating changes in tracheal anatomy, swallowing physiology, and QoL after thyroid surgery [7, 16, 19, 26, 27]. In part, the data have been reanalyzed, for the purpose of addressing a completely different issue.

MRI and Esophageal Anatomy

Magnetic resonance imaging (MRI) of the neck was performed using an Achieva D-stream (Phillips, Eindhoven, The Netherlands) operating at 1.5 tesla, using a repetition time of 680 ms, an echo time of 12 ms, and a slice thickness of 7 mm. Scans were performed at a median of 13 (range 1–90) days before and 180 (148–210) days after surgery. To assess esophageal compression, the smallest cross-sectional area of the esophagus (SCAE) was assessed from esophageal cross-sectional areas at the level of the thyroid gland before surgery and from the corresponding level following surgery.

To reflect the shape and surroundings of the esophagus, the anterior-to-posterior (AP) depth and medial-to-lateral (ML) width of the esophagus were measured. Esophageal deviation was measured as the distance from the esophageal center to the midline. In addition, contact between the circumference of the esophagus (in degrees) and closely related structures (within 2 mm) was measured as esophageal contact to the spine, trachea, and thyroid lobes.

Prior to the study, 10 random MRI scans were analyzed twice (by F.A.B.) as part of a training program. The observer performed all measurements using a computer-generated randomization algorithm for blinding. Two to six weeks after the initial examinations, a second evaluation of each patient was performed to allow for intraobserver variation analyses.

Patient Reported Outcomes

Goiter symptoms were evaluated by means of the thoroughly validated Thyroid-Specific Patient-Reported Outcome (ThyPRO) questionnaire [28–32]. Single scales of the ThyPRO measure can be used for measuring specific areas of interest [31]. We selected the 11-item Goiter Symptom Scale which has previously been found to reflect symptoms of swallowing difficulties well [19]. Each item was rated on a Likert scale of 0 (no symptoms) to 4 (severe symptoms), referring to the last 4 weeks. The combined scores of the items were linearly transformed to a scale of 0–100 points, with lower scores meaning fewer symptoms. The questionnaire was completed after the first consultation, and at follow-up 6 months after surgery, without supervision from health care professionals.

Surgical Procedure

A thyroid lobectomy or a total thyroidectomy was performed under general anesthesia by a consultant in head and neck surgery. Patients were discharged on the first postoperative day after a thyroid lobectomy if no clinical or biochemical complications had been encountered. On the first day after a total thyroidectomy, levothyroxine (LT_4) was administered and calcium levels were monitored, followed by discharge if these levels were normal. Postsurgical follow-up was scheduled for 2–4 weeks after surgery, and a follow-up with the focus on thyroid hormone levels 2–3 months after surgery. Thereafter, further LT_4 adjustment was made by the local department of endocrinology or the patient's general practitioner.

Fig. 1. Flow chart of recruitment and follow-up of patients with benign symptomatic goiter scheduled for thyroid surgery.

Statistics

Mean values were calculated from the first and the second measurements, to be used for statistical analyses. A paired *t* test was used to compare pre- and postsurgical values of esophageal compression, esophageal deviation, and goiter symptoms. Effect sizes (ES) were calculated by Cohen's *d* as mean change divided by the standard deviation at baseline. Accordingly, ES were defined as 0.2–0.5 being a small change, 0.5–0.8 a moderate change, and >0.8 a large change [33].

To estimate the relationship between esophageal parameters at baseline and swallowing difficulties, multiple regression analyses were used for the independent variables: age, sex, and weight of removed thyroid tissue. Multiple regression analyses were also used to compare changes in symptom scores with changes in SCAE, ML width, and esophageal contact to the trachea, spine, and thyroid. A linear mixed model was used to evaluate the influence of gender, age, and intraobserver differences on the esophageal parameters. Bland-Altman plots were used to illustrate intraobserver differences.

Results

Patient Characteristics

A total of 229 patients were initially assessed for eligibility (Fig. 1), 90 of whom were excluded based on pre-defined exclusion criteria. Sixty-four declined to participate, 5 were unable to complete the examination, and 6

Table 1. Surgical and demographic characteristics of patients with benign symptomatic goiter (*n* = 64)

Sex	
Male	10 (16)
Female	54 (84)
Age of patients, years	
Included	52 (21–77)
Not included	55 (19–92)
Surgical procedure	
Total thyroidectomy	20 (31)
Hemithyroidectomy	43 (66)
Isthmectomy	2 (3)
Volume of goiter, mL	57 (14–642)
Weight of removed thyroid, g	40 (7–607)
Thyrotropin	
Before surgery, mU/L	0.99 (0.05–3.90)
After surgery, mU/L	2.30 (0.22–10.60)
LT ₄ treatment after hemithyroidectomy	8 (19)
RLN paralyses 6 months after surgery	3 (5)

Values are expressed as *n* (%) or median (range). RLN, recurrent laryngeal nerve.

were lost to follow-up, resulting in a total of 64 patients completing all analyses. Eighty-five percent of included patients were females, and the median age was 52 (range 21–77) years, compared to 55 (19–92) years for the pa-

Fig. 2. Plot depicting the relation between changes in smallest cross-sectional area of the esophagus (SCAE) after surgery and the weight of the removed thyroid tissue ($n = 64$).

Table 2. Esophageal compression variables before and after surgery in patients with benign symptomatic nodular goiter ($n = 64$)

Parameters	Before	After	<i>p</i> value	Effect size ^b
AP, mm	9 (5–14)	9 (5–16)	0.70	0.04
ML, mm	15 (10–21)	17 (12–24)	<0.001	0.94
AP/ML ratio	0.57 (0.35–1.29)	0.52 (0.27–1.21)	<0.001	0.53
SCAE, mm ²	95 (47–147)	137 (72–286)	<0.001	1.31
Esophageal deviation, mm	4 (0–23)	3 (0–10)	0.004	0.54
Degrees of contact ^a				
Spine	74 (0–114)	78 (0–124)	0.033	0.31
Thyroid, left side	47 (0–101)	0 (0–68)	<0.001	1.38
Thyroid, right side	28 (0–101)	0 (0–54)	<0.001	1.24
Trachea	105 (38–154)	210 (123–266)	<0.001	0.68

A comparison is made of values before and after surgery, using a paired *t* test. Values are given as median (range). SCAE, smallest cross-sectional area of the esophagus; AP, anterior-posterior depth; ML, medial-lateral width.

^a Degrees of the esophageal circumference (maximum 360°) which has contact to surrounding structures.

^b Defined according to Cohen et al. [33] as: 0.2–0.5, a small change; 0.5–0.8, a moderate change; >0.8, a large change.

tients who were not included ($p = 0.76$) (Table 1). The median weight of surgically removed thyroid tissue for the included patients was 40 (7–607) g.

MRI and Esophageal Anatomy

The reproducibility in identifying the most affected esophageal level was within 3 mm on MRI scans (0.5 slice thickness, $p = 0.007$). The AP depth of the esophagus did not change significantly ($p = 0.70$) following surgery, while the ML width of the esophagus showed a significant increase from a median of 15 (range 10–21) to 17 (12–24) mm after surgery ($p < 0.001$, ES = 0.94) (Table 2). Based

on the above, the AP/ML ratio decreased from a median of 0.57 (0.35–1.29) to 0.52 (0.27–1.2) ($p < 0.001$, ES = 0.53), reflecting a change from a rounder to a more ellipsoid shape of the esophagus following surgery. The median SCAE increased significantly after surgery, from 95 (47–147) to 137 (72–286) mm² (ES = 1.31, $p < 0.001$), corresponding to a median increase of 34% (–17 to 253%). The most pronounced improvement occurred in the patients with the largest volume of removed thyroid tissue (Fig. 2).

The median esophageal deviation decreased moderately from 4 (0–23) to 3 (0–10) mm after surgery ($p =$

Fig. 3. Bland-Altman plots visualizing intraobserver differences for medial-lateral (ML) width (**a**) and esophageal deviation (**b**). The solid lines indicate the mean value of differences, while the dotted lines illustrate mean ± 2 SD.

0.005, ES = 0.54). For structures surrounding the esophagus, the degrees of esophageal contact to the spine increased from a median of 74° (0–114°) before surgery to 78° (0–124°) after surgery ($p = 0.03$, ES = 0.31). An increase was also seen for the contact to the trachea, from a median of 105° (38–145°) prior to surgery to 118° (83–165°) ($p < 0.001$, ES = 0.67) following surgery.

Using multiple regression analyses, the preoperative volume of the thyroid and SCAE was significantly inversely correlated, with a reduction in SCAE of 0.35 mm² for every 10% increase in goiter volume ($p = 0.01$). In parallel, a 10% increase in the weight of the removed thyroid tissue increased SCAE by 1% ($p = 0.03$), implying that patients with the largest goiters experienced the highest percent improvements in SCAE.

Observer Variation

From the Bland-Altman plots (Fig. 3) and intraobserver measurements, the ML width was (mean $\pm$ SD) 1.1 $\pm$

1.4 mm smaller at the second measurement, corresponding to a mean measurement difference of $7.2 \pm 9.3\%$ (Fig. 3a). For esophageal deviation, the mean intraobserver agreement was 1.4 ± 1.8 mm (Fig. 3b), while the degrees of contact between the esophagus and the trachea were $6.3 \pm 18.5^\circ$ higher ($p < 0.001$) in the second measurement. The remaining parameters did not vary significantly between the first and the second measurement.

Patient Reported Outcomes

The mean goiter symptom score of (mean $\pm$ SD) 40 ± 21 points before surgery improved to 10 ± 10 points after surgery (ES = 1.5, $p < 0.001$) (Table 3). All 11 items of the goiter symptom scale improved after surgery. These included symptoms closely related to swallowing difficulties, such as “discomfort swallowing”, with scores reduced from a mean of 1.8 ± 1.2 to 0.3 ± 0.6 points post-operatively (ES = 1.6, $p < 0.001$). Similarly, the mean score for “difficulty swallowing” decreased from 1.2 ± 1.2 to 0.2

Table 3. The symptom scores in patients with benign nodular goiter before and after surgery

Symptoms	Before	After	<i>p</i> value	Effect size
Sensation of fullness in neck	2.2±1.3	0.4±0.7	<0.001	1.7
Visible swelling in front of the neck	2.3±1.3	0.2±0.5	<0.001	2.1
Pressure in throat	2.3±1.1	0.6±0.8	<0.001	1.0
Pain in front of the throat	1.0±1.3	0.3±0.8	<0.001	0.6
Pain in neck radiating to ears	0.8±1.2	0.2±0.5	<0.001	0.7
Globus sensation	2.3±1.3	0.7±0.9	<0.001	1.1
Frequent need to clear throat	1.8±1.4	0.7±0.8	<0.001	1.0
Discomfort swallowing	1.8±1.2	0.3±0.6	<0.001	1.6
Difficulty swallowing	1.2±1.2	0.2±0.5	<0.001	1.1
Sensation of suffocating	0.8±1.2	0.1±0.4	<0.001	0.8
Feeling hoarse	1.0±1.3	0.5±0.8	0.003	0.5
Goiter Symptom Score	40±21	10±10	<0.001	1.5

Values are mean ± SD. Effect sizes were defined according to Cohen et al. [33]: 0.2–0.5, a small change; 0.5–0.8, a moderate change; >0.8, a large change.

± 0.5 points (ES = 1.1, $p < 0.001$) after surgery. The “globus sensation” also improved, with a large postsurgical mean decrease from 2.3 ± 1.3 to 0.7 ± 0.9 points (ES = 1.1, $p < 0.001$). The largest improvement was observed for “visible swelling in front of the neck” with a reduction from a mean 2.3 ± 1.3 to 0.2 ± 0.5 points (ES = 2.1, $p < 0.001$).

Five patients (7.8%) reported either no improvement or worsening symptoms after surgery. The most pronounced deterioration was an increase of 5 points on the Goiter Symptom Scale in 1 of these patients, who experienced a decrease in SCAE, from 115 to 95 mm².

Correlations between goiter volume, esophageal compression/deviation, and goiter symptoms were evaluated by multiple regression analyses. A 10% increase in SCAE was found to correlate with a 0.6-point improvement in Goiter Symptom Score ($p = 0.03$). However, none of the remaining parameters of esophageal anatomy were found to correlate with changes in goiter symptoms.

Discussion

This study demonstrated significant postoperative improvements in the esophageal anatomy in patients with benign nodular goiter. The ML width of the esophagus as well as the SCAE increased considerably following surgery. In addition, the esophageal deviation decreased, and the esophageal contact to the spine and the trachea increased, likely due to a widened esophagus. All but 4 patients showed an improvement in SCAE, thus reflecting that fibrotic tissue formation around the esophagus dur-

ing goiter development as well as in the postoperative period is of no major concern.

The Goiter Symptom Score decreased significantly after surgery with large reductions in both globus sensation and swallowing difficulties. We have demonstrated, for the first time, that symptoms related to the esophageal function improve along with the changes in the esophageal anatomy. The correlation between changes in SCAE and goiter symptoms indicates that this parameter may be a useful marker of esophageal compression in future studies. However, SCAE alone is not sufficient for explaining the developments in goiter symptoms, as the Goiter Symptom Score improved postoperatively by 30 points on average, while SCAE accounted for a reduction of only 0.6 points in goiter symptoms per 10% increase in SCAE. Compression of other neck structures, e.g., the trachea and spine, by goiter, might also contribute significantly to the various items included in goiter symptoms [7].

Instead of thyroidectomy, patients with benign goiter may undergo radioiodine therapy [34] or laser thermal or radiofrequency ablation [35], with which side effects such as voice changes and postoperative hypothyroidism are more likely avoided [36–39]. However, the effects on the esophageal anatomy of these nonsurgical treatment options remain to be evaluated. Monitoring the impact of these treatments on the esophagus, functionally or anatomically, should be considered in future trials, the main aim being to obtain comparisons with the effects of thyroid surgery.

Hitherto, research regarding esophageal compression and deviation has been sparse and inconclusive. A study

on patients with substernal goiter investigating dysphagia and esophageal compression, detected by computed tomography, did not identify any correlation, but the study was characterized by a small number of highly selected patients [24]. Other studies found positive correlations between esophageal compression and symptoms [22, 23], but definitions of esophageal compression and deviation were lacking, thereby hindering meaningful comparisons with our results. A retrospective study on 198 patients found a positive correlation (of unreported magnitude) between preoperative dysphagia and image findings, without defining what these findings represented [23]. A previous study by our group found no major association between esophageal motility disturbances and swallowing difficulties in patients with goiter [27], but that study may have been underpowered as it included only 33 patients. An alternative explanation may be that esophageal compression does not cause significant esophageal dysfunction, despite being symptomatic.

The strengths of our study include the several precautions taken to improve the validity. Measurements were performed twice to enable intraobserver analysis, blinding of the observer was done by computer randomization, and training sessions were performed to minimize the impact of a potential learning curve. In addition, the reasonable population size with a low drop-out rate, well-characterized patients, and the use of a thoroughly validated questionnaire improved the internal validity of the results. Importantly, the exact definition of the measured parameters of esophageal compression makes it feasible to compare interventional techniques in future studies.

A few limitations also need to be addressed. Due to the lack of a control group, we were not able to demonstrate whether the esophageal anatomy normalized completely after surgery. In addition, although our center receives a

large number of unselected patients, the study possibly suffered from selection bias, since only 64 of 267 patients with symptomatic goiter were included. Finally, an assessment was made only at 6 months after surgery, thus excluding us from making any conclusions about the relationship between symptoms and the esophageal anatomy in the early postoperative period and in the long term.

Conclusion

Thyroidectomy leads to substantial improvements in esophageal anatomy, as assessed by MRI, and this correlates with swallowing symptoms in patients with goiter. This information is valuable when offering goiter patients guidance on which effects of surgery to expect. This information is not yet available for the nonsurgical alternatives for goiter reduction in toxic or nontoxic goiter patients.

Statement of Ethics

The study was approved by The Regional Scientific Ethics Committee for Southern Denmark (S-20130096).

Disclosure Statement

The authors have no conflicts of interest.

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