

To explore the risk factors and preventive measures affecting the treatment of retrosternal goiter

An observational study

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Abstract

The definition of substernal goiter (SG) is based on variable criteria, leading to considerable variations in the reported incidence (from 0.2% to 45%). The peri- and postoperative complications are higher in total thyroidectomy (TT) for SG than that for cervical goiter. This study aimed to evaluate the preoperative risk factors associated with postoperative complications.

From 2002 to 2014, 142 (8.5%; 98 women and 44 men) of the 1690 patients who underwent TT had a SG. We retrospectively evaluated the following parameters: sex, age, histology, pre- and retro-vascular position, recurrence, and extension beyond the carina. These parameters were then related to the postoperative complications: seroma/hematoma, transient and permanent hypocalcemia, transient and permanent laryngeal nerve palsy, and the length of surgery. The results were further compared with a control group of 120 patients operated on in the same period with TT for cervical goiter (CG).

Statistical analysis (Student *t* test and Fisher exact test) indicated an association between recurrence and extension beyond the carina with all postoperative complications. The group that underwent TT of SG showed a statistically significant higher risk for transient hypocalcemia (relative risk = 1.767 with 95% confidence interval: 1.131–2.7605, *P* = .0124, and need to treat = 7.1) and a trend toward significance for transient recurrent laryngeal nerve palsy (relative risk = 6.7806 with 95% confidence interval: 0.8577–53.2898, *P* = .0696, and need to treat = 20.8) compared with the group that underwent TT of cervical goiter. The major risk factors associated with postoperative complications are recurrence and extension beyond the carina.

TT is the procedure to perform in SG even if the incidence of complications is higher than cervical goiters. The major risk factors associated with postoperative complications are recurrence and extension beyond the carina.

Abbreviations: CG = cervical goiter, CI = confidence interval, NNT = number needed to treat, SG = substernal goiter, ST = sternotomy, TT = total thyroidectomy.

Keywords: complications, substernal goiter, total thyroidectomy

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1. Introduction

Total thyroidectomy (TT) is the most suggested treatment for substernal goiter (SG). Several studies attribute the SG with a degree of variability between 2% and 48%.^[1] This high degree of variability is mainly due to the fact that there is a lack of a unanimous definition of SG, making it difficult to compare results.^[2] The symptoms reported by patients are caused by the compression of the SG on the trachea, on the esophagus, and on the vascular structures. Even in few cases where the SG is asymptomatic, surgery is the most suggested treatment because of the continuous growth of the goiter and also there is a high risk that it turns malignant.^[3] SG is classified as primary and secondary depending on the origin of the blood supply: the primary, rare (1%), originates in the mediastinum vessels, whereas the secondary originates in the cervical vessel.

The extension into the mediastinum is aided by the anatomical continuity between the neck and the thorax, by the traction caused from the negative intra-thoracic pressure and by constitutional factors such as short neck and strong muscles. In the majority of cases, surgery with thyroidectomy is feasible through a cervical access, while sternotomy (ST) is required only in those cases of suspected infiltration of mediastinal structures, extension beyond the carina, or recurrence following a partial

thyroidectomy. The incidence of intraoperative and postoperative complications is generally higher in ST than in thyroidectomy for cervical goiter (CG).^[4] Reoperation, the size of the extension of the goiter in the thorax, and/or the retrovascular position are all factors that explain the difference of thyroidectomy in SG and could affect the outcome of the surgery. The aim of this study is to identify which of those above-mentioned preoperative risk factors are associated with a higher incidence of post thyroidectomy complications for SG.

2. Methods

2.1. Patients selection

Patients undergoing thyroidectomy surgery with full medical records in our hospital were selected. From January 2002 to December 2014, we performed 1690 thyroidectomy and SG (8.5%) was diagnosed in 142 cases (98 females and 44 males with a mean age of 58 years [35–78]). We defined SG as a goiter which extends at least 3 cm from the sternal manubrium when the patient is in an operative position and with a hyper-extended neck. Anatomically, we divided SG into pre-arterial (103 patients) and retro-arterial (39 patients). All patients underwent TT.

2.2. Parameter evaluation

We retrospectively evaluated the following parameters: sex, age, histology, anatomical classification, recurrence, and extension beyond the carina. These parameters were then related to the postoperative complications: seroma/hematoma, transient and permanent hypocalcemia, transient and permanent laryngeal nerve palsy (recurrent laryngeal nerve), and the length of surgery. Indices of thyroid functionality and calcemia were controlled before surgery. One hundred and twenty patients showed compressive symptoms, including dry cough (110 patients), dyspnea under strain (15 patients), dysphagia (35 patients), and dysphonia (1 patient). Hypocalcemia is defined as a calcium level of 8 mg/dL, which is defined as permanent for 1 year above that level. We did not use post-prophylactic therapy for hypocalcemia after thyroidectomy. We performed daily controls of calcium level values and adapted therapy to the patient's clinical condition. In the last 3 years, we utilized the parathyroid hormone dosage at 1 hour to evaluate early the patients to treat. All the patients were examined pre- and postoperatively with a laryngoscope. For patients with paralysis of the vocal cords for .1 year from the operation, this condition is considered permanent. The scheduled follow-ups of the main parameters were set at 1, 6, and 12 months postoperatively. The results were further compared with a control group including 120 patients operated in the same period with thyroidectomy for CG with matched gender ratio and age with the SG group (Table 1).

2.3. Ethical approval

The informed consent of the patients were obtained preoperatively, and this study was approved by the Ethics Committee of our Hospital. Moreover, the study was conducted according to the guidelines of the Declaration of Helsinki.

2.4. Statistical analysis

All qualitative parameters were summarized as frequency and percentage and quantitative parameters as mean and standard

Table 1

Basic clinic characters of the substernal goiter (SG) and cervical goiter (CG) group.

Item	Substernal goiter (n=142)	Cervical goiter (n=120)	χ^2/t	P
Age (yr)			0.0732	.7867
<50	41	37		
≥50	101	83		
Gender			0.0313	.8596
Male	44	41		
Female	98	79		
Average postoperative hospital stay (d)	3.8 (3–8 d)	2.5 (2–4 d)	1.1497	.6191

deviation. Between-group differences for intraoperative parametric and nonparametric values were evaluated with the 2-tailed Student *t* test and the Fisher exact test. The effect of the selected surgical procedure was evaluated with relative risk (RR), 95% confidence intervals (95% CI), and need to treat (NTT). An alpha level of 0.05 was deemed statistically significant.

3. Results

3.1. Correlation between postoperative complications and clinicopathological features

There is no significant difference regarding gender and age in the 2 groups shown in Table 1. Also, operative mortality did not occur in neither groups. All the surgical procedures were conducted through the cervical access except in 2 cases in which a partial ST was necessary: 1 due to adherence following recurrence and the other for extension beyond the carina. All the patients had preoperatively normal calcemia while for preoperative laryngoscopy, 1 patient reported a paralysis in the inferior laryngeal nerve due to a former surgery. The average postoperative hospital stay in the SG group was of 3.8 days (3–8 days), and 1 patient required a blood transfusion. The median stay in the control group was of 2.5 days (2–4 days). Concerning complications, in the SG group, we had 3 patients (2.1%) with postoperative seroma and/or hematoma. Only 1 patient required a surgical revision. Temporary hypocalcemia occurred in 46 patients (33%), reaching higher levels in patients with goiter extended beyond 3 carinas (66.6%) and in those in whom it recurred after primary surgery (52.1%). Permanent hypocalcemia occurred in 4 patients (2.8%), also belonging to the 2 aforementioned subgroups (Table 3). Temporary dysphonia occurred in 8 patients (5.6%), among which 6 were in the group with extension beyond the carina. Permanent paralysis affected 5 patients (3.5%). Finally, the duration of surgery had a median of 118 minutes – longer for relapse cases (165 minutes) and carina extension (160 minutes). Compressive symptoms disappeared within 12 months except for 5 patients (4%) who were still affected by dysphagia. Statistical analysis (Student *t* test and Fisher exact test) showed a significant correlation between relapse cases ($P=.0119$), those with extension beyond the carina and the incidence of postoperative transient ($P=.0369$) and permanent hypocalcemia and transient and permanent laryngeal nerve palsy in the SG group (Table 2).

Table 2
Univariate analysis of risk factors and complications of total thyroidectomy for substernal goiter.

Subgroup	No. of patients	Complications		χ^2	P-value
		Yes	No		
Age (yr)	2.2991	.1294
<50	41	13	28
≥50	101	46	55
Gender	2.4859	.1149
Male	44	14	30
Female	98	45	53
Extension beyond the carina	4.3568	.0369
Yes	15	10	5
No	127	49	78
Pre- or retrovascular	2.5728	0.1087
Pre	103	47	56
Retro	39	12	27
Recurrence	6.3306	0.0119
Yes	23	15	8
No	119	44	75
Malignancy	0.5729	0.4491
Yes	18	6	12
No	124	53	71

The results show an increase of postoperative complications in recurrence and extension beyond the carina cases.

3.2. Comparison of complications

Statistically significant differences in intraoperative parameters were not observed in the control group. The group that underwent thyroidectomy of SG showed a significantly higher risk of transient hypocalcemia (RR = 1.767 with 95% CI: 1.131–2.7605, P = .0124, and NTT = 7.1) and a trend toward significance for transient recurrent laryngeal nerve palsy (RR = 6.7806 with 95% CI: 0.8577–53.2898, P = .0696, and NTT = 20.8) compared with the group that underwent thyroidectomy of CG (Table 3 and Fig. 1).

4. Discussion

The mechanisms that lead to the development of SG are diverse and contribute to the growth of the goiter in the mediastinum. Unfortunately, there is no consensus on the definition of SG, so the incidence varies across different case studies, and, above all,

makes it difficult to compare results.^[5] The indication for surgery is not strongly supported by scientific evidence,^[6] even though many authors believe SG to be a surgical indication due to the ineffectiveness of medical treatment and the risks of obstruction of breathing patterns/airways and the risk it will turn into malignancy.^[7] Various studies have suggested that postoperative morbidity for SG may be higher compared to CG surgery.^[8] Many authors^[9] emphasized the necessity of planning in advance the ST in the treatment of SG. On the other hand, we believe that only in few cases, 2% in our studies, ST is required. A good surgical preparation, following a surgical plan of dissection, will permit a safe thyroidectomy. A preoperative study with a cervical–thorax computed tomography scan allows also the extension and intra-thoracic assessment of the goiter.^[10] The case of ectopic goiter is peculiar, so an extra-cervical access is necessary. Postoperative mobility for SG is reported to be higher than to CG surgery.^[11] Our study confirms this data. In particular, temporary postoperative hypocalcemia had a greater occurrence when compared to TTs for CG. Various factors can influence the incidence of postoperative hypocalcemia for TTs.^[12] Also, temporary palsy of the recurrent laryngeal nerve has shown a trend toward significantly greater occurrence in SG surgery.

Postoperative hospital stay was longer for patients with SG but not with statistically significant data. In the majority of cases, temporary postoperative hypocalcemia is the reason for the delay in discharge.^[13] The use of early markers for hypocalcemia allowed an earlier treatment and a more rapid discharge for these patients.^[14]

In our study, we evaluated the preoperative risk factors that could be associated with a higher incidence of postoperative complications in patients with SG. Statistical analysis has shown that the major risk factors are recurrence and extension of the goiter beyond the carina. We considered the growth of the goiter beyond the carina a more significant risk factor compared to the volume of the goiter itself. In the case of relapse, in fact, adhesions and neo-blood supply are often present and can interfere with the correct surgical dissection. Furthermore, the intra-thoracic extension of SG is a significant factor in postoperative risk.^[15] Only 1 patient necessitated a blood transfusion due to a very expanded goiter.

Sancho et al reported an incidence of 37% in temporary hypoparathyroidism and 14% of temporary vocal paralysis for SG cases where the tracheal carina is reached.^[16] Concerning the

Table 3
Complications post total thyroidectomy for cervical and substernal goiter.

Surgical procedure	Transient hypocalcemia	Permanent hypocalcemia	Transient RLN palsy	Permanent RLN palsy	Sieroma
Total thyroidectomy of substernal goiter					
Yes	46 (32.4%)	4 (2.8%)	8 (5.6%)	5 (3.5%)	3 (2.1%)
Total thyroidectomy of cervical goiter					
Yes	22 (18.3%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	1 (0.8%)
Relative risk	1.767	1.6901	6.7806	4.2254	2.5352
95% CI (lower)	1.131	0.315	0.8577	0.5005	0.2672
95% CI (upper)	2.7605	9.0678	53.2898	35.6735	24.0584
z-statistic	2.501	0.612	1.814	1.324	0.81
P-value	.0124	.5403	.0696	.1855	.4178
nnT (harm)	7.112	86.939	20.831	37.205	78.185
95% CI (lower)	28.22	20.907	242.49	15.851	23.5
95% CI (upper)	4.069	40.28	10.883	107.167	58.942

CI = confidence interval, NNT = number needed to treat, RLN = recurrent laryngeal nerve.

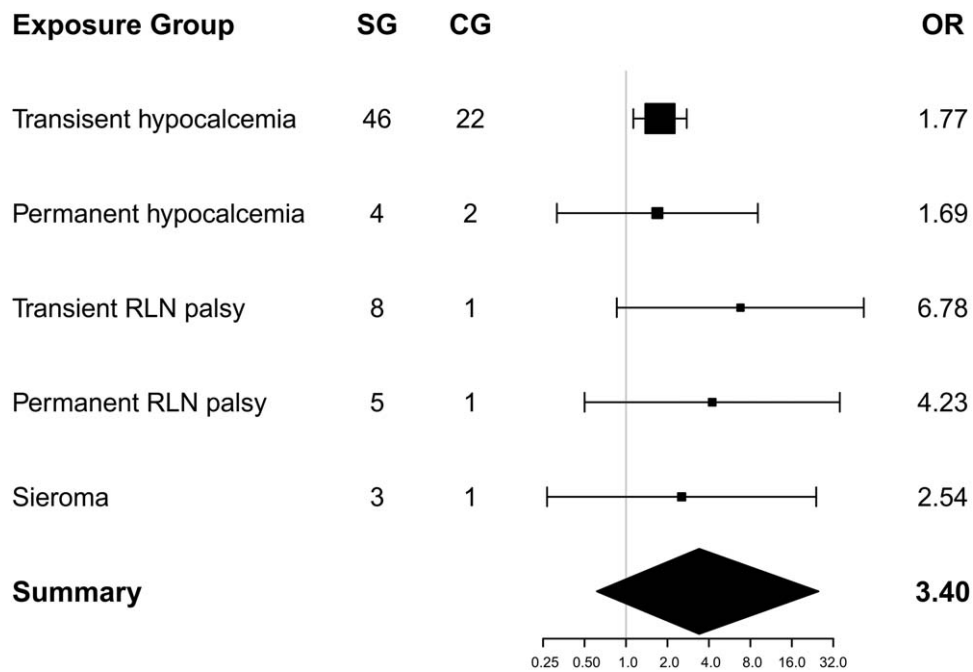


Figure 1. Complications post total thyroidectomy for cervical and substernal goiter.

goiter's position (pre-or retroarterial), we are aware that the retroarterial ones lead to a higher risk of complications. However, this data has not been confirmed by the statistical analysis, maybe because of the small number of cases reported. On the other hand, it is remarkable that 5 patients presented with dysphagia 1 year after the surgery. This is probably caused by swallowing motor disorders.

In a study by Raffaelli et al, the duration of surgery and postoperative hospital stay was longer for patients operated for SG. They conclude that the experience of the surgical team is essential to obtain good results.^[17] Certainly, a dedicated surgical team can handle complex cases with the minimum postoperative complications.

In our study, however, after extensive statistical analysis of patients undergoing thyroidectomy surgery, we found some risk factors. Such as recurrence and extension beyond the carina may increase the risk of postoperative complications. We tried to demonstrate that these 2 risk factors, recurrence and extension beyond the carina, make surgery more challenging. In the presence of these factors, greater care should be taken and the patients should be directed to a dedicated team. And a further Cohort study with larger sample size is still needed to further verify this finding.

5. Conclusion

Thyroidectomy is the procedure to perform in SG even if the incidence of complications is higher than for CGs. The major risk factors associated with postoperative complications are recurrence and extension beyond the carina. In the presence of these factors, greater care should be taken.

Author contributions

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Writing – review & editing: Junping Cheng.

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