RESEARCH ARTICLE

REVIEW: THE MANAGEMENT OF AN INTRATHORACIC GOITER

Pace-Asciak P.*, Higgins K.

Authors' affiliations:

1. Pia Pace-Asciak, MASc, MD, FRCSC
2. Kevin Higgins, MD, MSc, FRCSC

*** Corresponding author:** E-mail - piapaceasciak@gmail.com

Intrathoracic thyroid masses are rare but occur in 5.8% of all mediastinal masses (1). The definition of the mediastinal thyroid mass seems to vary across the literature. Generally, the most accepted definition of a retrosternal goiter is a thyroid gland which extends below the thoracic inlet. A mediastinal mass can also be described by its association with the aortic arch or whether it reaches the level of T4 on a chest XRAY, or whether more that 50% of the gland is below the thoracic inlet (2). The definition becomes important when planning surgical removal.

An intrathoracic (substernal) goiter can be either primary or secondary. Primary posterior substernal goiters arise from accessory or aberrant thyroid tissue within the mediastinum and consist of only less than 1% of retrosternal goiters. Their blood supply is derived from the intrathoracic arteries and do not have connections with the cervical thyroid gland and have an origin that is embryologic (3, 4). Secondary mediastinal goiters (MG) are more common than primary MG and are more likely to present to the Head and Neck surgeon. MG goiters are mostly located in the anterior and middle mediastinum, and rarely (10-15% of cases) in the posterior mediastinum (5). The blood supply is derived from the inferior thyroid arteries.

A secondary mediastinal goiter can be further subdivided into whether it is a "forgotten goiter". Massard et al. coined this rare entity as a goiter that identified post thyroidectomy but is not connected to the cervical thyroid. It may represent residual thyroid remnant or an incompletely resected cervical goiter or a completely separate and autonomously functioning thyroid tissue that becomes hypertrophic following removal of the cervical thyroid (6,7).

In secondary MG, swallowing, gravity and thoracic negative pressure can promote growth of a large thyroid nodule into the anterior mediastinum by following the path of least resistance between the trachea and sternum (8). Anterior extension is more frequently seen however, less commonly if the goiter extends posterior behind the brachiocephalic artery, the large space can

accommodate a goiter without notable symptoms until it is of significant size (9).

Up to 40% of substernal goiters are asymptomatic and found incidentally (10). If symptoms are present, the most common symptom of a substernal goiter is dyspnea with a feeling of being short of breath that may or may not be positional (11). The second most common symptom is dysphagia mostly to solids and can be associated with laryngopharyngeal reflux (12). Dysphonia is less common but an important factor to note preoperatively with assessment of vocal cord mobility with laryngoscopy. Less frequently, superior vena cava syndrome is noted and can be assessed by Pemberton's maneuver (the face turns red once the patient raises their arms above their head for a few minutes).

Ultrasound is the first line imaging in a patient with a cervical goiter followed by fine needle aspirate of any suspicious nodules. If a substernal goiter is suspected a CT scan with contrast of the neck and chest is recommended as the gold standard for further work up. The relationship between the goiter and the vasculature (aortic arch, common carotid artery, brachiocephalic artery, subclavian artery and veins) is noted, which can help anticipate whether or not a sternotomy will be required. When the goiter extends below the aortic arch, this makes removal more difficult and can be a risk factor for requiring a sternotomy (13). As part of the biological work up, TSH, TSH – receptor, thyroperoxidase and thyroglobulin antibodies should be drawn since autoimmune dysfunction of the thyroid is a risk factor for surgical difficulties (14).

Patients with an asymptomatic goiter is not in itself an indication for surgery, however in a young patient the risk of the goiter growing, becoming compressive, or malignant is a strong indication for surgery even in the absence of symptoms (15,16). Medical management with exogenous thyroxine will not reduce the size of the gland enough to relieve symptoms and often surgery is required (17). Generally, there is a consensus that most MG can be removed transcervically with an incision through the neck. Primary sternotomy is not the standard approach for most mediastinal goiters especially if they are located in the anterior mediastinum. Anticipation for a sternotomy approach is required if the goiter extends below the aortic arch and/or if malignancy is suspected but does not necessitate this procedure.

The incident of sternotomy is rare, but occurs anywhere from 0-11% (18,19). The variability of this number can be explained by the lack of a uniform definition of a substernal goiter. Historically, De Perrot reported the indication for sternotomy is a goiter of 10 cm in size, which was later revised to 15-20 cm (20). Further experience has demonstrated that size is a consideration in addition to the extent of the goiter below the tracheal bifurcation, vascular structures, associated lymphadenopathy with suspicious malignancy, and whether the goiter is localized to the posterior or anterior mediastinum (21). Predicting whether a sternotomy is required is important because it poses greater risk to the patient with a prolonged recovery compared to a cervical incision with risks including hematoma, mediastinitis, abscess, osteomyelitis, chest bone fracture and sternal dehiscence (22).

Cho et al. found the preoperative imaging

feature that was most predictive for safe cervical removal of a goiter was the presence of a clear tissue plane around the nodule in the mediastinum (23). Later work by Nankee et al. found in their retrospective review of 220 patients with large thyroid glands, that patient with chest pressure and voice changes were more likely to receive sternotomy, and had thyroid tissue below the level of the aortic arch. In their series, 7 (5.5%) required sternotomy (24). In more recent literature, Cohen et al. summarized 4 main factors had an increased likelihood of sternotomy in their retrospective review; malignancy, posterior mediastinal involvement, substernal extension inferior to the aortic arch, and ectopic goiter (25).

The rate of malignancy is reported to range from 3-21% in patients with substernal goiters (26). In a multicenter retrospective study involving 19,662 patients involving 6 large centers, 1055 patients had a cervicomediastinal goiter treated with a cervical approach, and 69 patients were treated with a sternal split approach. The malignancy rate was higher in patients with cervical mediastinal extension (22.4%), and in patients treated with sternotomy (36.2%) compared with patients treated for their cervical goiter (10.4%) (27). Complications were also higher in the group of patients treated with a cervical mediastinal goiter compared with the cervical goiter including transient and permanent hypocalcemia, transient and permanent recurrent laryngeal nerve palsies, phrenic nerve palsy, and seroma/hematoma (28). In Cohen's smaller series, they found a 11.5% rate of malignancy which excluded micro-carcinomas. Only 1 out of the 13 cancers required a sternotomy. Consideration should be given for a sternotomy if malignancy is suspected and adherence to mediastinal blood vessels is encountered.

The size of the goiter can play an important role in whether a sternotomy is required since the goiter needs to be pulled up through the thoracic inlet. However, goiter weight or volume is not predictive in patients with a large cervical component (29). Extra room can be temporarily acquired with temporary trachea compression; however, care is required to keep the capsule of the tumor intact to avoid potentially seeding malignant cells. Different studies have shown that size or volume can play a role in determining whether the goiter will fit through the thoracic inlet, however the best predictive factor for a sternotomy is the degree of inferior extension of the goiter beyond the aortic arch seen on CT or MRI (30). Cohen et al. showed that this led to a 50% chance of requiring a sternotomy.

Most substernal goiters are removed transcervically, however in the event of difficult to control bleeding the procedure can be converted to a sternotomy incision. Migliore et al. demonstrated situations where video mediastinoscopy can be useful for safe mediastinal goiter removal potentially reducing the risk for hemorrhage and sternotomy (31). In their cohort of seven patients, video mediastinoscopy was a useful tool in situations where adherence to the mediastinal pleura and vascular structures were present. Direct visualization of surrounding vessels enabled the surgeons to avoid hemorrhage and potentially a sternotomy as well as leaving a residual thyroid behind.

In patients where more definitive surgical treatment is not possible due to their poor candidacy for a general anesthetic, medical

therapy can be considered in select patients. Generally, the effectiveness of levothyroxine treatment in large goiters is limited and suppressive treatment is not recommended (32). Long term suppressive treatment can lead to symptoms of thyrotoxicosis, reduction in bone mineral density and atrial fibrillation making this form of treatment less desirable, and less effective in volume reduction. Radioactive iodine ablation has been associated with a 40-60% reduction in volume within two years of therapy (33). Pretreatment with recombinant human TSH (rh TSH) can improve the long-term effect of radioactive iodine therapy reduce the required dose of radioactive iodine (34). However, treatment is not without side effects such as transient goiter swelling (up to 15-25% increase in size), radiation thyroiditis, hypothyroidism, secondary hyperthyroidism, or radiation induced malignancies such as breast cancer (35).

In conclusion, safe removal of a mediastinal goiter can occur majority of the time through a cervical excision. The potential for a sternotomy should be reserved for worrisome features seen on CT scan or suspected malignancy that may make cervical removal difficult. Video mediastinoscopy can be a useful adjunct to safe removal of a mediastinal goiter for effective visualization in the mediastinum. Recovery from a sternotomy can take longer in comparison with a cervical approach with a greater risk for potential complications. When surgical therapy is not possible, radioactive iodine treatment is more effective than levothyroxine treatment for shrinkage of a large goiter, but is not free from complications or side effects (36).

References:

1. Di Crescenzo V., Vitale M., Valvano L., et al. Surgical management of cervico-mediastinal goiters: Our experience and review of the literature. *International Journal of Surgery*. 2016; 28: S47-S53.

2. Huins C.T, Georgalas C., Mehrzad H., Tolley N.S. A new classification system for retrosternal goiters based on a systematic review of its complications and management. *International Journal of Surgery*. 2008; 6: 71-76.

3. Mack E. Management of patients with substernal goiters. *Surgical clinics of North America*. 1995; 75: 377-394.

4. Cirocchi R., D'Ajello F, Trastulli S et al. Meta-analysis of thyroidectomy with ultrasonic dissector versus conventional clamp and tie. *World Journal of Surgery*. Oncology. 2010; 8:112.

5. Kacprzak G., Karas J., Rzechonek A., Blaskiak P. Retrosternal goiter localized in the mediastinum: surgical approach and operative difficulties. *Interact.Cardiovasc Thorac.Surg*. 2012; 15:935-937.

6. Patel K., Parsons C. Forgotten goiter: Diagnosis and management. A case report and literature review. *International Journal of Surgery case reports*. 2016; 27: 192-194.

7. Massard G., Wihlm JM., Jeung MY., et al. Forgotten mediastinal goiter: seven cases. *Ann. Chir*. 1992; 46: 770-773.

8. Di Crescenzo V., Vitale M., Valvano L., et al. Surgical management of cervico-mediastinal goiters: Our experience and review of the literature. *International Journal of Surgery*. 2016; 28: S47-S53.

9. Brenet E., Dubernard X., Merol JC., Louges MA., Labrousse M., Makeieff M. Assessment and management of cervico-mediastinal goiter. *European Annals of Otorhinolaryngology, Head and Neck diseases*. 2017; 678, 1-5.

10. Di Crescenzo V., Vitale M., Valvano L., et al. Surgical management of cervico-mediastinal goiters: Our experience and review of the literature. *International Journal of Surgery*. 2016; 28: S47-S53.

11. Brenet E., Dubernard X., Merol JC., Louges MA., Labrousse M., Makeieff M. Assessment and management of cervico-mediastinal goiter. *European Annals of Otorhinolaryngology, Head and Neck diseases*. 2017; 678, 1-5.

12. Brenet E., Dubernard X., Merol JC., Louges MA., Labrousse M., Makeieff M. Assessment and management of cervico-mediastinal goiter. *European Annals of Otorhinolaryngology, Head and Neck diseases*. 2017; 678, 1-5.

13. Nankee L., Chen H., Schneider DF., Sippel RS., Elfenbein DM. Substernal goiter: when is a sternotomy required? *Journal of Surgical Research*. 2015; 199: 121-125.

14. Pellizzo MR. Difficult thyroidectomies. *Il G Chir*. 2015; 36: 2:49-56.

15. Brenet E., Dubernard X., Merol JC., Louges MA., Labrousse M., Makeieff M. Assessment and management of cervico-mediastinal goiter. *European Annals of Otorhinolaryngology, Head and Neck diseases*. 2017; 678, 1-5.

16. Sanders LE., Rossi R., Shahian DM, Williamson WA. Mediastinal goiters. The need for an aggressive approach. *Arch Surg.* 1992; 127:5:609-613.

17. Casella C., Pata G., Cappelli C., Salerni B. Preoperative predictors of sternotomy need in mediastinal goiter management. *Head Neck.* 2010;32:1131-5.

18. Netterville JL., Coleman SC., Smith JC., Smith MM, Day TA, Burkey BB. Management of a substernal goiter. *Laryngoscope.* 1998;108 (11 pt 1):1611-1617.

19. Mussi A., Ambrogi MC, Iacconi P., Spinelli C., Miccoli P., Angeletti CA. Mediastinal goiters: when the transthoracic approach? *Acta Chir Belg*. 2000; 100:6:259-263.

20. De Perrot M., Fadel E., Mercier O., et al. Surgical management of mediastinal goiters: when is a sternotomy required? *J. Thorac. Cardiovasc Surgery*. 2007: 55: 39-43.

21. Polistena A., Sanguinetti A., Lucchini R. et al. Surgical approach to mediastinal goiter: An update based on a retrospective cohort study. *International journal of surgery*. 2016: 28: S42-S46.

22. Nankee L., Chen H., Schneider DF., Sippel RS., Elfenbein DM. Substernal goiter: when is a sternotomy required? *Journal of Surgical*

Research. 2015; 199: 121-125.

23. Cho HT., Cohen JP., Som ML. Management of substernal and intrathoracic goiters. *Otolaryngol Head Neck Surgery*. 1986;94:282-287.

24. Nankee L., Chen H., Schneider DF., Sippel RS., Elfenbein DM. Substernal goiter: when is a sternotomy required? *Journal of Surgical Research*. 2015; 199: 121-125.

25. Cohen JP. Substernal goiters and sternotomy. *Laryngoscope*. 2009; 199:683-688.

26. Randolph GW. Surgery of cervical and substernal goiter. In: Randolph GW, ed. *Surgery of the Thyroid and Parathyroid glands*. Philadelphia, PA: Saunders; 2003:70-99.

27. Testini M., Gurrado A., Avenia N. et al. Does mediastinal extension of the goiter increase morbidity of total thyroidectomy? A multicenter study of 19,662 patients. *Annals of Surgical Oncology*. 2011; 18:8:2251-2259.

28. Testini M., Gurrado A., Avenia N. et al. Does mediastinal extension of the goiter increase morbidity of total thyroidectomy? A multicenter study of 19,662 patients. *Annals of Surgical Oncology*. 2011; 18:8:2251-2259.

29. Cohen JP. Substernal goiters and sternotomy. *Laryngoscope*. 2009; 199:683-688.

30. Cohen JP. Substernal goiters and sternotomy. *Laryngoscope*. 2009; 199:683-688.

31. Migliore M., Costanzo M., Cannizzaro MA. Cervico-mediastinal goiter: is telescopic exploration of the mediastinum (video mediastinoscopy) useful? *Interactive Cardiovascular and Thoracic surgery*. 2010; 10: 439-440.

32. Chen AY., Bernet VJ., Carty SE., et al. American Thyroid Association Statement on Optimal Surgical Management of Goiter. *Thyroid*. 2014; 24:2:181-189.

33. Bonnema SJ., Hegedus L. Radioiodine therapy in benign thyroid diseases: effects, side effects, and factors affecting therapeutic outcome. *Endocrine Review*. 2002; 33: 920-980.

34. Fast S., Hegedus L., Grupe P. et al. Recombinant human thyrotropin-stimulated radioiodine therapy of nodular goiter allows major reduction of the radiation burden with retained efficacy. *Journal of Clinical Endocrinology Metabolism*. 2010; 95:3719-3725.

35. Chen AY., Bernet VJ., Carty SE., et al. American Thyroid Association Statement on Optimal Surgical Management of Goiter. *Thyroid*. 2014; 24:2:181-189

36. Fast S., Hegedus L., Grupe P. et al. Recombinant human thyrotropin-stimulated radioiodine therapy of nodular goiter allows major reduction of the radiation burden with retained efficacy. *Journal of Clinical Endocrinology Metabolism*. 2010; 95: 3719-3725.

