



Predictors of the need for an extracervical approach to intrathoracic goitre

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Background: Sternotomy and lateral thoracotomy are required infrequently to remove an intrathoracic goitre (ITG). As few studies have explored the need for an extracervical approach (ECA), the aim of this study was to examine this in a large cohort of patients.

Methods: A prospective database of all patients who had surgery for ITG between 2004 and 2016 was interrogated. Patient demographics, preoperative characteristics and type of operation were analysed to identify factors associated with an ECA.

Results: Of 237 patients who had surgery for ITG, 29 (12.2 per cent) required an ECA. ITGs below the aortic arch (odds ratio (OR) 10.84; $P = 0.004$), those with an iceberg shape (OR 59.30; $P < 0.001$) and revisional surgery (OR 4.83; $P = 0.022$) were significant preoperative predictors of an ECA.

Conclusion: The extent of intrathoracic extension in relation to the aortic arch, iceberg goitre shape and revisional surgery were independent risk factors for ECA. Careful preoperative assessment should take these factors into consideration when determining the optimal surgical approach to ITG.

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Introduction

Intrathoracic goitre (ITG) is a rare entity. It generally refers to a multinodular thyroid that extends below the level of the thoracic inlet^{1,2}. Since it was first described by Haller¹ in 1749, many attempts have been made to define and subgroup the condition accurately^{3–9}. There is no universal definition of ITG, which makes comparison of management approaches and surgical outcomes challenging^{2,10–12}.

Because of the controversy regarding definition, the incidence of ITG varies significantly, from as low as 0.2 per cent to more than 40 per cent in some series¹³. ITG is three times more common in women^{8,9}. The majority of patients present with compressive symptoms involving the trachea, oesophagus and, rarely, the major vessels¹⁴. As the goitre is slow growing, it takes many years for it to cause significant

symptoms; hence the reported age at diagnosis is usually after the fifth decade of life^{8,9}. ITG may require surgical removal for resolution of compressive symptoms or for diagnostic and therapeutic purposes, including diagnosis and treatment of malignancy. Reported rates of malignancy range from 6 to 21 per cent^{15–17}.

The decision regarding the optimal surgical technique to remove an ITG is taken on a patient-by-patient basis. There is currently no agreed standard surgical approach based on the goitre characteristics alone^{10,11}. Most ITGs are delivered successfully through a transcervical approach (TCA), with an extracervical approach (ECA) – either sternotomy or lateral thoracotomy – being reserved for the most challenging goitres¹². Available evidence, based on relatively small numbers of patients, suggests that ITGs with giant intrathoracic extension, recurrent goitres,

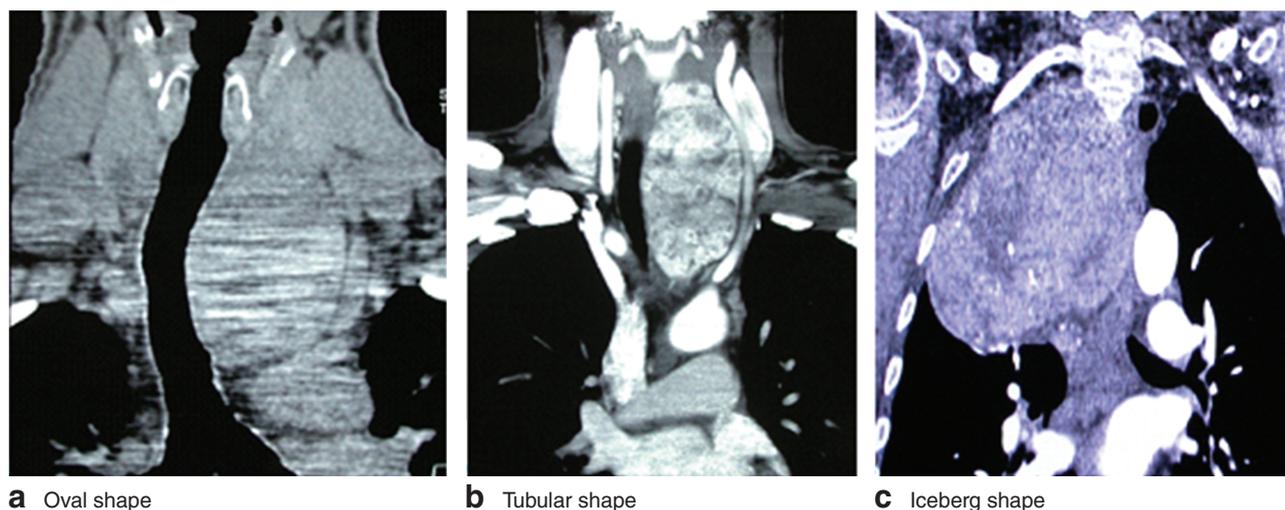


Fig. 1 Classification of goitres depending on their shape. **a** Oval, **b** tubular and **c** iceberg shape

extension posterior to both trachea and oesophagus, extension between trachea and oesophagus, isolated mediastinal goitre and an ITG diameter greater than the thoracic inlet diameter are associated with the need for ECA. These parameters can be evaluated before surgery using cross-sectional imaging, with extension beyond the aortic arch being described as the strongest predictor of a need for ECA¹³. The presence of malignancy with extrathyroidal extension is an independent factor for ECA, reflecting the need to control potentially invaded major vessels in the mediastinum and to access the regional mediastinal lymph nodes^{15,16}.

There have been no attempts to quantify the likelihood of an ECA based on statistical modelling. The aim of this study was to determine the risk of requiring an ECA excision of a non-malignant ITG and to identify predictors of ECA based on preoperative patient evaluation.

Methods

This cohort study was conducted in the Head and Neck and Thoracic Surgery departments of a UK teaching hospital, Guy's and St Thomas' NHS Foundation Trust. It included all patients who had surgery for ITG between 2004 and 2016. All operations were performed by the same principal surgeon, and when an ECA was required the operation was performed with the assistance of the same thoracic surgical team. Patient demographics, preoperative characteristics and surgical approach were collected and updated in a prospectively developed database using Microsoft Excel® (Microsoft, Redmond, Washington, USA) from August 2004 to 2012, and using exported

personal data from the British Association of Endocrine and Thyroid Surgeons (BAETS) (in Microsoft Excel® workbook) from November 2012 to October 2016. The BAETS national registry is registered under the Data Protection Act. Data are anonymized and ethics committee approval was not required. The study was registered with the hospital's audit department. The study was conducted in accordance with ethical requirements regarding the protection of the rights and welfare of human subjects participating in medical research, and has been reported in line with the STROCSS (Strengthening the Reporting of Cohort Studies in Surgery) criteria¹⁸.

All patients were evaluated with a full otorhinolaryngological clinical examination including fiberoptic laryngoscopy, thyroid function testing and estimation of thyroid autoantibodies. Ultrasound imaging was performed in all patients and used to characterize the goitre and its nodularity, and to guide fine-needle aspiration cytology (FNAC). When the cervical component was not palpable or was deemed inaccessible, FNAC was not performed. Multislice, multiplanar CT of the neck and chest with intravenous contrast was used in all patients. Those with iodine allergy or hyperthyroidism underwent either CT without contrast or MRI.

The Huins *et al.*¹⁰ criteria for classification of ITGs, as adopted by BAETS, were used to classify the degree of intrathoracic extension. This classification categorizes ITGs as retroclavicular, upper border of aortic arch or below aortic arch. Goitres were also classified regarding the shape on coronal imaging and categorized as: 'iceberg' or conical¹⁹, 'tubular' or 'oval' (Fig. 1). The radiological classification was performed by the senior author and confirmed

by a radiologist, who independently reviewed the scans. Any disagreement in the classification was resolved by consensus. This novel shape classification of ITGs is subsequently referred to as the Simo classification²⁰.

Cytological analysis was categorized using the British Thyroid Association guidelines for the management of thyroid cancer; from 2004 to July 2014 the second edition²¹ was used, and from July 2014 to 2016 the third edition²².

Patient selection

Patients were selected for an ECA based on preoperative evaluation, using the multiplanar CT scans in a setting where thoracic surgical support was available. All patients with goitres reaching or extending below the aortic arch, and patients undergoing revisional surgery were risk-assessed for the potential need for an ECA. They were discussed with the thoracic team at a dedicated multidisciplinary clinic and, when deemed appropriate, an ECA was planned. There were no unplanned ECA operations during the study period.

All consecutive goitres categorized using the BAETS criteria as retrocervical, up to the level of the aortic arch and below the level of the aortic arch were included. Patients with non-toxic multinodular goitres, toxic multinodular goitres, goitres with benign cytological results, goitres with indeterminate cytological results and goitres with suspected but not proven malignancy were included. Patients with evidence of malignancy on either FNAC or core biopsy, evidence of malignancy with mediastinal involvement from either the primary site or metastatic lymphadenopathy, recurrent thyroid cancer requiring ECA, revisional surgery for cancer requiring an ECA, or patients in whom the indication for an ECA was different (for example, access to mediastinal main vessels) were excluded.

Statistical analysis

Univariable and logistic regression analysis was performed to identify factors associated with an ECA. For categorical data, χ^2 and Fisher's exact tests were used as appropriate. The independent-samples Student's *t* test was used for normally distributed continuous data. The Mann-Whitney non-parametric test was applied for continuous variables that were not normally distributed. Multivariable analysis was performed using the binary logistic regression with a backward elimination process, with 0.050 being set as the level of significance. SAS[®] version 9.3 software (SAS Institute, Cary, North Carolina, USA) was used for statistical analysis.

Table 1 Patient demographic and preoperative characteristics stratified by type of operation

	Extracervical approach (n = 29)	Transcervical approach (n = 208)	P†
Age (years)*	62.9 (59.1, 66.8)	58.6 (56.6, 60.5)	0.044§
Sex ratio (M:F)	11:18	55:153	0.196‡
Indication			
Compressive symptoms	29 (12.7)	200 (87.3)	1.000
Biopsy	0 (0)	5 (100)	
Thyrotoxicosis	0 (0)	3 (100)	
OSAS			1.000
Yes	0 (0)	5 (100)	
No	29 (12.5)	203 (87.5)	
Onset			1.000
Acute	0 (0)	4 (100)	
Subacute	0 (0)	2 (100)	
Chronic	29 (12.6)	202 (87.4)	
Thyroid status			0.842
Euthyroid	26 (12.2)	187 (87.8)	
Hyperthyroid	3 (15)	17 (85)	
Hypothyroid	0 (0)	4 (100)	
FNAC finding			0.553
Thy1	0 (0)	9 (100)	
Thy2	28 (13.5)	180 (86.5)	
Thy3	0 (0)	18 (100)	
Thy4	1 (50)	1 (50)	
BAETS classification			< 0.001‡
Upper border of AA	2 (2)	95 (98)	
Below AA	26 (36)	47 (64)	
Retroclavicular	1 (1)	66 (99)	
Simo classification			< 0.001
Iceberg	17 (89)	2 (11)	
Tubular	5 (14)	31 (86)	
Oval	7 (3.8)	175 (96.2)	
Reoperation			< 0.001
Yes	12 (40)	18 (60)	
No	17 (8.2)	190 (91.8)	
Preoperative voice change			0.683
Yes	2 (14)	12 (86)	
No	27 (12.1)	196 (87.9)	

Values in parentheses are percentages unless indicated otherwise; *values are mean (95 per cent c.i.). OSAS, obstructive sleep apnoea syndrome; FNAC, fine-needle aspiration cytology; BAETS, British Association of Endocrine and Thyroid Surgeons; AA, aortic arch. †Fisher's exact test, except ‡ χ^2 test and §Student's *t* test.

Results

A total of 237 patients, of mean age 59 (95 per cent c.i. 57 to 61) years, had surgery for ITG during the study interval. More than two-thirds of patients were women (171 patients, 72.2 per cent). The main indication for operation was the presence of compressive symptoms (229 patients, 96.6 per cent) (Table 1). The majority of patients were euthyroid (213 patients, 89.9 per cent). All patients with hyperthyroidism had their thyroid status optimized before surgery. Fourteen patients (5.9 per cent) reported voice

Table 2 Multivariable regression analysis of independent risk factors for an extracervical approach for intrathoracic goitre

	Estimate	s.e.	P	Odds ratio
Intercept	-4.4625	0.8034	<0.001	
Goitre type			0.004	
Below AA <i>versus</i> upper border of AA	2.3831	0.8336	0.004	10.84 (2.12, 55.54)
Retroclavicular <i>versus</i> upper border of AA	0.0187	1.2742	0.988	1.02 (0.08, 12.38)
Goitre shape (Simo classification)			<0.001	
Iceberg <i>versus</i> oval	4.0825	0.9332	<0.001	59.30 (9.52, 369.27)
Tubular <i>versus</i> oval	0.3995	0.6930	0.564	1.49 (0.38, 5.80)
Reoperation (yes <i>versus</i> no)	1.5753	0.6883	0.022	4.83 (1.25, 18.6)

Values in parentheses are 95 per cent confidence intervals. AA, aortic arch.

changes before surgery, and 18 (7.6 per cent) had a pre-operative vocal cord palsy on the side of the goitre.

Eighty-three patients had a total thyroidectomy and 154 a thyroid lobectomy. There were no subtotal or near-total thyroidectomies. Some 208 patients (87.8 per cent) had the goitre excised via a TCA, with the remaining 29 (12.2 per cent) undergoing an ECA. Of these, 27 had a combined transcervical and midline sternotomy approach, and two patients underwent a combined transcervical and right thoracotomy approach.

In univariable analysis, patients were at higher risk of requiring an ECA when the goitre was below the aortic arch compared with patients whose goitre was above the aortic arch or retroclavicular (36, 2 and 1 per cent respectively; $P < 0.001$); when the goitre had an iceberg shape compared with a tubular or oval shape (89, 14 and 3.8 per cent respectively; $P < 0.001$); and when the patient required reoperation (40 per cent *versus* 8.2 per cent when reoperation was not needed; $P < 0.001$). These variables remained significant as independent predictors of an ECA in multivariable analysis (Table 2). Patients with a goitre below the aortic arch were more than tenfold more likely to require an ECA than those with a goitre in the upper border of the aortic arch ($P = 0.004$). No difference in surgical approach was found for retroclavicular goitres when compared to those extending up to the upper border of the aortic arch. An iceberg shape dramatically increased the likelihood of an ECA compared with an oval shape (odds ratio 59.30; $P < 0.001$). Patients who required a reoperation were 4.8 times more likely to have an ECA than those having a single operation ($P = 0.022$) (Table 2).

Discussion

It has been widely reported that more than 90 per cent of ITGs can be removed safely using a cervical approach. CT with contrast is the most accurate investigation to characterize ITG; it helps to determine whether patients are surgical candidates and can be used to predict the surgical

approach². The reported incidence of an ECA for ITG varies significantly. In prospective studies^{23–25} the range is relatively small (0–1.7 per cent), whereas in retrospective series^{13,26–28} the need for an ECA ranges from 0 to 45 per cent, reflecting the lack of consensus as to what represents an ITG and the fact that ITGs can be managed by a mix of surgical specialties, with different sets of operative expertise. It is also possible that patients with such goitres are offered non-surgical treatment as they are often elderly and with significant co-morbidity.

In the present series of 237 patients, 29 (12.2 per cent) had an ECA over a 13-year period. It is likely that this relatively high percentage is related to the nature of the referral pattern, the setting where the surgery was performed, and the strict definitions applied to inclusion criteria. The service reflects a tertiary referral centre for thyroid disease covering a population of over 3.5 million. The approach to surgical planning was multidisciplinary, with involvement of otolaryngology, anaesthesia and thoracic surgery, as well as having input from cytopathology and radiology. In this setting, surgical plans were individualized to each patient.

Specific preoperative factors have been linked previously with the need for an ECA. These factors have been based primarily on descriptive analyses or expert opinion. Thyroid cancer with or without recurrence, need for reoperation, emergency surgery, extension down to the aortic arch, primary ITG, iceberg shape and the presence of a large ITG, especially in the posterior mediastinum or causing superior vena cava syndrome, have all been cited as factors with significant association with an ECA^{13,29–32}. The present study identified independent predictive factors for an ECA in a large cohort of patients with ITG. Multivariable analysis quantified the likelihood of an ECA based on preoperative characteristics that can be used in the surgical planning of patients with an ITG. Extension of the goitre below the aortic arch, ITG with an iceberg shape and ITG requiring reoperation were features with a significantly increased likelihood of needing an ECA.

The present study classified ITG based on shape²⁰. It confirmed that an iceberg shape was a significant predictor of an ECA, as described previously¹⁹. This was quantified to be increased almost 60-fold when compared to an oval-shaped ITG. Reoperation also increased the risk of ECA by almost fivefold. The significance of reoperation was known but not quantified previously^{13,32}.

Malignancy was deliberately excluded from the present analysis. The need for an ECA in this subgroup seemed evident as, in order to resect macroscopic disease safely from mediastinal structures, adequate access is necessary.

One of the main limitations of this study is that it was performed in a non-controlled setting and the study groups were of different size. Despite the size of the cohort, limitations in the sample size and event rate generated large confidence intervals in some analyses, which probably reduced the power of multivariable modelling. A prospective trial in which all patients could initially be approached via a TCA and the procedure converted only if the goitre could not be excised would be ideal from a scientific standpoint, although this might be considered unethical if patients were at risk of significant predictable complications. For this reason, patients were selected for an ECA in the present study based on preoperative evaluations, using multiplanar CT in a setting where thoracic surgical support was available. In no patient was the preoperative decision to perform a transcervical operation changed during surgery. Differing criteria for selecting patients for an ECA may limit the applicability of the present findings to other units.

The position of the goitre relative to the aortic arch was made using the classification of Huins and colleagues¹⁰, as adopted by BAETS. This system fails to account for ITGs extending below the upper border of the aortic arch but not below the lower border. This is addressed in the classification of Mercante and co-workers³³, validated by Malvemyr *et al.*³⁴, underlining the increased risk of an ECA for ITGs extending below the lower border of the aortic arch. It was not possible in the present series to reclassify patients using the Mercante classification as the data were recorded at time of the patients' initial presentation. Further prospective studies using the latter classification would be beneficial.

The degree and character of intrathoracic extension as well as the need for revisional surgery were independent risk factors that led to the recommendation of an ECA in this study. Careful preoperative assessment, taking these factors into consideration, is recommended for optimal surgical management of ITGs.

Disclosure

The authors declare no conflict of interest.

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