Universitat Autònoma de Barcelona

Intrathoracic Goitres: Comparative study of the transcervical approach versus the combined cervicothoracic approach

Ricard Simó i Sanchez

Intrathoracic Goitres:
Comparative study of the transcervical approach versus the combined cervicothoracic approach

Ricard Simó i Sanchez

2017

Departament de Cirurgia

Universitat Autonoma de Barcelona

Intrathoracic Goitres:
Comparative study of the transcervical approach versus the combined cervicothoracic approach

Doctoral Thesis presented by Ricard Simo LMS, FRCS(Glas)
FRCS (ORL-HNS) to opt for the title of Doctor in Medicine

PhD Supervisors

Professor Miquel Quer
Dr Xavi Leon

London – Barcelona 2017

ADDRESS FOR CORRESPONDENCE

Ricard Simo FRCS(ORL-HNS)

Department of Otorhinolaryngology Head and Neck Surgery

St Thomas's Street

London SE1 9RT

United Kingdom

E-mail: ricard.simo@gstt.nhs.uk

Tel: +44 207 1882216

Fax: + 44 207 1882206

To Rachel, Joe and Anna.

CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENTS

Undertaking a Doctoral Thesis, has been an extraordinary journey and experience. It has required a lot of hard work, self-discipline, sacrifices and time.

I would like to thank first and foremost my wife Rachel, who has been a constant unconditional support and motivation and without her, writing this thesis would not have been possible. I would therefore like to dedicate this work to her.

I also would like to thank my children Joe and Anna for their encouragement and motivation to take upon such work so late in my life.

A special thanks to my father Josep a retired surgeon, from whom I learnt about work ethic, dedication and self-appraisal which makes surgeons strive to become better at their job. To my mother Conxita as well as my sisters Beti and Marta for their encouragement and support.

I would like to thank my supervisors Professor Miquel Quer and Dr Xavi Leon, who have been so inspirational, accommodating, flexible and encouraging. They have created a framework and a setting that has converted something potentially very difficult into something very enjoyable and achievable.

To Mr Iain Nixon, Mr Enyi Ofo and Dr Paul Carroll for their advice, encouragement, proofreading and correction of the manuscript.

To Dr Theofano Tikka for her laborious and methodical statistical analysis and advice.

To Ms Karen Harrison-Phipps, Mr Tom Routlege and Ms Juliet King, Thoracic Surgeons for their advice, for sharing the responsibility, the planning and the surgery of the cases treated, and helping with the post-operative care of all patients requiring extra-cervical approaches and for being on standby when needed.

To Dr Selvam Tharavaj, Professor Edward Odell, Professor Peter Morgan, Dr Ash Chandra and Dr Muffadal Moonim for their cytological and histopathological analysis of all these patients.

To Rose Ngu for being so systematic and patient in obtaining all the cytological samples, to Steve Connor and Ata Siddiqui for reporting all the complex multiplanar scans and their teaching.

To Richard Oakley, my clinical lead and Jean-Pierre Jeannon my colleague in the Head and Neck and Thyroid Unit for their constant encouragement, advice and support.

ABREVIATIONS

AA	Aortic arch
BAA	Below aortic arch
ATA	American thyroid association
BAETS	British Association of Endocrine and Thyroid Surgeons
CT	Computerised Tomography
ECA	Extracervical approach
FNAC	Fine needle aspiration cytology
ITG	Intrathoracic goitres
IONM	Introperative neuromonitoring
LOS	Length of stay
MNG	Multinodular goitre
MPTC	Micropapillary thyroid carcinomas
MTC	Medullary thyroid carcinoma
NED	No evidence of disease
OSAS	Obstructive sleep apnoea syndrome
PTC	Papillary thyroid carcinoma
RLN	Recurrent laryngeal nerve
RLNP	Recurrent laryngeal nerve palsy
RIA	Radioiodine ablation
TCA	Transcervical approach
TFT	Thyroid Function Tests
TSH	Thyroid Stimulating Hormone
UBAA	Upper border aortic arch
USS	Ultrasound scan

"Cases will be found to be operable in which the tumour at first sight seemed to be quite inaccessible"

–Operation for Intrathoracic Goitre.
Theodor Kocher 1911[1, 2]

"The extirpation of the thyroid gland for goitre typifies perhaps better than any other operation the supreme triumph of the surgeon's art"

–The operative story of the goiter: the author's operation.
William S. Halstead 1920[1]

SUMMARY

Introduction

MNGs with intrathoracic extension often present with compressive symptoms and pose specific management challenges requiring specialised care by experienced surgical teams. Most ITG can be accessed by a TCA and only between 5 and 15% will require an ECA. Many controversies exist regarding the clinical presentation, evaluation, and selection of cases for ECA, surgical technique and outcomes.

Aim

The aim of this study is to evaluate, analyse and compare the outcomes of patients undergoing surgery for ITG by the two main approaches.

Materials and Methods

An ambispective study of 237 patients undergoing surgery for ITG was undertaken. 27 patients underwent a combined cervical and midline sternotomy and 2 underwent a combined cervical and right lateral thoracotomy and the rest by a TC approach. Data on clinical presentation, investigations, complications and outcomes was collected prospectively and analysed.

Results

The rate of malignancy in ITG was 8.01% with a rate of occult malignancy of 5.0%. The USS FNA had poor sensitivity (33%) but high specificity (93.3%) to exclude cancer. The risk of sternotomy was 12.2% and the extension BAA ($p<0.001$), iceberg shape ($p<0.001$) and reoperation ($p<0.001$) were the best predictors of needing an ECA. The risk of RLNP and hypocalcaemia are higher in ECA ($p<0.003$ and $p<0.002$). The risk of tracheomalacia was 1.6% and the risk of tracheostomy was 2.5%. The median LOS in TCA was 3 days and 6 days in the ECA ($p<0.0001$).

Conclusions

Surgery for ITG is challenging. It requires accurate evaluation and a multidisciplinary approach by specialised teams. Despite the nature and anatomical complexities of these goitres most of them can be excised via a TCA. The rate of complications is relatively low but higher in patients undergoing ECA.

RESUM

Introducció

Els golls amb extensió intratoràcica es presenten sovint amb símptomes compressius i comporten reptes en el seu maneig requerint atenció per equips quirúrgics amb experiència. La majoria dels golls intratoràcics poden accedir-se amb un abordatge transcervical i nomes d'entre el 5 i el 15% requereixen abordatges extracervicals. Existeixen moltes controvèrsies referents a la presentació clínica, avaluació, selecció de casos per abordatges extracervicals, tècnica quirúrgica i resultats.

Objectiu

L'objectiu d'aquest estudi és avaluar, analitzar i comparar els resultats dels pacients sotmesos a cirurgia per golls intratoràcics pels dos abordatges principals.

Materials i Mètodes

S'ha fet una revisió de 237 pacients sotmesos a cirurgia per golls intratoràcics. 27 pacients varen ser operats per via cervical i esternotomia mitja, 2 per via cervical i toracotomia lateral dreta i la resta per via transcervical. Es varen recollir prospectivament dades de la presentació clínica, exploracions, tractament, complicacions i resultats.

Resultats

L'índex de malignitat en golls intratoràcics va ser del 8.01% i l'índex de malignitat oculta del 5.0%. L'ecografia amb punció d'agulla fina te una sensitivitat dolenta (33%) però una especificitat alta (93.3%) per excloure càncer. El risc d'esternotomia fou del 12.2% i l'extensió per sota de l'arc de l'aorta ($p<0.001$), la forma d'iceberg ($p<0.001$) i la cirurgia de revisió ($p<0.001$) van ser els millors predictors de necessitar un abordatge extracervical. El risc de lesió recurrencial i hipocalcemia va ser més alt en els abordatges extracervicals ($p<0.003$ i $p<0.002$, respectivament). L'índex de traqueomalacia va ser del 1.6% i el risc de traqueotomia del 2.5%. La mitjana en els períodes d'ingrés en els abordatges transcervicals va ser de 3 dies, i de 6 dies en els extracervicals ($p<0.0001$).

Conclusions

La cirurgia per golls intratoràcics representa un repte. Requereix un avaluació acurada i un abordatge multidisciplinar amb equips especialitzats. A pesar de les característiques I de les complexitats anatòmiques d'aquest golls, la majoria es poden abordar per una via transcervical. L'índex de complicacions es baix però mes alt en pacients que necessiten un abordatge extracervical.

1

INTRODUCTION

1.1 GENERAL ASPECTS

Multinodular Goitre (MNG), defined as an enlarged thyroid gland with multiple nodules, may present to the surgeon for diagnostic and/or therapeutic purposes. Challenges specific to this condition include patient evaluation, determination of the risk of malignancy within the multiple nodules of the gland, selecting patients who require surgical management, and planning a surgical approach to deal with the disease process or processes without un-due risk of complications. Classic indications for surgery in these patients include pressure effects and cosmesis, a recognized risk of malignancy in MNG and intrathoracic extension [(3)].

Palpable nodules occur in 4-7% of the adult population [(4)]. In non-iodine deficient patients USS, can detect thyroid nodules in over 20% of patients and multiple nodules in 9%. As expected, rates are higher in females and in older patients [(3, 5)]. These results suggest that with the ageing population currently encountered, an increasing number of patients with MNG will require appropriate management.

With the advent of high resolution USS, nodules and nodular thyroids can be detected up to 50-70% of the adult population [(6)].

MNG is an irregular enlargement of the thyroid gland generally arising in response to a presumed over-secretion of Thyroid Stimulating Hormone (TSH). MNG is charecterised by a benign proliferation of hyperplastic follicles, adenomatoid nodules and nodules with cystic degeneration. Such thyroid hyperplasia is probably due to a decrease in the production of thyroid hormones in relation to the metabolic demand of the human body. This can occur as a result of a congenital or an acquired defect. Morphological and molecular studies suggest a degree of polyclonal etiology. MNGs are sometimes familial and one study suggests linkage to a DNA mother as chromosome 14 q [(7)].

MNG affects 4% of the USA population and 10% of the British population [(8)] and it is estimated to affect 1.5 billion people globally. Iodine-deficiency contributes to the vast majority of cases of MNG worldwide and in endemic or iodine-deficient regions such as Bangladesh, the prevalence is even higher than encountered in the West. The majority of the natural existing iodine is in sea-water and it is therefore that the mountainous and lowland regions far from the sea where there is a higher risk of endemic goitre [(9)].

Retrosternal, substernal and intrathoracic goitres are terms referring to a subgroup of MNG that extend inferiorly towards the thoracic cavity. Such goiters raise a number of specific problems in terms of preoperative evaluation and surgical management. The most common recognised and appropriate term is probably the one of intrathoracic goitre (ITG) (10) and for the purpose of this PhD Thesis this term will be applied throughout.

It is not uncommon for ITG to manifest in elderly patients who often present with associated co-morbidities. This therefore requires a thorough preoperative evaluation and appropriate patient selection followed by careful operative planning and meticulous surgical technique. The extent of such goitres may require the option of an extracervical approach, therefore it is essential that the surgeon has the understanding, knowledge and experience of surgical techniques used to access the mediastinum and the pleural spaces as well as being part of a dedicated and expert multidisciplinary team including thoracic or cardiothoracic surgeons (11).

Surgery for ITG is thought to carry a higher risk of complications of both intra and postoperative complications and therefore it is imperative that the surgeons dealing with such cases have the knowledge and ability to deal with these complications when they arise (11).

1.2 CONCEPT OF INTRATHORACIC GOITRE

Haller first provided an anatomical description of the ITG in 1794 and in 1820 Klein was credited with removing the first mediastinal goitre. Since then as indicated, ITG has referred to under various names and descriptions including, retrosternal, substernal, retroclavicular and intrathoracic amongst others. The reason for this diversity is probably due to the fact that, unanimity in terms of the volume of the thyroid gland that must be in an intrathoracic position, nor how far down into the mediastinum has descended, has not been reached (12). Over the years numerous classifications have been used but none of them have been universally validated nor accepted.

Some authors have tried to compare these definitions in an attempt to clarify its utility and allow sensible comparisons [10, 13]. Huins et al have indicated the need to standarize the classification in 3 grades depending on the relationship of the ITG with the aortic arch and the right auricle. More recently Rios et al al critically analysed all previous classifications with the aim of determining the most useful definition of ITG for predicting intra-operative as well as postoperative complications. They found that most definitions of ITG can be ignored as they are not clinically relevant and concluded that Katlic's definition [10, 14] is the most useful for predicting a possible sternotomy for removing the goitre [10].

1.3 SURGICAL ANATOMY

The thoracic inlet, bounded by the clavicles, first rib, sternum and vertebrae contains many vital structures. In addition to the prevertebral muscles, the trachea, oesophagus, carotid and jugular vessels all pass through this region. As the thyroid gland enlarges, an increasing percentage of the cross sectional area of this inlet is occupied by goitre, leaving less room for additional structures. Pressure symptoms will tend to develop in low-pressure areas in the first instance, and a feeling of difficulty swallowing is a common initial symptom. As the degree of compression increases, along with increasing dysphagia, pressure on the trachea can lead to deformity of the tracheal rings and airway compression. In extreme cases as the goitre expands, pressure on the venous structures of the neck can lead to a superior vena cava syndrome, although this is rare (5%) [15].

ITGs can be classified as primary, secondary or recurrent depending on the site of origin [16] and this will be elucidated in the pathogenesis section. Some authors also classify ITGs dependant on the anatomical compartment in which they develop. Type I ITGs develop from the ipsilateral lobe into the anterior mediastinum, type II into the posterior mediastinum and type III may develop from ectopic thyroid tissue.

Table 1. ITG classification according to GW Randolph [17]

Type	Subtype	Location	Anatomy	Prevalence
I		Anterior Mediastinum	Anterior to great vessels trachea and RLN	85%
II		Posterior Mediastinum	Posterior to great vessels, trachea and RLN	15%
	IIA	Ipsilateral		
	IIB	Contralateral		
	IIB1	Posterior extension behind trachea and oesophagus		
	IIB2	Extension between trachea and oesophagus		
III	Isolated		Ectopic with no connection	1%

Over 90% of the posterior mediastinal goitres arise from the right thyroid lobe as the aortic arch, the subclavian and carotid arteries impede their descend in the left chest.

Goitres can be unilateral or bilateral and there is also the possibility that the intrathoracic growth can cross-over between the right and the left or viceversa [18]. The blood supply to secondary goitres is usually from the superior and infterior thyroid arteries [19]

1.4 PATHOGENESIS OF ITG

As indicated the pathogenesis of ITG is poorly understood. The cause of this inferior descent appears to be multifactorial but is partly a consequence of anatomical bony restrictions of the thoracic inlet and the limitation of the strap muscles anteriorly and the trachea medially. As Lahey and Swinton stated the neck is “a space with no bottom”. The repetitive forces of deglutition, the negative intrathoracic pressure during respiration and gravity appear to contribute to the downward growth of these hyperplastic glands into the mediastinum [9]. From the surgical point of view, ITG can be classified based on its anatomical origin into:

Primary ITG: This represents less than 1% of the ITGs, it is congenital and originates from an ectopic thyroidal tissue in the mediastinum. Primary ITGs also are known as mediastinal aberrant or isolated goitres and they have no connection with the cervical thyroid gland receiving their blood supply from the intrathoracic arteries including internal mammary arteries. Primary ITGs may be located in the anterior or posterior mediastinum [20]. In over 80% of cases, the ITG arises in the anterior mediastinum and often has no connection with the thyroid gland. The vascular supply is from mediastinal vessels and its removal requires an ECA [5].

Secondary ITG: These represent between 80 to 90% of ITGs arising from a pre-existing cervical MNG, which descends into the thorax as described above. Their blood supply is from the inferior thyroid arteries and the great majority can be accessed by a TCA [5]. The great majority of ITGs are secondary and develop from the downward growth of the cervical thyroid tissue. The majority of these goitres grow into the anterior mediastinum, anterior to the RLN, main vessels and anterolateral to the trachea. However 10 to 15% grow into the posterior mediastinum, descending posterior to the carotid sheath and the RLN [19, 21] and a small minority can grow into both the anterior and posterior mediastinum riding over the innominate vessels.

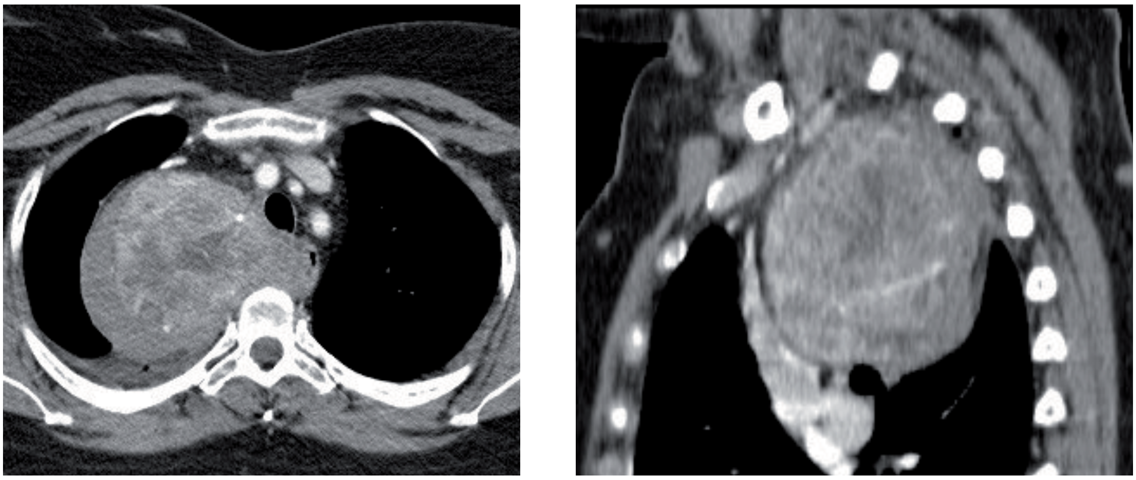


Figure 1. Axial and sagital views of a CT scan of a goitre growth into the posterior mediastinum.

Recurrent ITG: These represent between 10 and 20% of ITG. They develop following partial thyroidectomy, especially subtotal thyroidectomies with poor TSH control during follow-up. Recurrent ITGs often grow into the mediastinum as the scar tissue caused by the original surgery prevents their growth towards the lateral and medial aspect of the neck. The blood supply can be mixed as this tissue can develop neovascularization from the mediastinal vessels and often mandating an ECA [(5)].

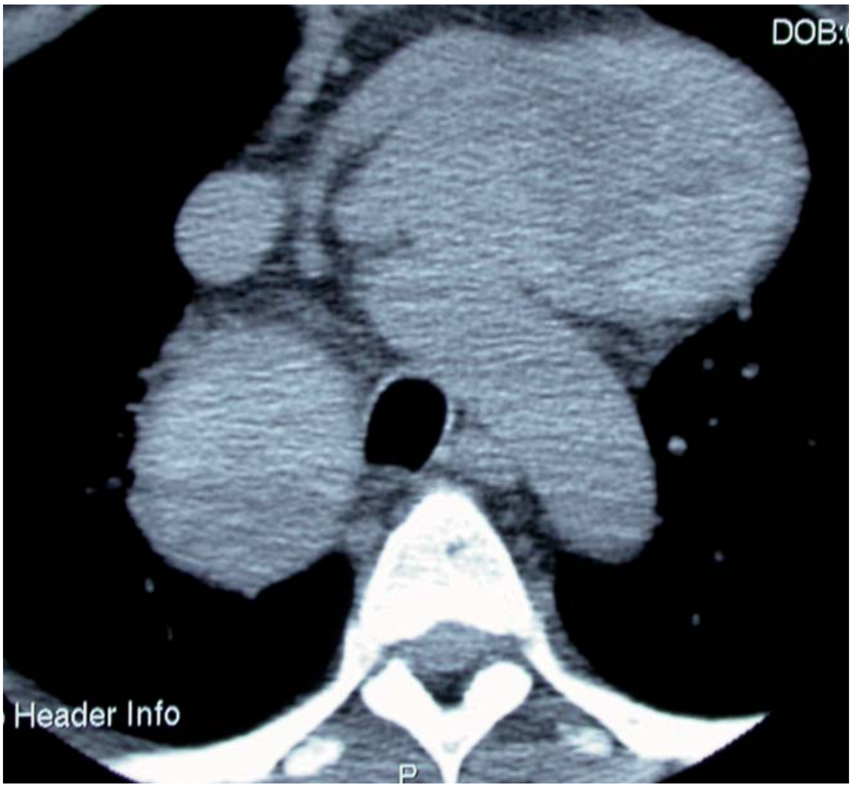


Figure 2. Axial CT scan of a recurrent ITG with double compartment components.

On completion of surgery, long standing pressure on the trachea has been suggested as a cause of tracheomalacia. However, few authors have encountered difficulty with this phenomenon, and postoperative tracheostomy should rarely be required (2%), but more commonly required following a traumatic intubation causing laryngeal oedema rather than for long standing weakness of the tracheal framework [(22)].

For a thyroid gland to reach sufficient size to pass into the mediastinum, the pathological processes involved must have been present for many years. It is therefore unsurprising that the vast majority of surgical specimens will demonstrate benign pathology.

Recently some authors have suggested that the smaller tracheal diameter – to thoracic – inlet ratio and the lower position of the thyroid gland are the main indicators for the development of ITG [(2)].

1.5 CLINICAL PRESENTATION

ITGs tend to grow slowly and they are usually diagnosed between the fifth and sixth decades. They appear to be more common in women with a female to male ratio of 3 to 1 [(14, 23)]. In 20% to 30% of cases the goitre is impalpable or barely palpable in the neck as most of the goitre is in the mediastinum [(5)]. Some ITGs are discovered as an incidental finding during other investigations such as magnetic resonance for neck pain or after trauma. The absence of symptoms from the ITG may cause a decision making conundrum [(24)]. However, the majority of ITGs cause compression symptoms, ranging from mild cough, shortness of breath on excertion to severe life-threatening stridor and asphyxia [(25, 26)]. ITG may also compress on other anatomical structures in its vicinity such as the RLN or the oeshopagus causing dysphonia due RLN palsy, dysphagia [(27)] or even obstructive sleep apnoea syndrome [(28)].

1.6 RISK OF MALIGNANCY IN THE INTRATHORACIC GOITRE

Ocasionallly thyroid malignancy presents with intrathoracic extent, however the majority of malignancies will present as occult findings in cases operated on due to compressive symptoms. The rate of malignancy in reported surgical series is low and ranges between 6-

21% in most reported series [15, 22, 29, 30]. However, malignancy is vital to consider as it may significantly alter the approach to management in these cases.

1.7 PREOPERATIVE EVALUATION INCLUDING VOCAL CORD ASSESSMENT

All patients who present with a goitre should have a full head and neck examination with particular focus on the presence of cervical lymphadenopathy and function of the vocal cords. Following initial examination, most clinicians use USS to assess the central and lateral neck and to guide fine needle aspiration. As stated earlier, rates of malignancy are low and in cases of intrathoracic nodules, access is limited. Nonetheless, cytological assessment of the gland may identify malignancy preoperatively and allow for accurate counselling and preoperative planning in terms of extent of surgical resection. Assessment of thyroid function and preoperative calcium levels is also of use prior to surgery.

Whereas most patients with cervical thyroid disease will require no further investigation, those with suspected to have an ITG should have cross sectional imaging to define the size, position and relation of the goitre to critical structures within the mediastinum. This will allow adequate preoperative planning. In most patients, the clinical impression will be of benign disease. Imaging should be used to assess the tissue planes surrounding the thyroid gland. Any evidence of extrathyroidal extension on imaging should be considered evidence of malignancy and the surgical approach tailored as appropriate [15].

In addition to assessment of the thyroid pathology, consideration should be given to the general condition of the patient. The average age of patients who undergo surgery for ITG is greater than for those with cervical goitre and varies between reports from 51 to 63 years [24, 30-32]. As such, other medical co-morbidities must be evaluated, particularly given the potential need for sternotomy or thoracotomy in this older patient group. Electrocardiography and echocardiography should be considered in any patient thought to be at risk of requiring sternotomy, and in all other patients with significant cardio-respiratory disease as part of assessment prior to general anaesthesia. The use of flow volume loops may be considerered as they may detect subradiological tracheal compression but rarely influence management in patients with ITG [33].

Ultrasound guided fine needle aspiration cytology is now considered the gold standard test to evaluate thyroid nodules. However, this does not appear to be standard practice in cases of ITGs. This is because access can be difficult or impossible and the risk of occult malignancy is thought to be low. However as the risk of occult malignancy in ITGs is between 10 and 35% in most surgical series, younger patients, those with prior irradiation, patients with a family history of thyroid malignancy and those with compression symptoms are reported to have higher rates of malignancy [3]. It is therefore, important that efforts are made to attempt a preoperative diagnosis in these patients despite the fact that samples may be non-diagnostic or very difficult to obtain. The results of the FNAC may also be useful in prioritizing patients in terms of clinical urgency.

1.8 CURRENT INDICATIONS FOR SURGERY

Most patients with ITGs present either with compression symptoms, mainly with increasing dyspnoea on exertion. ITGs can often be diagnosed as an incidental finding during chest radiography or other investigations such as USS, CT, MRI or PET which can be the case in up to 40% of these patients [21]. Patients with ITG can therefore be classified as symptomatic or asymptomatic. In the symptomatic group (dyspnoea, dysphagia or superior vena cava syndrome) surgery provides the only way of controlling local aerodigestive symptoms and provides tissue for histological analysis [22]. For the few patients who present with malignancy, surgical resection provides the mainstay of therapy, and allows for adjuvant radioiodine treatment when indicated [3].

However, as imaging becomes more widely available an increasing number of ITGs are detected incidentally during work up of other diseases (up to 40%) [15]. Indications for surgery in this patient group are unclear. Some authors consider the mere presence of an ITG as an indication for surgery [22] whereas others have questioned the need for surgery in all cases especially if malignancy is not suspected [24]. Therefore, any decision-making regarding surgery in this patient group should be individualised. An appropriate management plan can be decided based upon the size of the goitre, the degree of aero-digestive tract compression and the co-morbidities of the patient. For example, a patient with an asymptomatic ITG detected on imaging to stage an incurable aggressive malignancy clearly is not a candidate for surgery. In contrast, an otherwise well patient with asymptomatic tracheal compression and an excellent life expectancy will be a good surgical candidate. Surgery in this clinical setting will prevent increasing airway symptoms and avoid a situation where an intubation attempt is unsuccessful. This can occur in an emergency or elective situation and can place the patient in danger.

The difficult patient is one with minor co-morbidities and asymptomatic disease, which causes early tracheal compression. Such patients should be made aware of the risks and benefits of both a conservative and a surgical approach. Interval imaging often provides critical information about the trajectory of disease, which aids in borderline cases.

1.9 PREOPERATIVE CONSIDERATIONS AND ANAESTHESIA

Surgery for ITG may be associated with a high morbidity and it is essential to identify the most high-risk cases, which require a planned combined cervicothoracic approach either with sternotomy or lateral thoracotomy.

Once a patient has satisfied indications for surgery and given informed consent, the multi-disciplinary team must set aside time prior to surgery to ensure that the patient and conditions are favourable, in order to minimise the risk of complications.

Consideration should be given to:

1. Thyroid function
2. Coagulation status
3. Extent of goitre and relationship to mediastinal structures
4. Co-morbidities (in particular respiratory or cardiac disease)
5. Airway management for surgery and other anaesthetic issues

1. Thyroid Function

All patients with preoperative hyperthyroidism must be managed by an endocrinologist to achieve euthyroidism status, in order to prevent life threatening thyrotoxic crisis during or after surgery. This usually involves thionamide antithyroid drugs, or potassium iodide (40 mg three times daily for 10 days) +/- beta-blockade (e.g. propranolol 40 to 80 mg three times per day).

2. Coagulation status

Given the risk of bleeding, pre-existing clotting disorders must be identified, and anticoagulation such as warfarin or clopidogrel should be stopped and substituted for heparin if required depending on the underlying medical or coagulation disorder.

3. Extent of goitre and relationship to mediastinal structures

Once the diagnosis of ITG is suspected, preoperative cross sectional imaging of the neck and chest with an intravenous contrast agent is essential for surgical planning. CT or MRI may be used, however most surgeons may find it easier to interpret CT scan images. The relationship of the ITG to the trachea, oesophagus and great vessels should be easily appreciated on imaging, and this will guide the surgical approach (cervical +/- sternotomy) which may require the input of other surgical teams, as well as providing invaluable information to the anaesthetist on the presence of laryngotracheal compression and likely problems with endotracheal intubation.

4. Co-morbidities

Patients with significant cardiorespiratory disease requiring median sternotomy are at higher risk of post-operative complications, hence may require close monitoring post surgery in a high dependency or intensive care setting.

5. Airway management for surgery and other anaesthetic issues

ITG can be associated with significant laryngotracheal compression resulting in difficult orotracheal intubation. Prior to surgery, the surgeon and anaesthetist must discuss the airway plan and review all imaging together. In most cases tracheal compression is ‘soft in nature’ and can easily be overcome on gentle insertion of the endotracheal tube, which may need to be one size smaller than standard for the patient. In order to avoid the dreaded emergency scenario of ‘can’t intubate, can’t ventilate’ at induction of anaesthesia in a paralysed patient, the anaesthetic team may choose to perform an awake fibreoptic oral or nasal tracheal intubation with the aid of topical local anaesthesia (22, 34).

Although the majority of cases are amenable to endotracheal intubation, as the tube splints the trachea open at the area of maximal compression, airway management may not always be straightforward. Many patients will have variable symptoms related to head position. When the neck is fully extended, the goitre is pulled up towards the thoracic inlet, and the patient may find this position compromises the airway. In such cases awake fibreoptic intubation may be required in order to allow neck flexion during intubation. Truly difficult intubations are uncommon (22) but cooperation between the operating surgeon and anaesthetist is crucial in avoiding problems at this critical stage of the procedure (22).

In cases where extensive mediastinal dissection is anticipated, a double lumen endotracheal tube may be required to permit selective pulmonary ventilation. Such cases require an experienced anaesthetic team with appropriate head and neck and thoracic anaesthetic expertise, as these tubes can be challenging to place in patients with a difficult airway (22, 34).

Recurrent laryngeal nerve neuromonitoring has been reported to reduce nerve palsy rates following difficult thyroidectomy, such as ITG surgery (35). Where nerve monitoring will be employed and muscle relaxants are required at induction of anaesthesia, a short acting agent should be used so as not to interfere with neural monitoring during the operation.

Maintenance of anaesthesia is usually standard as per other surgical procedures, with no special requirements. At the end of surgery, tracheal compression resulting from longstanding goitres may cause a degree of tracheomalacia, however endotracheal extubation is almost always possible. In the highly unlikely event that the patient suffers airway obstruction on extubation due to tracheomalacia, reintubation should be straightforward and an elective tracheostomy performed at a later stage if necessary (36).

1.10 SURGICAL APPROACHES

Surgery for ITG poses a significant intraoperative and postoperative challenge and therefore should be carried out by experienced surgeons who are part of a dedicated multidisciplinary thyroid surgery team.

For patients with bilateral enlargement of the thyroid gland, total thyroidectomy is the procedure of choice however in patients with unilateral enlargement or in those patients in which there is a significant risk of injury to the recurrent laryngeal nerve or the parathyroid function, thyroid lobectomy is a perfectively accepted option as the majority of these patients will have benign goitres [22].

In 95% of cases of ITG, the approach and excision can be achieved by a transcervical approach. The risk of sternotomy increases substantially if a significant proportion (over 50%) of the gland is in the medistinum, the ITG is in a retrotracheal or retrooesophagic position, and if the volume of the intrathoracic component is significantly larger than that of the cervical component. Most authors also advocate sternotomy if there is evidence of malignancy [5, 13, 21, 30, 37, 38] .

The main reported indications for an ECA therefore include: giant intrathoracic extension, recurrent goitres, presence of malignancy with extrathyroidal extension, extension posterior to both trachea and oesophagus, extension between trachea and oesophagus, isolated ectopic mediastinal goitre and an ITG diameter greater than the thoracic inlet diameter [13, 39-41].

One very important point to be taken into account in the decision-making process is whether a lobectomy or a total thyroidectomy is undertaken and when and how the thyroid isthmus should be addressed.

If the decision is being made to do a lobectomy, it is the opinion of the author that dividing the isthmus earlier would facilitate the cervical dissection and therefore this should be done as early as possible. In very large bilateral goitres, this can be done earlier for the same reason so the procedure becomes essentially two lobectomies. In cases where, a total thyroidectomy is preferred then, the dissection should start with the smaller lobe and continued to the other side which will facilitate the dissection of the larger lobe [5, 9, 22].

1.11 OUTCOMES OF SURGERY FOR INTRATHORACIC GOITRES

Complications associated with thyroidectomy for ITGs have been underestimated due to the lack of precise definition of high-risk patients. ITG which extend to the carina tracheae are reported to carry a high risk of unplanned sternotomy, postoperative complications, return to the operating theatre for reoperation and even death [(42)].

There is little comprehensive evidence based data concerning the management of ITG especially when comparing surgical approaches and the majority of evidence is level V [(21)].

2

HYPOTHESIS

1. Multiplanar Computerised Tomography is the best predictor to determine the adequate surgical approach.
2. Ultrasound guided fine needle aspiration is a poor predictor of occult carcinoma in intrathoracic goitres.
3. Transcervical approach is equally effective as combined transcervical approach with midline sternotomy or lateral thoracotomy.
4. Midline sternotomy and lateral thoracotomy are necessary in selective cases including giant goitres and in reoperative procedures.
5. The risk of specific complications including recurrent laryngeal nerve injury and permanent hypocalcaemia is equal for both approaches.

3

OBJECTIVES

1. Determine the rate of malignancy in goitres with intrathoracic extension and the rate of occult malignancy.
2. Define the value of ultrasound guided fine needle aspiration in determining the rate of malignancy within ITG.
3. Determine the risk of sternotomy in non-malignant ITGs.
4. Determine the indications for transcervical and extracervical approaches in the management of ITG.
5. Compare the risk of injury to the recurrent laryngeal nerve between transcervical and extracervical approaches.
6. Determine the value of intraoperative neuromonitoring in preventing the risk of injury to the RLN in surgery for ITG.
7. Determine the risk of permanent hypoparathyroidism in surgery for ITG.
8. Determine the rate of tracheomalacia and rate and the indications of tracheostomy in patients undergoing surgery for ITG.
9. Analyse and compare the rate of extracervical complications is in patients undergoing surgery for ITG.
10. Compare the length of stay between patients undergoing transcervical versus extra-cervical approaches for ITG.

4

MATERIALS AND METHODS

Between August 2004 and August 2016, 1045 patients underwent thyroidectomy in our Unit. 237 patients had goitres with intrathoracic extension. 27 patients underwent a combined cervical and midline sternotomy and 2 underwent a combined cervical and right lateral thoracotomy.

4.1 CLINICAL EVALUATION

All patients were evaluated with a full otorhinolaryngological clinical examination including fibreoptic nasendoscopy, thyroid function test and thyroid autoantibodies.

4.2 RADIOLOGICAL EVALUATION

Ultrasound scanning: USS was done in all cases and was used to characterize the goitre and its nodularity and to guide FNAC. In patients in which the cervical component was not palpable or deemed to be inaccessible the FNAC was also attempted. From 2014, the characterisation was done using the British Thyroid Association guidelines for the management of thyroid cancer [(43)].

Computerized Tomography: Multislice, multiplanar CT scan of the neck and chest with intravenous contrast was used in all cases. Patients with iodine allergy underwent either CT without contrast or MRI scanning. The Huins et al criteria for classification of ITGs as adopted by the British Association of Endocrine and Thyroid Surgeons (BAETS) was used to classify the degree of intrathoracic extension [(13)]. This classification categorises ITG into retroclavicular, upper border of aortic arch and below aortic arch.

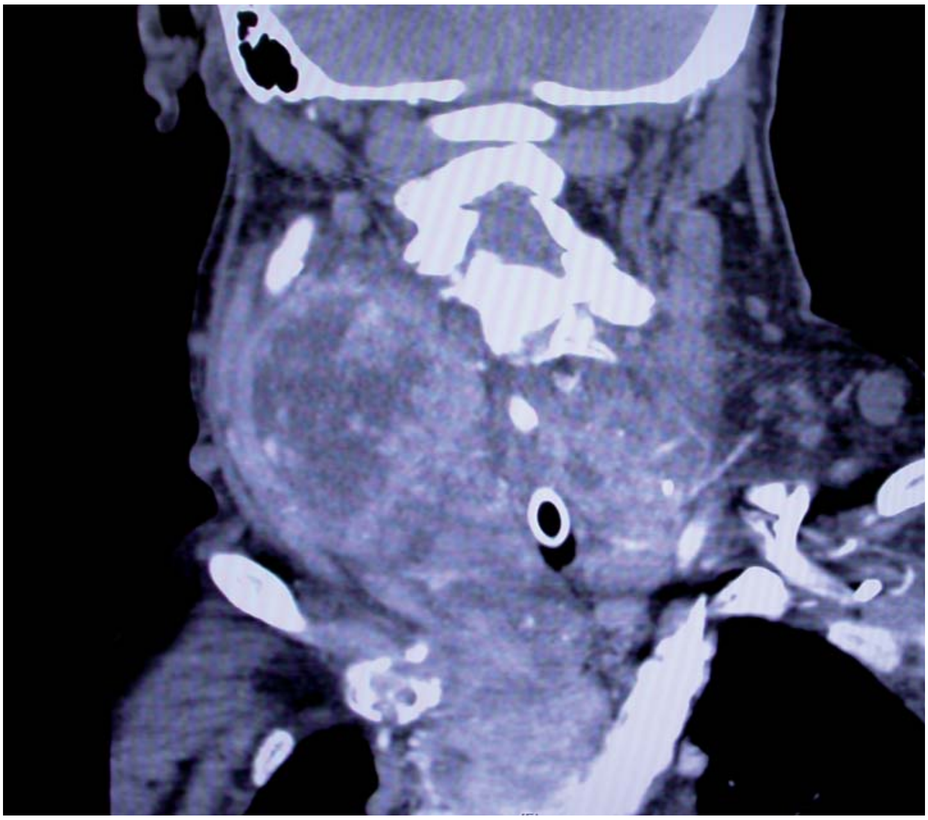


Figure 3. Retroclavicular goitre.

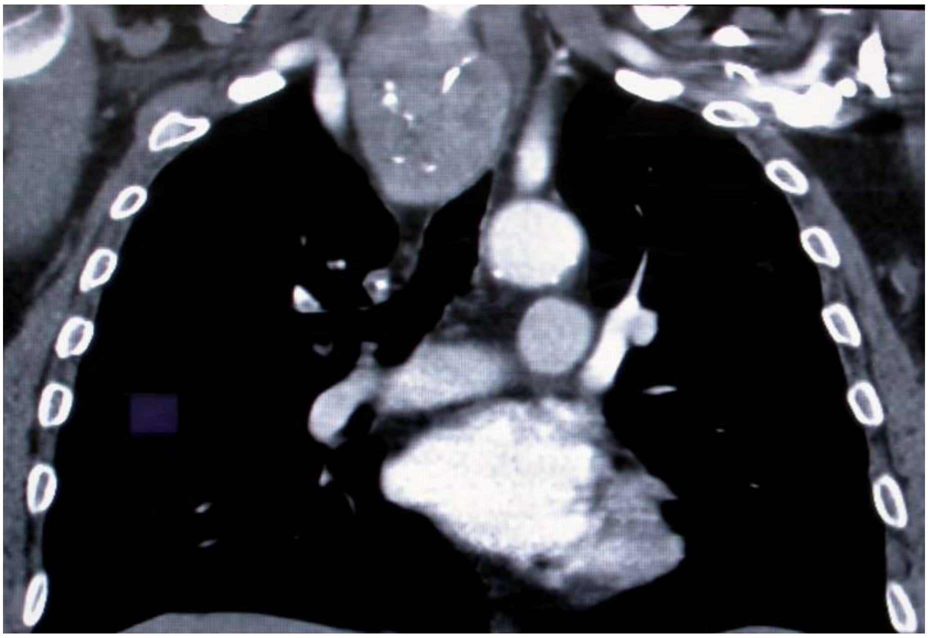


Figure 4. Goitre reaching the upper border of the aortic arch.

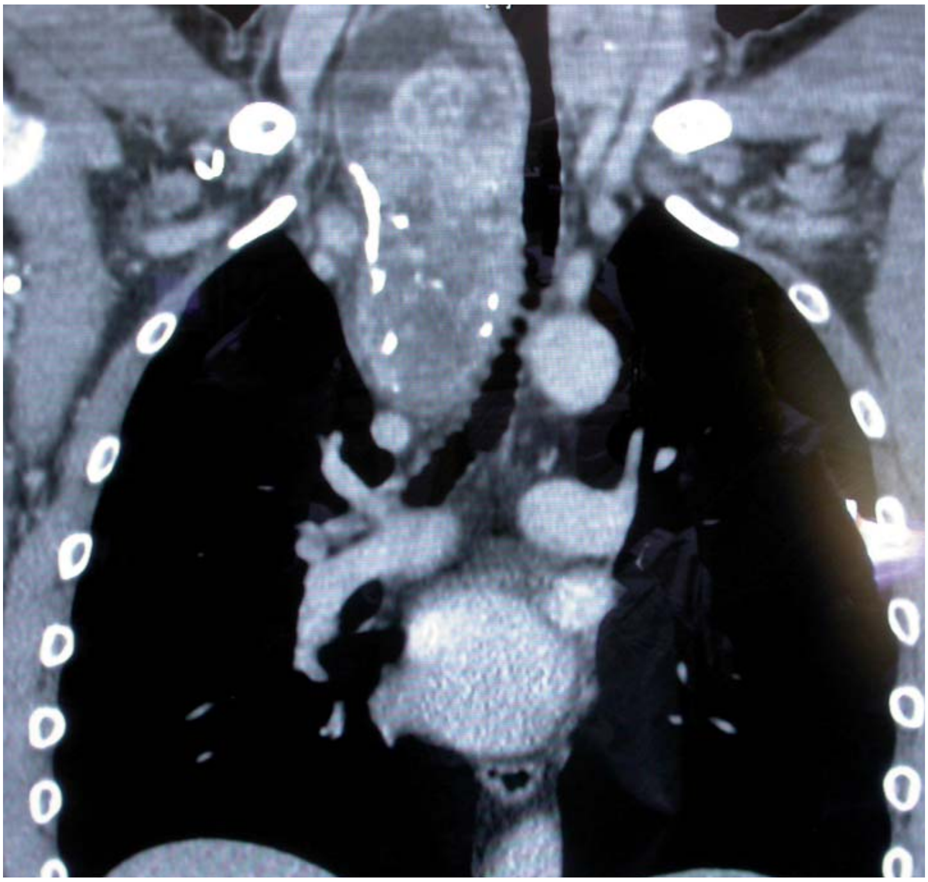


Figure 5. Goitre extending beyond the aortic arch.

We also classified goitres regarding the shape and we separated them into 3 categories: “iceberg”, “tubular” and “oval”. We also provided descriptions of some of the characteristics of the goitres that could help to determine the risk of an extra-cervical approach.

4.3 CYTOLOGICAL EVALUATION

Cytological analysis was categorized using the British Thyroid Association Guidelines for the management of thyroid cancer (BTA). From 2004 to 2014 the 2nd Edition was used and from 2014 to 2016 the 3rd Edition [43] .

Table 2. BTA Cytological Classification 2014 [43]

Category	Description	Action
Thy 1	Insufficient sample	Repeat FNAC
Thy 1c	Cyst	Observation vs surgery if patient symptomatic
Thy 2	Benign	Observation vs surgery if patient symptomatic
Thy 3a	Atypia	Surgery vs observation
Thy 3f	Follicular neoplasm	Surgery
Thy 4	Suspected malignancy	Surgery
Thy 5	Malignant	Surgery

4.4 HISTOLOGICAL ANALYSIS

All pathological specimens were orientated, placed in 10% buffered formal saline and submitted to the histopathology laboratory. The preoperative cytological result was noted. Following adequate fixation, the specimen was then weighted and measured. The capsule was examined for integrity and the inclusion of possible parathyroid glans noted. The specimens were sliced in the transverse plane from superior to inferior at 1 cm intervals. If a true multinodular macroscopic architecture was demonstrated, a representative slice of each nodule was submitted for standard processing and paraffin embedding. If a single or dominant nodule was demonstrated, then the entire periphery of the nodule was submitted for embedding. Five micrometer sections cut from each block using standard microtomy procedure and stained with haematoxilin and eosin (H&E).

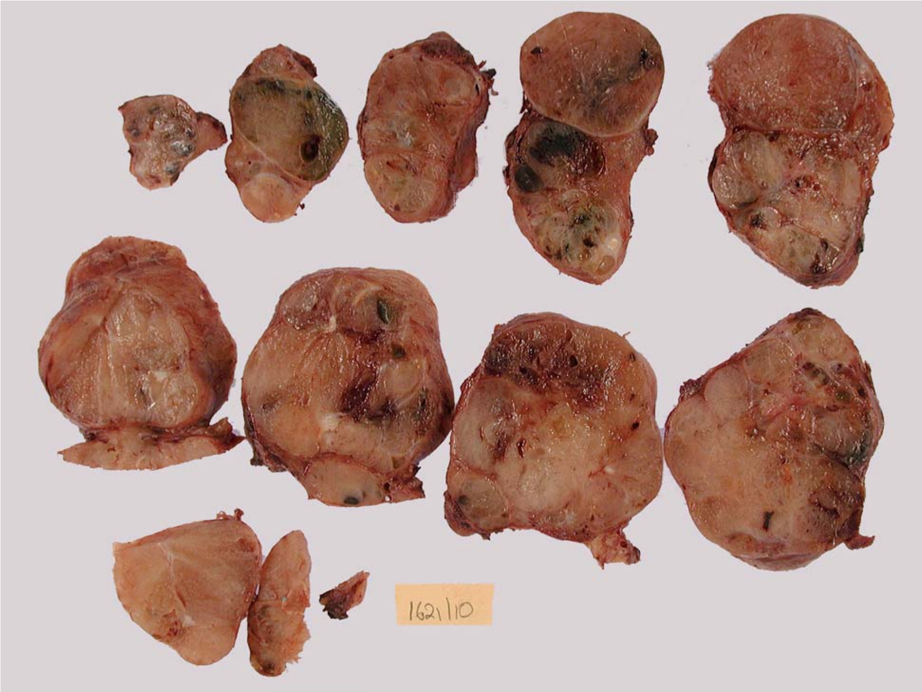


Figure 6. Macroscopic view of cut surface of a fixed MNG specimen demonstrating nodular architecture. Milimeter scale positioned at the bottom of the image.

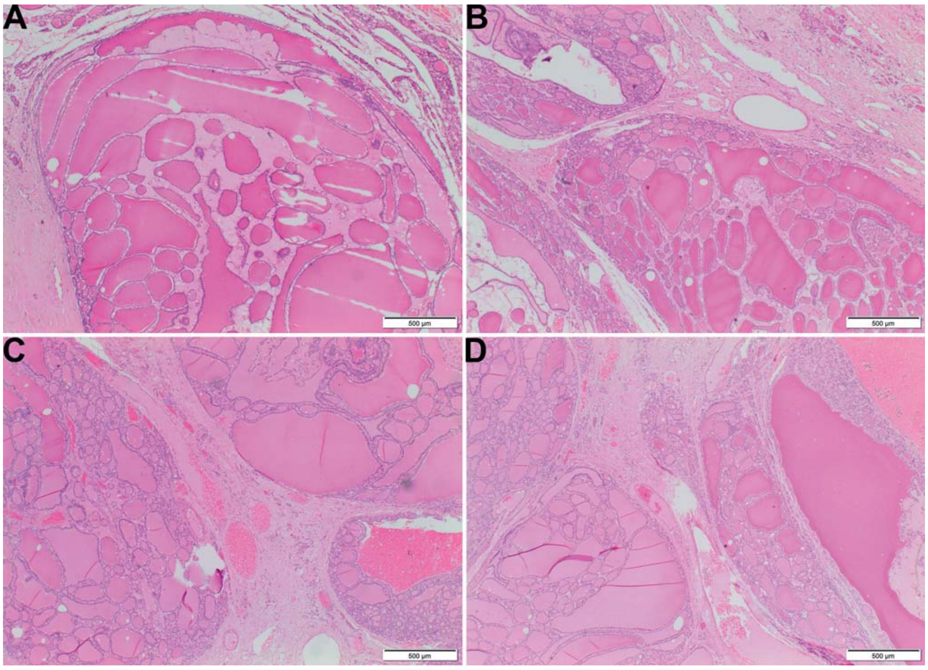


Figure 7. A-D Low-power representaive photomicrographs from specimen in figure 5 above demonstrating MNG.

4.5 INCLUSION CRITERIA

All consecutive goitres were categorised as per the BAETS as retroclavicular, up to the level of the aortic arch and below the level of the aortic arch. The following pathological entities were included:

1. Non-toxic multinodular goitres.
2. Toxic multinodular goitres.
3. Goitres with benign cytological results (Thy 2).
4. Goitres with indeterminate cytological results (Thy 3).
5. Goitres with suspected but not proven malignancy (Thy 4).

4.6 EXCLUSION CRITERIA

The following pathological categories were excluded:

1. Proven evidence of malignancy either on FNAC, CNB or histological analysis and advanced stages T3 or T4.
2. Proven evidence of malignancy with mediastinal involvement either from the primary site or metastatic lymphadenopathies.
3. Recurrent thyroid cancer requiring sternotomy.
4. Revision surgery for metastatic thyroid cancer requiring sternotomy.
5. Patients in which the indication of sternotomy was different.

4.7 MULTIDISCIPLINARY SETTING

All patients with goitres reaching the AA, those extending below the AA and patients undergoing revision surgery were risk assessed for the potential need of an ECA. These patients were discussed with the Thoracic Team at a dedicated multidisciplinary clinic.

All patients with abnormal TFT underwent endocrinology evaluation to optimize the thyroid function prior to surgery and to confirm the indication for surgery.

4.8 INDICATIONS FOR EXTRACERVICAL APPROACH

Preoperative indications for ECA were predetermined as shown. Indications for ECAs were categorized as high risk, moderate risk and low risk. This categorisation was based on current available literature and the previous experience of the surgical team. A member of the thoracic surgery team was always on stand-by for high and moderate risk patients.

4.8.1 High-risk patients for ECA

- ITG below the AA
- Recurrent goitres with intrathoracic extension to and below the AA
- Giant extension
- Goitres involving multiple mediastinal compartments
- Goitres with separate components
- Goitres with “iceberg” or inverted cone shape
- Goitres with extension to the posterior pleura
- Primary goitres

Figure 8. CT scan demonstrating a typical giant goitre extending to the diaphragm.

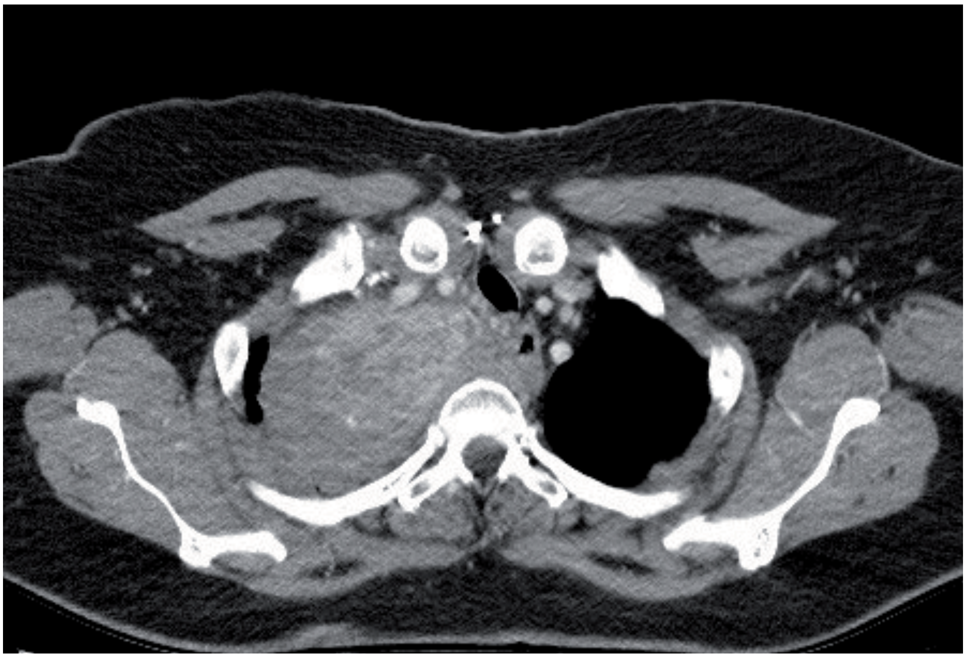


Figure 9. CT scan demonstrating a goitre with extension to the posterior pleura.

4.8.2 Moderate risk patients for ECA

- Goitres reaching the aortic arch
- Goitres reaching the aortic arch with oval or tubular shape
- Goitres with minimal posterior mediastinal, retrotracheal

4.8.3 Low risk for ECA

- Goitres with retroclavicular extension

4.9 DATA COLLECTION AND DATA FIELDS

Data collection was done prospectively using Microsoft excel ® workbook from August 2004 to 2012 and using exported personal data from the British Association of Endocrine and Thyroid Surgeons National Audit (in Microsoft excel workbook ®) from November 2012 to August 2016. The data was automatically anonimized to comply with data protection regulations by BAETS. Participation in the National Audit is considered an obligatory requirement for BAETS Full Members. The BAETS National Registry is operated in partnership with Dendrite Clinical Systems Ltd and is registered under the Data Protection Act (Number Z9844379).

4.9.1 Data group fields collected included:

- Demographic data and date of surgery
- Preoperative evaluation
- Intraoperative data
- Discharge data
- Follow-up

Complete set of data fields is shown in annex 1.

4.10 ANTIBIOTIC PROPHYLAXIS

Our protocol for antibiotic prophylaxis in surgery for ITG is as follows:

Table 3. Protocol for antibiotic prophylaxis in surgery for ITGs

Approach	Non-Penicillin Allergy	Penicillin Allergy
Transcervical	Co-Amoxyclav 1.2 g at induction	Teicoplanin 400 mg at induction
Extracervical and Revision Surgery	Co-Amoxyclav 1.2 g and Teicoplanin 400 mg at induction and for further 3 doses	Teicoplanin 400 mg at induction and for further 3 doses

The dose is repeated if there is more than 500 mls of blood loss.

4.11 HYPOCALCAEMIA PROPHYLAXIS

All patients undergoing total thyroidectomy or completion thyroidecomies for ITG were considered high risk patients in our protocol of postoperative hypocalcaemia and they were given Calcium carbonate po 1g bd and started in 1 alfa calcidol 1 microgram daily. For patients undergoing thyroid lobectomies, no prophylaxis was given. The calcium levels were measured the following day to obtain a baseline. See annex 2.

4.12 SURGICAL TECHNIQUE

4.12.1 Transcervical approach

4.12.1.1 Incision, approach and thyroid isthmus

The incision for approaching ITG was always generous to allow adequate exposure and excision of the goitre. An extended Kocher incision was placed in the lower aspect of the neck. This allowed adequate exposure of the goitre at the thoracic inlet and, if a midline sternotomy was required, there was a minimal vertical element of the scar in the neck. If however, a lateral neck dissection was required then a modified extended Kocher incision was used [(44)].

When doing a total thyroidectomy, the dissection was started in the smaller of the lobes. In selected cases a full total lobectomy on the side of the smaller lobe, with division of the isthmus was performed. This allowed better mobilization of the dominant lobe, reducing cervical pressure and helping to locate the RLNs and the parathyroid glands more easily [(5, 45)].

The thyroid isthmus was identified, scheletonised and divided using Harmonic Scalpel ®.

4.12.1.2 Strap muscles

In large MNGs the strap muscles (SM), in particular sternothyroid, was divided. The main advantages of this approach were: better control of the regional veins, improved exposure to the lateral aspect of the goitre and superior vascular pedicle, and better access to mobilize the goitre and visualize the anatomical structures that must be preserved.

Following division of the SM, the middle thyroid vein was identified, dissected, ligated and divided. Rough manipulation of the gland was avoided to prevent avulsion of the internal jugular vein [(46)].

4.12.1.3 Superior Thyroid Pole

The thyroid lobe was dissected from the prethyroid strap muscles and then the sternothyroid muscle was divided for access to gain access to the upper pole. The superior thyroid pole was identified and individual vessels ligated and divided closer to the gland to avoid injury to the external branch of the superior laryngeal nerve. The upper pole was dissected from the attachments to the cricothyroid muscle and the RLN was identified at the cricothyroid junction at its entry to the larynx. The RLN was then dissected in a caudal direction tunnelling the tissue surrounding the nerve with a fine-tip mosquito dissector. The RLN was dissected inferolateraly as much as the approach allowed it under the common carotid artery and brachiochepalic artery and gently controlled with a rubber vessel sling. Then the thyroid lobe was dissected from its cervical attachements (oesophagus and trachea) into the thoracic inlet as much as possible so it was free from the upper mediastinal attachments.

4.12.1.4 Management of the Recurrent Laryngeal Nerve.

The RLN was either identified at the cricotracheal junction, in its lateral position or inferiorly at the Baehr's triangle depending on the size and shape of the goitre.

A – Superior Approach: Once the upper pole had been dissected and mobilized, then the RLN was identified at the cricotracheal junction and dissected in a caudal direction tunnelling the tissue surrounding the nerve with a fine-tip mosquito dissector. The RLN was dissected inferolateraly as much as the approach allowed it under the common carotid artery and brachiochepalic artery and gently controlled with a rubber vessel sling. Then the thyroid lobe was dissected from its cervical atachements (oesophagus and trachea) into the thoracic inlet as much as possible so it is free from the upper mediastinal attachments [(46-48)].

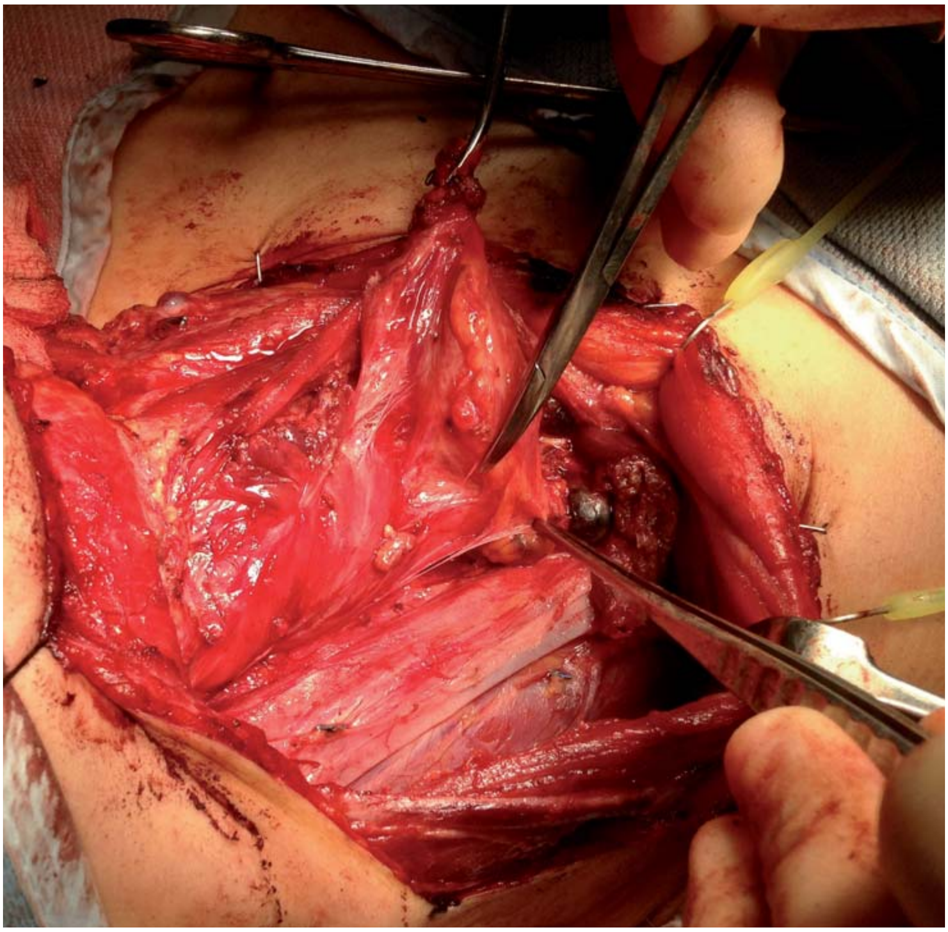


Figure 10. Identification of the RLN at the cricotracheal joint.

B – Lateral Approach: In some cases the RLN was identified in its lateral position above the axis of the ITA close to the tubercle of Zuckerkandl and followed up superiorly and or inferiorly depending on the size and shape of the goitre.

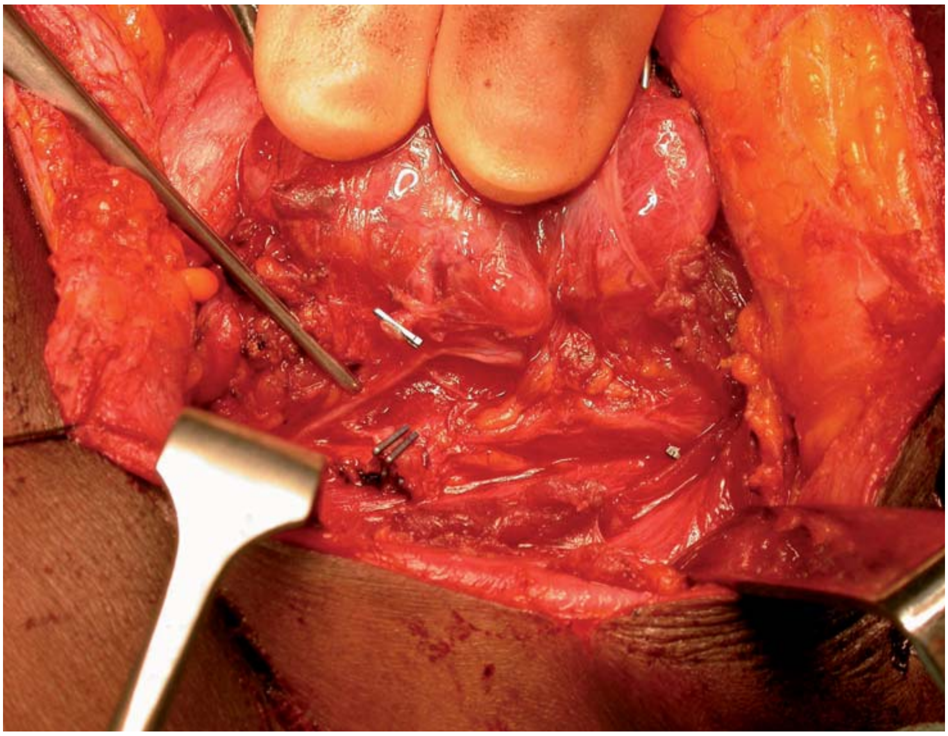


Figure 11. Identification of the RLN laterally at the level of the Tubercle of Zuckerkandl.

C – Inferior Approach: In some cases the RLN was identified in its most inferior position in Beahr's triangle and then followed cranially to the crico-tracheal joint and caudally to the mediastinum, depending on the shape and size of the goitre.

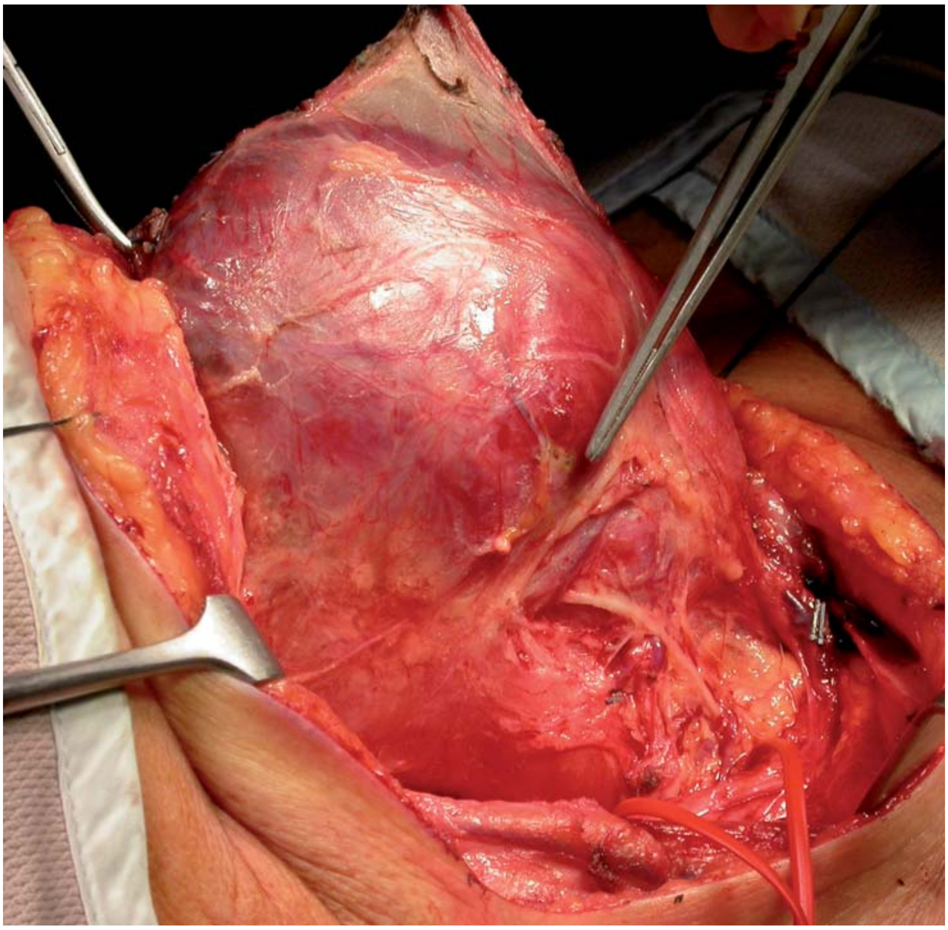


Figure 12. Identification of the RLN inferiorly at the level of Beahr's Triangle.

4.12.1.5 Neuromonitoring

A nerve stimulator hand held locator (Medtronic ®) was used up to 2012 and then a nerve stimulator (NIM III Medtronic ®) from 2012 to 2016.

4.12.1.6 Management of the Parathyroid Glands

In surgery for large MNG the parathyroid glands may be displaced due to the aberrant growth of the thyroid gland. In order to minimise the risk of hypocalcaemia the following surgical principles were adopted; the superior pole of the thyroid gland was first systematically dissected and its contour was followed down to the position of the superior parathyroid gland. Dissection was performed close to the capsule or pseudocapsule to avoid unintentional removal of the glands. The thyroid gland was inspected before its final removal to ensure that there were no parathyroid glands in the main specimen. In the event of an inadvertent removal, part of the gland was sent for frozen section, cut in small fragments and autotransplanted in the ipsilateral sternocleidomastoid muscle pocket which was then marked with ligaclips ®. All total or completion thyroidectomies for ITGs were treated as high risk in our protocol and therefore given calcium as well as 1 alfa calcidol as prophylaxis as indicated.

4.12.1.7 Management of Berry's Ligament

Once the dissection reached the Berry's ligament, minimal traction was applied when holding the thyroid lobe to avoid traction injury to the nerve. The ligament was dissected from the nerve with fine instruments, usually with judicious usage of bipolar diathermy and fine scalpel dissection [46].

4.12.2 Extra-Cervical Approaches

4.12.2.1 Combined cervical and midline sternotomy approach

This approach was composed of 3 main stages:

1. Cervical stage
2. Sternotomy and Mediastinal stage
3. Thoracic inlet stage

Cervical Stage

A standard Kocher incision was made. Subplatysmal flaps were elevated and then the dissection proceeded as described in the cervical approach.

Sternotomy and Mediastinal dissection

The chest was completely exposed and prepared from neck to umbilicus and areola mammae to areola mammae. A midline incision was made from the cervical wound to xiphisternum in T fashion. The subcutaneous fat was incised down to the periostieum with cautery or scalpel. At this point the midline was identified superiorly at the sternal notch, inferiorly at the xiphisternum and at a midpoint by digital palpation of the rib spaces on each side. A linear incision in the sternal periosteum from top to bottom was then made with electrocauthery precisely in the midline in preparation for the saw. The xiphisternum was cut with curved Mayo scissors and the suprasternal ligament with electrocautery. Blunt dissection with a finger sweep retrosternally was then performed at the top and bottom to visualise the path of the saw and prepare a space for its path. The anaesthetist was instructed to stop ventilation while the sternum was split with the saw. Once the sternotomy was completed, ventilation was resumed and the bleeding from the periosteal edges controlled with electrocautery and the Holmes-Sellars retractor places to expose the mediastinum. The mediastinum was inspected to identify and clarify the extent and location of the goitre. The brachiocephalic or innominate vessels were identified and controlled with soft rubber vascular slings if necessary. Care was taken to minimize unnecessary pleural or pericardial breach especially if malignancy was suspected. In these cases it is preferred to start the dissection as caudally as possible to clear out mediastinal fat containing lymph nodes. Once the goitre was identified and the mediastinal vessels controlled, the dissection was commenced in the extracapsular plane anteriorly to inferiorly ligating any extracapsular vessels that were encountered. The dissection proceeded posteriorly and laterally delivering the specimen in an upward direction until the thoracic inlet was reached. At this point, the cavity was inspected for haemostasis and to ensure that no mediastinal structures were inadvertently injured [(49)].

Figure 13. Clinical photograph demonstrating the T cervicothoracic incision and the subplatysmal flaps in the neck.

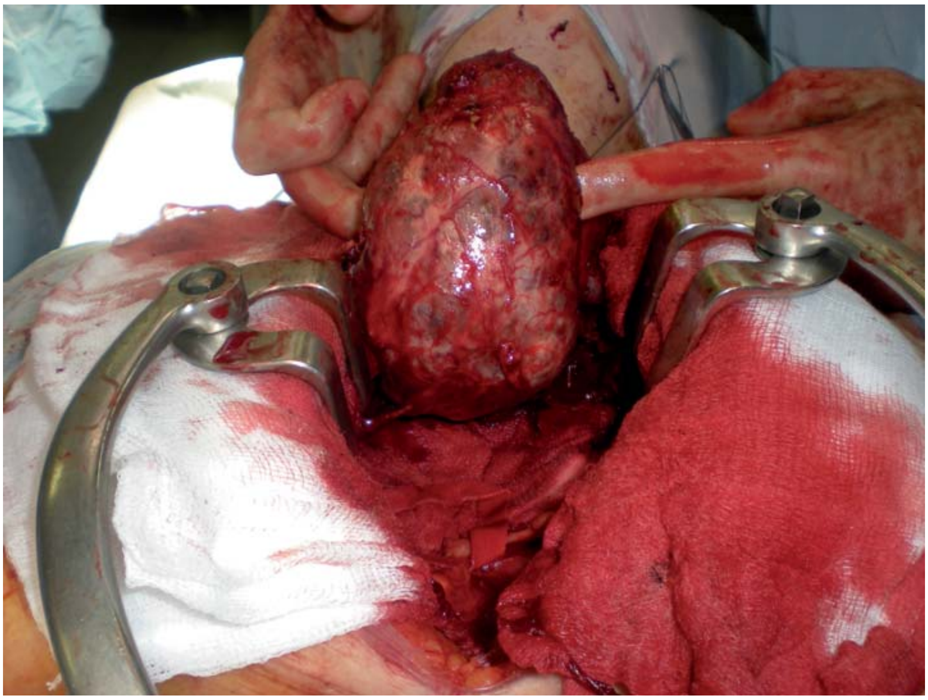


Figure 14. Mobilization of the goitre inferiorly from its mediastinal bed.

Thoracic Inlet stage

Once the thyroid gland had been mobilized superiorly and inferiorly, then the dissection was commenced to mobilize the gland at the thoracic inlet. This is the narrowest part of the dissection and by doing this at the end, allowed an easier mobilisation of the gland. This also allowed better visualisation of the RLN, which was carefully dissected from the remaining thyroid gland [49].

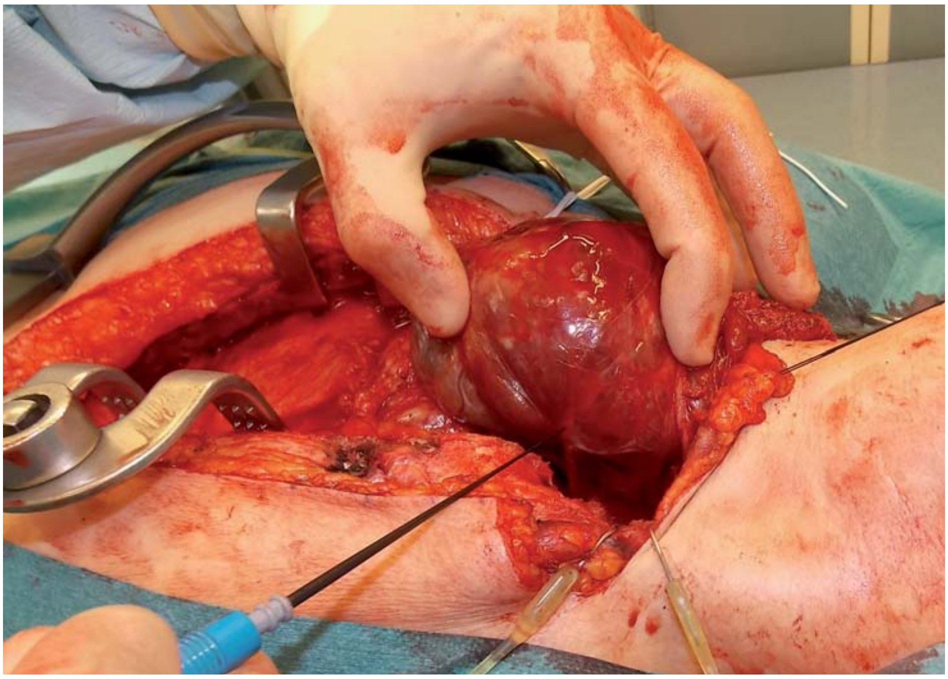


Figure 15. Mobilsation of the thyroid gland at the level of the thoracic inlet with the exposure of the RLN being checked with the IONM probe.

4.12.2.2 Combined cervical and lateral thoracotomy approach

This approach was indicated when the goitre had grown into the posterior mediastinum and reached the posterior pleura. In these cases it was considered that a midline sternotomy would not offer enough space to dissect the goitre from its posterior position. This approach was performed in 2 main stages:

1. Cervical Stage
2. Thoracotomy and intrathoracic and mediastinal stage

Cervical Stage

The cervical stage followed the same approach as described above. The thyroid lobe was dissected from its cervical attachments (oesophagus and trachea) into the thoracic inlet as much as possible and it was free from the upper mediastinal attachments. At this point the cervical portion of the thyroid lobe was amputated using Harmonic Scalpel and the tissue between the recurrent nerve and the intrathoracic portion of the goitre was packed with 2 or 3 layers of Surgicel Fibrillar ® absorbable haemostat. This was done to facilitate the identification of the RLN and protect it during the final stages of the thoracotomy approach.

Thoracotomy and Posterior Mediastinal Dissection Stage

The patient was repositioned laterally, but rolled back to allow access to the anterior neck simultaneously with the thoracotomy as needed. A high posterolateral thoracotomy was made, usually through the right chest, as from the left, the aortic arch and its branches impede access. The latisimus dorsi muscle was divided, the serratus anterior muscle preserved, and the chest entered through the 4th intercostal space. It was usually necessary to separate the goitre from the superior vena cava anteriorly and from the trachea, taking care not to injure the phrenic nerve. Special care was taken not to injure the right RLN as it recurs around the great vessels at the thoracic inlet. By dividing Sibson's fascia, it was possible to join the thoracic inlet with the cervical planes of dissection. Lower down, the innominate vein was often stretched across the goitre and in mobilising it care was taken not to tear this, or to avulse the feeding veins from the goitre. Mobilisation of the goitre was best achieved by blunt dissection within the capsule. Any bleeding from the vascularised surface of the goitre was controlled by gauze packing during the dissection. A surface cautery device such as the aquamantys was used as a heamostatic adjunct [(49)].

4.13 POSTOPERATIVE CARE

Patients with transcervical approaches were transferred, nursed and monitored in a dedicated head and neck ward.

Patients undergoing ECA were transferred, nursed and monitored in the Intensive Care Unit for 24 hours and then transfered to a dedicated head and neck ward once stable.

Postoperative care Pathway for Thyroid Surgery is shown in annex 3.

4.14 FOLLOW-UP

All patients were followed-up as per the Unit protocol and were seen in out-patients at 2 weeks from surgical discharge. During the consultation patients underwent:

1. Questioning about well-being and any symptoms occurred following discharge.
2. Inspection of the neck.
3. Fibreoptic Laryngoscopy for vocal cord assessment.
4. Analysis of FBC, TFT in all patients and bone profile and PTH in patients who underwent total thyroidectomy.

Patients were then followed up at 3 months and then discharged if there were no clinical concerns. If there were any clinical concerns, then further follow-up was arranged accordingly.

4.15 STATISTICAL ANALYSIS

Categorical data are presented with raw values and percentages. The mean value and 95% confidence interval is shown for normally distributed continuous data, whereas the median and range values for not normally distributed continuous variables. Presence of association between categorical data was assessed using the Pearson Chi-Square Test. When more than 20% of the cross-tabulation cells have an expected frequency of less than 5, the Fisher's Exact test was used instead to assess association between categorical variables. Continuous data were analysed following assessment of normality of distribution using the

Kolmogorov-Smirnov test. For normally distributed data, the t-test was used to assess association. For not normally distributed data the Mann-Whitney non-parametric test was applied for comparisons between two groups.

Multivariate logistic regression analysis was performed to assess for presence of statistically significant variables when the dependent variable is binary. The estimate statistics, standard errors, p-values and odds ratios with 95% confidence intervals were computed for the final selected model. The backward elimination process was used to exclude non-significant variables. Presence of multicollinearity was tested using the variance inflation factor (VIF) and tolerance (TOL) statistic. The Hosmer and Lemeshow goodness-of-fit test and the c-statistic were computed to assess the suitability and predictive power of the model.

Sensitivity, Specificity, negative and positive predictive values were calculated using standard methodology.

To assess for differences in the sensitivity and specificity of a test for two different groups of patients the two-sample tests for binomial proportions was used (Chi-square/Fisher's exact as appropriate) and exact 95% confidence intervals for the tests were calculated.

The statistical analysis was performed using the programmes SPSS 20 ® and SAS 9.3®.

5

RESULTS

5.1 RESULTS

Two hundred and thirty seven consecutive patients underwent excision of an ITG between August 2004 and August 2016. There were 171 (72.1%) females and 66 (27.8%) males. The age ranged from 16 to 87 years with a median of 59 years of age and a mean of 59.1 years of age.

5.2 THYROID STATUS

Two hundred and thirteen patients were euthyroid, 4 patients were hypothyroid and 20 had a history of hyperthyroidism. All patients with hyperthyroidism had their thyroid status optimised before the surgery (Figure 16).

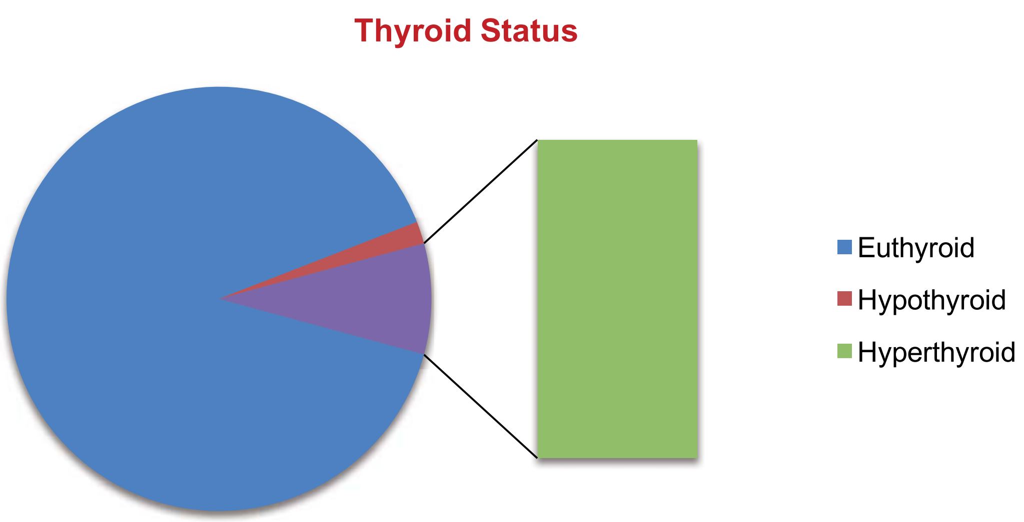


Figure 16. Distribution of the thyroid status of patients.

5.3 SURGICAL INDICATIONS AND EXTENT OF SURGICAL PROCEDURE

The main indication for surgery was compressive symptoms in 232 patients, followed by the biopsy result in 5 patients and thyrotoxicosis in 3 patients.

Four patients required surgery due to acute airway obstruction, 2 due to subacute airway obstruction and 233 had long-standing chronic progressive symptoms of compression. Five patients presented with Obstructive Sleep Apnoea Syndrome (OSAS).

Twenty-four (10.1%) patients reported voice changes before surgery. Ten of these patients (0.4%) had a pre-operative vocal cord palsy on the side of the goitre.

5.4 PREOPERATIVE CYTOLOGICAL ANALYSIS

Preoperative cytological analysis included 9 patients with Thy 1 results, 208 with Thy 2 results, 19 with Thy 3 results and 1 with Thy 4 results (Figure 17).

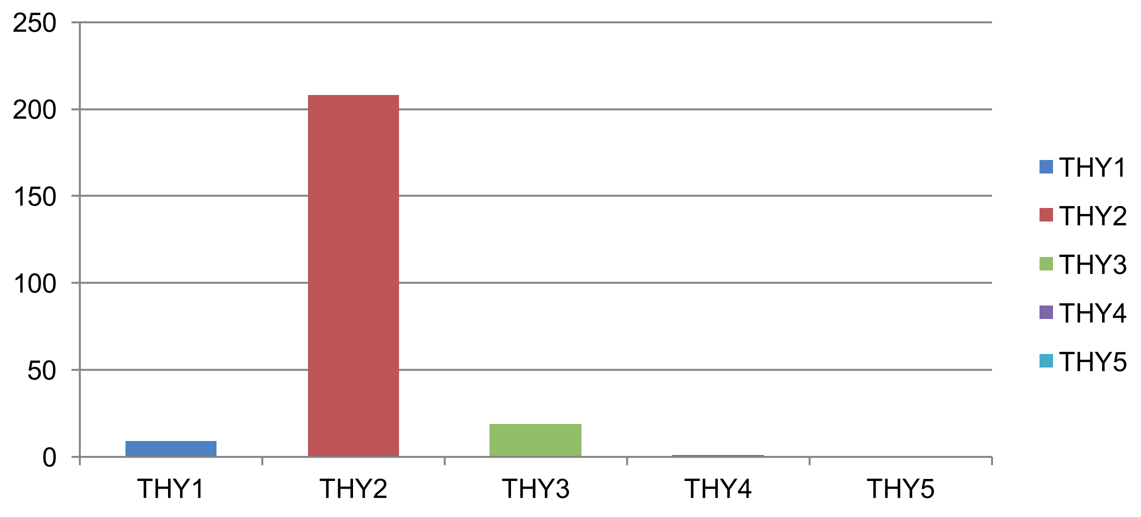


Figure 17. Distribution of the preoperative cytological analysis.

5.5 GOITRE WEIGHT

Goitre weight ranged from a minimum of 20 grams to a maximum of 1200 grams with the median of 153 grams and a mean of 183.8 grams. The distribution of the goitre weights is shown in Figure 18.

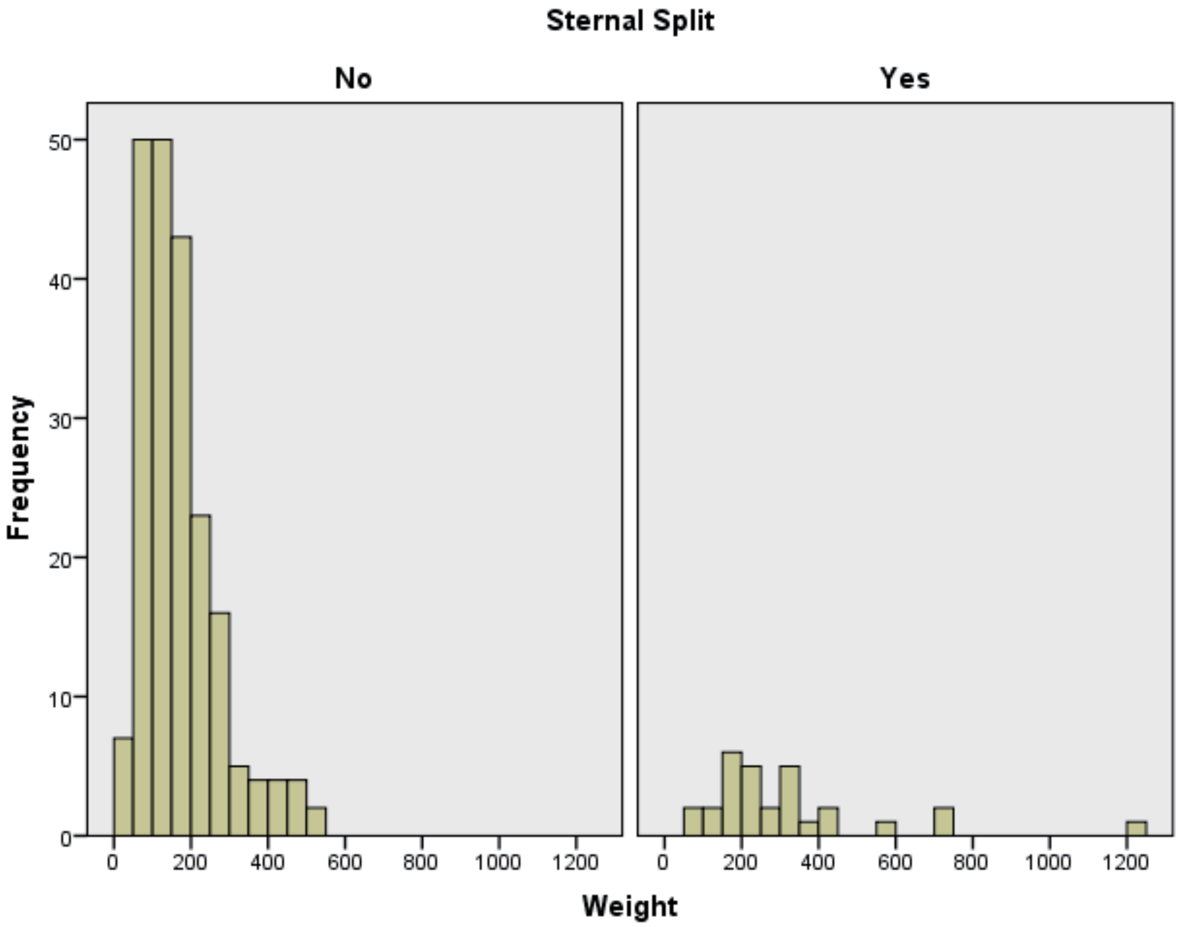


Figure 18. Distribution of the goitre weight in both study subgroups.

5.6 HISTOPATHOLOGY

The primary histopathological diagnosis was multinodular colloid goitre in 235 patients, medullary thyroid cancer in 1 patient and a giant adenoma in another one. Additional secondary diagnosis included 18 papillary thyroid cancers, Graves disease and thyroiditis. An example of an incidental papillary thyroid carcinoma is shown in Figure 19.

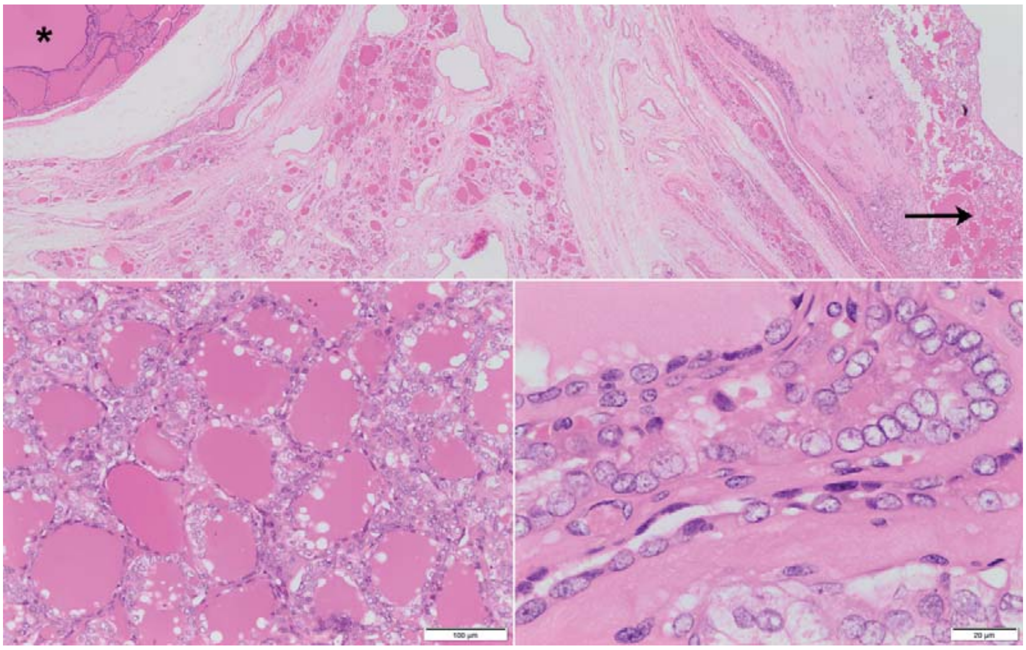


Figure 19. Representative photomicrographs of incidental thyroid papillary carcinoma in multinodular goitre. Top panel: whole mount view of the section. Arrow indicates thyroid papillary carcinoma. Asterisk indicates a hyperplastic nodule. Lower left panel: medium power view demonstrating a predominantly microfollicular architecture. Lower right panel: high power view demonstrating typical nuclear features of optical clearing, grooving and overlapping.

5.7 RATE OF MALIGNANCY

The number of patients with malignancy was 19 patients making a rate of 8.01% patients with thyroid cancer identified.

Twelve patients had benign preoperative benign cytology results and had unexpected occult malignancy in the histopathological analysis resulting in a rate of 5.0%. There was no statistical significance regarding the rate of malignancy in the two study groups (Table 4 and 5). USS guided FNAC when Thy1 are included, had a sensitivity of 31.6% (6/19), the specificity of 93.6% (204/218), positive predicted value of 30% (6/20) and negative predicted value of 94% (204/217) to indicate malignancy within the ITG.

Table 4. Contingency table demonstrating no statistical difference regarding rate of malignancy by sternotomy approach. Fisher's exact test, p=0.065.

Cancer * Sternotomy approach

		Sternal split		Total
		No	Yes	
Cancer	No	194	24	218
	Yes	14	5	19
Total		208	29	237

Table 5. Contingency table demonstrating no statistical difference regarding rate of malignancy having excluded all Thy 1 results. Fisher's exact test, p=0.051.

		Sternal split		Total
		No	Yes	
Occult cancer	No	191	25	216
	Yes	8	4	12
Total		199	29	**228**

One patient had medullary thyroid cancer, 6 patients had papillary thyroid cancer one of them with tall cell features and 10 patients had papillary microcarcionomas. Only one patient with micropapillary thyroid cancer required a completion thyroidectomy as the contralateral lobe grew causing compression symptoms. A further micropapillary thyroid cancer foci was identified in the contralateral lobe. The characteristics of this subgroup of patients are shown in Table 6.

Table 6. Characteristics of patients with ITG diagnosed with thyroid cancer.

N	Age	Gender	Goitre Type	Thy	Histology	TNM	Initial Surgery	Completion Surgery	RIA / PORT	Current Status
1	34	M	RC	4	PTC	T3N1a	TL	Yes	Yes	NED
2	36	F	RC	3	PTC	T3N0	TL	Yes	Yes	NED
3	68	F	UBAA	2	PTC	T3N0	L	Yes	Yes	NED
4	72	F	BAA	2	PTC	T1aN0	L	No	No	NED
5	53	F	UBAA	2	PTC	T1aN0	L	Yes	Yes	NED
6	55	M	UBAA	2	PTC	T1aN0	TT	N/A	No	NED
7	71	F	UBAA	2	PTC	T1aN0	L	No	No	NED
8	57	F	RC	3	PTC	T1aN0	TT	N/A	No	NED
9	67	F	BAA	2	PTC	T1aN0	T	No	No	NED
10	64	F	BAA	3f	PTC	T1aN0	L	No	No	NED
11	42	M	AA	2	PTC	T1aN0	L	No	No	NED
12	77	F	RC	2	PTC	T2N0	TT	N/A	No	NED
13	55	M	RC	1c	PTC	T1aN0	L	No	No	NED
14	58	F	BAA	2	PTC	T3N1a	TT	N/A	Yes	NED
15	45	F	RC	3f	PTC	T1aN0	TT	N/A	No	NED
16	76	F	UBAA	2	PTC	T1bN0	L	Yes	Yes	NED
17	40	M	BAA	2	PTC	T3N0	L	Yes	Yes	NED
18	71	F	UBAA	2	PTC	T2N0	L	Yes	Yes	NED
19	56	F	BAA	3	MTC	T3N0	TT	N/A	Yes	NED

The preoperative cytological results of the patients diagnosed with thyroid are demonstrated in Figure 20.

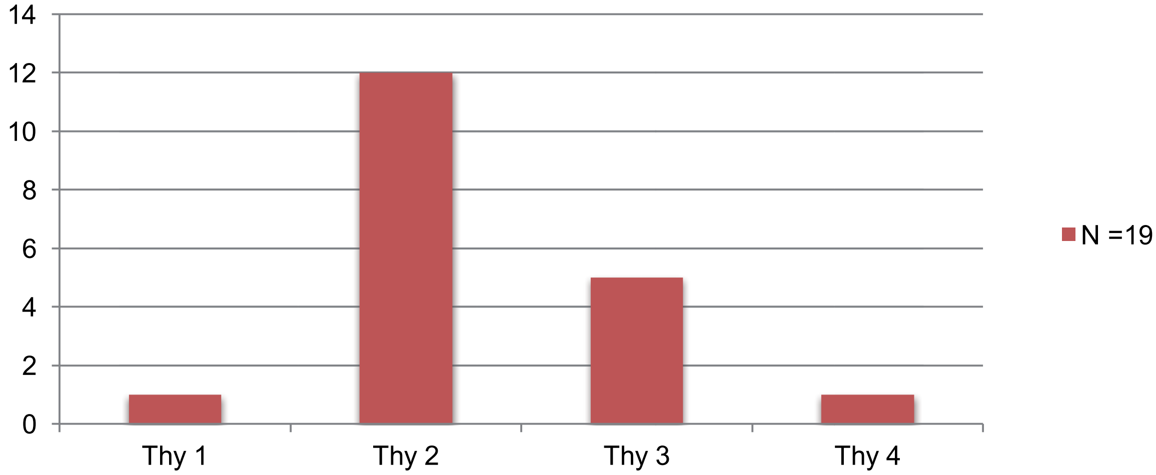


Figure 20. Cytological results of patients diagnosed with thyroid cancer.

5.8 CT SCAN FEATURES

Sixty-seven patients had goitres extending to the retroclavicular region, 97 up to the level of the aortic arch and 73 below the level of the aortic arch. The distribution is shown in Figure 21.

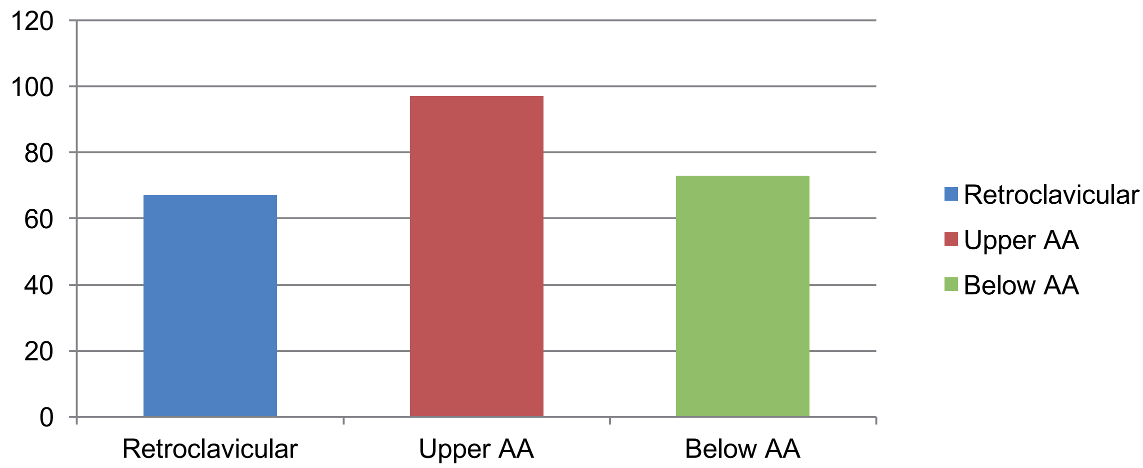


Figure 21. Distribution of the patients by intrathoracic extension.

One hundred and eighty-two patients had goitres with an oval shape, 36 with a tubular shape and 19 patients had goitres with an iceberg shape. The distribution of the different goitre shapes is shown in Figure 22.

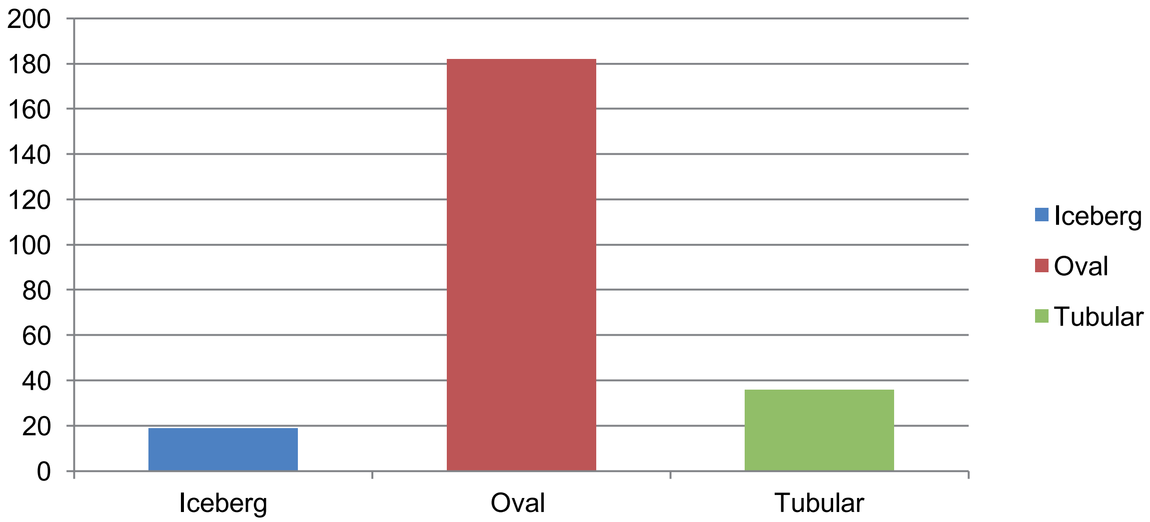


Figure 22. Distribution of the goitres by anatomical shape.

Further anatomical characteristics included, extension to the posterior mediastinum including retropharyngeal, retrotracheal and retroesophageal, multiple components and goitre crossing to the contralateral side.

5.9 SURGERY

5.9.1 Extent of surgery

Eighty-three patients (35%) underwent a total thyroidectomy and 154 (65%) a lobectomy. Of these 66 were right lobectomies and 88 left lobectomies. There were no subtotal thyroidectomies or near-total thyroidectomies. The distribution of the extent of the surgical procedures is shown in Figure 23.

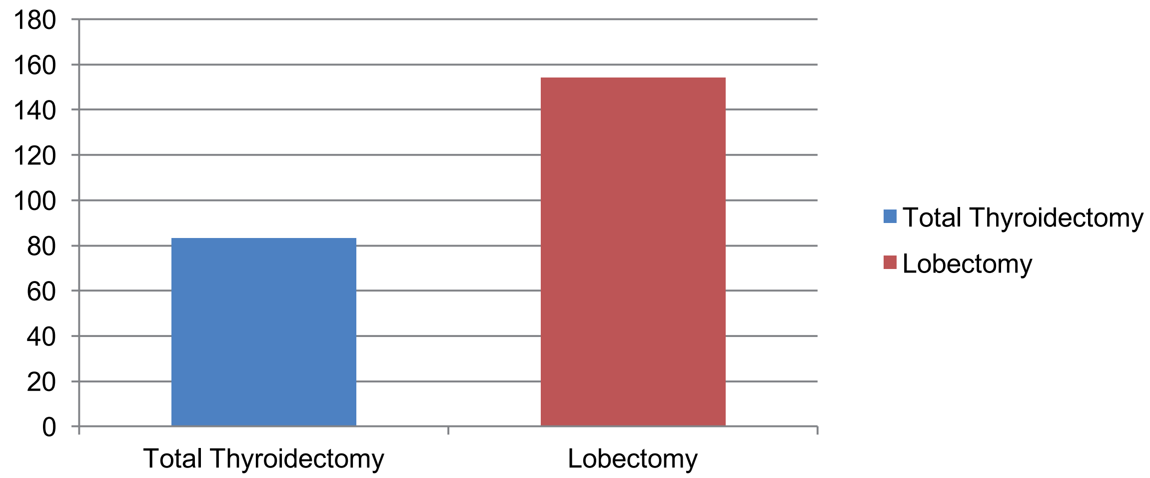


Figure 23. Distribution of the extent of the surgical procedures.

5.9.2 Surgical approach

Transcervical approach: Two hundred and eight (87.7%) patients had their goitre excised via a transcervical approach.

Extracervical approach: Twenty-nine (12.3%) patients required extracervical approaches. Twenty-seven patients underwent a combined transcervical and a midline sternotomy approach and 2 patients a combined transcervical and a right thoracotomy approach (Figure 24).

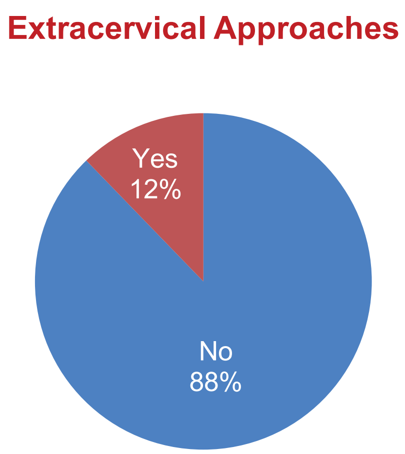


Figure 24. Distribution of the extracervical approaches.

5.10 RISK OF STERNOTOMY

The risk of sternotomy was 12.2%. In univariate analysis, the patients who had higher risk of sternotomy were patients in whom the goitre was below the aortic arch (p<0.001), patients with “iceberg” shape (p<0.001) and patients who underwent reoperation (p <0.001). All factors are shown in Tables 7 and 8.

Table 7. Contingency table of the univariate analysis excluding cancer of variables assessing the risk of sternotomy.

Non-malignant cases		Sternal split: yes N=24	Sternal split: no N=194	P value
Age	**Mean**	62.8	58.9	0.198 [a]
	(95% CI)	58.4 – 67.3	(56.9 – 60.9)	
Gender	**Male**	10	49	0.088 [b]
	Female	14	145	
Indication	**Compressive**	24	188	1 [c]
	Biopsy	0	3	
	Thyrotoxicosis	0	3	
OSAS	**Yes**	0	5	1 [c]
	No	24	189	
Onset	**Acute**	0	4	1 [c]
	Subacute	0	1	
	Chronic	24	189	
Thyroid status	**Euthyroid**	21	173	1 [c]
	Hyperthyroid	3	17	
	Hypothyroid	0	4	
FNAc	**Thy1**	0	8	0.436
	Thy2	24	172	
	Thy3	0	14	
	Thy 4	-	-	
BAETS	**Upper border AA**	2 (8.3%) *	86 (44.3%) **	<0.001 [b]
	Below AA	22 (91.7%) *	46 (23.7%) **	
	Retroclavicular	0 *	62 (32%) **	

Non-malignant cases		Sternal split: yes N=24	Sternal split: no N=194	P value
Simo	Iceberg Tubular Oval	13 (54.2%) * 4 (16.7%) * 7 (29.2%) *	2 (1%) ** 28 (14.4%) * 164 (84.5%) **	<0.001 [c]
Re-operation	Yes No	11 (45.8%) 13 (54.2%)	18 (9.3%) 176 (90.7%)	<0.001 [c]
Pre-op voice changes	Yes No	2 22	11 183	0.614 [c]

[a] *T-test,* [b] *Chi-square,* [c] *Fisher's exact*

Table 8. Contingency table of the univariate analysis including cancer of variables assessing the risk of sternotomy.

		Sternal split: yes N=29	Sternal split: no N=208	P value
Age	Mean (95% CI)	62.9 59.1 – 66.8	58.6 (56.6 – 60.5)	0.044 [a]
Gender	Male Female	11 18	55 153	0.196 [b]
Indication s	Compressive Biopsy Thyrotoxicosi	29 0 0	200 5 3	1 [c]
OSAS	Yes No	0 29	5 203	1 [c]
Onset	Acute Subacute Chronic	0 0 29	4 2 202	1 [c]
Thyroid status	Euthyroid Hyperthyroid Hypothyroid	26 3 0	187 17 4	0.84 [c]
FNAc	Thy1 Thy2 Thy3 Thy 4	0 28 19 1	9 180 18 1	0.55 [c]

		Sternal split: yes N=29	Sternal split: no N=208	P value
Cancer	**Yes**	5	14	0.065 [c]
	No	24	94	
BAETS	**Upper border AA**	2 (6.9%) *	95 (45.7%) **	<0.0001 [b]
	Below AA	26 (89.7%) *	47 (22.6%) **	
	Retroclavicular	1 (3.4%) *	66 (66%) **	
Simo	**Iceberg**	17 (58.6%) *	2 (1%) **	<0.0001 [c]
	Tubular	5 (17.2%) *	31 (14.9%) *	
	Oval	7 (24.1%) *	175 (84.1%) **	
Re-operation	**Yes**	12 (41.4%)	18 (8.7%)	<0.0001 [c]
	No	17 (58.6%)	190 (91.3%)	
Pre-op voice changes	**Yes**	2	12	0.683 [c]
	No	27	196	

[a] T-test, [b] Chi-square, [c] Fisher's exact

This was confirmed by the multivariate analysis as shown below (Figure 9). This was done by backward elimination process. The indication, onset, preoperative voice change, age, FNAC result, thyroid status, cancer diagnosis and gender were non-significant (p-value>0.05) therefore they were excluded during the backward elimination process. The final model had a good fit for the dataset (Hosmer and Lemeshow Goodness-of-fit test, p=0.66; c-statistic 0.926) and the degree of multicollinearity between variables was low (tolerance statistic <0.4; variance inflator factor<10 for all variables included in the model).

Patients with a goitre below the AA were more than 10 times more likely to require sternotomy compared to a goitre in the upper border of the AA (odds ratio 10.8, 95% CI 2.1 – 55.5; p=0.0043). An "iceberg" shaped goitre had 59 times more chances of requiring a sternotomy compared to an oval shaped goitre, despite the small number of cases the 95% confidence interval range was large (odds ration 59.3, 95% CI 9.5 – 369.3, p< 0.0001). Patients that required a reoperation were 4.8 times more likely to have a sternotomy compared to first operation cases (odds ratio 4.83, 95% CI 1.25 – 18.6; p=0.0221).

Table 9. Contingency table of the multivariate analysis (including all cases) of the risk of sternotomy for the cohort.

Parameter	Estimate	Standard Error	P value	Odds ratio (95% CI)
Intercept	-4.4625	0.8034	<.0001	
Goitre type			0.0042	
Below AA vs Upper border AA	2.3831	0.8336	0.0043	10.84 (2.12 – 55.54)
Retroclavicular vs Upper border AA	0.0187	1.2742	0.9883	1.02 (0.08 – 12.38)
Goitre Shape	4.0825	0.9332	<0.0001	59.3
Iceberg vs Oval			<.0001	(9.52 – 369.27)
Tubular vs Oval	0.3995	0.6930	0.5643	1.49 (0.38 – 5.80)
Reoperation yes vs no	1.5753	0.6883	0.0221	4.83 (1.25 – 18.6)

Table 10. Contingency table of the multivariate analysis (excluding cancer) of the risk of sternotomy for the cohort.

Parameter		Estimate	Standard Error	P value	Odds Ratio (95% CI)
Intercept		-3.4494	0.4332	<.0001	
Goitre shape	**Iceberg vs Oval**	4.7794	0.8768	<.0001	119.03 (21.35 – 663.72)
Goitre shape	**Tubular vs Oval**	0.9348	0.6907	0.1760	2.55 (0.66 – 9.86)
Reoperation	**Yes vs No**	1.6871	0.6472	0.0091	5.40 (1.52 – 19.21)

Multivariate analysis was also repeated this time excluding the cancer cases. Again using a backward elimination process, only the statistically significant variables were included in the final model (p<0.05). Goitre shape and reoperation were statistically significant predictors of sternotomy in this group of patients. The model was a good fit for the dataset and no multicollinearity were detected (Hosmer and Lemeshow Goodness-of-Fit test p=0.98; c-stat: 0.85).

5.11 SURGICAL OUTCOMES

5.11.1 Intraoperative Blood Loss

Intraoperative blood loss ranged from 10 mls to 4000 mls with a median of 98 mls and a mean of 209.8 mls. Patients with larger volumes of blood loss were in the extracervical approaches. The blood loss was found to be not normally distributed (KS test p <0.001) therefore a t-test was not appropriate. A Mann-Whitney U test was performed instead. There was statistically significant difference between the two groups p<0.0001(Figure 25).

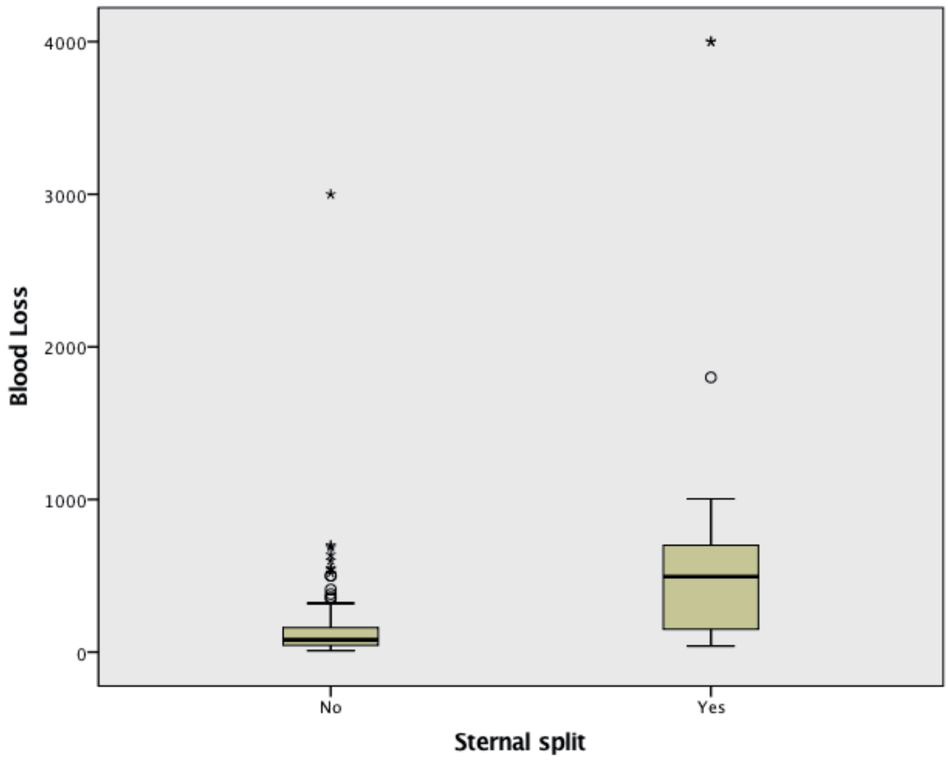


Figure 25. Distribution of the blood loss in both study subgroups.

Table 11. Contingency table demonstrating the differences between the 2 study groups regarding blood loss.

	Sternal split			Statistic
Bloodloss	No	Mean		137.66
		95% Confidence Interval for Mean	Lower Bound	105.04
			Upper Bound	170.29
		Median		80.00
		Std. Deviation		238.641
		Minimum		10
		Maximum		3000
		Range		2990
	Yes	Mean		727.83
		95% Confidence Interval for Mean	Lower Bound	355.96
			Upper Bound	1099.69
		Median		495.00
		Std. Deviation		977.614
		Minimum		40
		Maximum		4000
		Range		3960

5.11.2 Postoperative heamorrhage and return to theatre

Three patients representing 1.2% had postoperative haemorrhage that required return to theatre and evacuation of the haematoma. These three patients were in the transcervical approach group. Two patients had a history of hypertension and had an episode of postoperative peroxismal cough within 8 hours of surgery. All 3 patients underwent re-exploration of the surgical wound. There was no evidence of major vessel bleeding and a drain was reapplied. All 3 patients underwent an uneventful recovery.

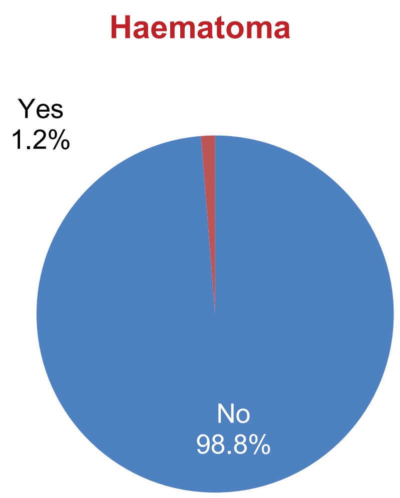


Figure 26. Distribution of the postoperative haemorrhage and the proportion of patients requiring return to theatre.

5.11.3 Wound infection

The risk of wound infection in this cohort was 0%.

5.11.4 Pre-existing Recurrent Laryngeal Palsy

Ten patients (4.2%) had pre-existing RLNP. Nine patients had RLNP and one due to previous surgery. Nine were potentially recoverable and one was not due to previous surgery. In those patients where the RLNP was due to thyroidal compression, 6 recovered the nerve function within 6 months of the procedure.

5.11.5 Recurrent Laryngeal Nerve Palsy

There were 237 thyroidectomies with 320 nerves at risk. Ten patients were excluded as indicated above resulting in a total of 227 thyroidectomies and 306 nerves at risk. The rate of temporary RLNP (of nerves at risk) was 10 out of 310 (3.22%) in all cases, Hemi-thyroidectomies: 7 out of 170 (4.12%) in hemi-thyroidectomies and in total thyroidectomies 3 out of 162 (1.85%) (Table 12).

Table 12. Crosstabulation of the presence of temporary RLNP by side of thyroidectomy.

Side thyroid * temporary RLNP Crosstabulation					
Count		Temporary RL			Total
		No	Yes	Pre-existing	
Side of thyroidectomy	Right	63	3	0	66
	Left	78	4	6	88
	Total	76	3	4	83
Total		217	10	10	237

Temporary RLN Injury: Ten patients sustained a temporary RLN injury or neuropraxia making a rate of 3.2% of nerves at risk. In this group 4 patients had the goitre in a posterior position in relationship to the RLN (Riding RLN). Patients undergoing an ECA were at higher risk of both temporary and persistent RLNP (p=0.003 and p=0.013). With regards to temporary RLNP, the "Iceberg" shape (p=0.006), tracheostomy (p=0.002) and high intraoperative blood loss (p=0.031) had a higher risk. With regards to persistant RLNP, patients with "Iceberg" shape (p=0.006), reoperation (p=0.013), sternal split (p=0.013), did not have IONM (p =0.023) and had a tracheostomy (p=0.043) were at higher risk. Patients with pre-existing palsies were excluded from this analysis (Tables 13, 14 and 15).

Table 13. Contingency table of the Recurrent Laryngeal Nerve Temporary and Permanent palsies in both study groups.

		Sternal split		P value
		No	Yes	
Temporary RLNP	No	195 (97.5%)	22 (81.5%)	0.003 [a]
	Yes	5 (2.5%)	5 (18.5%)	
Persistent RLNP	No	199 (99%)	24 (88.9%)	0.013 [a]
	Yes	2 (2%)	3 (11.1%)	

[a] *Fisher's exact*

Table 14. Table demonstrating Univariate Analysis of Temporary RLNP demonstrating the variables, which are statistically significant.

1. Temporary RLNP

(Pre-existing palsies excluded)		Temporary palsy: yes N=10	Temporary palsy: no N=217	P value
Age	**Mean**	58.6	58.8	0.952 [a]
	(95% CI)	49.9 – 67.3	(56.9 – 60.7)	
Gender	**Male**	5	59	0.150 [c]
	Female	5	158	
Indication	**Compressive**	10	209	1 [c]
	Biopsy	0	5	
	Thyrotoxicosis	0	3	
OSAS	**Yes**	0	5	1 [c]
	No	10	212	
Onset	**Acute**	0	2	1 [c]
	Subacute	0	2	
	Chronic	10	213	
Thyroid status	**Euthyroid**	9	195	0.664 [c]
	Hyperthyroid	1	18	
	Hypothyroid	0	4	
FNAc	**Thy1**	0	9	1 [c]
	Thy2	9	189	
	Thy3	1	18	
	Thy 4	0	1	
Cancer	**Yes**	2	16	0.183 [c]
	No	8	201	
BAETS	**Upper border AA**	3	89	0.138 [c]
	Below AA	6	63	
	Retroclavicular	1	65	
Simo	**Iceberg**	4 (40%) *	14 (6.5%) **	0.006 [c]
	Tubular	1 (10%) *	33 915.2%) *	
	Oval	5 (50%) *	170 (78.3%) **	
Re-operation	**Yes**	3	24	0.102 [c]
	No	7	193	

(Pre-existing palsies excluded)		Temporary palsy: yes N=10	Temporary palsy: no N=217	P value
Sternal split	**Yes**	5 (50%)	22 (10.1%)	0.003 [c]
	No	5 (50%)	195 (89.9%)	
Preop voice changes	**Yes**	1	3	0.166 [c]
	No	9	214	
Monitor	**NIM**	4	116	0.522 [c]
	Stimulator	6	101	
IONM	**Yes**	4	116	0.522 [c]
	No	6	101	
Tracheostomy	**Yes**	2	0	0.002 [c]
	No	8	217	
Side thyroid	**Right**	3	63	1 [c]
	Left	4	78	
	Total	3	76	
Bloodloss	**Median (IQR)**	292.5 (487)	90 (150)	0.031 [d]
Weight	**Median (IQR)**	214 (224)	150 (124)	0.118 [d]

[a] *T-test,* [b] *Chi-square,* [c] *Fisher's exact,* [d] *Mann-Whitney*

Table 15. Table demonstrating Univariate Analysis of Persistent RLNP demonstrating the variables, which are statistically significant.

2. Persistent RLNP

(Pre-existing palsies excluded)		Persistent palsy: yes N=4	Persistent palsy: No/resolved N=224	P value
Age	**Mean (95% CI)**	62.8 52.4 – 73	58.8 (56.9 – 60.6)	0.570 [a]
Gender	**Male**	1	63	0.684 [c]
	Female	3	160	
Indication	**Compressive**	4	215	1 [c]
	Biopsy	0	5	
	Thyrotoxicosis	0	3	

(Pre-existing palsies excluded)		Persistent palsy: yes N=4	Persistent palsy: No/resolved N=224	P value
OSAS	**Yes**	0	5	0.914 c
	No	4	218	
Onset	**Acute**	0	2	1 c
	Subacute	0	2	
	Chronic	4	219	
Thyroid status	**Euthyroid**	4	200	1 c
	Hyperthyroid	0	19	
	Hypothyroid	0	4	
FNAc	**Thy1**	0	9	0.423 c
	Thy2	3	195	
	Thy3	1	18	
	Thy 4	0	1	
Cancer	**Yes**	2	16	0.032 c
	No	2	207	
BAETS	**Upper border AA**	1	91	0.004 c
	Below AA	3	66	
	Retroclavicular	0	66	
Simo	**Iceberg**	3 (75%) *	15 (6.7%) **	0.004 c
	Tubular	0 (0%) *	34 (15.2%) *	
	Oval	1 (40%) *	174 (78%) **	
Reoperation	**Yes**	3 (75%)	24 (10.8%)	0.006 c
	No	1 (25%)	199 (89.2%)	
Sternal split	**Yes**	3 (75%)	24 (10.8%)	0.006 c
	No	1 (25%)	199 (89.2%)	
Preop voice changes	**Yes**	1	3	0.069 c
	No	3	220	
Monitor	**NIM**	0	120	0.048 c
	Stimulator	4	103	
IONM	**Yes**	0	120	0.048 c
	No	4	103	
Tracheostomy	**Yes**	0	0	-
	No	4	223	
Side thyroid	**Right**	1	65	0.839 c
	Left	1	81	
	Total	2	77	

(Pre-existing palsies excluded)		Persistent palsy: yes N=4	Persistent palsy: No/resolved N=224	P value
Bloodloss	**Median (IQR)**	600 3078	92 (150)	0.079 [d]
Weight	**Median (IQR)**	275 (381)	151 (125)	0.167 [d]

[a] *T-test,* [b] *Chi-square,* [c] *Fisher's exact,* [d] *Mann-Whitney*

Table 16. Multivariate analysis was also attempted to identify independent predictors of temporary and persistent RLNP. Nevertheless, the generalisability of the findings is limited because of the small number of events. Backward elimination process was used with only the statistically significant variables included in the final models. No multicollinearity problems were detected (VIF<10, TOL <0.4) but both models were not a good fit for the dataset (Hosmer and Lemeshow Goodness-of-Fit p, value <0.05). That is likely to be because of the small number of events.

1. Temporary (n=10)

Parameter	Estimate	Standard Error	P value	Odds ratio (95% CI)
Intercept	-3.8712	0.5052	<.0001	
Pre voice change (yes vs no)	2.7726	1.2604	0.0278	16 (1.35 – 189.21)
Sternal split (yes vs no)	2.3896	0.7076	0.0007	10.9 (2.73 – 43.66)

2. Persistent(n=4)

Parameter	Estimate	Standard Error	Pr > ChiSq	Odds Ratio (95% CI)
Intercept	-5.2933	1.0025	<.0001	
Reoperation (yes vs no)	3.2139	1.1747	0.0062	24.88 (2.49 – 248.7)

5.11.5.1 Persistent RLN Injury

The risk of persistent RLNP in the whole cohort (excluding pre-existing RLNP) was 2.1% (5/233). The rate of persistent RLNP rate (nerves at risk) was 1.27% (4/316), 1.32%(2/151) in hemithyroidectomies and 1.21% (2/165) in total thyroidectomies.

Table 17. Crosstabulation of the risk of persistent recurrent laryngeal nerve palsy by side.

Side thyroid * persistent RLNP Crosstabulation						
Count		Persistent RL				Total
		No	Yes	Pre-existing	Resolved	
Side thyroid	Right	65	1	0	0	66
	Left	81	1	3	3	88
	Total	77	2	1	3	83
Total		223	4	4	6	237

But 4 pre-existing persistent palsies = 316 nerves at risk for persistent RLNP.

5.11.6 Intraoperative Neuromonitoring (IONM)

Intraoperative Neuromonitoring was used in 120 patients as opposed to 103 who only had a nerve locator or stimulator. There were no statistically significant differences regarding the rate of temporary RLNP (p=0.522) but the use of IONM had an impact in preventing permanent RLNP (p=0.048) (Figures 14, 15, 16 and 17).

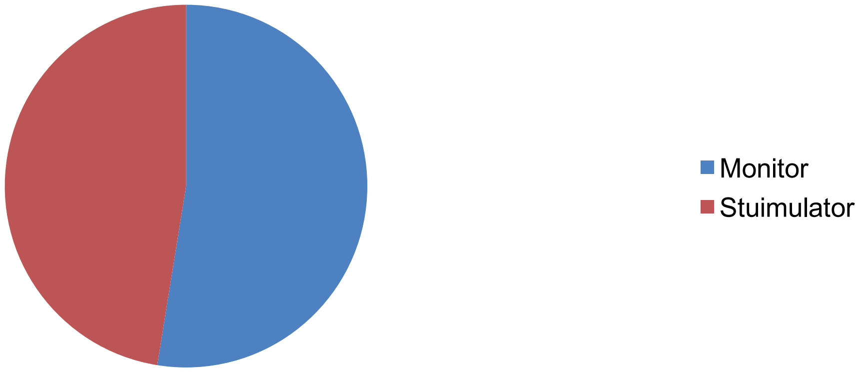


Figure 27. Distribution of patients who underwent thyroidectomy with nerve stimulator and with nerve monitor.

5.11.7 Hypoparathyroidism

5.11.7.1 Permanent Hypoparathyroidism

Of the 83 patients undergoing total thyroidectomy, 5 patients developed permanent hypoparathyroidism making a rate of 6.02%. On univariate analysis, the extent of intrathoracic extension, shape, sternal split, tracheostomy, intraoperative blood loss, weight of the goitre, and RLNP, have an influence of the development of permanent hypoparathyroidism.

Figure 28. Univariate analysis for the whole cohort demonstrating the statistically significant factors for permanent hypocalcaemia.

		Permanent hypoCa: yes N=5	Permanent hypoCa: No/resolved N=223	P value
Age	**Mean**	63.4	58.4	0.482 [a]
	(95% CI)	49.7 – 77.1	(54.9 – 61.9)	
Gender	**Male**	1	15	1 [c]
	Female	4	63	
Indication	**Compressive**	5	73	1 [c]
	Biopsy	0	3	
	Thyrotoxicosis	0	2	

		Permanent hypoCa: yes N=5	Permanent hypoCa: No/resolved N=223	P value
OSAS	Yes	0	4	1 [c]
	No	5	74	
Onset	Acute	1	1	0.118 [c]
	Subacute	0	0	
	Chronic	4	77	
Thyroid status	Euthyroid	4	62	1 [c]
	Hyperthyroid	1	13	
	Hypothyroid	0	3	
FNAc	Thy1	0	2	0.583 [c]
	Thy2	4	66	
	Thy3	1	10	
	Thy 4	0	0	
Cancer	Yes	1	5	0.320 [c]
	No	4	73	
BAETS	Upper border AA	1 *	31*	0.027 [c]
	Below AA	4 **	18 *	
	Retroclavicular	0 *	29 *	
Simo	Iceberg	3 *	5 *	0.003 [c]
	Tubular	0 **	10 *	
	Oval	0 **	63 *	
Reoperation	Yes	2	6	0.071 [c]
	No	3	72	
Sternal split	Yes	4	9	0.002 [c]
	No	1	69	
Preop voice changes	Yes	2	4	0.040 [c]
	No	3	74	
Monitor	NIM	1	33	0.644 [c]
	Stimulator	4	45	
IONM	Yes	4	33	0.644 [c]
	No	1	45	
Preop tracheostomy	Yes	1	78	0.060 [c]
	No	4	0	
Tracheostomy	Yes	2	1	0.009 [c]
	No	3	77	

		Permanent hypoCa: yes N=5	Permanent hypoCa: No/resolved N=223	P value
Bloodloss	**Median (IQR)**	400 (373)	142.5 (223)	0.022 [d]
Weight	**Median (IQR)**	380 (227)	212 (139)	0.016 [d]
Heamatoma	**Yes**	0	1	1 [c]
	no	5	77	
Tracheomalacia	**Yes**	1	1	0.118 [c]
	No	4	77	
Temporary RLNP	**Yes**	3 *	0 **	<0.0001 [c]
	No	0 *	76 **	
	Pre-existing	2 *	2 **	
Persistent RLNP	**Yes**	2*	0 **	<0.0001 [c]
	No	1 *	76 **	
	Pre-existing	1 *	0 **	
	Resolved	1 *	2 **	

[a] *T-test,* [b] *Chi-square,* [c] *Fisher's exact,* [d] *Mann-Whitney*

5.11.7.2 Multivariate analysis (number of events = 5/83)

Table 18. Multivariate analysis was also attempted to identify independent predictors of permanent hypocalcaemia. Once again the number of events were too small to allow generalisability of the findings. Backward elimination process was used with only the statistically significant variables included in the final model($p<0.05$). No multicollinearity problems were detected (VIF<10, TOL <0.4) but the model is not a good fit for the dataset (Hosmer and Lemeshow Goodness-of-Fit p, value <0.05). As a rule of thumb 1 variable should be included in a multivariate model for every 10 events. This condition is not met in our analysis which limits the value of multivariate statistical modelling to analyse this outcome.

Parameter		Estimate	Standard Error	P value	Odds Ration (95% CI)
Intercept		-4.6330	1.1314	<.0001	
Tracheostomy	**Yes vs No**	4.1126	1.4349	0.0042	**61.1 (3.67 - >999.999)**
Bloodloss		0.00416	0.00210	0.0475	1.004 (1 – 1.008)

Table 19. Table showing univariate analysis for the total thyroidectomy cohort demonstrating the statistically significant factors for persistent hypocalcaemia.

		Permanent hypoCa: yes N=5	Permanent hypoCa: No/resolved N=78	P value
Age	**Mean**	63.4	58.4	0.482 [a]
	(95% CI)	49.7 – 77.1	(54.9 – 61.9)	
Gender	**Male**	1	15	1 [c]
	Female	4	63	
Indications	**Compressive**	5	73	1 [c]
	Biopsy	0	3	
	Thyrotoxicosi	0	2	
OSAS	**Yes**	0	4	1 [c]
	No	5	74	
Onset	**Acute**	1	1	0.118 [c]
	Subacute	0	0	
	Chronic	4	77	
Thyroid status	**Euthyroid**	4	62	1 [c]
	Hyperthyroid	1	13	
	Hypothyroid	0	3	
FNAc	**Thy1**	0	2	0.583 [c]
	Thy2	4	66	
	Thy3	1	10	
	Thy 4	0	0	
Cancer	**Yes**	1	5	0.320 [c]
	No	4	73	
BAETS	**Upper border AA**	1*	31*	0.027 [c]
	Below AA	4 **	18 *	
	Retroclavicular	0 *	29 *	
Simo	**Iceberg**	1. *	5 *	0.003 [c]
	Tubular	2. **	10 *	
	Oval	0**	63 *	
Reoperation	**Yes**	2	6	0.071 [c]
	No	3	72	
Sternal split	**Yes**	4	9	0.002 [c]
	No	1	69	

		Permanent hypoCa: yes N=5	Permanent hypoCa: No/resolved N=78	P value
Preop voice changes	Yes No	2 3	4 74	0.040 [c]
Monitor	NIM Stimulator	1 4	33 45	0.644 [c]
IONM	Yes No	4 1	33 45	0.644 [c]
Preop tracheostomy	Yes No	1 4	78 0	0.060 [c]
Tracheostomy	Yes No	2 3	1 77	0.009 [c]
Bloodloss	Median (IQR)	400 (373)	142.5 (223)	0.022 [d]
Weight	Median (IQR)	380 (227)	212 (139)	0.016 [d]
Heamatoma	Yes No	0 5	1 77	1 [c]
Tracheomalacia	Yes No	1 4	1 77	0.118 [c]
Temporary RLNP	Yes No Pre-existing	3 * 0 * 2 *	0 ** 76 ** 2 **	<0.0001 [c]
Persistent RLNP	Yes No Pre-existing Resolved	2* 1 * 1 * 1 *	0 ** 76 ** 0 ** 2 **	<0.0001 [c]

[a] T-test, [b] Chi-square, [c] Fisher's exact, [d] Mann-Whitney

5.11.8 Tracheomalacia

Four patients developed tracheomalacia resulting in a rate of 1.68%. All patients were female and older than 70 years. In all patients the tracheomalacia was developed preoperatively resulting in airway obstruction.

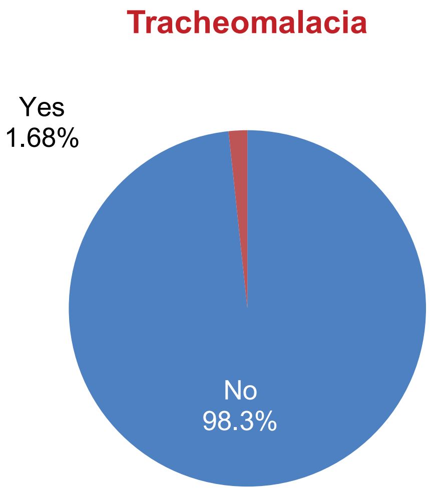


Figure 29. Distribution of patients who developed tracheomalacia.

Table 20. Characteristics of patients diagnosed with tracheomalacia.

N	Age	Gender	Goitre Type	Surgery	Trach	RLNP	Decannulation
1	81	Female	UBAA	TT	Yes	Yes	Yes
2	80	Female	BAA	TT	Yes	Yes	Yes
3	71	Female	UBAA	CT	Yes	Pre-existing	Yes
4	74	Female	UBAA	TT	No	No	N/A

5.11.9 Tracheostomy

Two patients required preoperative tracheostomy, 3 required it intraoperatively and one patient had a pre-existing tracheostomy. Preoperative tracheostomy was required for acute airway obstruction in 2 patients. Intraoperative tracheostomy was required for tracheomalacia, bilateral RLN, LOS during IONM and to aid weaning assisted ventilation.

All patients who underwent postoperative tracheostomy were successfully decannulated during their initial hospital admission.

Table 21. Table demonstrating the characteristics of patients who required tracheostomy. (TRM: Tracheomalacia. VCPO: Vocal cord palsy outcome).

N	Age	Gender	Timing	Aetiology	TRM	RLNP	VCPO	Outcome
1	81	Female	Preop	Acute	Yes	Yes	Resolved	Decannulated
2	80	Female	Preop	Acute	Yes	Yes	Resolved	Decannulated
3	60	Female	Intraop	Chronic	No	Yes	Persistent	Decannulated
4	71	Female	Pre-existing	Previous	Yes	Yes	Persistent	Not decannulated
5	81	Female	Intraop	Chronic	No	Yes	Resolved	Decannulated
6	83	Female	Intraop	Chronic	No	Yes	Resolved	Decannulated

5.11.10 Extracervical and other complications

5.11.10.1 Pneumothorax

5 patients sustained a controlled intraoperative pneumothorax. This was a consequence of the need to open the pleura to resect the intrathoracic portion of the goitre. No patients underwent unexpected postoperative pneumothorax.

5.11.10.2 Pneumonia

One patient developed a postoperative pneumonia. She was in the TCA group.

5.11.10.3 Subclavian artery injury

One patient sustained a right subclavian artery injury. This was a patient with a recurrent goitre who had undergone a subtotal thyroidectomy 20 years, prior to the recurrence.

5.11.10.4 Rare Complications

Left upper limb neuropraxia and oedema: One patient sustained left upper limb neuropraxia and oedema secondary to brachiocephalic vein removal.

Hypertrophic and keloid scarring: Five patients developed hyperthropic scarring. All patients were treated conservatively using silocone gel therapy.

Other unusual complications are shown in table 22.

Table 22. Table of rare postoperative complications.

Complications (>1/patient)	Frequency
Seroma (local)	1
Hypertrophic scar(local)	5
AF (extrathyroidal)	1
Horner's syndrome (extrathyroidal)	1
Pneumonia (extrathyroidal)	2
Hungry bone syndrome (extrathyroidal)	1
Left arm oedema (extrathyroidal)	1
Keloid scar (local)	1

Table 23. Table demonstrating whether the development of rare complications can be affected by performing a sternal split or not. Overall there was a statistically significant difference between the two groups (p=0.001). As the variable of interest has 3 levels, chi-square post-hoc analysis was also performed. Results remained statistically significant different for 2 out of the 3 levels of the variable (see annotation in Table 23). 13.8 % of patients developed a local complication in the sternal split group compared to only 1.4% in the non-sternotomy group. 96.6% of patients did not develop a complication in the first group as opposed to 79.3% in the sternal split group These differences remained statistically significant in post-hoc subgroup analysis, whereas the number of extrathyroidal complication was not statistically significant different in the two groups (1.9% vs 6.9%).

Postoperative complications * sternal split Crosstabulation				
Count		Sternal split		Total
		No	Yes	
Postop complications	No	201	23	224
	Seroma	0	1	1
	Hypertrophic scar	3	2	5
	AF	1	0	1
	Horner's syndrome	0	1	1
	Pneumonia	2	0	2
	Hungry bone syndrome	1	0	1
	Left arm oedema	0	1	1
	Keloid scar	0	1	1
Total		208	29	237

Rare complications * sternal split Crosstabulation				
Count		Sternal split		Total
		No	Yes	
Rare complications	No	201_a (96.6)	23_b (79.3%)	224
	Local	3_a (1.4%)	4_b (13.8%)	7
	Extrathyroidal	4_a (1.9%)	2_a (6.9%)	6
Total		208	29	237

Each subscript letter denotes a subset of sternal_split categories whose column proportions do not differ significantly from each other at the .05 level. Fisher's exact p-value = 0.001

5.11.11 Mortality

The rate of mortality in this cohort was 0%.

5.11.12 Length of Stay

The median length of stay for cervical approaches was 3 days – range minimum 2 and maximum 14 and the median for ECA was 6 with a range between 2 and 14. The length of stay was not normally distributed therefore median (range) rather than mean (SD) was used.

Table 24. Distribution of the length of stay in both study groups.

	Sternal split			Statistic
LOS	No	Mean		2.98
		95% Confidence Interval for Mean	Lower Bound	2.72
			Upper Bound	3.24
		Median		3.00
		Std. Deviation		1.908
		Minimum		2
		Maximum		14
	Yes	Mean		6.45
		95% Confidence Interval for Mean	Lower Bound	5.64
			Upper Bound	7.25
		Median		6.00
		Std. Deviation		2.114
		Minimum		2
		Maximum		14

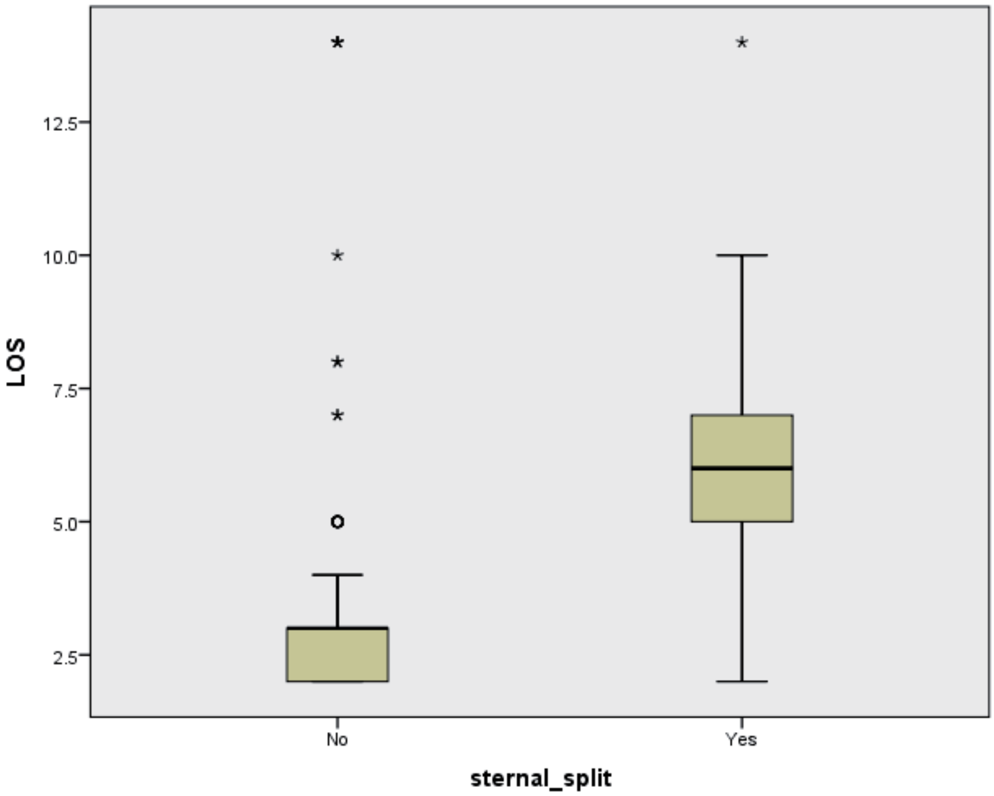


Figure 30. Distribution of the length of stay in both study groups.

6

DISCUSSION

6.1 GENERAL ASPECTS

Intrathoracic goitres are a challenging group of goitres that cause specific problems regarding the preoperative evaluation and surgical management.

It is not uncommon that patients presenting with ITG causing compression symptoms are elderly and with multiple co-morbidities. It is therefore essential that this group of patients are thoroughly preoperatively evaluated and their surgical management carefully planned and addressed.

As these patients may require combined extracervical approaches, it is necessary that the surgeon understands the anatomy, the histopathological features and has the knowledge and experience to be able to safely remove these goitres.

Surgery for ITG is associated with a higher risk of anaesthetic, intraoperative and postoperative complications than surgery performed for purely cervical goitres.

In view of this it is important that surgeons managing patients with ITG not only have the expertise and surgical skills, but also understand the indications and limitations of the available surgical approaches.

Therefore, it is essential that surgeons undertaking surgery for ITG, work as part of an expert and dedicated multidisciplinary team and undertake this surgery in a setting where it can be done safely and with minimal complications.

6.2 RATE OF OCCULT MALIGNANCY

In a recent series of 462 patients who underwent a total thyroidectomy for MNG without the suspicion of malignancy, Burtrugno et al reported a malignancy rate of 8.9% (50). Dogan et al reported a PTC rate of 17.5% in 154 patients who underwent total thyroidectomy for MNG without any evidence of malignancy(51). Higher still was the rate reported by Luo et al, at 31% of 1791 patients and 35% in a series of 813 reported by

Agarwal [52, 53] . It is very likely that this rate will depend on patients selected to undergo surgical resection and may also reflect the different approaches to pathological analysis of surgical specimens [3].

In ITG, the rate of malignancy ranges between 0 to 22.6%, however if we look at the rates in series that include over 50 patients this rate ranges from 2.5 to 22.6% with a mean rate of 10.1% [21].

In our cohort, the rate of malignancy was 8.01%, which is slightly lower than the mean of large published series of 50 patients or more but in range with series of similar number of patients such as those published by Rios or Hsu [54, 55].

In our cohort, the rate of unexpected occult malignancy meaning the patients with benign cytological results in which a cancer was diagnosed was 5.0%.

Although the rate is relatively low, the clinical implication is important and the extent of the original surgery is essential. If the original surgery was a total thyroidectomy, then there is no issue provided that a bilateral total lobectomy or a near total lobectomy has been performed. If on the contrary the patient has undergone a unilateral lobectomy and tumour stage and applied risk stratification is such that the patient requires further surgery, then it is imperative that the surgeon would have performed an appropriate surgical procedure in the first place and that the completion procedure can be done safely.

In our cohort, 3 patients required completion thyroidectomy either, immediately or at later stage. All patients had successful completion surgeries and all are to date well with no signs of recurrent disease.

Table 25. Rate of Occult Malignancy in reported series of over 50 patients with intrathoracic goitre.

Author	Year	Country	N	Type of study	% of cancer
Torre et al	1995	Genoa - Italy	237	Retrospective	6.8
Nervi et al	1998	Pisa - Italy	621	Retrospective	3.7
Hsu et al.	1996	Sydney - Australia	234	Prospective	7.7
Vadasz et al	1998	Budapest - Hungary	175	Retrospective	5.7
Shai et al.	2000	Taichung - China	55	Retrospective	5.4
Arici et al.	2001	Antalya - Turkey	52	Retrospective	11.5
Cui et al.	2002	Beijing - China	64	Retrospective	15.6
Hedayati et al.	2002	Cleveland - USA	116	Prospective	21.6
Parra-Membrives et al	2003	Seville - Spain	83	Retrospective	9.6
Erbil et al.	2004	Istambul - Turkey	170	Retrospective	12.9
Shen et al.	2004	San Francisco - USA	60	Retrospective	6.7
Rios et al.	2004	Murcia - Spain	247	Retrospective	5.7
Ben Hun et al	2006	Haifa - Israel	75	Retrospective	12.0
Chauhan et al.	2006	Frankston - Australia	199	Prospective	2.5
De Perrot et al.	2007	Paris - France	185	Retrospective	9.7
Pieracci et al.	2007	New York - USA	1153	Retrospective	22.6
White et al.	2008	Ann Arbor - USA	115	Retrospective	15.7
Simo	2016	London - UK	237	Prospective	8.01

6.3 ULTRASOUND GUIDED FINE NEEDLE ASPIRATION

USS guided FNAC has become the standard of care for the initial evaluation of thyroid nodules. Most current clinical guidelines recommend their use in patients with STN or long standing MNG with rapid growth. USS guided FNAC has a significant lower yield of inadequate aspirates than palpable FNAC. Current rates of overall accuracy of FNAC analysis for malignancy are around 97%, with sensitivity rates of 83% and specificity of 98%. The positive predictive values are around 71.4% and the negative predictive value of

98.4%. Difficulties of cytological diagnosis are often associated with lymphoid infiltrates and degenerative changes in follicular adenomas [56]. In our study the USS guided FNAC, had a sensitivity of 31.6%, the specificity of 93.6%, a PPV of 30% and a NPV of 94% to indicate the presence of malignancy within the ITG. These results are in keeping with current literature.

Recent guidelines have introduced a very useful USS characterisation of thyroid nodules that may help standardization of the reporting but also guiding clinicians as to which nodules may target for their biopsy [43].

The use of USS guided FNAC in long-standing MNG and ITG remains a subject of controversy. Some clinicians feel that that their use in this setting is not useful as the majority of patients will undergo surgery to alleviate their symptoms and therefore will not change practice. However recent reports suggest that the incidence of thyroid cancer in patients with MNG and benign FNAC is significant. In a recent report of 134 patients, Campbell et all found a rate of 15% of micropapillary thyroid cancers and a 7.5% rate of patients with other forms of thyroid cancer [57]. It is also difficult if the cervical component is minimal and there is poor access to the potential target nodule. One should bare in mind that as previously stated, some of these patients are elderly and may have kyphosis making it difficult to access the thyroid gland which may be completely in the intrathoracic position.

An optimal preoperative assessment will guide clinicians as to the extent of the surgery required. Patients can also be appropriately counselled as this will give them the information required to help them to make an informed decision about their treatment.

For patients with indeterminate thyroid nodules FNAC results, there is a rate of malignancy between 10 and 29% and for suspicious FNAC results of about 70% [58]. However it is clear that the rate of occult malignancy ranges from 2.5% to 22.6% and this may not be addressed by the FNAC result [57]. The majority of these will be MPTC less than 10 mm in maximum diameter and will have no clinical consequence. However, if patients have only undergone a hemithyroidectoy, as stated earlier, this will have implications for follow-up and the potential need to perform a completion procedure if there is contralateral nodularity and the patient or the clinician feel that they will benefit from further surgery.

It is however important for clinicians to recognise their institutional rate of occult malignancy in ITG and advice patients accordingly.

6.4 MULTIPLANAR COMPUTERISED AXIAL TOMOGRAPHY

Multiplanar Computerised tomography is the best predictor to determine the adequate surgical approach. This has been appropriately addressed in many papers in recent years [13, 38, 59].

In this study multiplanar CT scan of the neck and chest with intravenous contrast was used in all cases where possible. Patients with iodine allergy underwent either CT without contrast or MRI scanning. The Huins et al criteria for classification of ITGs as adopted by the BAETS [13] was used to classify the degree of intrathoracic extension. This paper proposed to classify the ITG into retroclavicular, upper border of aortic arch and below aortic arch. We adopted Huins et al classification as the best predictor of surgical approach. This classification has been adopted by the British Association of Endocrine and Thyroid Surgeons and provides a very simple and reproducible classification [13].

Multiplanar CT scan provides the best characterisation, anatomical location and relationships for ITG and it has shown to be the best investigation to help surgical planning in this condition. It defines the extent of the ITG, demonstrates its anatomical location and the relationships of the goitre to the trachea, oesophagus, great vessels, main bronchi, lungs and perichardium. It provides an objective and reproducible measure of the tracheal calibre and therefore will aid preoperative anaesthetic planning. Thyroid tissue in the mediastinum is identified as likely thyroid based on high attenuation of 15 Hounsfield units or 25 units or greater postcontrast and is higher than for mediastinal lymphoma or thymoma. CT also helps to exclude nodal disease and other potential correlates of malignant disease such as irregular margins, heterogeneous internal features and the presence of microcalcification. The presence of gross capsular calcification in our opinion represents an indicator of the natural history of the goitre and also may help to select patients for extracervical approaches as it would be difficult to dissect from the surrounding anatomical structures [21, 60, 61].

CT scan with contrast is the most accurate investigation to characterise ITG and invariably helps to determine whether patients are surgical candidates and aid to predict the surgical approach.

Table 26. Factors increasing the risk of Extracervical Approaches in published series over 50 patients with ITG [21].

Reference	Year	N Patients	ECA %	Risk Factors
Cleveland	2006	116	1.7	Primary Goitre
Sidney	2006	234	1.7	Mass larger than TI
Ann Arbor	2007	115	5.3	Invasive Carcinoma Mass larger thant TI Primary Goitre Reoperation
Dublin	2007	140	2.1	Extension BAA Extension to AA Adherence on CT
Amiens	2007	223	1.3	Anatomical Findings on CT
Plessis-Robinson	2007	185	7.0	Invasive Carcinoma Primary Goitre Reoperatrion
Istambul	2004		7.1	Posterior Mediastinum Reoperation
Pisa		374	16.4	Giant Extension Posterior Mediastinum

Sancho et al in 2006 reported a series of 35 patients undergoing surgery with ITG. They found that a goitre weight of 260 gr and extension to the tracheal carina were significant predictors of ECA ($p<0.02$). Their ECA rate was 37% which is significantly higher than any other series in the literature [42].

Flati et al in 2005 introduced the term “iceberg” shape as a potential factor leading to an ECA [62]. We have also adopted this term in this study as shown in the results.

In our series patients who required ECA included revision surgery, recurrent goitres, giant goitres, complex anatomical goitres involving multiple mediastinal compartments, retrotracheal and retroesophageal goitres and primary goitres. Furthermore 2 patients with goitres involving the posterior mediastinum and reaching the posterolateral pleura, required combined cervical and right lateral thoracotomy approach. One patient required a midline sternotomy for the simultaneous presence of an ITG and at the same time a thymoma.

6.5 CLINICAL PRESENTATION AND SURGICAL INDICATIONS

Intrathoracic goitres tend to grow slowly and are most commonly discovered during the fifth and sixth decades of life. They are found more often in women with a female to male ration of about 3 to 1 (21). This has been clearly reflected in our experience with 72% of women in the cohort.

It is reported that between 20 % and 30% of patients do not have a palpable cervical goitre or it is only palpable when swallowing or when extending the neck. The most common presenting symptoms are compression of the airway ranging from vague positional pressure symptoms, globus pharyngeus, mild cough and shortness of breath on exertion. A minority of patients will present with acute or subacute airway obstruction (26), thyrotoxicosis, obstructive sleep apnoea (28) and recurrent laryngeal nerve paralysis (27).

6.5.1 Acute airway obstruction

Patients presenting with an ITG and acute airway obstruction represent an obvious management challenge. In our cohort 4 (1.6%) patients presented with acute airway obstruction requiring airway management, either with endotracheal intubation or tracheostomy. There is much debate as to what is the optimal management in this situation. On the one hand a surgical airway may be difficult to establish due to the position of a large goitre in the pretracheal area and on the other a conventional endotracheal intubation would not be possible as the patient’s laryngotracheal airway will obstruct. A fibreoptic laryngoscopic intubation via an experienced difficult airway team may be necessary (63).

6.5.2 OSAS

Patients with ITG and OSAS represent an interesting group of patients as when the goitre is removed the symptoms of OSAS may resolve almost immediately [28]. In this group of patients the goitres appear to have large volumes and have a retropharyngeal or retrosophageal component. In our cohort 4 patients presented with OSAS. Our group reported a series of MNG goitres causing OSAS in 2012. The paper reported 5 patients diagnosed with OSAS who had large MNG with retropharyngeal extension and were treated with a total thyroidectomy. There was a complete and immediate resolution of the OSAS and it was recommended that patients diagnosed with OSAS should have appropriate thyroid screening to exclude the presence of a MNG. The experience with this subgroup of patients is identical. It has to be emphasised that in this subgroup of patients total thyroidectomy is the treatment of choice [28].

6.5.3 Recurrent laryngeal nerve paralysis due to ITG

The association between a preoperative RLN injury and thyroid disease is usually indicative of locally advanced invasive thyroid malignancy. However between 2-3% of patients with benign MNGs or ITGs may develop RLN paralysis [27]. Up to 50% of these patients may not have dysphonia as laryngeal symptoms often develop gradually and the laryngeal muscles compensate. Our group reported a series of 5 patients with benign MNG who developed RLN paralysis and after thyroidectomy 50% of them recovered their function [27]. In this study cohort 9 (3.7%) patients presented with a preoperative RLN paralysis due to compression of the RLN. After thyroidectomy 6 recovered the function. In this subgroup, it is therefore imperative to have cytological evidence of benign disease, as a thyroid lobectomy may be more appropriate than a total thyroidectomy in order to reduce the potential risk of bilateral paralysis.

6.6 SURGICAL INDICATIONS

Surgery for the MNG can be challenging due to the distortion of the anatomy and potential involvement of vital structures. It is therefore advisable that this surgery is carried out by experienced surgeons in specialized centres and as part of multidisciplinary teams.

Surgery is the treatment of choice for symptomatic ITG. The reasons for this include: a. there is no other effective treatment, b. the radioactive iodine could potentially cause an acute reaction causing airway obstruction, c. most ITG have a tendency to grow and therefore cause increasing compression of surrounding anatomical structures and local complications such as RLNP d. a significant proportion (up to 25%) of ITG can yield malignant disease and e. up to 90 % of ITG could be safely excised via a cervical approach (5, 64).

However some authors argue the need for surgical intervention in patients with asymptomatic goitres that have been diagnosed as incidental findings during other investigations or in the preoperative evaluation for surgery in other causes (24, 65). This may represent up to 40% of all ITG. Elderly individuals or patients with significant co-morbidities may be included in this group. In our study group all patients were symptomatic and agreed that surgery was the best way forward to help to resolve their symptoms.

The only alternative treatment for patients in which surgery is contraindicated due to medical reasons is radioiodine ablation. A recent paper suggests that RIA may reduce the volume of the goitre by 40% inducing significant reduction in symptoms (5).

6.6.1 Surgical strategy and extent of the surgery

Most ITG arise from one lobe of the thyroid gland. Our surgical philosophy has been to perform a lobectomy when the main pathological component is unilateral and a total thyroidectomy if the nodular growth is bilateral and compresses the adjacent anatomical structures. This philosophy is shared by some authors (22) but not by others (66). Using a selective strategy will allow the resolution of symptoms and could significantly reduce the risk of significant complications such as bilateral recurrent laryngeal nerve paralysis, tracheostomy and permanent hyperparathyroidism.

In order to safely follow a selective approach, appropriate evaluation with TFT, USS guided FNAC with adequate cytological report and accurate multiplanar CT scanning is imperative.

TFT will help determine the extent of the surgery. Euthyroid patients with unilateral goitres are likely to be helped by a selective approach whereas hyperthyroid patients are likely to require a total thyroidectomy to eradicate symptoms of toxicity.

Adequate cytological analysis also will help to council patients preoperatively as to the extent of surgery. Truly benign (Thy2) unilateral goitres can safely undergo a selective approach whereas cytologies with follicular neoplasm or malignant features are likely to be offered a total thyroidectomy approach.

Surgery for ITG is deemed to be high-risk surgery as it is likely to pose significant surgical technical problems with higher risk of complications [5]. Some authors recommend that, these surgeries should be performed by experienced surgeons [67, 68]. Experience however comes with a learning curve, and therefore surgery for ITG should be done in specialised centres preferably by high volume surgeons where there is appropiate expertise.

In our study, all patients with ITG are discussed in a multidisciplinary setting by an endocrinologist, head and neck, endocrine and thoracic surgeons. This allows adequate planning, a reduction of unplanned extracervical approaches and a decreased rate of unexpected morbidity and mortality. High-risk patients are carefully discussed and specialist difficult airway anaesthetists consulted to allow appropriate anaesthetic planning and postoperative care. In this study, no patients underwent unplanned ECA and there were no deaths.

6.6.2 Surgical approach

The majority of ITG can be excised via a TCA with most reported series around 95% of cases [5].

When prospective data is reviewed the rate of ECA is low ranging from 0 to 1.7%, therefore nearly 99% of the time these goitres can be accessed by a TC approach. In other words, only 2% of ITG will require an ECA when patients are operated by experienced surgeons [21].

When retrospective data is reviewed the rate of ECA for ITG is more variable and ranges from 0 to 45%[21].

This variable rate is probably a reflection of lack of consensus as to what represents an ITG, the quality of reported work, attempting TC when not indicated and then abandoning surgery and the fact that some of these cases may not performed by the endocrine or head and neck surgeons but by cardiothoracic or thoracic surgeons and therefore never reported. It is also possible that patients with such goitres are offered non-surgical treatment as they often are elderly and with significant co-morbidities.

The factors leading to an extra-cervical approach are summarised in Table 26.

In our series the rate of ECA is 12.1% with 27 sternotomies and 2 lateral thoracotomies. This is relatively higher than the mean of the prospective data available in the current literature.

It is thought that this relatively high percentage is related to the nature of the patients that were referred and the setting that we work in. Our unit is a tertiary referral centre for thyroid disease covering a population of over 3.5 million and we are therefore more likely to deal with complex problems. The availability and immediate access to a thoracic surgery team could also lower the threshold of ECA.

We deliberately excluded malignancy from this analysis. It was felt that the intrinsic nature of this pathology would have a negative impact on the outcomes of these patients and therefore requires a detailed separate study. The need for sternotomy in this subgroup is evident as in order to resect macroscopic disease safely from mediastinal structures requires adequate access. It is also obvious that due to the intrinsic nature of this disease the risk of complications mainly RLN injury and HPT are higher. By definition malignant ITG will be either in advanced stages (T3 and T4) and will require extensive dissection leading to an increased risk of complications.

Based on the analysis of this cohort, we concluded that the need for an ECA in non-neoplastic goitres from the outset should be considered and the presence of a thoracic or cardiothoracic team should be available in the following situations:

1. ITG with extension beyond the AA
2. Revision cases and or recurrent ITG with extension to the AA

3. ITG extending to the posterior mediastinum, retrotracheal and retroesophageal.
4. ITG Multiple compartments anterior and posterior mediastinum
5. “Iceberg” or “Inverted cone” - Intrathoracic component much larger than cervical component.
6. Giant extensions
7. Multiple components – Primary intrathoracic goitres and or minimal cervical component.
8. Adverse body habitus eg OSAS, High Body Mass Index.
9. Posteriorly based goitres with extension to posterior thoracic pleura or thoracic wall.
10. Combination of the above.

In our methods, we stated the preoperative risk stratification of those patients in whom the CT scan findings could put them in a high-risk category for an ECA. Using this approach no unexpected or unplanned ECA had to be performed.

6.6.2.1 ITG with extension beyond the AA

Extension of ITG beyond the AA has been one of the most frequent factors reported to increase the risk of an ECA. Grainger et al found that CT scan evidence of ITG reaching or extending to the AA increased the risk of sternotomy in univariate and multivariate analysis [38]. Riffat el al reported similar findings in a cohort of 97 patients with ITG. They found that when using preoperative CT scanning, there was a “relative” but statistically significant risk of sternotomy in patients with posterior mediastinal extension, extension into the posterior mediastinum, “conical” shape, ectopic goitre, and evidence of nodal disease [59].

6.6.2.2 Revision cases and recurrent ITG with extension to the AA

For most surgeons, revision cases require significant surgical experience as they have been associated with a high risk of complications mainly due to fibrosis, distortion of anatomy and surgical planes. This leads to increased rates of haemorrhage and injury to vascular and visceral structures [21, 69].

Surgery for ITG is no exception and there is evidence to suggest that revision or reoperative surgery is associated with an increased risk of complications [21].

In order to facilitate surgical access and find an adequate surgical plane of dissection as well being able to identify anatomical structures appropriately, surgical approach through the mediastinum will provide a clearer plane of dissection.

6.6.2.3 ITG extending to the Posterior mediastinum – Retrotracheal and retroesophageal

Goitres with extension to the posterior mediastinum pose a significant challenge making the access via a single TCA difficult and hazardous. The angle of dissection is awkward and makes the visualization of the anatomy difficult. In these cases the RLN is likely to be in a more anterior position and therefore make it more vulnerable to injury [2]. We will discuss the approach to the RLN further down in this section. If these goitres also reach the posterior pleura the risk of iatrogenic uncontrolled pneumothorax is much higher.

6.6.2.4 ITG Multiple compartments anterior and posterior mediastinum

The risk of an ECA in these goitres has been recognised. By definition these goitres ride over the brachiochephalic vascular bundle causing distortion of these vessels and possibly the RLN [2, 70]. It is therefore much safer to approach them from the anterior position via midline sternotomy rather than from a craniocaudal angle where these structures are not in direct view.

6.6.2.5 "Iceberg" or "Inverted Cone" – Intrathoracic component greater than cervical component

The issue of the shape of the goitre has been described in the literature as a potential risk factor for an ECA approach. The terms such as iceberg and conical have been described in the literature [59]. The shape of the goitre and its impact on the approach has been analysed in this study. The shape has been classified in 3 main categories oval, tubular and iceberg or inverted cone. The analysis has proved that there is statistically significant risk of needing an ECA with iceberg or inverted cone shapes, and this should be taken into consideration when planning surgery for ITG.

6.6.2.6 Giant extensions

Sancho et al reported the weight of over 250 grams as a statistically significant factor for an ECA [42]. This is perhaps the most obvious indication of needing an ECA as the size will make it imposible to deliver the goitre via the thoracic inlet [2].

6.6.2.7 Multiple components. Primary Goitres – Isolated intrathoracic goitres – minimal cervical component

One of the problems with ITG, is the presence of primary thyroid nodules in the mediastinum, ectopic goitres and goitres with multiple components which are either not connected or they have a minimal fibrotic connecting remnant [70]. Unless this ectopic element can be accessed via a TC approach, it would be extremely difficult to be able to hold on to the tissue and exert upward traction so it can be removed in a cranial direction.

6.6.2.8 Thyroid cancer with mediastinal involvement

Thyroid cancer cases have been explicitly excluded from this study as stated in the materials and methods section. There is no question that when reviewing the literature this group represents perhaps one of the most evident indications for an ECA. It is imperative that there is access to the superior mediastinum for appropriate dissection and excision of all macroscopic disease with preservation of vital structures [43, 65].

Two of the ECA patients included in the study, had locally advanced thyroid cancer. One was a sporadic MTC and the other one a PTC. None of them had overt evidence of thyroid cancer on FNAC or CT scanning. There was also no evidence of metastatic lymphadenopathies in the neck or the mediastinum. One patient had a total thyroidectomy and the other one required a completion thyroidectomy of a truly cervical component with no additional morbidity. Both patients are well with no evidence of recurrent disease, in the primary site, neck or mediastinum.

6.6.2.9 Other factors

Whilst undertaking this surgery regularly and with increasing numbers of cases and experience, we developed a protocol of risk for potential ECA. This was based on the experience of the team of surgeons and the evidence available in the literature. It has been demonstrated that the risk stratification protocol generated correlates very well with current evidence and that the findings of this study confirm this. It is also thought that the introduction of a simple shape classification may help to determine an additional risk for an ECA. The findings of this study have indicated that the introduction of such guidance, helps counselling patients and helps an informed decision.

6.7 INJURY TO THE RECURRENT LARYNGEAL NERVE

Voice changes are very common after thyroid surgery some being of neural but others from non-neural origin. This latter group include endotracheal tube injury and oedema, laryngeal oedema secondary to venous stasis and fibrosis. Between 30% and 87% of patients may complain of subjective voice changes without neural injury [(71)].

Recurrent laryngeal nerve injury resulting in vocal fold immobility can be the source of significant morbidity causing symptoms profound enough to warrant change of vocation. Unilateral vocal fold immobility can also be associated with dysphagia mainly for liquids and be associated with aspiration pneumonia. Bilateral RLNP can be associated with acute airway obstruction and the need for tracheostomy or other airway widening procedures which themselves cause a negative impact in voice and QOL [(71)].

The rate of RLN injury in ITG ranges from 0 to 14.3% with a mean rate of 2.7%. The risk of 0% on one hand is almost not credible and should probably not be taken in consideration. On the other hand a risk of 14.3% is somehow very high. Most series report a permanent rate between 2 and 4% and in view of the complexity of these cases, this would appear to be an acceptable rate [(72, 73)].

There is also variability in reporting the risk as authors refer to total cases as opposed to nerves at risk. It is obvious that the risk of RLN injury should be referred to the number of nerves at risk rather than the procedure as for hemithyroidectomies the risk is half to those of total thyroidectomies.

In a recent review over 10 years in high volume centres in Italy, the authors compared the rate of RLNP in 14993 patients undergoing total thyroidectomy for cervical MNG and ITG via a transcervical vs a manubriectomy. The rate of transient RLNP ranged from 0.5% in the cervicotomy group to 8% and in the manubriotomy group the rate of permanent RLNP ranged from 0% to 4% respectively. A statistical significant difference was found between the two groups concluding that there was an increased risk of transient as well as permanent RLNP in surgery for goitres extending to the mediastinum in which an ECA was needed [32].

The factors for increased risk of RLNP have been found to be diverse. The volume of the glands, the distortion of the anatomy often with nerves riding over the intrathoracic component requiring longer segment dissections, the complexity of the surgery, elderly patients with comorbidities with less resilient neural tissues have an influence [32, 45].

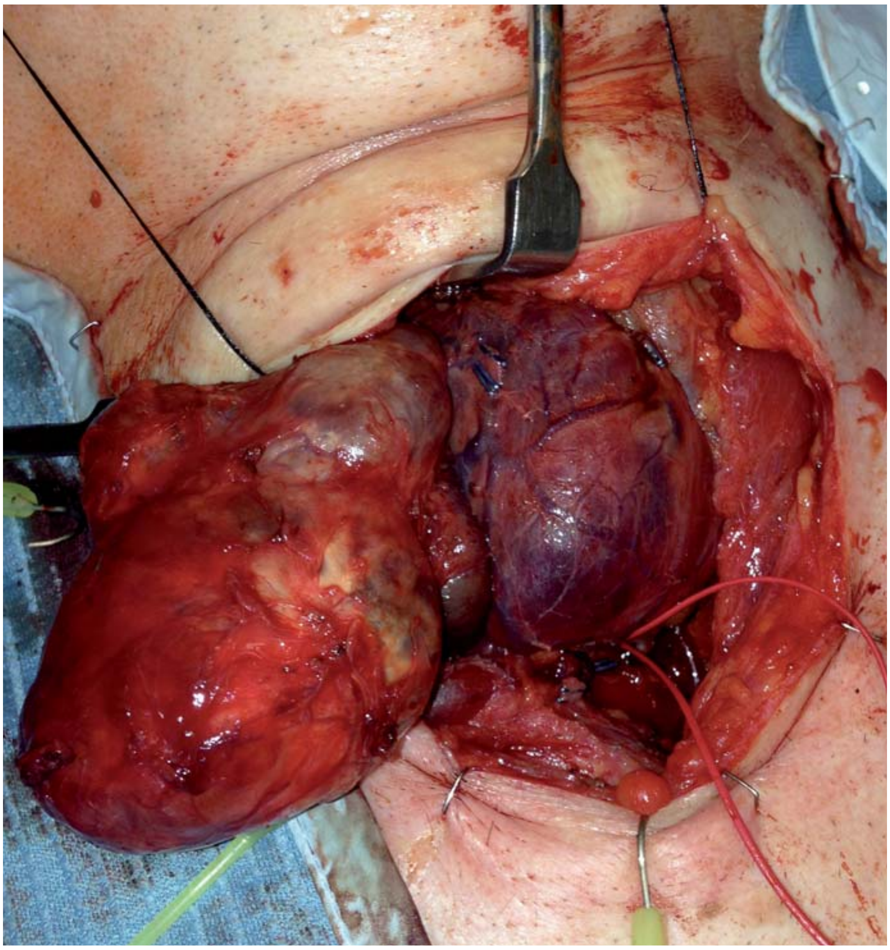


Figure 31. Intrathoracic goitre with RLN riding over the posterior component.

Figure 32. Postoperative picture of the intrathoracic goitre in Figure 31 with a blue sling demonstrating the course of the recurrent laryngeal nerve riding over the posterior component.

In our series the risk of permanent RLN was 1.6% (4 out of 237 patients, excluding patients with pre-operative palsy) but when we relate the rate to nerves at risk the percentage is reduced to 1.6%.

There is also no consensus regarding reporting of temporary vs permanent RLN injury. Most authors report rates of permanent injury as an endpoint outcome rather than rates of temporary injury as these vary significantly in regards the timing and method of vocal cord examination. The only true way of finding the true figure of transient and permanent RLNP after thyroid surgery would be by ensuring that all thyroid surgeries are registered in national data bases such as the BAETS or Danish Society of Otorhinolaryngology Head and Neck Surgery and all patients undergo appropriate laryngeal examination preferably by independent clinicians at agreed intervals [72, 74].

It is well known however that the rate of RLNP is increased in those series in which the laryngoscopic assessment is systematically performed [72].

Current Clinic Practice Guidance by the American Academy of Otorhinolaryngology Head and Neck Surgery recommends a. the documentation of any voice change after thyroid surgery, b. the examination of the vocal folds in the event of voice change after thyroid surgery and the referral to an otolaryngologist if there is an abnormal vocal fold abnormality identified after thyroid surgery [75].

Interestingly we found 2 patients who had documented delayed vocal cord paresis over 2 weeks after the original procedure. They both underwent thyroidectomies with IONM and both had satisfactory amplitude and action potential (AP) readings at the end of their procedures. They also both had normal FON 2 weeks after their procedures but they returned with evident RLNP, which resolved spontaneously in both occasions within 6 weeks. The phenomenon of delayed RLNP after thyroid surgery is not clearly understood and poorly reported [76]. It is possible that fibrosis could have lead to temporary segmental ischeamia of the nerve or that patients could have developed viral conditions that could have affected the nerve function.

6.8 INTRAOPERATIVE NEUROMONITORING

The RLN and ESBLN are at risk of iatrogenic injury during thyroidectomy given their close anatomical relationship to the thyroid and parathyroid glands. Despite appropriate surgical training and experience, these nerves may be difficult to identify and protect intraoperatively, especially in cases of invasive thyroid cancer, large goitres, or revision surgery. Intraoperative neuromonitoring is a useful aid for localising and monitoring the electrophysiological status of the RLN and EBSLN during surgery, however routine use of IONM remains controversial.

Current guidelines recommend definitive visual identification of the RLN as the best way of avoiding injury to the nerve and ensuring protection of the EBSLN during thyroid surgery [71, 77]. Historical surgical training promoted complete avoidance of exposure of the

RLN as a means of preventing nerve injury. However, following descriptions of newer surgical techniques over 70 years ago [78, 79], during which an attempt was made to systematically recognise the RLN, visual nerve identification became acceptable practice. Further supporting evidence for routine RLN visualisation to prevent iatrogenic injury comes from Hermann et. al. [80] who compared two historical cohorts (of over 26,000 patients) undergoing thyroidectomy for benign disease, from a period when RLN identification was not performed (1979 to 1990), to more recent times (1991 to 1998), when RLN visualisation was routine practice, and the authors demonstrated that the rate of permanent RLN palsy was significantly lower with RLN identification (0.4%) versus non-identification (1.1%).

In spite of relatively low rates of permanent vocal fold paralysis with RLN visualisation alone during thyroidectomy (i.e. < 2%) [81], the negative impact on laryngeal function [82-85] and the medico-legal implications [86, 87] of vocal fold paralysis has prompted thyroid surgeons to seek further reductions in the incidence of RLN injury, through the use of surgical adjuncts such as IONM. Notwithstanding the purported benefits, several studies over the past twenty years have failed to demonstrate an obvious statistically significant difference in the rates of permanent vocal fold paralysis when comparing routine use of IONM versus visual RLN identification alone [81, 88-90], a result that was confirmed in a recent systematic review of 42 studies and over 64,000 nerves at risk [91]. With the lack of strong evidence for a clinical advantage of IONM in thyroid surgery, the additional costs associated with specialised equipment and consumables [92], surgeon learning curve, and theatre staff training time, are cited as further reasons why its routine use may not be justified. However, whilst the benefits of IONM for routine thyroid surgery are debated, IONM has been shown to reduce the rate of RLN injury during revision surgery [93], or when neck anatomy is complex e.g. large goitres [35]. Therefore, in the context of high-risk thyroidectomies, IONM is widely accepted to be beneficial. Conversely, for surgeons to gain experience with IONM for difficult cases, it is important that they are familiar with its use during routine procedures, so that they can precisely interpret electrophysiological information acquired during complex surgeries.

There are several additional benefits of routine IONM during thyroid surgery which include, earlier identification of the RLN and EBSLN and a consequent reduction in operative time [35, 94], more accurate prediction of postoperative vocal fold palsy, given that an anatomically intact RLN may not be functional (especially if neuropraxia has occurred secondary to blunt or stretch injury), and clearer identification of the site of neuronal injury. Surgeon recognition of RLN injury from visual inspection only is very poor, at around 15% of cases [95], and this is particularly relevant in the context of bilateral RLN injury which is also poorly recognised from inspection alone [96]. The use of IONM can prevent bilateral RLN paralysis and its life threatening complication of airway obstruction. Failed IONM stimulation of the RLN after hemithyroidectomy has resulted in some surgeons changing the operative strategy and delaying contralateral thyroid lobectomy, with a significant reduction in bilateral RLN palsy rates, compared to a reliance on visual neural integrity alone [97]. Overall, the benefits of IONM appear to outweigh any potential disadvantage from increased equipment or training costs, hence current guidelines recommend the use of laryngeal electromyography (EMG) monitoring during thyroid surgery [71].

The principles of IONM are two fold:

1. Stimulation of the RLN or EBSLN
2. Evaluation of vocal fold musculature response to RLN or EBSLN stimulation

Stimulation of the RLN or EBSLN may be achieved using low current (1 to 2mA) applied directly to the nerves, or indirectly by stimulation of the ipsilateral vagus nerve. Stimulator probes may be monopolar or bipolar, with the latter producing less stimulation artefact and consequently has a greater sensitivity. Bipolar stimulating electrodes must be used in the correct orientation of the anode and cathode for effective nerve stimulation [98].

Monitoring of vocal fold response to RLN or vagal stimulation can be accomplished in a number of ways:

1. Finger palpation of the posterior cricoarytenoid muscle during stimulation [45, 99-102]
2. Direct observation of vocal fold mobility via flexible laryngoscopy [103]
3. Interpretation of EMG data acquired from intramuscular vocal fold electrodes [104, 105]
4. Interpretation of EMG data acquired from endotracheal tube (ET) surface electrodes [93, 106]

Of all the monitoring techniques mentioned above, endotracheal tube surface electrodes are most commonly used worldwide [98], because it is a simple, non-invasive, commercially available technique that does not require additional skill or expertise from the operating surgeon for correct electrode placement. There are several manufacturers of neuromonitoring equipment, and a popular commercially available system is the Medtronic Nerve Integrity Monitoring (NIM®) 3.0 unit (Figure 7) which consists of surface electrodes integrated into endotracheal tubes, and a monitor that provides a visual EMG waveform and auditory signal of vocal fold activity following appropriate stimulation using a probe attached to the NIM system. An advantage of the NIM unit is that it is also widely used to facial nerve monitoring during parotid or otological surgery, making it readily available in most hospitals. However the use of ET tubes with integrated electrodes restricts the anaesthetist to using Medtronic supplied tubes, which reduces flexibility given the limited range of Medtronic endotracheal tube sizes. Other manufacturers, such as Inomed (Inomed Medizintechnik GmbH) produce adhesive laryngeal electrodes for use with their nerve monitoring units that can be applied to standard endotracheal tubes.

Regardless of the ET surface electrode or EMG monitoring system employed, a number of essential aspects require consideration prior to IONM use. The surgeon must be familiar with the neuro-monitoring equipment, and may have to attend additional training sessions with the manufacturer to achieve this. Unambiguous communication between the operating surgeon and anaesthetist on the pre-operative laryngoscopy findings, especially if abnormal, is also important. The anaesthetist should be made aware of the need for accurate placement of the ET tube so that surface electrodes are between the vocal folds, a process that should be relatively straighforward, especially if the vocal folds are clearly visualised during intubation. Long acting neuromuscular blocking agents must be avoided during ET intubation, so as not to interfere with neural stimulation.

During thyroid and parathyroid surgery, surgeons may use IONM to aid identification of the RLN or EBSLN. This usually involves intermittent stimulation of the area being dissected with interpretation of the auditory signal and EMG waveform from the nerve monitor to confirm whether or not the RLN has been stimulated. The International Neural Monitoring Study Group (INMSG) has produced thorough guidelines on IONM equipment set-up for thyroid/parathyroid surgery, anaesthetic considerations, interpretation of electrophysiological data, and have also standardised loss of signal troubleshooting algorithms [98]. As experience with IONM increases, it has become more evident that reliance on auditory signals of RLN stimulation is unreliable with a reported positive predictive value ranging from 9.2% to 94% [98]. A four-step procedure for IONM during thyroid surgery has been advocated [98, 107]:

1. Initial ipsilateral vagal stimulation prior to RLN identification i.e **V1 signal**. An EMG waveform with amplitude >100μV should be achieved at stimulation currents between 0.5mA to 1mA. This initial process confirms integrity of the neuromonitoring circuit and may alert the surgeon to the presence of a non-recurrent RLN (on the right side) which can occur in up to 3% of patients [108].
2. EMG waveform obtained upon stimulation of the RLN on its first identification i.e. **R1 signal**.
3. EMG trace derived from stimulation of the most proximal portion of the RLN at the end of thyroidectomy i.e. **R2 signal**.
4. EMG waveform derived following stimulation of the ipsilateral vagus nerve prior to closure, once haemostasis has been achieved i.e **V2 signal**. This final EMG trace again confirms that the whole neuromonitoring circuit remains intact at the end of surgery provided the desired event threshold (i.e. EMG amplitude >100μV) is achieved at appropriate stimulation currents.

Quantification of the laryngeal EMG for prognostication of postoperative vocal fold function is a key advantage of neuromonitoring systems which provide a visual EMG waveform, however this requires a basic understanding of waveform amplitude, threshold, and latency, for the surgeon to interpret and act on the information provided. The INMSG has attempted to standardise these EMG waveform characteristics [98]. Repeated stimulation of the RLN and vagus nerve has so far not been shown to cause permanent neurological deficits [98].

The EBSLN is closely related to the superior thyroid pole vessels, and is at risk of injury during ligation of the superior thyroid pole. This may result in difficulty with voice projection and pitch [109], especially in females. Through the human communicating nerve, the EBSLN innervates the anterior half of the ipsilateral vocal fold in up to 85% of patients [110], and this forms a basis that current IONM systems use can monitor the electrophysiological status of the EBSLN [111].

As with IONM for the RLN, the INMSG has proposed an algorithm with a sequence of neural stimulation steps to minimise the risk of EBSLN injury [111]. Standards for equipment set-up, endotracheal tube placement, anaesthetic considerations, etc, are the same as for RLN IONM, with a number of additional steps required for the EBSLN. Similar to the RLN, identification of the EBSLN prior to ligation of superior thyroid pole vasculature is recommended in all patients. The anatomy of the EBSLN has been described earlier. It is worth remembering that the EBSLN may not be visually identifiable in up to 20% of patients because the nerve runs in a subfascial or intramuscular plane. IONM is particularly useful in this case, because neural mapping with a stimulation current of 1 to 2mA can be used to detect these otherwise ‘hidden’ nerves.

IONM of the EBSLN is a two-step process. Firstly, upon visualisation of the nerve in the sternothyroid-laryngeal triangle, it is stimulated at a current of 1mA whilst observing for contraction of the cricothyroid muscle (CTM). The presence of an unambiguous CTM contraction or ‘twitch’ confirms positive identification of the EBSLN. Additionally, prior to ligation of the superior thyroid pole, stimulation of the tissue to be divided should be performed, with concurrent inspection for a negative CTM twitch to confirm the absence of neural tissue. Secondly, upon EBSLN stimulation, the nerve monitor is observed for a laryngeal EMG waveform, with an amplitude that is usually one-third that of the ipsilateral RLN in comparison. Currently, EBSLN stimulation will result in an identifiable laryngeal EMG waveform in only 70% to 80% of patients [111]. The reasons for this are not clearly understood, but the INMSG has proposed that it is more likely related to equipment issues, such suppression of early evoked potential responses, or the influence of endotracheal tube positioning, given that terminal branches of the EBSLN innervate only the anterior 50% of the ipsilateral vocal fold [111]. Using the two techniques described above, the thyroid surgeon should be able to identify the EBSLN in 100% of cases.

In a very recent paper of 2556 patients undergoing total thyroidectomy, both univariate and multivariate analysis showed that no use of IONM was an independent risk factor for RLN injury. The authors found the technology of IONM safe and reliable and its use an important adjunct in nerve dissection and functional neural integrity. The routine ues of IONM reduced pitfalls and provides guidance for surgeons in difficult cases, reoperations and high-risk patients [112].

Despite advocating the use of IONM, this has not had an effect on the rate of temporary RLN injury in our experience, but has a positive impact on permanent palsy.

6.9 POSTOPERATIVE HYPOCALCAEMIA

Postoperative hypocalcaemia is the most common complication after total thyroidectomy. A review by Pattou et al reported that the prevalence of transient hypocalcaemia ranges from 19 to 38% and the rate of permanent hypoparathyroidism varies from 0 to 3% (113)The main cause of postoperative hypocalcaemia is parathyroid insufficiency (114). These values are however likely to be an underestimate due to lack of complete follow-up and the lack of an accepted definition regarding the value and the timing. Additionally some of the reports include hemithyroidectomies as well as total thyroidectomies, which makes more difficult to interpret the results (115).

The BAETS has established a clear definition as well as aknowledging the fact that surgeons provide prophylactic calcium following total thyroidectomies as well as completion thyroidectomies. BAETS has also established the end point of hypocalcaemia at 6 months from the procedure episode (116). This is still a matter for debate, as it is known that some patients may recover the parathyroid function even after 12 months from surgery. For the purpose of this analysis and due to the fact that the data collection has been done using this national database we set up the definition of permanent postoperative hypocalcaemia at 6 months.

It has been shown that the failure of identifying the parathyroid glands during thyroidectomy may increase the risk of injury and inadvertent removal. Additionally intraoperative damage of these glands either due to mechanical or thermal trauma, devascularisation of the gland and unintentional removal, all lead to hypocalcaemia either temporary or permanent.

Surgery for ITG has been shown to be high-risk surgery leading to an increased risk of complications. With regards to the parathyroid glands, the large volume of the thyroid glands with its anatomical distortion can make the identification of the glands difficult. In reoperative or revision surgery this is even more evident (21).

With ITG, the inferior parathyroid glands become more displaced and by definition they may become intrathoracic, whereas the superior parathyroid often maintains a more constant position and it is more readily identifiable.

In order to minimise the risk of hypocalcaemia we have adopted the following principles; 1.- Check the calcium level preoperatively and correct any abnormal results, 2.- Dissect the superior pole of the thyroid gland first and follow its contour down to the position of the superior parathyroid gland, 3.- Dissect close to the capsule or pseudocapsule to avoid unintentional removal of the glands, 4.- Inspect the gland before its final removal to ensure that there are no parathyroid glands in the main specimen, 5.- In the event of an inadvertent removal, part of the gland is sent for frozen section, cut in small fragments and auto-transplanted in the ipsilateral sternocleidomastoid muscle pocket which is then marked with ligaclips ® and finally 6.- all total or completion thyroidectomies for ITG are treated as high risk in our protocol and therefore are given calcium as well as 1 alfa calcidol as prophylaxis.

Lorente-Poch et all demonstrated the importance of in situ preservation of parathyroid glands during parathyroidectomy. They described and tested a scoring system named PIGRIS (Parathyroid Glands Remaining In Situ) in which clearly demonstrated that the higher the PIGRIS score, the less likely that they will encounter postoperative hypocalcaemia. They followed up their patients for 1 year (114).

In our study, it was felt that measuring the rate of temporary hypocalcaemia was not indicated due to the fact that we follow a selectively proactive protocol and no patients required acute reactive postoperative calcium replacement. However 2 patients had to be readmitted for acute symptomatic hypocalcaemia in this cohort. Both patients had borderline calcium levels on the day of discharge and had prophylactic calcium treatment. One patient who underwent a left thyroid lobectomy but also had a contralateral parathyroid adenoma, which was also removed. She was sent home with prophylactic calcium and despite this she was readmitted requiring calcium replacement therapy. The second patient was a male with an overactive gland who developed Hungry Bone Syndrome and within 6 months he recovered his parathyroid function.

In our study the rate of permanent hypocalcaemia in total thyroidectomy at 6 months is 6.02%. The rates are similar to those reported in the literature.

6.9.1 Tracheomalacia

Postoperative tracheomalacia in ITG is both rare and controversial. Recent studies in Western Countries have suggested that the incidence and risk of tracheomalacia is between 0.001 and 1.5% with some series being 0% (117, 118). In contrast, surgeons working in endemic goiter areas have reported much higher rates (eg 3.1% and 5.8%) during the last decade (119, 120).

Recent studies have concluded that tracheomalacia is minimal in modern thyroid surgery (ranging from 0.001% to 0.05%; see Table 4) (117, 118, 121). The highest incidence (1.5%) reported was in ITG [4]. We note that, recently, case series studying the incidence of tracheomalacia and the risks of this condition have not come from groups specializing in complex thyroid pathology. This rises the issue of what could represent the common denominator and what will be a true rate. For the purpose of this study the rate is applied to ITG.

A retrospective review from India by Agarwal et al identified 28 (3.1%) of 900 patients undergoing a thyroidectomy who required any treatment for tracheomalacia, with 26 (2.8%) receiving a tracheostomy (122). This group recently published additional work noting the persistence of the tracheomalacia phenomenon in patients with large goitre (119). In another report from Sudan, 6 (5.8%) of 103 patients undergoing thyroid surgery for a large goitre had tracheomalacia, with 5 (4.8%) requiring a tracheostomy (123).

Another factor that accounts for the variation in tracheomalacia incidence is the heterogeneity of goitre sizes used in studies about the incidence of this condition. For example, Lacoste et al followed a cohort of 3,008 patients undergoing thyroidectomy none of whom developed tracheal collapse after surgery (124). Benett et al conducted a study with over 2000 patients that had a heterogeneous definition criteria of ITG that included goitres of different sizes rather than the compressible definition (goitre size greater than 100g) (121).

Our rate of tracheomalacia in patients presenting with ITG is 1.6% (4 out of 237 patients). It is difficult to make robust conclusions as to what is the factors leading to tracheomalacia however it appears that preoperative acute airway obstruction is one of them as two of them presented with acute airway obstruction due to a large bilateral ITG. It is obvious however that the great majority of patients with ITG will not develop the condition.

It is nevertheless important that surgeons undertaking surgery for large goitres recognises it existence as this may lead to significant management implications as some patients will require tracheostomy.

Classically, tracheomalacia has been defined as an extreme degree of compression of the airway resulting in the cross-sectional area of the trachea being reduced to less than half its accepted size [120, 125]. This airway alteration produces a progressive asphyxia not responding to increasing fractionated inspired oxygen concentration (FiO2). Stridor becomes evident only when the tracheal diameter is reduced to less than 3.5 mm, signalling critical functional obstruction [126].

Lacoste et al suggested that the main causes of postoperative respiratory obstruction are wound hematoma, bilateral recurrent laryngeal nerve palsies, and laryngeal oedema [117]. These findings were supported by several other groups, and therefore necessitate the exclusion of these diagnoses before a diagnosis of tracheomalacia can be made [118, 123-125].

The diagnosis of tracheomalacia is not consistent; there are no “reproducible” radiological criteria that permit the comparisons between the different series. Preoperative imaging studies of the trachea compression (such as anterior–posterior chest X-ray or CT of the neck and upper chest do not predict to the risk of tracheomalacia. Findlay et al estimated the risk of tracheomalacia in patients with goitres causing significant tracheal compression. The study included 18 patients with critical compression <5 mm and 35 patients with compression between 6-10 mm in a series of 334 patients with thyroid surgery [118]. No patients required tracheostomy placement or were diagnosed with tracheomalacia.

Although there is no accepted intraoperative diagnosis of tracheomalacia, Agarwal et recently proposed a definition for the intraoperative diagnosis of tracheomalacia that has to include one or more of the following criteria: (1) Soft and floppy trachea on palpation by the surgeon at the end of thyroidectomy. It is worth noting that, because of the splinting effect of the endotracheal tube in *situ,* it may be difficult to appreciate a soft trachea. One could ask the anaesthetist to gradually withdraw the tube for a short distance and then feel the trachea without the tube in site. This maneuver may also help the surgeon recognize an obvious collapse of the tracheal wall. (2) Obstruction to spontaneous respiration during gradual withdrawal of the endotracheal tube after thyroidectomy. (3) Difficulty in negotiating the suction catheter beyond the endotracheal tube after gradual withdrawal. (4)

After closure of the wound, tracheomalacia can be suspected if there is (a) absence of peri-tubal leak on deflation of the endotracheal tube cuff, (b) absence of volume pressure loop on ventilator or (c) development of respiratory stridor along with a falling hemoglobin oxygen saturation (SpO2) on pulse oximetry despite the administration of increasing FiO2 [122].

In our series, Agarwal diagnostic criteria was used intraoperatively, and the diagnosis was made by the author and the consultant anaesthetist [126]. We recommend that when tracheomalacia is suspected every effort is made to achieve the diagnosis intraoperatively as making the postoperative diagnosis of tracheomalacia could result in potential airway complications.

Large series of tracheomalacia patients have not revealed a clinically significant link between stridor and tracheomalacia as either a sensitive or specific diagnostic criteria. For example, Agarwal found stridor in only a quarter of patients (7/28) [122]. In our study, only 2 out of the 4 patients presented with preoperative stridor and also had evidence of recurrent laryngeal nerve paralysis.

The management of tracheomalacia is controversial. It is recommended that tracheostomy is avoided if possible. As an alternative, in mild cases keeping the patient intubated for 24 to 48 hours or keep the patient with CPAP (Continous Pressure airway ventilation and allow the trachea to re-expand may be advised. However in severe cases it may be very difficult to avoid tracheostomy. In our 4 cases, 1 had already a pre-operative long-standing tracheostomy due to a previous complicated thyroidectomy in another centre, 2 had pre-operative tracheostomies due to acute airway obstruction and 1 patient had mild tracheomalacia which was managed conservatively with CPAP for 24h. Both patients who had pre-operative tracheostomies due to acute airway obstruction were successfully decannulated.

6.9.2 Other complications

Thyroid surgery outcomes usually relate to resolution of the pathology, rates of RLNP and hypoparathyroidism [127]. However surgery for ITG is regarded as high risk surgery and therefore there is an associated risk of other important complications especially those related mediastinal structures [5].

Other complications to neightbouring anatomical organs reported by some other authors include injury to trachea, injury to oesophagus, injury to phrenic nerve, and cardiac arrytmias [(29)]. These occur mainly in patients with malignant disease but there are extremely rare in dealing with benign goitres. None of them have occurred in our experience.

The rate of unusual complications is higher in extracervical approaches and this is a reflection of the extent of the disease and dissection.

6.10 MORTALITY

Mortality is the worse complication that can occur following surgery for intrathoracic goitres. The rate of mortality ranges from 0 to15.3% in some series. The incidence of mortality appears to be higher in patients who have malignant disease such as anaplastic carcinoma or the surgery has been indicated for severe worsening respiratory symptoms [(128)].

Di Crescenzo et al reported a mortality rate ranging from 2% in cervical approaches to 15.3% in patients requiring sternotomy [(115)]. Sancho et al also reported an increased risk of mortality in patients in which the goitre reached the carina trachea. In their series, the incidence of mortality was 5.7% and they felt that this was significantly higher than in other series [(42)].

The risk factors for increased mortality were malignant disease such as anaplastic carcinoma and rapidly worsening respiratory symptoms before surgery. The causes of death are attributed to severe postoperative complications such as sternotomy dehiscence and tracheobronchial fistula.

In this series, no patients died as a consequence of the surgical procedure and therefore the incidence of mortality is 0%. This incidence is in line with other reported experience from specialized thyroid surgery centres such as the Massachusetts Eye and Ear Infirmary[(22)].We attribute this to careful patient selection, preoperative evaluation, preoperative optimization, multidisciplinary team working with experienced thoracic surgeons and exemplary postoperative care. All patients requiring sternotomy or lateral thoracotomy were kept intubated and ventilated overnight in the Intensive Care Unit and this reduces the risk of severe postoperative events such as bleeding and cardiovascular events.

6.11 INFECTION

Infection risk is always included as part of the consent for patients undergoing surgery and thyroidectomy is no exception. Postoperative haemorrhage, injury to recurrent laryngeal nerve and hypocalcaemia are the main outcome measures referring to thyroid surgery. However, infection is rarely included as part of the outcomes of thyroid surgery. The risk of infection is often low and represents around 1% to 2% of patients undergoing thyroid surgery [(129)]. The risk of infection increases with the complexity of the procedure, whether neck dissection is done or not and of course if an extracervical approach is used [(42)].

The risk of wound infection is not discussed in most recent papers reporting outcomes of surgery for ITGs.

Sancho et al reported a 6% incidence of pneumonia a 3% of catheter related sepsis and 3% of postoperative urinary track infection but there is no indication of wound infection despite one patient suffering sternotomy dehiscence which resulted in death [(42)].

Antibiotic prophylaxis was also not discussed as needed in patients undergoing surgery for ITG in any of the literature reviewed.

The rate of postoperative wound infection in our series has been 0%. 2 patients in the extracervical approach group developed lobar atelectasis and pneumonia which was successfully treated with intravenous antibiotic therapy. Systemic infections are most likely to occur in patients undergoing extracervical approaches.

The role of prophylactic antibiotic therapy in patients undergoing surgery for ITG is yet to be elucidated. Our protocol, which is stated in the methods section appears to be effective in preventing postoperative wound infection.

The true rate of postoperative wound infection in thyroid surgery may be able to be elucidated when national databases such as in Denmark or the United Kingdom are analyzed.

6.12 HAEMORRHAGE

Postoperative haemorrhage after thyroid surgery can be one of the most devastating and life-threatining complications despite of not being included in the main outcomes in most series reporting outcomes in thyroid surgery.

Postoperative haemorrhage can lead to laryngeal oedema and potential airway obstruction including death. The majority of these episodes occur in the first 8 hours after surgery.

Goodballe et al in 2009 collected data from the National Danish Thyroid Data Base. This paper represents the most complete account on postoperative bleeding after thyroid surgery. The rates of haemorrhage ranged from 1.9 to 14.3% with a mean rate of 4.2% [(130)].

As per the reporting of complications, units with better outcomes are more likely to publish their results and therefore complication rates may appear to be falsely low leading to a publication bias. Anonimized national data collection may overcome this problem as units are obligated to submit their outcome.

Factors increasing the risk of postoperative haemorrhage include patients over the age of 50 years, malignant histology, male gender and bilateral procedures. Most of these factors are patient related and therefore difficult to adjust.

In our study the rate of postoperative haemorrhage was low (1.2%) only occurring in 3 patients. In all patients the onset of the bleeding was in the first 8 hours after surgery and it was caused in all patients by episodes pof coughing. No obvious bleeding was found in the reexploration.

Interestingly, the patients in whom the haemorrhage occurred were in the transcervical group. In this group the patients were fully awake and had cervical drains as opposed to the patients in the extracervical approaches who were recovered in the intensive care unit, had large mediastinal drains and were more heavily sedated and some of them intubated and ventilated for the first 24 h.

6.13 PNEUMOTHORAX

The risk of pneumothorax in patients undergoing cervical approach is minimal. The risk of pneumothorax in patients undergoing extracervical approach is obviously higher.

In some patients, a pneumothorax was created by the opening of the mediastinal pleura at the time of dissection, and it was necessary to be able to resect the goitre from this structure. In patients in which an intentional pneumothorax was necessary, a second mediastinal intrapleural drain was inserted and all patients had their drains removed within 5 days of surgery. None of them required further drainage.

6.14 TRACHEOSTOMY

Tracheostomy after thyroidectomy is rare. Published rates average between 2 to 3% and are related to bilateral RLN injury or tracheomalacia [22, 126].

Randolph et al reported a rate of 3% of patients undergoing thyroidectomy for ITG. There was a low threshold for temporary tracheostomy in cases where there was a concern for laryngeal oedema or in cases of known preoperative uniteral vocal cord dysfunction where contralateral vocal cord integrity was in question during the surgery [22].

In our experience the rate of tracheostomy was 2.5%. The risk of undergoing a tracheostomy was higher in patients with severe tracheomalacia, patients with bilateral recurrent laryngeal nerve injuries, those undergoing total thyroidectomies, those who have undergone previous surgery and patients presenting with acute airway obstruction. Fortunately, the risk is low as in the majority of patients, the goitre compression appears to be unilateral rather than bilateral.

Regardless of the low risk of tracheotomy, we recommend that patients with ITG undergoing total thyroidectomy, with previous preoperative RLN injury and with preoperative acute or incipient airway obstruction or suspected tracheomalacia, should be consented for elective tracheostomy.

6.15 LENGTH OF STAY

The LOS in thyroid surgery has reduced significantly over the past two decades and in many centres, has become an ambulatory or less than a 23h stay procedure. This has been a consequence of better surgical planning and techniques, improved technical advances, better anaesthetic techiniques and more efficient postoperative care. This has also been driven by the need for reducing health care costs.

In surgery for ITGs these changes have had a positive impact in reducing significantly the postoperative LOS. As shown, surgery for ITG is complex and in a significant proportion of patients it does require ECA which will require more time and care until the patient is ready for discharge. Also, patients undergoing this surgery are often elderly and have multiple co-morbidities. Additionally most of this surgery is now done in tertiary referral centres and patients have to travel long distances for their procedures. It is therefore difficult for these patients to be sent home in the first 23 hours after their procedure.

However, there is no excuse for the care not to be streamlined and the postoperative pathway should be efficient and appropriate to current standards of care.

A mean LOS of 3.5 days appears to be entirely appropriate for the magnitude of these procedures bearing in mind that some patients, may have ECA, additional procedures such as tracheostomies and may have complex discharge needs.

6.15.1 Limitations and weaknesess of the study

This study has the limitations of any retrospective cohort analysis. The study was not controlled and the study groups are different is size. This is unfortunately part of the intrinsic nature of such a study. Limitations both in sample size and complication rate resulted in a low number of adverse events which restricted multivariate modeling. However, although a prospective randomised controlled trial setting would be ideal to determine outcomes in a more scientific manner, this is clearly impossible given ethical limitations in clinical surgical practice. This study was performed by a single surgical clinical team in a large University Teaching Hospital and although this eliminates surgical variability it also inflicts bias into the surgical results should these be extrapolated to other settings.

6.15.2 Strengths of the study

Despite being a retrospective analysis review, the data was collected prospectively and the dataset complete. This is one of the largest European and worldwide surgical series addressing the management of ITG. Many studies have addressed only a single aspect in the complex overall management of these patients. In contrast, this study addresses the whole spectrum of challenges involving the management of ITG, from the clinical presentation and evaluation, rate of malignancy, prediction of surgical approach and clinical outcomes both overall and in relation to the surgical approach required. Very few studies to date have had sufficiently robust a dataset to achieve this.

6.16 VALUE OF THE STUDY

This study will help surgeons and clinicians managing patients with ITG. It describes issues relating to the presentation and assessment of this group of patients as well as both intra and postoperative challenges. This will allow surgeons to understand outcomes relating to surgery for ITG, ensure adequate resource allocation to minimise complications and improve informed consent.

7

CONCLUSIONS

1. The rate of malignancy in goitres with intrathoracic extension is 8.01% and the rate of occult malignancy is 5.0%.
2. Ultrasound guided fine needle aspiration has a sensitivity of 31.6%, the specificity of 93.6%, PPV of 30% and a NPV of 94% to indicate malignancy with in the ITG.
3. The rate of sternotomy in non-malignant ITG is 12.2%.
4. Over 87% of intrathoracic goitres can be successfully delivered and excised via a transcervical approach. An increased risk of needing an extracervical approach occurs with goitres extending beyond the aortic arch, “iceberg” shapes and revision surgery.
5. The risk of temporary injury to the recurrent laryngeal nerve was 3.22% and the risk of permanent injury was 2.1% of nerves at risk. The risk of temporary and permanent RLNP is significantly higher if sternotomy is undertaken ($p<0.003$ and $p<0.006$).
6. The use of neuromonitoring does not reduce the risk of the rate of temporary injury to the recurrent laryngeal nerve ($p=0.522$), however it reduces the risk of permanent injury and it may be useful in selected cases including revision surgery.
7. The risk of permanent hypoparathyroidism is 6.4% and should only apply to total thyroidectomies.
8. The rate of tracheomalacia was 1.6% and often presents preoperatively with acute airway obstruction and the risk of tracheostomy was 2.5 % and this should be included in the consent form when doing total thyroidectomies for intrathoracic goitres.
9. The rate of extrathyroidal complications was 2.5% but 20% in extracervical approaches and this is a reflection of the extent of the disease and dissection.
10. The length of stay in surgery for ITG ranged from 2 to 14 days. The median for transcervical approaches was 3 days and the median for extracervical approaches was 6.0 days.

8

REFERENCES

1. Hannan SA. The magnificent seven: a history of modern thyroid surgery. International journal of surgery 2006;4(3):187-91.

2. Vaiman M, Bekerman I. Anatomical approach to surgery for intrathoracic goiter. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies 2017;274(2):1029-1034.

3. Nixon IJ, Simo R. The neoplastic goitre. Current opinion in otolaryngology & head and neck surgery 2013;21(2):143-9.

4. Association BT. Guidelines for the Management of Thyroid Cancer (Second Edition). In: Physicians RCo, editor. 2 ed. Great Britain: The Lavenham Press, Suffolk; 2007. p. 92.

5. Rios A, Sitges-Serra A. [Surgical treatment of intrathoracic goitre]. Cirugia espanola 2012;90(7):421-8.

6. Ezzat S, Sarti DA, Cain DR, Braunstein GD. Thyroid incidentalomas. Prevalence by palpation and ultrasonography. Arch Intern Med 1994;154(16):1838-40.

7. Brix TH, Hegedus L. Genetic and environmental factors in the aetiology of simple goitre. Ann Med 2000;32(3):153-6.

8. Gittoes NJ, Miller MR, Daykin J, Sheppard MC, Franklyn JA. Upper airways obstruction in 153 consecutive patients presenting with thyroid enlargement. Bmj 1996;312(7029):484.

9. Randolph G. Surgery of the thyroid and parathyroid glands: Elsevier; 2013.

10. Rios A, Rodriguez JM, Balsalobre MD, Tebar FJ, Parrilla P. The value of various definitions of intrathoracic goiter for predicting intra-operative and postoperative complications. Surgery 2010;147(2):233-8.

11. Rugiu MG, Piemonte M. Surgical approach to retrosternal goitre: do we still need sternotomy? Acta otorhinolaryngologica Italica : organo ufficiale della Societa italiana di otorinolaringologia e chirurgia cervico-facciale 2009;29(6):331-8.

12. Randolph G. Surgery of The Thyroid and Parathyroids; 2003.

13. Huins CT, Georgalas C, Mehrzad H, Tolley NS. A new classification system for retrosternal goitre based on a systematic review of its complications and management. International journal of surgery 2008;6(1):71-6.

14. Katlic MR, Grillo HC, Wang CA. Substernal goiter. Analysis of 80 patients from Massachusetts General Hospital. American journal of surgery 1985;149(2):283-7.

15. Cohen JP. Substernal goiters and sternotomy. The Laryngoscope 2009;119(4):683-8.

16. Hashmi SM, Premachandra DJ, Bennett AM, Parry W. Management of retrosternal goitres: results of early surgical intervention to prevent airway morbidity, and a review of the English literature. The Journal of laryngology and otology 2006;120(8):644-9.

17. Shin JJ, Grillo HC, Mathisen D, et al. The surgical management of goiter: Part I. Preoperative evaluation. The Laryngoscope 2011;121(1):60-7.

18. Buckley JA, Stark P. Intrathoracic mediastinal thyroid goiter: imaging manifestations. AJR American journal of roentgenology 1999;173(2):471-5.

19. Mack E. Management of patients with substernal goiters. The Surgical clinics of North America 1995;75(3):377-94.

20. Hall TS, Caslowitz P, Popper C, Smith GW. Substernal goiter versus intrathoracic aberrant thyroid: a critical difference. The Annals of thoracic surgery 1988;46(6):684-5.

21. White ML, Doherty GM, Gauger PG. Evidence-based surgical management of substernal goiter. World journal of surgery 2008;32(7):1285-300.

22. Randolph GW, Shin JJ, Grillo HC, et al. The surgical management of goiter: Part II. Surgical treatment and results. The Laryngoscope 2011;121(1):68-76.

23. Allo MD, Thompson NW. Rationale for the operative management of substernal goiters. Surgery 1983;94(6):969-77.

24. Landerholm K, Jarhult J. Should asymptomatic retrosternal goitre be left untreated? A prospective single-centre study. Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society 2015;104(2):92-5.

25. Melliere D, Saada F, Etienne G, Becquemin JP, Bonnet F. Goiter with severe respiratory compromise: evaluation and treatment. Surgery 1988;103(3):367-73.

26. Shaha AR, Burnett C, Alfonso A, Jaffe BM. Goiters and airway problems. American journal of surgery 1989;158(4):378-80; discussion 380-1.

27. Moorthy R, Balfour A, Jeannon JP, Simo R. Recurrent laryngeal nerve palsy in benign thyroid disease: can surgery make a difference? European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies 2012;269(3):983-7.

28. Gutierrez T, Leong AC, Pang L, Chevretton E, Jeannon JP, Simo R. Multinodular thyroid goitre causing obstructive sleep apnoea syndrome. The Journal of laryngology and otology 2012;126(2):190-5.

29. Sancho JJ, Prieto R, Duenas JP, et al. A randomized trial of hemithyroidectomy versus Dunhill for the surgical management of asymmetrical multinodular goiter. Annals of surgery 2012;256(5):846-51; discussion 851-2.

30. Coskun A, Yildirim M, Erkan N. Substernal goiter: when is a sternotomy required? International surgery 2014;99(4):419-25.

31. Vasica G, O'Neill CJ, Sidhu SB, Sywak MS, Reeve TS, Delbridge LW. Reoperative surgery for bilateral multinodular goitre in the era of total thyroidectomy. The British journal of surgery 2012;99(5):688-92.

32. Testini M, Gurrado A, Bellantone R, et al. Recurrent laryngeal nerve palsy and substernal goiter. An Italian multicenter study. Journal of visceral surgery 2014;151(3):183-9.

33. Stevens JL, Constantinides V, Todd J, et al. Do flow volume loops alter surgical management in patients with a goitre? Clinical endocrinology 2014;81(6):916-20.

34. Dempsey GA, Snell JA, Coathup R, Jones TM. Anaesthesia for massive retrosternal thyroidectomy in a tertiary referral centre. British journal of anaesthesia 2013;111(4):594-9.

35. Chiang FY, Lu IC, Chen HC, et al. Intraoperative neuromonitoring for early localization and identification of recurrent laryngeal nerve during thyroid surgery. The Kaohsiung journal of medical sciences 2010;26(12):633-9.

36. Findlay JM, Sadler GP, Bridge H, Mihai R. Post-thyroidectomy tracheomalacia: minimal risk despite significant tracheal compression. British journal of anaesthesia 2011;106(6):903-6.

37. McKenzie GA, Rook W. Is it possible to predict the need for sternotomy in patients undergoing thyroidectomy with retrosternal extension? Interactive cardiovascular and thoracic surgery 2014;19(1):139-43.

38. Grainger J, Saravanappa N, D'Souza A, Wilcock D, Wilson PS. The surgical approach to retrosternal goiters: the role of computerized tomography. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2005;132(6):849-51.

39. Hajhosseini B, Montazeri V, Hajhosseini L, Nezami N, Beygui RE. Mediastinal goiter: a comprehensive study of 60 consecutive cases with special emphasis on identifying predictors of malignancy and sternotomy. Am J Surg 2012;203(4):442-7.

40. Casella C, Pata G, Cappelli C, Salerni B. Preoperative predictors of sternotomy need in mediastinal goiter management. Head Neck 2010;32(9):1131-5.

41. Cichon S, Anielski R, Konturek A, Baczynski M, Cichon W, Orlicki P. Surgical management of mediastinal goiter: risk factors for sternotomy. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie 2008;393(5):751-7.

42. Sancho JJ, Kraimps JL, Sanchez-Blanco JM, et al. Increased mortality and morbidity associated with thyroidectomy for intrathoracic goiters reaching the carina tracheae. Archives of surgery 2006;141(1):82-5.

43. Perros P, Boelaert K, Colley S, et al. Guidelines for the management of thyroid cancer. Clinical endocrinology 2014;81 Suppl 1:1-122.

44. Simo R, Nixon I, Tysome J, Balfour A, Jeannon JP. Modified Extended Kocher Incision for Total Thyroidectomy with Lateral Compartment Neck Dissection - A critical Appraisal of Surgical Access and Cosmesis in thirty one patients. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 2012.

45. Randolph GW, Kobler JB, Wilkins J. Recurrent laryngeal nerve identification and assessment during thyroid surgery: laryngeal palpation. World journal of surgery 2004;28(8):755-60.

46. Bliss RD, Gauger PG, Delbridge LW. Surgeon's approach to the thyroid gland: surgical anatomy and the importance of technique. World journal of surgery 2000;24(8):891-7.

47. Darr EA, Randolph GW. Management of laryngeal nerves and parathyroid glands at thyroidectomy. Oral oncology 2013;49(7):665-70.

48. Hisham AN, Lukman MR. Recurrent laryngeal nerve in thyroid surgery: a critical appraisal. ANZ journal of surgery 2002;72(12):887-9.

49. Simo R NI, Ofo E. Surgery for Intrathoracic Goitre (Retrosternal) goitres. In: J F, editor. Open access atlas of otolaryngology, head and neck operative surgery. Cape Town Southafrica: University of Cape Town; 2015.

50. Botrugno I, Lovisetto F, Cobianchi L, et al. Incidental carcinoma in multinodular goiter: risk factors. The American surgeon 2011;77(11):1553-8.

51. Dogan L, Karaman N, Yilmaz KB, Ozaslan C, Atalay C. Total thyroidectomy for the surgical treatment of multinodular goiter. Surgery today 2011;41(3):323-7.

52. Luo J, McManus C, Chen H, Sippel RS. Are there predictors of malignancy in patients with multinodular goiter? The Journal of surgical research 2012;174(2):207-10.

53. Agarwal A, Agarwal S, Tewari P, et al. Clinicopathological profile, airway management, and outcome in huge multinodular goiters: an institutional experience from an endemic goiter region. World journal of surgery 2012;36(4):755-60.

54. Rios A, Rodriguez JM, Canteras M, Galindo PJ, Balsalobre MD, Parrilla P. Risk factors for malignancy in multinodular goitres. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 2004;30(1):58-62.

55. Hsu B, Reeve TS, Guinea AI, Robinson B, Delbridge L. Recurrent substernal nodular goiter: incidence and management. Surgery 1996;120(6):1072-5.

56. Cai XJ, Valiyaparambath N, Nixon P, Waghorn A, Giles T, Helliwell T. Ultrasound-guided fine needle aspiration cytology in the diagnosis and management of thyroid nodules. Cytopathology : official journal of the British Society for Clinical Cytology 2006;17(5):251-6.

57. Campbell MJ, Seib CD, Candell L, et al. The underestimated risk of cancer in patients with multinodular goiters after a benign fine needle aspiration. World journal of surgery 2015;39(3):695-700.

58. Tysome JR, Chandra A, Chang F, et al. Improving prediction of malignancy of cytologically indeterminate thyroid nodules. The British journal of surgery 2009;96(12):1400-5.

59. Riffat F, Del Pero MM, Fish B, Jani P. Radiologically predicting when a sternotomy may be required in the management of retrosternal goiters. The Annals of otology, rhinology, and laryngology 2013;122(1):15-9.

60. Bin Saeedan M, Aljohani IM, Khushaim AO, Bukhari SQ, Elnaas ST. Thyroid computed tomography imaging: pictorial review of variable pathologies. Insights into imaging 2016;7(4):601-17.

61. Qureishi A, Garas G, Tolley N, Palazzo F, Athanasiou T, Zacharakis E. Can pre-operative computed tomography predict the need for a thoracic approach for removal of retrosternal goitre? International journal of surgery 2013;11(3):203-8.

62. Flati G, De Giacomo T, Porowska B, et al. Surgical management of substernal goitres. When is sternotomy inevitable? La Clinica terapeutica 2005;156(5):191-5.

63. El-Boghdadly K AI. Anaesthesia for the difficult airway. Journal of the ENT Masterclass 2015;8(1):118 - 123.

64. Shaha AR, Alfonso AE, Jaffe BM. Operative treatment of substernal goiters. Head & neck 1989;11(4):325-30.

65. Chen AY, Bernet VJ, Carty SE, et al. American Thyroid Association statement on optimal surgical management of goiter. Thyroid : official journal of the American Thyroid Association 2014;24(2):181-9.

66. Nakaya M, Ito A, Mori A, et al. Surgical treatment of substernal goiter: An analysis of 44 cases. Auris, nasus, larynx 2016.

67. Nouraei SA, Virk JS, Middleton SE, et al. A national analysis of trends, outcomes and volume-outcome relationships in thyroid surgery. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 2016.

68. Gourin CG, Tufano RP, Forastiere AA, Koch WM, Pawlik TM, Bristow RE. Volume-based trends in thyroid surgery. Archives of otolaryngology--head & neck surgery 2010;136(12):1191-8.

69. Watkinson JC. Fifteen years' experience in thyroid surgery. Annals of the Royal College of Surgeons of England 2010;92(7):541-7.

70. Foroulis CN, Rammos KS, Sileli MN, Papakonstantinou C. Primary intrathoracic goiter: a rare and potentially serious entity. Thyroid : official journal of the American Thyroid Association 2009;19(3):213-8.

71. Chandrasekhar SS, Randolph GW, Seidman MD, et al. Clinical practice guideline: improving voice outcomes after thyroid surgery. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2013;148(6 Suppl):S1-37.

72. Jeannon JP, Orabi AA, Bruch GA, Abdalsalam HA, Simo R. Diagnosis of recurrent laryngeal nerve palsy after thyroidectomy: a systematic review. Int J Clin Pract 2009;63(4):624-9.

73. Rios A, Rodriguez JM, Galindo PJ, et al. Results of surgical treatment in multinodular goiter with an intrathoracic component. Surgery today 2008;38(6):487-94.

74. Godballe C, Madsen AR, Sorensen CH, et al. Risk factors for recurrent nerve palsy after thyroid surgery: a national study of patients treated at Danish departments of ENT Head and Neck Surgery. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies 2014;271(8):2267-76.

75. Sinclair CF, Bumpous JM, Haugen BR, et al. Laryngeal examination in thyroid and parathyroid surgery: An American Head and Neck Society consensus statement: AHNS Consensus Statement. Head & neck 2016;38(6):811-9.

76. Melin M, Schwarz K, Pearson MD, Lammers BJ, Goretzki PE. Postoperative vocal cord dysfunction despite normal intraoperative neuromonitoring: an unexpected complication with the risk of bilateral palsy. World journal of surgery 2014;38(10):2597-602.

77. Barczynski M, Konturek A, Pragacz K, Papier A, Stopa M, Nowak W. Intraoperative nerve monitoring can reduce prevalence of recurrent laryngeal nerve injury in thyroid reoperations: results of a retrospective cohort study. World journal of surgery 2014;38(3):599-606.

78. Lahey F. Routine dissection and demonstration of the recurrent laryngeal nerve in subtotal thyroidectomy. Surg Gynecol Obstet 1938;66:775-777.

79. Riddell VH. Injury to recurrent laryngeal nerves during thyroidectomy; a comparison between the results of identification and non-identification in 1022 nerves exposed to risk. Lancet 1956;271(6944):638-41.

80. Hermann M AG, Roka R, Glaser K, Freissmuth M. Laryngeal recurrent nerve injury in surgery for benign thyroid diseases: effect of nerve dissection and impact of individual surgeon in more than 27,000 nerves at risk. Ann Surg 2002;235(2):261-268.

81. Shindo M, Chheda NN. Incidence of vocal cord paralysis with and without recurrent laryngeal nerve monitoring during thyroidectomy. Archives of otolaryngology--head & neck surgery 2007;133(5):481-5.

82. Brunner E, Friedrich G, Kiesler K, Chibidziura-Priesching J, Gugatschka M. Subjective breathing impairment in unilateral vocal fold paralysis. Folia phoniatrica et logopaedica : official organ of the International Association of Logopedics and Phoniatrics 2011;63(3):142-6.

83. Leder SB, Ross DA. Incidence of vocal fold immobility in patients with dysphagia. Dysphagia 2005;20(2):163-7; discussion 168-9.

84. Ollivere B, Duce K, Rowlands G, Harrison P, O’Reilly BJ. Swallowing dysfunction in patients with unilateral vocal fold paralysis: aetiology and outcomes. The Journal of laryngology and otology 2006;120(1):38-41.

85. Stojadinovic A, Shaha AR, Orlikoff RF, et al. Prospective functional voice assessment in patients undergoing thyroid surgery. Annals of surgery 2002;236(6):823-32.

86. Kern KA. Medicolegal analysis of errors in diagnosis and treatment of surgical endocrine disease. Surgery 1993;114(6):1167-73; discussion 1173-4.

87. Singer MC, Iverson KC, Terris DJ. Thyroidectomy-related malpractice claims. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2012;146(3):358-61.

88. Dralle H, Sekulla C, Haerting J, et al. Risk factors of paralysis and functional outcome after recurrent laryngeal nerve monitoring in thyroid surgery. Surgery 2004;136(6):1310-22.

89. Barczynski M, Konturek A, Cichon S. Randomized clinical trial of visualization versus neuromonitoring of recurrent laryngeal nerves during thyroidectomy. The British journal of surgery 2009;96(3):240-6.

90. Dralle H, Sekulla C, Lorenz K, Brauckhoff M, Machens A, German ISG. Intraoperative monitoring of the recurrent laryngeal nerve in thyroid surgery. World journal of surgery 2008;32(7):1358-66.

91. Higgins TS, Gupta R, Ketcham AS, Sataloff RT, Wadsworth JT, Sinacori JT. Recurrent laryngeal nerve monitoring versus identification alone on post-thyroidectomy true vocal fold palsy: a meta-analysis. The Laryngoscope 2011;121(5):1009-17.

92. Dionigi G, Bacuzzi A, Boni L, Rausei S, Rovera F, Dionigi R. Visualization versus neuromonitoring of recurrent laryngeal nerves during thyroidectomy: what about the costs? World journal of surgery 2012;36(4):748-54.

93. Chan WF, Lang BH, Lo CY. The role of intraoperative neuromonitoring of recurrent laryngeal nerve during thyroidectomy: a comparative study on 1000 nerves at risk. Surgery 2006;140(6):866-72; discussion 872-3.

94. Sari S, Erbil Y, Sumer A, et al. Evaluation of recurrent laryngeal nerve monitoring in thyroid surgery. International journal of surgery 2010;8(6):474-8.

95. Lo CY, Kwok KF, Yuen PW. A prospective evaluation of recurrent laryngeal nerve paralysis during thyroidectomy. Archives of surgery 2000;135(2):204-7.

96. Bergenfelz A, Jansson S, Kristoffersson A, et al. Complications to thyroid surgery: results as reported in a database from a multicenter audit comprising 3,660 patients. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie 2008;393(5):667-73.

97. Goretzki PE, Schwarz K, Brinkmann J, Wirowski D, Lammers BJ. The impact of intraoperative neuromonitoring (IONM) on surgical strategy in bilateral thyroid diseases: is it worth the effort? World journal of surgery 2010;34(6):1274-84.

98. Randolph GW, Dralle H, Abdullah H, et al. Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. Laryngoscope 2011;121 Suppl 1:S1-16.

99. James AG, Crocker S, Woltering E, Ferrara J, Farrar W. A simple method for identifying and testing the recurrent laryngeal nerve. Surgery, gynecology & obstetrics 1985;161(2):185-6.

100. Tomoda C, Hirokawa Y, Uruno T, et al. Sensitivity and specificity of intraoperative recurrent laryngeal nerve stimulation test for predicting vocal cord palsy after thyroid surgery. World journal of surgery 2006;30(7):1230-3.

101. Loch-Wilkinson TJ, Stalberg PL, Sidhu SB, Sywak MS, Wilkinson JF, Delbridge LW. Nerve stimulation in thyroid surgery: is it really useful? ANZ journal of surgery 2007;77(5):377-80.

102. Cavicchi O, Caliceti U, Fernandez IJ, et al. Laryngeal neuromonitoring and neurostimulation versus neurostimulation alone in thyroid surgery: a randomized clinical trial. Head & neck 2012;34(2):141-5.

103. Eltzschig HK, Posner M, Moore FD, Jr. The use of readily available equipment in a simple method for intraoperative monitoring of recurrent laryngeal nerve function during thyroid surgery: initial experience with more than 300 cases. Arch Surg 2002;137(4):452-6; discussion 456-7.

104. Rice DH, Cone-Wesson B. Intraoperative recurrent laryngeal nerve monitoring. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 1991;105(3):372-5.

105. Tschopp KP, Gottardo C. Comparison of various methods of electromyographic monitoring of the recurrent laryngeal nerve in thyroid surgery. The Annals of otology, rhinology, and laryngology 2002;111(9):811-6.

106. Eisele DW. Intraoperative electrophysiologic monitoring of the recurrent laryngeal nerve. The Laryngoscope 1996;106(4):443-9.

107. Chiang FY, Lu IC, Kuo WR, Lee KW, Chang NC, Wu CW. The mechanism of recurrent laryngeal nerve injury during thyroid surgery--the application of intraoperative neuromonitoring. Surgery 2008;143(6):743-9.

108. Donatini G, Carnaille B, Dionigi G. Increased detection of non-recurrent inferior laryngeal nerve (NRLN) during thyroid surgery using systematic intraoperative neuromonitoring (IONM). World journal of surgery 2013;37(1):91-3.

109. Sulica L. The superior laryngeal nerve: function and dysfunction. Otolaryngologic clinics of North America 2004;37(1):183-201.

110. Maranillo E, Leon X, Quer M, Orus C, Sanudo JR. Is the external laryngeal nerve an exclusively motor nerve? The cricothyroid connection branch. The Laryngoscope 2003;113(3):525-9.

111. Barczynski M, Randolph GW, Cernea CR, et al. External branch of the superior laryngeal nerve monitoring during thyroid and parathyroid surgery: International Neural Monitoring Study Group standards guideline statement. The Laryngoscope 2013;123 Suppl 4:S1-14.

112. Vasileiadis I, Karatzas T, Charitoudis G, Karakostas E, Tseleni-Balafouta S, Kouraklis G. Association of Intraoperative Neuromonitoring With Reduced Recurrent Laryngeal Nerve Injury in Patients Undergoing Total Thyroidectomy. JAMA otolaryngology-- head & neck surgery 2016;142(10):994-1001.

113. Pattou F, Combemale F, Fabre S, et al. Hypocalcemia following thyroid surgery: incidence and prediction of outcome. World journal of surgery 1998;22(7):718-24.

114. Lorente-Poch L, Sancho JJ, Ruiz S, Sitges-Serra A. Importance of in situ preservation of parathyroid glands during total thyroidectomy. The British journal of surgery 2015;102(4):359-67.

115. 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 Suppl 1:S47-53.

116. Surgeons BAoEaT. Guidelines for for the surgical management of endocrine disease and training requirements for endocrine surgery. British Association of Endocrine and Thyroid Surgeons 2016.

117. Randolph GW, Shin JJ, Grillo HC, et al. The surgical management of goiter: Part II. Surgical treatment and results. The Laryngoscope 2011;121(1):68-76.

118. Findlay J, Sadler G, Bridge H, Mihai R. Post-thyroidectomy tracheomalacia: minimal risk despite significant tracheal compression. British journal of anaesthesia 2011;106(6):903-906.

119. Agarwal A, Agarwal S, Tewari P, et al. Clinicopathological profile, airway management, and outcome in huge multinodular goiters: an institutional experience from an endemic goiter region. World journal of surgery 2012;36(4):755-760.

120. Jokinen K, Palva T, Sutinen S, Nuutinen J. Acquired tracheobronchomalacia. Annals of clinical research 1977;9(2):52-57.

121. Bennett A, Hashmi S, Premachandra D, Wright M. The myth of tracheomalacia and difficult intubation in cases of retrosternal goitre. The Journal of Laryngology & Otology 2004;118(10):778-780.

122. Agarwal A, Mishra AK, Gupta SK, et al. High incidence of tracheomalacia in longstanding goiters: experience from an endemic goiter region. World journal of surgery 2007;31(4):832-837.

123. Ahmed ME, Ahmed EO, Mahadi SI. Retrosternal goiter: the need for median sternotomy. World journal of surgery 2006;30(11):1945-1948.

124. Lacoste L, Montaz N, Bernit A-F, et al. Airway complications in thyroid surgery. Annals of Otology, Rhinology & Laryngology 1993;102(6):441-446.

125. Johnson TH, Mikita JJ, Wilson RJ, Feist J. Acquired Tracheomalacia 1. Radiology 1973;109(3):577-580.

126. Agarwal A, Mishra AK, Gupta SK, et al. High incidence of tracheomalacia in longstanding goiters: experience from an endemic goiter region. World journal of surgery 2007;31(4):832-7.

127. Duclos A, Peix JL, Colin C, et al. Influence of experience on performance of individual surgeons in thyroid surgery: prospective cross sectional multicentre study. Bmj 2012;344:d8041.

128. Gomez-Ramirez J, Sitges-Serra A, Moreno-Llorente P, et al. Mortality after thyroid surgery, insignificant or still an issue? Langenbeck’s archives of surgery / Deutsche Gesellschaft fur Chirurgie 2015;400(4):517-22.

129. Dionigi G, Rovera F, Boni L, Castano P, Dionigi R. Surgical site infections after thyroidectomy. Surgical infections 2006;7 Suppl 2:S117-20.

130. Godballe C, Madsen AR, Pedersen HB, et al. Post-thyroidectomy hemorrhage: a national study of patients treated at the Danish departments of ENT Head and Neck Surgery. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies 2009;266(12):1945-52.

9

ANNEXES

Annex 1 Data Fields British Association of Endocrine and Thyroid Surgeons National Registry

Basic Patient Details

- Date of operation
- Gender
- Age at operation
- Endocrine case type
- Hospital where the procedure was performed
- Dueal-operating case
- Name of the principal consultant surgeon

Pre-operative Thyroid Details

- Main indication for thyroid surgery
- Thyroid status at presentaion
- Goitre type
- Sternal split / thoracotomy required
- Preoperative voice change
- Preoperative laryngoscopy
- Reoperation
- FNAC
- FNAC result
- MEN

Thyroid Surgery Procedure

- Grade of principal surgeon
- Grade of assistant surgeon
- Side of thyroid procedure
- Side of nodal procedure
- Previous contralateral lobectomy

- Isthmusectomy alone
- Thyroid procedure right
- Thyroid node dissection right
- Thyroid procedure left
- Thyroid node dissection left
- Recurrent laryngeal nerve sacrificed
- Thymectomy
- Nerve monitoring used
- Nerve monitoring method
- Monitor
- ET tube with integraded electrodes
- Energy source used
- Other energy source used

Primary Thyroid Pathology

- Thyroid pathology
- Primary Thyroid Pathology
- Thyroid malignancy resectable (only if pathology is thyroid cancer)
- TNM (only if pathology is thyroid cancer)
- Was patient discussed at MDM before first operation
- Was patient discussed at MDM after first operation
- Side of this malignancy (only if pathology is thyroid cancer)

Thyroid Surgery Discharge Details

- Reoperation for haemorrhage
- Hypocalcaemia
- Hypocalcaemia treatment given
- Postoperative complications
- Patient survival
- Date of discharge/death

Thyroid Follow up

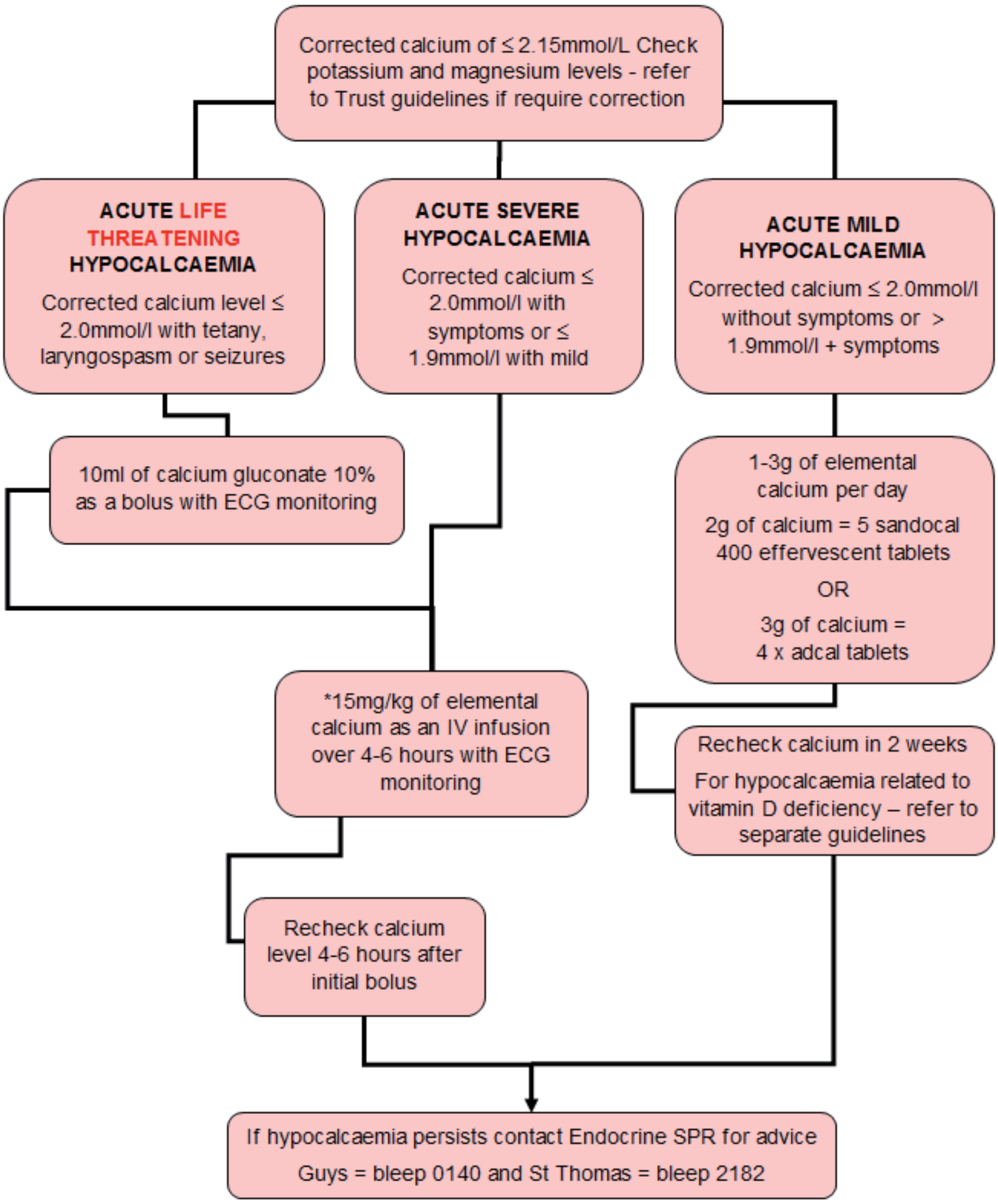
- Patient lost to follow up within 6 months after surgery
- Date of follow up
- Related to re-admission
- Date of related re-admission
- Voice change
- Vocal cord check
- Date of first post-operative vocal cord check
- Is the patient on T3/T4
- Is the patient taking calcium or Vitamin D to maintain normocalcaemia at 6 months

Comments

- Patient comments
- Database coments
- Follow up complete

Annex 2 Clinical Guidelines for the Treatment of Adult Patients with Hypocalcaemi. Guy's and St Thomas' Hospital NHS Foundation Trust

A2.1 Flow Chart for the Management of Acute Hypocalcaemia



** Dose of elemental calcium required = 15mg/kg*

1ml of calcium gluconate 10% contains 8.4mg of elemental calcium

Volume of calcium gluconate 10% = body weight (kg) x 1.8

Dilute calcium gluconate 10% in 1l of sodium chloride 0.9% or glucose 5% and infuse over 4-6 hours

Definition of hypocalcaemia

Hypocalcaemia occurs when there is a net efflux of calcium from the extracellular fluid often through renal mehanisms, in greater quantities than can be replaced by the intestine or bone.

- Serum corrected calcium <2.15 mmol/l

The serum calcium concentration must be interpreted in relation to serum albumin. Serum calcium exists in an ionised form (50%) or is bound to albumin or other ions. Only ionised calcium is biologically important. Serum calcium concentrations are therefore corrected to a reference albumin concentration of 40g/l and for every 1g/l above or below this value, the calcium is adjusted by decreasing or increasing by 0.02mmol/l. This estimation is often used but can be unreliable in some situations such as critical illness.

1. Causes of Hypocalcaemia

    1.1. Common

    - Hypoparathyroidism as a result of surgery or autoimmune disease
    - Chronic renal disease
    - Vitamin D deficiency as a result of low exposure to ultra violet light or low dietary intake, or malabsorption

    1.2. Rare

    - Parathyroid hormone resistance
    - Vitamin D resistance
    - Hypomagnesaemia
    - Sclerotic metastases
    - Autosomal dominant hypocalcaemia

    1.3. Other

    - Pseudohypoparpathyroidism
    - Acute pancreatitis
    - Tumour lysis syndrome
    - Rhabdomyolysis

- Hungry bone syndrome after parathyroidectomy for hyperparathyroidectomy
- Infusion of phosphate or calcium chelators
- Critical illness
- After intravenous infusion of bisphosphonates,especially high dose treatment in vitamin D deficient patients

2. Symptoms

The symptoms correlate with the magnitude and rapidity of the fall in serum calcium.

- Neuromuscular irritability – muscle weakness, twitching, spasms, myalgia and cramps, paraesthesia and numbness of extremities and circumoral region
- Confusion/altered affect (irritability/anxiety/depression)
- Dysphagia
- Shortness of breath secondary to bronchospasm, stridor
- Seizures
- Tetany ncluding laryngospasm

3. Signs

- Prolonged QT interval which may progress to ventricular fibrillation or heart block, arrhythmias, hypotension, congestive cardiac failure.
- Chvostek's sign – tapping over the parotid gland over the facial nerve can induce facial muscle spasm. (This sign may be observed in some normocalcaemic individuals).
- Trousseau's sign – mild hypoxia induced by inflation of a blood pressure cuff can precipitate carpopedal spasm. Carpopedal spasm can progress to tetany, seizures and cardiac dysrhythmias.

4. Investigations

- Bone profile
- U+Es
- Erum magnesium & phosphate
- parathyroid hormone
- 25-hydroxyvitamin D
- ECG

5. Management

- If possible identify and treat cause.
- Always check serum magnesium and treat if < 0.7mmol/l, otherwise the hypocalcaemia will be refractory to treatment.
- Monitor corrected calcium levels frequently
- Patients taking digoxin have increased cardiac sensitivity to fluctuations in serum calcium, so intravenous calcium administration must be more cautious in this setting with ECG monitoring.
- Calcium gluconate is the preferred form of intravenous calcium because calcium chloride is more likely to cause local irritation at the site of injection.

5.1. Life threatening hypocalcaemia (tetany, laryngospasm, seizures)

- 10 ml of calcium gluconate 10% as a slow IV bolus over 5 minutes with ECG monitoring.
- ECG monitoring is required because dysrrythmias can occur if correction is too rapid.
- Followed by:
    - Elemental calcium: 15mg/kg as an intravenous infusion. Dilute in 1 litre of sodium chloride 0.9% or glucose 5%. Infuse over 4-6 hours.[1]

How to calculate the volume of calcium gluconate 10% required:

Dose of elemental calcium required = 15mg/kg

1ml of calcium gluconate 10% contains 8.4 mg of elemental calcium[5]

Volume of calcium gluconate 10% required (ml) $= \frac{\text{body weight (kg) x 15}}{8.4}$

= body weight (in kg) x 1.8

e.g. a 70 kg man will need 70 x 1.8 = 126ml of calcium gluconate 10%

5.2. Acute severe hypocalcaemia

(Corrected $Ca^{2+} \leq 2.0$mmol/l + severe symptoms OR corrected $Ca^{2+} \leq 1.9$mmol/l and mild symptoms)

- Dose of elemental calcium: 15mg/kg elemental calcium (see instructions above)
- If corrected Ca2+ is ≤ 2.0mmol/l, consider starting alfacalcidol.

- This should be discussed with the endocrine SpR (Guy's bleep 0140, St. Thomas' bleep 2182, out of hours via switchboard).

5.3. Acute mild hypocalcaemia

(Corrected Ca^{2+}< 2mmol/l + no symptoms OR corrected Ca^{2+}> 1.9mmol/l + symptoms)

- 1–3g elemental calcium orally per day in divided doses, adjusted according to response.
- (2g elemental calcium = 5 x sandocal 400 effervescent tablets)
- (3g elemental calcium = 4 x adcal tablets)
- Ideally oral calcium should be taken between meals or on an empty stomach to improve absorption. If hypocalcaemia persists, consider initiating alfacalcidol. This should be discussed with the endocrine SpR (Guy's bleep 0140, StH bleep 2182).

5.4. Chronic hypocalcaemia

- If hypocalcaemia is due to vitamin D deficiency, use a calcium carbonate preparation with colecalciferol (e.g. Adcal D_3 1 tablet BD or TDS). In patients with renal failure alfacalcidol should be used. In patients with liver failure calcitriol should be used.
- If associated with hypoparathyroidism add alfacalcidol 0.5 micrograms daily, adjusted according to response.

Guy's and St Thomas' NHS
NHS Foundation Trust

Enhanced Recovery Programme

Head and Neck

Thyroid Surgery Pathway

Total Thyroidectomy / Hemithyroidectomy

Ward (circle): BLUNDELL ESTHER

Patient Label:

AFFIX PATIENT LABEL HERE

Admission date (dd/mm/yy)		
Planned discharge date (dd/mm/yy)		
Actual discharge date (dd/mm/yy)		
Consultant (name)		
Nurse Led Discharge (circle)	Yes	No
Admitted through Surgical Admission Lounge (circle)	Yes	No
Patient swabbed for MRSA	Yes	No
Diabetic Management Required	Yes	No
Patient has had previous chemo radiation therapy	Yes	No
Is this a diagnostic lobectomy or is post-op Radioiodine Treatment required or under consideration?	Yes	No
Nursing admission pack completed	Yes	No
Thyroidectomy procedure - hemi or total (circle)	HEMI	TOTAL
Patient has had neck dissection	Yes	No
Pectoralis major (PEC) flap	Yes	No
For patients without a PEC flap please strike through pages 10, 11,12, 13,14,15,16 and 17 For patients who have had a hemithyroidectomy please strike through pages 6 to 17		

Instructions for use:
This pathway is for patients who have had a total thyroidectomy or a hemithyroidectomy, with or without neck dissection and with or without PEC flap
Please ensure that you complete all boxes highlighted in grey and complete your details and signature on page 23
An **'A'** should be marked in the Day / Night shift box indicating the action / goal has been completed / **achieved**
A **'V'** should be marked in the Day / Night box if there is a **variance**. Inpatient evaluation sheets should then be used to describe the variance and action taken, using the Variance Number (e.g. A1) as a reference marker
N/A should be entered if the action / goal is not applicable

2 DAYS TOTAL LoS for Hemithyroidectomy
Day 0 (post op)
Day 1 (day of discharge)

3 DAYS TOTAL LoS for Total Thyroidectomy or Total Thyroidectomy with Neck Dissection
Day 0 (post op) Day 1 (ward based care) Day 2 (day of discharge)

5 DAYS TOTAL LoS for Total Thyroidectomy with Neck Dissection and PEC flap
Day 0 (post op) Day 1-3 (ward based care) Day 4 (day of discharge)

LoS = Length of stay

Version 1.3 December 2013 Page 1 of 23 For review July 2015

Day 0 (dd/mm/yy) POST-OP		Time of return to ward	
Named day nurse			
Named night nurse			

Ward round summary (if seen post-operatively):

Ward round led by Mr (please circle)	Lyons
	Jeannon
	Hussain
	Simo
	McGurk
	Oakley
No Consultant present	
SpR	
Completed by (FY/CT)	
(name)	
signature	

Acute Kidney Injury Risk*	Yes	No
Age > 65		
Diabetes		
Heart Failure		
Male		
Hypertension		
Ascities		
Obesity		
Medication (e.g. NSAIDs, Diuretics, ACEi, ARB)		

*Score 3 or more = HIGH RISK.

NURSING	Day	Night	Variance
Teeth brushed and mouth examined			A1
Hygiene needs met - please circle: Bed bath / Bowl Wash / Shower / Declined			A2
Hygiene needs met by - please circle: Assisted / Independent			A3
Staple remover and stitch cutter kept beside bed			A4
Hourly check of wound -Observe for haematoma (request medical review if present)			A5
Hourly check of drains - is it suctioned and drain in situ? **If drain is filling >30mls over any 15 min interval call doctor**			A6
Corrected calcium level checked 6 hours post op (state level) record as variance if out of range **NB** - not applicable for hemithyroidectomies unless patient has had previous thyroid surgery. Corrected calcium level:			A7
Is calcium <2.2? If **YES**, take blood for Magnesium level, ECG and contact doctor immediately			A8
Hypocalcaemia - is patient symptomatic (muscle weakness, malaise, muscle cramps, parasthesia and numbness of extremities and peri oral region?)	If **YES**, contact doctor immediately		
Hypocalcaemia - is patient showing signs? Prolonged QT interval, arrhythmias, hypotension, congestive cardiac failure; Chvostek's sign - tapping over the facial nerve results in contraction of the facial muscles. NB: This sign may be observed in some normocalcaemic individuals; Trousseau's sign - inflation of BP cuff above systolic BP for up to 3 mins produces carpo-pedal spasm that cannot be overcome NB: This sign is specific to hypocalcaemia			
Anti-embolism stockings prescribed as per Trust protocol			A9
Review pain score (below)			A10
Practice nurse letter written for removal of clips (sign on p14)			A11
If patient is for RadioIodine therapy (see front sheet) bleep Thyroid CNS 2219			A12
Ensure no concerns regarding functional abilities and/or discharge planning (consider occupational therapy referral/social services input)			A13
Post theatre drain output at 10pm (measurement since theatre) ml			A14
Assess if IVAD needed and remove if not			A15
Ensure patient is sat out in chair			A16
Ensure patients is moblising, request physio review if chest concerns			A17
Patient on track for discharge?			A18

FY1	Day	Night	Variance
Order calcium level on return to ward for total thyroidectomies			A19
Prescribe regular Paracetamol 1g QDS, Ibuprofen 400mg TDS, dihydrocodeine 30mg 4 hourly, morphine immediate release 10mg 4 hourly (or as required)			A20
Complete Acute Kidney Injury (AKI) risk assessment			A21
Complete VTE risk assessment and prescribe dalteparin 5,000iu SC OD unless contraindicated (see full guideline for dose adjustments if ClCl < 30ml/min or body weight <50kg or >99kg)			A22
Prescribe Senna II ON and / or Lactulose 10mls BD unless contraindicated			A23
Prescribe patient's regular drug history medications			A24
Prescribe calcium therapy if required. If oral therapy appropriate: sandocal 1000 1-3 tablets daily and/ or alfacalcidol. If IV therapy required: calcium gluconate 10%.			A25
Prescribe thyroxine replacement therapy if required. Levothyroxine once daily (dose in micrograms = body weight (kg) - age + 125); Liothyronine 20micrograms TDS if patient has had diagnostic lobectomy or may have radioiodine ablation (see front sheet).			A26
Electronic Discharge Letter complete (please sign p18)			A27

Pain Score			
0800 hrs	1200 hrs	1800 hrs	2200 hrs
0	1	2	3
None	Mild	Moderate	Severe
If >=1, REVIEW ANALGESIA (Medical team)			

ANY SUGGESTION OF AIRWAY REMOVE CLIPS AND SEEK ASSISTANCE

		Time
Sign off - Named day nurse		
Sign off - Named night nurse		

Guy's and St Thomas'
NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Guy's and St Thomas' NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

FOR HEMITHYROIDECTOMIES PLEASE CROSS THROUGH THIS PAGE AND GO STRAIGHT TO PAGE 13 (DAY OF DISCHARGE)

Day 1 (dd/mm/yy)	
Named day nurse	
Named night nurse	

Ward round summary:

Drains to be removed? Y N

Ward round led by Mr (please circle): Lyons / Jeannon / Hussain / Simo / McGurk / Oakley

No Consultant present

SpR (name)

Completed by (FY/CT) (name)

(sign)

NURSING					Day	Night	Variance
Teeth brushed and mouth examined							B1
Hygiene needs met - please circle	Bed bath	Bowl Wash	Shower	Declined			B2
Hygiene needs met by - please circle		Assisted	Independent				B3
Check all actions complete from previous day							B4
Corrected calcium level checked (state level) record as variance if out of range NB - not applicable for hemithyroidectomies unless patient has had previous thyroid surgery				Corrected calcium level:			B5
Is calcium <2.2? If YES, take blood for Magnesium level, take an ECG and contact doctor immediately							B6
Hypocalcaemia - is patient symptomatic (muscle weakness, malaise, muscle cramps, parasthesia and numbness of extremities and peri oral region?					If **YES**, contact doctor immediately		
Hypocalcaemia - is patient showing signs? Prolonged QT interval, arrhythmias, hypotension, congestive cardiac failure; Chvostek's sign - tapping over the facial nerve results in contraction of the facial muscles. Nb: This sign may be observed in some normocalcaemic individuals; Trousseau's sign - inflation of BP cuff above systolic BP for up to 3 minutes produces carpo-pedal spasm that cannot be overcome Nb: This sign is specific to hypocalcaemia							
Anti-embolism stockings prescribed as per Trust protocol							B7
Review pain score (below)							B8
Ensure no concerns regarding functional abilities and/or discharge planning (consider occupational therapy referral/social services input)							B9
Discharge planning discussed with patient.							B10
8 hour drain output at 6am (10pm - 6am). **If <10ml over 8 hrs remove**				ml			B11
24 hour drain output at 6am (6am - 6am). **If <30ml over 24hrs remove**				ml			
If drain is filling >30mls over any 15 min interval call doctor							B12
Ensure patient sat our in chair> 4 hrs							B13
Ensure patient is mobilising minimal 30 metres, request physio review if mobility concerns							B14
Request physio review if chest concerns/ neck dissection/ PEC flap							B15
If drains out, request physio review for neck / shoulder exercises							B16
Assess if IVAD needed and remove if not							B17
Patient on track for discharge on day 2							B18

Physio				Position tested in	Active Assisted	Day	Night	Variance
Neck AROM	rotation	R	L					B19
	side flexion	R	L					B20
	flexion							B21
	extension							B22
Shoulder AROM Please note resting posture	shrug	R	L					B23
	retraction	R	L					B24
	external	R	L					B25
	flexion	R	L					B26
	abduction	R	L					B27

FY1	Day	Night	Variance
Order calcium level (once per day)			B28
Review analgesia and step up / down as required			B29
Prescribe any medication not prescribed previously that is now required (dalteparin, laxatives, Drug History medications, calcium therapy, thyroid replacement therapy)			B30
Review Creatinine versus baseline and urine output			B31
Electronic discharge letter completed please sign p18			B32

ANY SUGGESTION OF AIRWAY REMOVE CLIPS AND SEEK ASSISTANCE

Pain Score			
0800 hrs	**1200 hrs**	**1800 hrs**	**2200 hrs**
0	**1**	**2**	**3**
None	Mild	Moderate	Severe
If >=1, REVIEW ANALGESIA (Medical team)			

		Time
Sign off - Named day nurse		
Sign off - Named night nurse		

Guy's and St Thomas'
NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Guy's and St Thomas'
NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

NOT APPLICABLE FOR PATIENTS WHO HAVE NOT HAD A PEC FLAP

Day 2 (dd/mm/yy)	
Named day nurse	
Named night nurse	

Ward round summary:

Drains to be removed? Y N

Ward round led by Mr (please circle)	Lyons
	Jeannon
	Hussain
	Simo
	McGurk
	Oakley
No Consultant present	
SpR (name)	
Completed by (FY/CT)	
(name)	
(sign)	

NURSING					Day	Night	Variance
Teeth brushed and mouth examined							C1
Hygiene needs met - please circle	Bed bath	Bowl Wash	Shower	Declined			C2
Hygiene needs met by - please circle		Assisted	Independent				C3
Check all actions complete from previous day							C4
Corrected calcium level checked (state level) record as variance if out of range NB - not applicable for hemithyroidectomies unless patient has had previous thyroid surgery				Corrected calcium level:			C5
Is calcium <2.2? If **YES**, take blood for Magnesium level, take an ECG and contact doctor immediately							C6
Hypocalcaemia - is patient symptomatic (muscle weakness, malaise, muscle cramps, parasthesia and numbness of extremities and peri oral region?					If **YES**, contact doctor immediately		
Hypocalcaemia - is patient showing signs? Prolonged QT interval, arrhythmias, hypotension, congestive cardiac failure; Chvostek's sign - tapping over the facial nerve results in contraction of the facial muscles. NB: This sign may be observed in some normocalcaemic individuals; Trousseau's sign - inflation of BP cuff above systolic BP for up to 3 minutes produces carpo-pedal spasm that cannot be overcome Nb: This sign is specific to hypocalcaemia							
Anti-embolism stockings prescribed as per Trust protocol							C7
Review pain score (below)							C8
Ensure no concerns regarding functional abilities and/or discharge planning (consider occupational therapy referral/social services input)							C9
Discharge planning discussed with patient.							C10
8 hour drain output at 6am (10pm - 6am). **If <10ml over 8 hrs remove**				ml			C11
24 hour drain output at 6am (6am - 6am). **If <30ml over 24 hrs remove**				ml			C12
Assess if IVAD needed and remove if not							C13
Ensure patient is mobilising minimal 60 metres, request physio review if mobility concerns							C14
Request physio review if chest concerns							C15
If drains out, request physio review for neck / shoulder exercises							C16
Patient on track for discharge?							C17

Physio				Position tested in	Active Assisted	Day	Night	Variance
Neck AROM	rotation	R	L					C18
	side flexion	R	L					C19
	flexion							C20
	extension							C21
Shoulder AROM Please note resting posture	shrug	R	L					C22
	retraction	R	L					C23
	external	R	L					C24
	flexion	R	L					C25
	abduction	R	L					C26

FY1	Day	Night	Variance
Order calcium level (once per day)			C27
Review analgesia and step up / down as required			C28
Prescribe any medication not prescribed previously that is now required (dalteparin, laxatives, Drug History medications, calcium therapy, thyroid replacement therapy)			C29
Review Creatinine versus baseline and urine output			C30
Electronic discharge letter completed please sign p18			C31

Pain Score			
0800 hrs	**1200 hrs**	**1800 hrs**	**2200 hrs**
0	**1**	**2**	**3**
None	Mild	Moderate	Severe
If >=1, REVIEW ANALGESIA (Medical team)			

ANY SUGGESTION OF AIRWAY REMOVE CLIPS AND SEEK ASSISTANCE

		Time
Sign off - Named day nurse		
Sign off - Named night nurse		

Guy's and St Thomas' NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Guy's and St Thomas' NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Day 3 (dd/mm/yy)	
Named day nurse	
Named night nurse	

Ward round summary:

Drains to be removed? Y N

Ward round led by Mr (please circle)	Lyons
	Jeannon
	Hussain
	Simo
	McGurk
	Oakley
No Consultant present	
SpR (name)	
Completed by (FY/CT)	
(name)	
(sign)	

NURSING					Day	Night	Variance
Teeth brushed and mouth examined							D1
Hygiene needs met - please circle	Bed bath	Bowl Wash	Shower	Declined			D2
Hygiene needs met by - please circle		Assisted	Independent				D3
Check all actions complete from previous day							D4
Corrected calcium level checked (state level) record as variance if out of range NB - not applicable for hemithyroidectomies unless patient has had previous thyroid surgery				Corrected calcium level:			D5
Is calcium <2.2? If **YES**, take blood for Magnesium level, take an ECG and contact doctor immediately							D6
Hypocalcaemia - is patient symptomatic (muscle weakness, malaise, muscle cramps, parasthesia and numbness of extremities and peri oral region?					If **YES**, contact doctor immediately		
Hypocalcaemia - is patient showing signs? Prolonged QT interval, arrhythmias, hypotension, congestive cardiac failure; Chvostek's sign - tapping over the facial nerve results in contraction of the facial muscles. Nb: This sign may be observed in some normocalcaemic individuals; Trousseau's sign - inflation of BP cuff above systolic BP for up to 3 minutes produces carpo-pedal spasm that cannot be overcome Nb: This sign is specific to hypocalcaemia							
Anti-embolism stockings prescribed as per Trust protocol							D7
Review pain score (below)							D8
Ensure no concerns regarding functional abilities and/or discharge planning (consider occupational therapy referral/social services input)							D9
Discharge planning discussed with patient.							D10
8 hour drain output at 6am (10pm - 6am). **If <10ml over 8 hrs remove**				ml			D11
24 hour drain output at 6am (6am - 6am). **If <30ml over 24 hrs remove**				ml			D12
Ensure patient is mobilising minimal 120 metres, request physio review for physical activity promotion/ exercise bike							D13
Request physio review if chest concerns							D14
If drains out, request physio review for neck / shoulder exercises							D15
Assess if IVAD needed and remove if not							D16
Patient on track for discharge?							D17

Physio				tested in	Assisted	Day	Night	Variance
Neck AROM	rotation	R	L					D18
	side flexion	R	L					D19
	flexion							D20
	extension							D21
Shoulder AROM Please note resting posture	shrug	R	L					D22
	retraction	R	L					D23
	external	R	L					D24
	flexion	R	L					D25
	abduction	R	L					D26

FY1	Day	Night	Variance
Order calcium level (once per day)			D27
Review analgesia and step up / down as required			D28
Prescribe any medication not prescribed previously that is now required (dalteparin, laxatives, Drug History medications, calcium therapy, thyroid replacement therapy)			D29
Review Creatinine versus baseline and urine output			D30
Electronic discharge letter completed please sign p18			D31

Pain Score			
0800 hrs	**1200 hrs**	**1800 hrs**	**2200 hrs**
0	**1**	**2**	**3**
None	Mild	Moderate	Severe
If >=1, REVIEW ANALGESIA (Medical team)			

ANY SUGGESTION OF AIRWAY REMOVE CLIPS AND SEEK ASSISTANCE

		Time
Sign off - Named day nurse		
Sign off - Named night nurse		

Guy's and St Thomas' NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Guy's and St Thomas'
NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Day of discharge (dd/mm/yy)	
Named day nurse	

Day 1 for hemithyroidectomy
Day 2 for total thyroidectomy with or without neck dissection
Day 4 for total thyroidectomy with neck dissection and PEC flap

Ward round summary:

Drains to be removed? Y N

Ward round led by Mr (please circle)	Lyons
	Jeannon
	Hussain
	Simo
	McGurk
	Oakley
No Consultant present	
SpR (name)	
Completed by (FY/CT)	
(name)	
(sign)	

NURSING		Day	Night	Variance
Check all actions complete from previous day				E1
8 hour drain output at 6am (10pm - 6am). **If <10ml over 8 hrs remove**	ml			E2
24 hour drain output at 6am (6am - 6am). **If <30ml over 24hrs remove**	ml			E3
Drains out				E4
Ensure patient is mobilising minimal 120 metres, request physio review if mobility concerns				E5
Request physio review if chest concerns				E6
If drains out, request physio review for neck/ shoulder exercises				E7

Physio		Day	Night	Variance
Ensure patient mobilising minimal 120 metres/ at baseline/ exercise bike/ physical				E8
Stairs assessement completed if required				E9
Post op exercises and advice booklet given				E10
MDT section on Electronic Discharge letter completed				E11
Referral to CHANT/ Guy's outpatient	Location			E12

Physio				Position tested in	Active Assisted	Day	Night	Variance
Neck AROM	rotation	R	L					E13
	side flexion	R	L					E14
	flexion							E15
	extension							E16
Shoulder AROM	shrug	R	L					E17
Please note resting posture	retraction	R	L					E18
	rotation	R	L					E19
	flexion	R	L					E20
	abduction	R	L					E21

DISCHARGE DAY CHECKLIST

Section	Tasks	PRINT NAME and sign	Date
TTOs	Dispensed, checked and explained to patient		
Planning	Follow up appointment in the following week's Friday Head and Neck clinic		
	Electronic Discharge Letter complete		
	Practice Nurse letter written		
	Transport arranged		

Extra day (dd/mm/yy)	
Named day nurse	
Named night nurse	

Ward round summary:

Drains to be removed? Y N

Ward round led by Mr (please circle)	Lyons
	Jeannon
	Hussain
	Simo
	McGurk
	Oakley
No Consultant present	
SpR (name)	
Completed by (FY/CT)	
(name)	
(sign)	

NURSING					Day	Night	Variance
Teeth brushed and mouth examined							F1
Hygiene needs met - please circle	Bed bath	Bowl Wash	Shower	Declined			F2
Hygiene needs met by - please circle		Assisted	Independent				F3
Check all actions complete from previous day							F4
Corrected calcium level checked (state level) record as variance if out of range NB - not applicable for hemithyroidectomies unless patient has had previous thyroid surgery				Corrected calcium level:			F5
Is calcium <2.2? If **YES**, take blood for Magnesium level, take an ECG and contact doctor immediately							F6
Hypocalcaemia - is patient symptomatic (muscle weakness, malaise, muscle cramps, parasthesia and numbness of extremities and peri oral region?					If **YES**, contact doctor immediately		
Hypocalcaemia - is patient showing signs? Prolonged QT interval, arrhythmias, hypotension, congestive cardiac failure; Chvostek's sign - tapping over the facial nerve results in contraction of the facial muscles. NB: This sign may be observed in some normocalcaemic individuals; Trousseau's sign - inflation of BP cuff above systolic BP for up to 3 minutes produces carpo-pedal spasm that cannot be overcome Nb: This sign is specific to hypocalcaemia							
Anti-embolism stockings prescribed as per Trust protocol							F7
Review pain score (below)							F8
Ensure no concerns regarding functional abilities and /or discharge planning (consider occupational therapy referral/social services input)							F9
Discharge planning discussed with patient.							F10
8 hour drain output at 6am (10pm - 6am). **If <10ml over 8 hrs remove**				ml			F11
24 hour drain output at 6am (6am - 6am). **If <30ml over 24hrs remove**				ml			F12
Ensure patient is mobilising minimal 120 metres/ off the ward, request physio review if mobility concerns							F13
Request physio review if chest concerns							F14
If drains out, request physio review for neck / shoulder exercises							F15
Assess if IVAD needed and remove if not							F16
Patient on track for discharge (state revised date)							F17

Physio				tested in	Assisted	Day	Night	Variance
Neck AROM	rotation	R	L					F18
	side flexion	R	L					F19
	flexion							F20
	extension							F21
Shoulder AROM Please note resting posture	shrug	R	L					F22
	retraction	R	L					F23
	external	R	L					F24
	flexion	R	L					F25
	abduction	R	L					F26

FY1	Day	Night	Variance
Order calcium level (once per day)			F27
Review analgesia and step up / down as required			F28
Prescribe any medication not prescribed previously that is now required (dalteparin, laxatives, Drug History medications, calcium therapy, thyroid replacement therapy)			F29
Review Creatinine versus baseline and urine output			F30
Electronic discharge letter completed please sign p18			F31

Pain Score			
0800 hrs	**1200 hrs**	**1800 hrs**	**2200 hrs**
0	**1**	**2**	**3**
None	Mild	Moderate	Severe

ANY SUGGESTION OF AIRWAY REMOVE CLIPS AND SEEK ASSISTANCE

If >=1, REVIEW ANALGESIA (Medical team)		Time
Sign off - Named day nurse		
Sign off - Named night nurse		

Guy's and St Thomas'
NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Guy's and St Thomas' NHS Foundation Trust
IN-PATIENT CLINICAL NOTES

Ward / clinic	Consultant
Surname	Unit No
First Name	
Date of Birth	
Address	Sex

Sheet Number

Date, time and Problem Number	

Signature Sheet

PRINT Name in Block Capitals	Signature	Role and Contact No/Bleep