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Review

Surgical management of cervico-mediastinal goiters: Our experience and review of the literature

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ABSTRACT

Aim: We analyze and discuss the clinical presentation, the diagnostic procedures and the surgical technique in relation to post-operative complications and results in cervico-mediastinal thyroid masses admitted in Thoracic Surgery Unit of AOU Second University of Naples from 1991 to 2006 and in Thoracic Surgery Unit of AOU "S. Giovanni di Dio & Ruggi D'Aragona" of Salerno over a period of 3 years (2011–2014).

Methods: We reviewed 97 patients who underwent surgical treatment for cervico-mediastinal goiters. 47 patients (49.2%) had cervico-mediastinal goiter, 40 patients (40%) had mediastino-cervical goiter and 10 patients (10.8%) had mediastinal goiter. 73 cases were prevascular goiters and 24 were retrovascular goiters. We performed total thyroidectomy in 40 patients, subtotal thyroidectomy in 46 patients and in 11 cases the resection of residual goiter. In 75 patients we used only a cervical approach, in 21 patients the cervical incision was combined with median sternotomy and in 1 patient with transverse sternotomy.

Results: Three patients (3.1%) died in the postoperative period (2 cardio-respiratory failure and 1 pulmonary embolism). The histologic study revelead 8 (7.7%) carcinomas. Postoperative complications were: dyspnea in 9 cases (10.7%), transient vocal cord paralysis in 6 patients (9.2%), temporary hypoparathyroidism in 9 patients (9.2%) and kidney failure in 1 case (0.9%).

Conclusions: The presence of a cervico-mediastinal thyroid mass with or without respiratory distress requires a surgical excision as the only treatment option. Thyroid masses extending to the mediastinum can be excised successfully by cervical incision. Bipolar approach (cervical incision and sternotomy) has an excellent outcome, achieving a safe resection, especially in large thyroid masses extending to the mediastinum with close relations to mediastinal structures and in some limited cases (carcinoma, thyroiditis, retrovascular goiter, ectopic goiter). Postoperative mortality and morbidity is very low, independent of surgical techniques. Other surgical approaches for excision of a Posterior Mediastinal Thyroid Goiter reported in literature are: VATS techniques to remove an ectopic intrathoracic goiter, robot-assisted technique for the removal of a substernal thyroid goiter, with extension into the posterior mediastinum.

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1. Introduction

Intrathoracic thyroid masses account for 5.8% of all mediastinal masses. The definition of mediastinal goiter (MG) generally refers to a struma with a location for at least 50% of its volume in substernal position into the mediastinum in the prevascular or

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retrovascular space, reaching at least the level of the aortic arch, penetrating into the mediastinum for at least two fingers transverse below the jugular incision with the head in iperextension; the radiological opacity must be projected at least at the level of D4 [1,2]. For embryologic reasons, MG are mostly located in the anterior and middle mediastinum, and rarely in the posterior mediastinum. Up to 40% of MG are asymptomatic and they are diagnosed incidentally. According to the originations of thyroid tissue, intrathoracic goiter can be divided into primary intrathoracic goiter and secondary intrathoracic goiter. The vast majority of intrathoracic goiters are secondary ones which arise from the lower part of one lobe or both lobes of cervical thyroid or isthmus and grow down through the thoracic inlet. Swallowing, gravity and thoracic negative pressure help the growing goiter direct into the chest cavity. Anatomically speaking, goiter in the chest cavity generally grows to the position of relatively low resistance. At first, the tumor will grow into the anterior superior mediastinum between trachea and sternum, forming the common retrosternal thyroid goiter.

Because there are thymus (may atrophy), left and right brachiocephalic veins and superior vena cava in the front, aortic arch and its three branches (phrenic nerve and vagus nerve have smaller resistance) in the middle left of retrosternal space, tumor growth will be resisted there. Right posterior mediastinum has relatively low resistance than left posterior mediastinum, and it helps form right posterior mediastinal goiter. The primary intrathoracic goiter only accounts for 0.2–1% of all the intrathoracic goiters, it affects females more often (male: female = 1: 3 or 1: 4). Its causes are totally different from the ones of secondary intrathoracic goiter. During the embryonic developmental period of thyroid gland, part or all of the thyroid blastoma leaves primordium and is pulled into the thoracic cavity by the descendent heart and great vessels, then continues to develop in the thoracic cavity, forming the final primary intrathoracic goiter. Because of different originations, secondary posterior mediastinal goiter is often continued with the cervical thyroid gland, with blood supply from inferior thyroid artery and its branches while primary posterior mediastinal goiter maintains little or no connection with the cervical thyroid gland, and has a blood supply derived from intrathoracic arteries [3–6].

2. Materials and methods

Over two different period, 1991–2006, in the Unit of Thoracic Surgery of Second University of Naples and 2011–2014 in the Unit Thoracic Surgery Unit of University of Salerno and General Surgery Unit of "S. Giovanni di Dio e Ruggi D'Aragona" Hospital of University of Salerno, were observed and treated 97 patients with cervical-mediastinal goiter (43 men and 54 women with a mean age of 63.6 years - range 36–81 years). Seven patients (6 women and 1 man) had already undergone previous surgery for goiter, and 2 of these for 2 times. The symptoms of 97 patients is summarized in Table 1. When clinically manifest MG is usually associated to compressive symptoms which mainly determine effects on surrounding structures. Respiratory distress suggest presence of tracheal compression, with consequent dislocation producing chough, dyspnea and sleeping apnea, asthma-like syndrome, acute upper airway obstruction (wheezing and stridor) (55 patients in our observations) or esophageal compression with dysphagia (15 cases). Less frequently are observed compressive effects on cervical and mediastinal neurovascular structures with rare cases of superior vena cava syndrome (4 cases) due to venous compression and thrombosis, tachycardia (12 cases), laryngeal nerve involvement with dysphonia (6 cases). Nine patients were asymptomatics.

Physical examination revealed in every case a cervical mass that moves on swallowing and in some patients a variable degree of kyphosis and a short, thick neck.

Table 1
Patients' symptoms on presentation (patients may have more than one clinical feature).

	Numbers	Percentage %
Patients	97	
Respiratory manifestations	55	57
- Dyspnea	50	52
- cough	22	23
- Asthma-like syndrome	7	7.6
Dysphagia	22	23
Hyperthyroidism	18	18.5
Tachycardia	18	18.5
Anxiety	9	9.2
Weight loss	6	6.1
Hyperhidrosis	4	4.6
Tremors	4	4.6
Dysphonia	9	9.2
Superior vena cava syndrome	6	6.1
Asymptomatic	13	13.8

The preoperative diagnosis was made by anamnesis, clinically examination, thoracic X-ray examination, cervical and thoracic CT scan exploration, laryngeal and tracheal endoscopy, thyroid scintigraphy, esophageal barium study, esophageal endoscopy and in some cases we performed fiberbronchoscopy, Nuclear Magnetic Risonance (NMR) scan and SPECT.

Forty-seven patients (49.2%) had cervico-mediastinal goiter, 40 patients (40%) had mediastino-cervical goiter and 10 patients (10.8%) had mediastinal goiter. In 73 cases it was a prevascular goiter and in 24 cases a retrovascular goiter (13 paratracheal, 8 retrotracheal and 3 retroesophageal).

Total thyroidectomy with en bloc removal of the intrathoracic portion of the thyroid, is the treatment of choice. We performed surgical interventions in all of the cases in order to achieve the removal of the thyroid mass and decompression of the trachea. These surgical interventions were performed under general anesthesia with tracheal intubation. In the cases of tracheal compression the anesthesiologist performed a difficult tracheal intubation with a thin single lumen tube under fiber-bronchoscope control.

The surgical approaches for cervico-mediastinal thyroid goiters were: Kocher type cervicotomy in 75 cases, cervicosternotomy in 22 cases (partial upper sternotomy in 12 cases, full sternotomy in 9 cases and 1 transverse sternotomy).

In our cases of cervico-mediastinal thyroid masses, we performed following operation types: total thyroidectomy (surgical removal of entire thyroid gland) (40 cases), subtotal thyroidectomy (both lobes were removed except of a small thyroid tissue from posterior part of the goiter) (46 cases), excision residual goiter (11 cases). In 2 cases has been associated tracheal resection, in 2 case a VATS procedure for pleural effusion, in 1 case the removal of a neurinoma of the phrenic nerve and finally, in another case, the removal of two ribs for metastatic follicular thyroid cancer.

3. Results

The standard thoracic X-ray revealed an enlargement of the mediastinal opacity and, in some cases, a tracheal compression with lateral tracheal deviation (Fig. 1). In some cases the presence of calcification within an enlarged thyroid gland, raised the risk of malignancy (5 cases). The esophageal barium study revealed in 16 cases the esophageal dislocation and in 8 cases, clear signs of dyskinesia. Computed tomography (CT) is part of a standard protocol of evaluation in all cases in order to define preoperatively the indication to the cervical or sternotomic approach or a combination of both and the technical issues related to each singular patient. CT, performed in 84 patients, has always consented to evaluate size,

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Fig. 1. Standard thoracic X-ray: enlargement of the mediastinal opacity with tracheal compression and left tracheal deviation.

location and relationships of enlarged thyroid gland. (Figs. 2–4). In some of the cases, the cervical sections of the CT scan showed a right thyroid lobe enlargement with laryngeal and tracheal deviation and doesn't show the contralateral thyroid lobe at this level because it was complete intrathoracic. Thoracic sections of the CT scan (transversal plane) revealed a partial mediastinal mass (thyroid lobe) located in the visceral compartment (behind the great vessels and in close relationship to the trachea) with different degrees of compression of the tracheal or esophageal lumen. The sagittal CT reconstruction revealed the degree of intra-thoracic protrusion of a cervico-thoracic goiter and helped us to evaluate the severity of compression and deviation of the trachea and relations to the esophagus, erector spinal muscles, and spine. Coronal CT reconstruction revealed the inferior limit of the mediastinal. Nuclear Magnetic Risonance (NMR), performed only in 5 cases, was useful to better define the relationship of continuity between the cervical and the mediastinal component and with the vascular

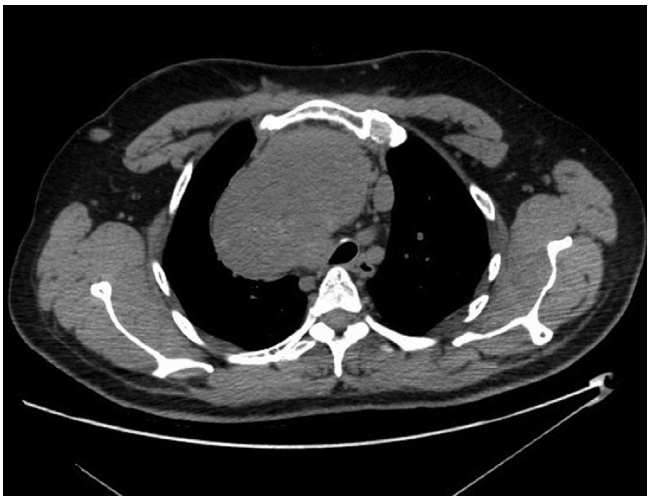

Fig. 2. Thoracic sections of the CT scan showing different type of mediastinal goiter and its relationship with surrounding structures.

Fig. 3. Thoracic sections of the CT scan showing different type of mediastinal goiter and its relationship with surrounding structures.

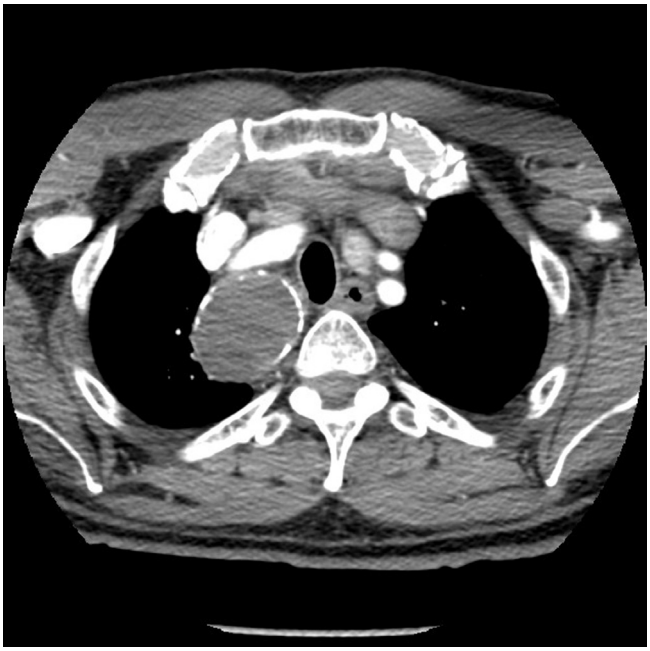

Fig. 4. Thoracic sections of the CT scan showing different type of mediastinal goiter and its relationship with surrounding structures.

structures. Thyroid scintigraphy, used in 68 cases, was insufficient in the evaluation of mediastinal component in 32 of the 60 cases in which we used ^{99m}Tc pertechnetate or ^{131}I; best results were obtained using the ^{99m}Tc-MIBI which allowed, in all 20 patients in which it was used, to highlight the retrosternal thyroid tissue. Recently, integrated I-131 SPECT-CT imaging has an additional value in patients with thyroid cancer, for characterization of tracer uptake seen on planar imaging as well as for precise localization of malignant lesions in the neck, chest, and skeleton. Histological examination revealed a simple colloid goiter in 51 cases (52.3%). For 37 patients (38.4%) the histological diagnosis was nodular goiter (Fig. 5). The incidence of thyroid malignancy in cervico-mediastinal thyroid masses was 7.7% (3 anaplastic carcinoma, 3 papillary carcinoma and 1 follicular type). Two cases were thyroiditis. Three patients (3.1%) died within 30 days after surgery: in 2 cases for respiratory failure and in 1 case for pulmonary embolism. Complications, (Table 2), showed no significant differences relating to

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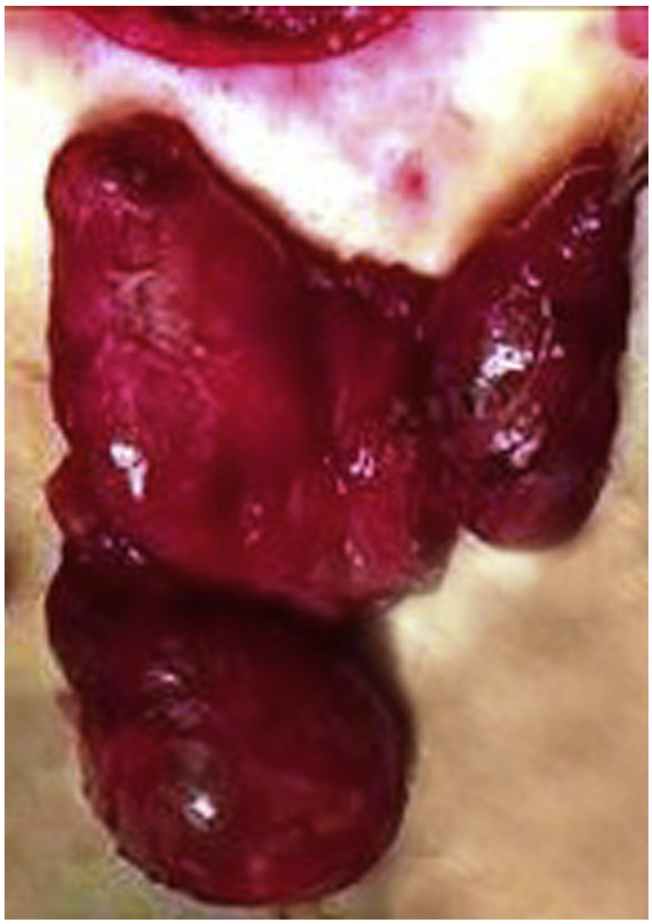

Fig. 5. Cervico-mediastinal goiter after surgical resection.

Table 2
Complications after surgical treatment for cervical-mediastinal goiter.

	Cervicotomy	Sternotomy	P
N. cases	75	22	
• Average length of postoperative stay	7.7 days	10.1 days	0.02
• Patients with complications	12 (16%)	7 (30.7%)	0.417
• Mortality	2 (2%)	3 (15.3%)	0.198
• Respiratory failure	7 (10%)	3 (15.3%)	NS
• Pulmonary embolism	–	1	NS
• Transient Hypoparathyroidism	7 (10%)	2 (7.6%)	NS
• Dysphonia	6 (8%)	2 (7.6%)	NS
• Hemorrhage	3 (4%)	0	NS
• Kidney failure	–	1 (4.6%)	NS

the type of surgical approach. Postoperative results have been very satisfactory with immediate disappearance of preoperative symptoms like dyspnea, dysphagia and cough, and relieve of the dysphonia in short time after operation. Two cases needed for reoperation due to postoperative hemorrhage, both after cervicotomy approach. The average hospital stay was significantly greater in patients undergoing sternotomy.

4. Discussion

According to Th. Shields, in most series, approximately 80% of the substernal thyroid masses are of the small substernal extension type (less than 50% of the thyroid gland was intrathoracic), 15% are "partial" intrathoracic (in which the major part of the mass but less than 80% was situated within the thorax) and only 2–4% are "complete" retrosternal (all of the mass lies within the thoracic cavity). The cervicomediastinal thyroid masses develop from the cervical region and descend to mediastinum, behind the great mediastinal vessels. Most of the retrosternal masses are situated in the anterior compartment of the mediastinum (prevascular goiters) (73 cases in our study) and only a few behind the great mediastinal vessels (13 cases), retrotracheally (8 cases) or even in the posterior mediastinum (posterior of the esophagus) (3 cases). In several percentages, 3/30% in the literature, (11 cases in our series) can be present a history of a previous thyroidectomy [7,8]. Up to 40% of mediastinal goiters are asymptomatic and they are diagnosed incidentally (14.2% of our patients). When clinically manifest mediastinal goiter is usually associated to compressive symptoms which mainly determine effects on surrounding structures, especially on the trachea with consequent dislocation producing chough, dyspnea and sleeping apnea or on the esophagus with dysphagia. Less frequently are observed compressive effects on cervical and mediastinal neurovascular structures with rare cases of superior vena cava syndrome due to venous compression and thrombosis and even of Horner's syndrome for chronic compression on the sympathetic chain. Sometimes the patient presented the clinical signs of an acute upper airway obstruction (wheezing and stridor) as a result of an important progressive tracheal compression, aggravated by an acute respiratory infection or a spontaneous hemorrhage within the thyroid mass [9–11]. The management of this event was promptly applied: intubation and emergency thyroidectomy through a combined cervical and thoracic approach (cervico-sternotomy). Through this approach it was achieved the complete removal of the thyroid mass from both cervical region and mediastinum and the decompression of the trachea without postoperative collapse or kinking of the tracheal wall. There may be signs of hyperthyroidism (18 among our patients), due to the plurinodular cervical component. Furthermore, cervical, thoracic or cervicobrachial pain may be indicative of a malignant neoplastic degeneration of goiter [12]. Cervical and thoracic CT scan was used for detecting the presence and the extent of retrosternal thyroid mass and their relation to adjacent structures in the neck and chest and for determining if mediastinal masses are of thyroid origin. In our series, CT of the neck and chest was routinely performed for diagnosis, which was also helpful in the decision-making process – which approach type of surgical intervention was mostly suited. In case of a big intrathoracic thyroid mass with the inferior limit below the aortic arch (at the level of the tracheal carina in one case), we consider that cervico-sternotomy is the most appropriate way for approaching the surgical patient. Clinical examination, cervico-thoracic CT scan and thyroid scintigraphy provide a positive diagnosis for 82% of the patients with cervico-thoracic thyroid masses [13–15]. Ultrasonography has a limited role to cervical component, for the difficult approach offered by the structure of the chest wall [16]. The standard thoracic X-ray, always supported by esophageal barium study, revealed an enlargement of the mediastinal opacity and, in some cases, a tracheal compression with lateral tracheal deviation (34 cases, 35%) [17,18]. Computed tomography (CT) scan and Nuclear Magnetic Risonance (NMR) are part of a standard protocol of evaluation in all cases in order to define preoperatively the indication to the cervical or sternotomic approach or a combination of both and the technical issues related to each singular patient. On CT images, MG usually appears as a clear boundary mass, its density varies due to the amount of iodine contained: when the amount of iodine in the mass is low, its density is close to the soft tissue of chest wall, and when the amount of iodine is high, its density could be greatly higher than soft tissue. In addition, its density can be uneven due to colloid cysts and calcified plaque [19]. NMR is useful to better define

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the relationship of continuity between the cervical and the mediastinal component and with the vascular structures [20–22].

Radionuclide scan with ^{131}I or ^{99}Tc is also one of the common diagnostic methods, but it is not so effective when compared with its usage in thyroid goiter of other regions because the intrathoracic goiter does not always uptake iodine; negativity is due to the reduction of the endocrine activity secondary to regressive disorders determined by the dislocation, the presence of the sternum and the great mediastinal vessels hiding the modest uptake [23–25]. In our experience, these methods consented to confirm the presence of retrosternal component only in 32 cases out of 60 (52.5%). Best results were obtained using the ^{99m}Tc-MIBI, a positive indicator, which allowed, in all 20 patients in which it was used, to highlight the retrosternal thyroid tissue. According to latest literature, integrated I-131 SPECT-CT imaging has an additional value in patients with thyroid cancer, for characterization of tracer uptake seen on planar imaging as well as for precise localization of malignant lesions in the neck, chest, and skeleton. With these indicators, used under scintigraphy, we are able to evaluate not only morphologically retrosternal thyroid tissue, but also to get information on the metabolic goiter, suspecting the neoplastic nature and also identifying the lymphnode metastases [26,27,49]. Tracheobroncoscopy is the only invasive diagnostic procedure of cervical mediastinal goiters, while fine needle ago biopsy (FNAB) has controversial indication [28]. Endoscopy should be performed in presence of clinical signs of a upper airway obstruction (wheezing and stridor), dyspnea, dysphonia and tracheal profile modifications. It becomes necessary for suspected malignancy of the thyroid mass to detect any irregularities in tracheal mucosa or neoplastic infiltration of the wall, and in cases of an important tracheal compression due to big cervico-mediastinal goiters, the anesthesiologist performed the tracheal intubation with a small single lumen tube and laringo-tracheal visualization under fiberbronchoscope control. The fine needle biopsy is rarely useful in mediastinal goiter: the taking is never representative for the entire gland. The neoplastic degeneration of a cervico-mediastinal goiter is in most cases an incidental finding. The malignant lesions are preoperative known (positive preoperative biopsy and presence of cervical adenopaties). In majority of the cases the malignant lesions are discovered at the time of the removal of the substernal thyroid mass as an occult thyroid tumor. Most of the mediastinal thyroid masses is represented by cystic or nodular colloid goiter. The neoplastic transformation is reported in literature with a frequency ranging from 3% to 5%; although in our case it was slightly higher, with 7 cases out of 97 (7.6%). When the trachea, esophagus or vena cava is compressed, surgical resection of intrathoracic goiter must be done. Preventive operation is also feasible for asymptomatic patients in order to avoid future compression [29]. The normal thyroid gland develops with the parathyroids and thymus from the primordial pharynx and its pouches during the first and second weeks of intrauterine life. When the median thyroid anlage comes in contact with the aortic sac it is pulled ventrocaudally as the sac descends. Following descent of the median thyroid anlage, its pharyngeal connection elongates as the thyroglossal duct. The thyroglossal duct normally disappears by the fifth to sixth week but the separated fragments of ectopic thyroid tissue may eventually reside anywhere in the midline along the embryologic pathway from the root of the tongue to the diaphragm. The blood supply in secondary MG comes from the inferior thyroid artery and its branches while primary posterior mediastinal goiter maintains little or no connection with the cervical thyroid gland and has a vascularization derived from intrathoracic arteries. These anatomical bases suggest that at least in the secondary MG located in the anterior mediastinum a complete control of the arterial supply (inferior thyroid arteries) is possible and safe via a cervical approach. In a thyroidectomy for primary MG, vascular control is possible only directly in the mediastinum. These differences are part of the evaluation for a proper surgical access.

Total thyroidectomy with en bloc removal of the intrathoracic portion of the thyroid, is the treatment of choice. Usually a cervical approach is appropriate in most of the cases (77% of our cases) being the mediastinal portion easily externalized by traction and digital maneuvers. In selected cases (posterior mediastinal goiters which extended beyond the aortic arch, severe kyphosis, caval syndrome compression) in situations when mediastinal structures were distorted by the presence of the cervico-mediastinal thyroid mass and strong adherences between the abnormal neovascularized capsule of the mass and the surrounding structures, the thoracic approach through partial upper sternotomy or total was important in order to minimize the bleeding due to vascular damage. Morcellation of the thyroid tissue was avoided in order to lessen the possibility of bleeding, which may be difficult to control, and because of the possible presence of an occult carcinoma within the gland, a partial or complete median sternotomy or a thoracotomy are required to achieve radical excision without haemorrhagic complications [30,40–48]. In fact en block thyroidectomy, at least radical lobo-isthmectomy plus contralateral lobectomy possibly without disruption of the thyroid capsule is the gold standard technique. This standard approach avoids the problem of the "forgotten" goiter which is defined as a mediastinal thyroid mass found after total thyroidectomy, rare condition whose incidence might increase after surgery for MG, if it is not performed according to the above criteria. In fact the "forgotten goiter" is usually the consequence of the incomplete removal of a plunging goiter, and moreover, sometimes it may be attributed to a concomitant, unrecognized mediastinal goiter which is not connected to the thyroid. Sternotomy, while conditioning the postoperative hospital stay, not aggravate the mortality and morbidity [31,32,50–59]. We performed sternotomy in 22 patients (Table 3). The need of performing an enlarged incision manifested in the totality of cases (11/11 of 100%) of "forgotten" goiter of previous interventions, and in almost totality of patients with neoplasia (6/7 cases corresponding to 80%). Another important factor conditioning the choice of approach has been the localization; sternotomy was necessary in almost half of patients with retrovascular goiter (11/24 43.7%) while only 16.3% of cases of prevascolar goiter (12/73 cases) needed sternotomic approach. In 12/22 cases we performed a sternal split. In one case we used the transverse sternotomy: it was a patient, already submitted twice thyroidectomy to for benign lesions, presenting a "forgotten" goiter in the mediastinum, and a rib metastasis. The patient underwent to removal of "forgotten" goiter and resection of two costal arches. The definitive diagnosis was suggestive for thyroid follicular carcinoma. A variety of operation modes exist, including sternotomy, clavicular resection, anterior posterolateral thoracotomy and Video Assisted Thoracoscopic Surgery (VATS). A specific mode depends on the location, size of the mass and its relationship with surrounding important organs. The posterolateral thoracotomy may be used in presence of posterior ectopic mediastinal goiters or in case of thyroid masses with uncertain diagnosis, with no relationship with the thyroid cervical [33,34]. Finally, in rare cases of posterior mediastinal goiter with

Table 3
Sternotomy (total or split) and morphological aspects of goiters.

	Sternotomy	%
• Thyroid cancers	6/7	80
• Retrovascular goiters	11/24	43.7
• Prevascular goiters	12/73	16.4
• "Forgotten" goiter	11/11	100

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mediastinal compressive symptoms lateral thoracotomy before cervicotomy is an alternative approach. In 40 patients (41.5%) we performed total thyroidectomy (surgical removal of entire thyroid gland), subtotal thyroidectomy (both lobes were removed except of a small thyroid tissue from posterior part of the goiter) in 46 cases (47.7%). Interdisciplinary assessment of these cases consists of cardiac evaluation (clinical examination, electrocardiography, and echography), otolaryngology (vocal cords exploration through laryngoscopy) and pre-anesthetic evaluation [35–38]. In six cases the thyroidectomy was completed with other surgical procedures: in two cases has been associated tracheal resection, in 2 case a VATS procedure for pleural effusion, in 1 case the removal of a neurinoma of the phrenic nerve and finally, in another case, the removal of two ribs for metastatic follicular thyroid cancer. Postoperative complications are typical of thyroid surgery: temporary or permanent recurrent laryngeal nerve palsy and hypoparathyroidism, respiratory failure and post-operative bleeding. The higher mortality (15.3% vs 2%) of patients undergoing sternotomy, in our series, should be evaluated considering that two patients had an anaplastic carcinoma and that the surgical procedure was necessary for a worsening respiratory failure [39,60,61]. Other surgical approaches for excision of a Posterior Mediastinal Thyroid Goiter reported in literature are: VATS techniques to remove an ectopic intrathoracic goiter, robot-assisted technique for the removal of a substernal thyroid goiter, with extension into the posterior mediastinum. This technique used a combination of a cervical incision and minimally invasive thoracic approach, without subjecting the patient to the morbidity of a thoracotomy.

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