A critical update on the management of retrosternal goiter

Cesare Miani[1], Luca Giovanni Locatello[2], Anna Maria Bergamin-Bracale[2], Nicole Caiazza[2], Stefania Rigo[2], Maria Gabriella Rugiu[3], Andrea Zuin[1], and RICARD SIMO[4]

[1]Universita degli Studi di Udine
[2]Presidio Ospedaliero Universitario Santa Maria della Misericordia
[3]Azienda sanitaria universitaria Friuli Centrale
[4]Guy's and St Thomas' NHS Foundation Trust Ear Nose and Throat Head and Neck Service

October 21, 2023

Abstract

Background: Retrosternal goiters (RGs) pose several challenges to head and neck surgeons because of the intricate anatomical relationships with major vessels and other mediastinal structures. Methods: A scoping review of the last five years in the PubMed database was conducted and a total of 105 articles were discussed, along with methodological issues and future directions in the research on RGs. Results: The surgical excision of RGs may be accomplished by standard transcervical approach in the vast majority of cases, yet the potential need for a transthoracic approach must be always kept in mind. Great expertise in referral centers is required to maintain an acceptable rate of postoperative complications, and a thorough diagnostic work-up is mandatory. Several non-surgical treatments in addition to mini-invasive approaches have been proposed for RGs. Conclusions: RGs require a multidisciplinary thyroid team in order to eventually minimize the risk of complications and avoid extracervical approaches.

Introduction

Retrosternal goiter (RG), also referred to as intrathoracic or retrosternal, or cervico-mediastinal goiter, was first described by Haller in 1794 but it still represents a challenge for inexperienced head and neck and thoracic surgeons, as well as for anesthesiologists[1,2]. Clinically RGs are usually incidental findings, yet they can present sometimes with life-threatening dyspnea. They pose many issues in terms of airway management: because of tracheal deviation, external compression, and risk of tracheomalacia and cardiovascular collapse, RGs should be managed only in referral centers where expected difficulties can be safely managed. In this regard, an accurate preoperative work-up is mandatory in order to avoid complications and to reduce the need for an extra-cervical approach. The most recent review available on RG dates back to some years ago, and since then the evolution of technology has brought in different innovations, especially in new mini-invasive techniques such as image-guided ablation or robotic-assisted transthoracic surgery[3].

The present review aims to critically discuss the published evidence in the last five years on the medical and surgical management of RG, with particular attention to the need for multidisciplinary management of these patients.

Materials and Methods

The PRISMA statement (*https://www.equator-network.org/reporting-guidelines/prisma/*) was followed in the preparation of the present paper, and a modified PRISMA flowchart is given in **Figure 1** [4]. No institutional review board approval was necessary for the present work. The PubMed database was used in order to perform the review of the literature from January 1st 2017 to January 1st 2023. The following search

string was used: "(intrathoracic OR retrosternal OR cervico-mediastinal OR substernal) AND (goiter OR goitre)". All the pertinent articles were included after careful reading of the titles and abstracts. Full texts of the included articles were then retrieved by the first author (LGL) and quantitative and qualitative data were synthesized accordingly. Papers reporting surgical outcomes of RG mixed with other thyroid disorders (Reason 1); studies other than original articles or reviews or case series/reports (Reason 2), or written in languages other than English or French, or Italian were excluded (Reason 3).

The search strategy retrieved a total of 172 articles and, after applying the selection criteria, a total of 98 articles were ultimately analyzed. Additionally, a further 7 articles were retrieved and included in the discussion after checking through the reference lists of the relevant studies. Quantitative and qualitative data regarding surgical outcomes were summarized and systematically reported in tables.

Definition, Classification, and Pathogenesis of RG

From an etymological point of view, RG must at least partially be located in the mediastinum, but a myriad of factors affects this seemingly simple definition: a clinical versus a radiological evaluation, the extension of the head at the time of examination, the proportion of thyroid mass that is required to extend into the thoracic cavity, just to name a few. As of today, we still haven't found a commonly accepted definition of RG which suffers from an "identity crisis"[2], and a historical overview of the over ten definitions available has just been published[5]. Notably, Rios et al. analyzed the various criteria to define RGs and they found none to be clinically meaningful[6]. The most recent (and somehow broadest) definition comes from the 2020 American Association of Endocrine Surgeons (AAES) guidelines, where "if a mediastinal extension is present, meaning that the gland extends caudally past the sternal notch on physical examination, computer tomography (CT) imaging, or at the time of surgery" it can be considered as a true RG[7]. Since an authoritative international consensus has not been reached, the most recent literature is still heavily affected by these heterogeneous definitions (see**Table 1**), and this represents an enormous obstacle for comparing surgical outcomes.

RGs can be variously defined according to their extension and relationships with anatomical structures of the mediastinum: the most recent classification divides them into a Type I RG (extending anteriorly to the trachea and RLN), a Type II RG (where at least a part of the mass extends posteriorly to the mediastinal vessels, the trachea, and the RLN), and a Type III (purely mediastinal) RG[8]. Unfortunately, a formal correlation of these classifications with surgical outcomes has not been performed. We must remember that over 99% of RGs are secondary (type I and II), *i.e.* they represent an inferior extension of the normal thyroid gland, and they are vascularized by branches of superior and inferior thyroid arteries. Instead, primary (type III) RGs are clearly separated from the orthotopic cervical thyroid, they receive arterial branches from intrathoracic arteries, and they are usually incidental findings[9]. In these cases, a missed gland can be diagnosed only when postoperative TSH levels remain unchanged or a (functional) imaging of the chest is performed[10–13]. From an embryological point of view, type III RG is explained by an erroneous migration of the two median and lateral anlagen from the pharyngeal pouch and the ultimobranchial body, as it was recently reviewed by Rico and Lung[14]. Migration of the median anlage may also lead to a presternal goiter, and in 2019 the seventh case worldwide was reported[15]. Sometimes, after subtotal thyroidectomy, patients may present with only a residual central mediastinal mass shifting the trachea laterally ("pseudo-primary RG")[16–18]. This may also happen decades after the initial surgery and it may mimic other mediastinal or pulmonary pathologies, such as paraganglioma or adenocarcinoma of the lung[19,20].

Regarding the pathogenesis of RG, no recent study has ever explored if there are different molecular mutations in RG compared to non-intrathoracic goiters. The issue remains unsolved and anatomical and functional factors (no limitations downwards encountered by the expanding gland, traction forces associated with swallowing, a negative intrathoracic pressure during inspiration), and gravity itself has been called into question[21]. A 1939's study by Crile proposed that patients with a short neck and hypertrophic cervical muscles might theoretically favor the retrosternal expansion of the goiter[22], but no formal anthropometric study exists to corroborate this assumption. In the end, and besides the simple time during which a goiter has been allowed to grow undisturbed, risk factors for the development of RGs remain still unexplored.

Clinical Presentation

A chronic and slowly progressive airway compression is the usual presentation of RG, and this can last many years in areas where iodine deficiency is endemic[23]. A choking sensation exacerbated by the supine position, globus, wheezing, and exercise-induced dyspnea (both mistaken for asthma), or dysphagia are the symptoms most commonly reported by patients, that on the other hand are asymptomatic at presentation in over one-third of cases[5]. Mechanisms of dyspnea are believed to be direct extrinsic tracheal compression, dysfunction of the recurrent laryngeal nerve, and lung atelectasis[24]. Instead, in less than 5 % of cases the clinical presentation of RG may be acute: spontaneous hemorrhagic enlargement of RG may occur during pregnancy[25,26] or for unclear reasons[27,28], acute asphyxia and cardiac arrest have been described[29,30], and some authors have hypothesized a direct phrenic nerve compression by the RG as the main cause of these dramatic scenarios[31].

Rarer presentation may be constituted by thyrotoxicosis or symptoms of superior vena cava syndrome (facial plethora and congestion, upper neck cyanosis, or a positive Pemberton's sign with facial flushing and engorgement of superficial jugular veins upon raising the arms)[5]. While it had been previously reported that this syndrome was more often associated with malignancy, this remains unproven[21]. Isolated dysphagia is also possible in case of goiter growing only in the retro-esophageal plane[32,33], while the only presenting symptom may also be represented by oropharyngeal bleeding because of pharyngolaryngeal "downhill" (*i.e* ., without venous portal hypertension) varices[34]. Furthermore lower and upper extremities edema[35], pericardial effusion, chylothorax, or hemoptysis because of tracheal varices have been also described[21].

Diagnostic Work-up and Anesthesiologic Considerations

The diagnostic workup of a goiter begins with simple palpation of the neck and performing an ultrasound. Regarding the former, Pattashanee and colleagues have shown that clinical examination in modified Rose's position (*i.e.* , supine, a roll under the shoulders, and by hyperextending the neck) has an excellent sensitivity (98%) and a variable specificity (46.7-91.1%) to identify substernal extension[36]. Another interesting result is that, in the absence of the Pemberton's sign, the probability of getting a false positive finding of a substernal extension was only 4%, and this is quite relevant in the context of low-income countries where the availability of CT scan is scarce[3633], an 89% sensitivity and 87% specificity for any degree of tracheal narrowing were registered (AUC = 0.90)[37].

CT scan of the neck and thorax remains the gold standard for a full assessment and classification of RG because it evaluates the dimensions, the morphology, and the relationships to the adjacent mediastinal anatomical structures (**Figure 2**). It is usually performed with the aid of intravenous iodine contrast agents, despite a theoretical more than a real risk of precipitate thyrotoxicosis (Jod-Basedow phenomenon)[5,21]. Some authors have proposed a simple yet not validated rule-of-thumb: if the RG remains cranial to the aortic arch in the sagittal plane of CT performed while the patients maintain a full neck extension, then sternotomy is usually not necessary[38]. Classical predictors of the need for sternotomy are based on the craniocaudal length of the retrosternal extension, the ratio between the retrosternal portion and the diameter of the upper thoracic inlet (so-called "iceberg" or "cone-shaped RG"), and the anterior or posterior relationships with major vessels[2,393] had a negative predictive value for the extra-cervical approach of 100%[40]. Volume was manually outlined on axial sections by two radiologists, but interrater agreement and kappa coefficients were not calculated thus leaving doubts on the applicability of this technique. The value of imaging in the prediction of an exclusive transcervical approach to RG will be discussed further in the next sections.

CT scan lets a clear assessment of both tracheal deviation and extrinsic compression, which are both reasons why airway management is usually labeled as difficult in RG patients, and a very low threshold for endoscopic-assisted awake intubation is kept by anesthesiologists. This fear mostly derives from anecdotal evidence of extreme RG where emergency tracheostomy[29], or the need for a pediatric flexible bronchoscope were necessary[41]. In the most extreme case, the application of extracorporeal membrane oxygenation (ECMO) before the induction of general anesthesia has been described with success[42,43]. Actual evidence instead dispels the myth of a difficult airway, in the absence of classical risk factors (mouth opening less than 4

cm, a thyromental distance less than 6 cm, Mallampati Class III or higher, etc.)[39]. In a 2020 paper, 22 cases of "giant" type I RG (defined as trespassing the aortic arch on CT scan), with a mean maximum diameter of 114.2 ± 19.5 mm were all successfully intubated with standard laryngoscopy or awake tracheal intubation (for 5 patients, 22%) using flexible bronchoscopy[44]. A larger multi-institutional series from the USA, confirmed that direct laryngoscopy or videolaryngoscopy techniques were sufficient in 162 patients (90.5%), while transnasal of transoral fiberoptic was intubation used for the remaining 17 patients[45]. The authors did not give a clear-cut definition of RG, yet they performed a multivariate analysis where the body mass index was the only factor to positively correlate with the number of attempted intubations[45].

Non-surgical management of RG

When surgery is not indicated or it is not feasible because of the patient's general status, frailty, or comorbidities, a wait-and-see approach or medical treatment of RG may be proposed[5,21]. In the most recent literature, no new studies regarding levothyroxine supplementation or radioiodine treatment have been published. For both options many drawbacks are present (missed malignancy, risk of thyrotoxicosis or of an increase airway obstruction) and only with the advantage of a slow and modest size reduction at best[21]. Instead minimal-invasive techniques such as transcervical microwave ablation (TcMA), transcervical radiofrequency ablation (TcRfA), or selective embolization of the thyroid arteries (SETA), whose preliminary reports date back to the 2000s, are being further explored.

Ultrasound-guided microwave TCA of RG combined with ethanol injection was reported as an effective and safe treatment for solitary nodular RG, especially for patients who are ineligible or unwilling to receive surgical treatment [46,47]. A first preliminary experience was presented by Cui et al in 2018 on 10 patients a mean volume reduction ratio (VRR) of around 67% was reported after one month, while no local (pain, hematoma, etc.) or functional (thyrotoxicosis crisis, changes in TSH, etc.) adverse events were reported[46]. In a subsequent prospective study from the same hospital involving 72 patients (mean age 47.8 years) and with a mean follow-up of 23.9 months, TCA yielded a mean VRR of 83.12 ± 12.74 % (range: 52.01–100%) after one year; 57 patients (79.2%) showed a total regression of the intrathoracic extension (by CT scan) while 8 patients (11.1%) needed a second procedure because of "regrowth of unsatisfactory reduction". 4.2% (3/72). Two patients complained of temporary neck pain/discomfort, while there was a case of postprocedural dysphonia, which resolved spontaneously after 1 month, for an overall complication rate of 4.2%[47].

It should be noticed that in both studies, a significant reduction in terms of RG-associated signs and symptoms (*i.e.* , neck circumference and a VAS scale measuring pain, shortness of breath, positional dyspnea, dysphagia, and dysphonia) was obtained, despite the fact that the procedure focused only on the largest retrosternal nodule[46,47].

TcRfA is another option and Chiang et al. recently showed a VRR of 75.5% ($p<0.001$) in a series of 16 RGs[48]. In this series, only 4 (25%) patients showed complete regression of the substernal portion of the goiter, while there was a case of temporary hoarseness and a case of subcutaneous/focal mediastinal hematoma, which was managed conservatively (complication rate 12.5%). Nonetheless, all the patients reported significantly lower cosmetic and symptom scores on the VAS scale at 6 months[48].

Regarding the SETA procedure, a small Italian series of 10 patients reported complete success in reducing the thyroid function and RG dimensions but no formal endpoints were used, and follow-up time was not reported. In addition, all patients developed transient thyrotoxicosis requiring corticosteroids, antibiotics, and methimazole, while one patient (10%) had right vocal cord fixation lasting around 6 months[49]. Yilmaz and coworkers instead presented their experience with SETA in 56 goiters, and among them 47 were considered "intrathoracic"[50]. The procedure was conducted successfully in 145 out of the 146 thyroid arteries and complications occurred in 27 patients (48%), but if we eliminate a case of intraoperative blurry vision, one case of groin hematoma, and 23 cases of hyperthyroidism (since it is a predictable effect because of the necrosis of the gland), only 3 (5%) patients developed temporary hoarseness. Notably, after 6 months, the mean thyroid volume was reduced from 147.0 mL to 62.6 mL, while the mean retrosternal extension was reduced from 31.7 mm to 15.9 mm ($P < .001$). Quality of life was measured by the popular ThyPRO tool

and the mean scores improved from 155.4 to 70.4 ($P < .001$)[50]. These authors also reported that one patient died of myocardial infarction two weeks after SETA, and a possible causative effect cannot be excluded. Despite the absence of a comparative study, SETA is reported to be applicable irrespective of the goiter dimensions but this does not fit the preprocedural reported mean dimensions of the nodules (80.2 ± 46.7 mL for SETA[50], versus 76.10 ± 50.56 mL for TcMA[47]).

In summary, all these non-surgical approaches have many advantages (no reported risk of iatrogenic hypothyroidism or hypoparathyroidism; they are a day or one-day procedures for ablation and SETA, respectively; they can be performed even in very fragile patients, etc.) but they retain the fundamental limit of not permitting any histological evaluation of the RG, even though at least one[50], or two[47] consecutive non-malignant (up to Bethesda category 3) fine-needle core biopsies were required as an inclusion criterion. The clinical experience remains however limited and, most importantly, the lack of a head-to-head comparison between standard surgical resection and these techniques remains their central limit.

Indications and Classical surgical approaches to RG

Classical indications for surgically removing a simple/non-toxic goiter date back to the beginning of the twentieth century: relief from compression symptoms, prevention of or suspicion of an associated malignancy, or for cosmetic purposes[51]. Unfortunately, these criteria are somehow vague and, because ultimately the surgeon is the sole responsible for the outcomes of thyroidectomy, in 2018 a "Choosing wisely" initiative from Germany proposed more reproducible criteria: compression symptoms (dyspnea, stridor, dysphagia) must be directly attributable to goiter while a reasonable suspicion of malignancy must be documented (*i.e.* , TI-RADS category 4c/ 5, Tir 3 or higher class at FNAC in the presence of risk factors for thyroid cancer, basal calcitonin serum level increase >26 pmol/L in women and 60 pmol/L in men, cN+ status at ultrasound). In the absence of the above, surgery may also be indicated for "prevention of complications" that may derive from a *progressive* RG (defined as tracheal compression >35%, superior vena cava syndrome)"[52–54]. Again the progression must be documented but the very natural history of untreated RG is still poorly understood[2].

An exhaustive explanation to the patient and their caregivers is the key to surgical success[3]. A detailed technical overview of the classical surgical approaches to RG has been recently given by Uludag et al and it will briefly be discussed here[39]. A Kocher incision, ligation of the superior and inferior vascular peduncles, and digital dissection remain the standard surgical steps, but resection of the pre-laryngeal musculature is often necessary for delivering large goiters. A 2022 study has for the first time evaluated its consequences on vocal and swallowing function: by using patient-reported impairment scores, a prospective head-to-head study of 34 patients revealed no significant differences when strap muscles are transected or not[55].

In 2021, the International Neural Monitoring Study Group (INMSG) published the most important study of surgical anatomy since the introduction of intraoperative neuromonitoring (IONM). The authors have meticulously evaluated the course and anatomical relationships of 1000 RLNs: strikingly, among other findings, it emerged that in 50% of cases of RG (versus 30% in standard thyroidectomies), the RLN was fixed, splayed, or entrapped at the level of the capsule of the thyroid, thus rendering at high risk for loss of signal[56]. IONM is thus mandatory for every RG operation and, in the case of "giant" RG, many authors suggest the upfront use of a transcervical medial approach, which implies the separation of the isthmus and dissection of Berry's ligament in a layered fashion along the trachea and towards the RLN. In a series from the USA, successful identification of the RLN was reported to be 84% with this approach and postoperative vocal cord dysfunction (assessed by flexible laryngoscopy) was null[57]. A very high rate (17%) of postoperative hematoma was reported, yet the authors declared that revision in the operative room was deemed necessary only for one patient[57]. Another larger case series from Greece declared instead no postoperative bleeding, and a permanent RLN damage rate comparable with classic lateral approaches[58].

Regarding the extent of the resection, even in the most recent series total thyroidectomy is the preferred strategy for RG, which however can harbor one or more foci of malignancy in up to 40% of cases[21]. When the intrathoracic part is well lateralized, or there are anatomical constraints or technical issues during the dissection, a subtotal resection or a simple hemithyroidectomy may help relieve the compression symptoms

while minimizing the postoperative complications. New technologies are being exploited also in this type of operation: in 2018, some authors have proposed a microdebrider-assisted intracapsular reduction thyroidectomy on a small series of 26 patients. According to the proponents, a standard sinus suction debrider may morcellate the intracapsular part of the RG, it has no effect on the risk of major bleeding, and may avoid the need for sternotomy in selected patients[59]. Instead, recent retrospective papers on transoral endoscopic thyroidectomy vestibular approach (TOETVA) or transoral robotic thyroidectomy (TORT) consider RG as an exclusion criterion because of intrinsic limitations in terms of surgical exposure[60].

Current Indications for combined surgical approaches to RG

Several goiter-related and patient-related factors must be considered in the surgical plan. The former are usually evaluated by neck and chest imaging, and as already mentioned patients are deemed at high risk for an extra-cervical approach when: RG extends below the aortic arch, it has multiple or separate mediastinal compartments, it has an "iceberg" or conical shape (*i.e.* , it extends to both sides of the thorax or it has a diameter that is larger than the upper thoracic inlet)[3,21,38,61]. Some authors believe that in presence of possible malignancy, sternotomy may be favored, but there is no consensus on this point[62]. In extreme cases, RG may be strictly adherent to the pericardium[63], or it can even invade it: in these exceedingly rare cases of intrapericardial RG, sternotomy and the availability of a cardiopulmonary bypass are essential[64]. Instead, patient-related features that may favor an extracervical approach include a history of previous thyroid or thoracic surgery, previous irradiation in the neck or chest areas, preoperative dysfunction of the vocal cords, coagulopathies, or platelet disorders (*e.g.* , Bernard-Soulier syndrome)[2,21,65].

The most important study that has corroborated these factors was published in 2019: in a cohort of 237 RGs where 29 (12.2%) required sternotomy, on multivariate logistic regression analysis, extension below the aortic arch (OR 10.84), an iceberg shape (OR 59.30), and previous neck surgery (OR 4.83) were all significantly associated with an extra-cervical approach[66]. For the sake of completeness, another group has suggested the presence of an inflammatory component in the excised RG as a predictor for sternotomy (only on univariate analysis and in a small series)[67], while in another series of 109 RGs, only the part extending beyond the sternal notch into the mediastinum would predict sternotomy (univariate only, odds ratio 3.43, confidence interval 1.65-6.41), with a sensitivity of 94% and specificity of 86.5% when it is more than 5 cm[68]. Unmeasurable aspects such as the surgeon's expertise do however exist since there are case series where RG cases below the aortic arch or in the posterior mediastinum were reported to be completely excised through a purely transcervical approach[69].

Complete sternotomy is the gold standard access for RG but less extensive approaches have been devised, namely partial or split sternotomy[70], manubriotomy[71], anterolateral or posterolateral thoracotomy, the hemi-clamshell approach (partial median sternotomy plus an anterolateral thoracotomy)[72], and they are all technically described in the work of Uludag et al[39]. Endoscopic-assisted approaches are another option but in the last years, video-assisted mediastinoscopy has lost its interest in favor of thoracoscopic approaches[3,73]. For example, the subxiphoid thoracoscopic approach is a novel alternative proposed by a Chinese group for median RGs[74]. Robotic-assisted procedures are being also actively explored but they are always combined with a transcervical incision[75–77].

Interestingly, in the 2016 American Thyroid Association (ATA) Statement on Remote-Access Thyroid Surgery (RATS), the substernal extension was considered a contraindication, but the latest papers seem to overcome this limit. A RATS by an axillo-thoracic endoscopic approach has been applied on very selected patients with RG[78]. The excellent view of the surgical field provided by high-definition cameras is obviously very helpful in the identification of critical neurovascular structures (RLN and phrenic nerves, etc.) but, at present, all these approaches remain preliminary and a formal comparison with standard techniques is lacking. Finally and in very rare cases, a straightforward indication for combined approaches to RG is given by a coexisting thoracic condition: for instance, a minimally invasive transcervical and robotic transthoracic approach has been described for RG and concurrent thymoma[79], or RG excision and aortic valve replacement were performed through a mini-J sternotomy[80].

Complications associated with surgery for RG

The presence of RG is historically known to carry a higher risk of finding a malignancy and of the development of postoperative complications (hematoma, transient/permanent hypoparathyroidism, and RLN dysfunction) compared to cervical goiters[81]. The most recent evidence has further confirmed these findings: for example, in a cohort of 1500 RLNs at risk, substernal extension and a thyroid volume >100 mL were the only significant factors for postoperative transient or permanent VC paralysis[82]. In the IONM era, a study extracting 42341 operations from the UK Thyroid database found that RG was an independent factor (OR= 1.36, 95%CI 1.05- 1.77) that predicted the risk of RN injury, along with revision surgery and patient age.[83] A recent anatomical study has revealed that iatrogenic lesions of the RNL after RGs' resections are more frequent on the right side in comparison to the left one because of the known anatomical and embryological differences in the development of the RLN on either side of the neck[84].

Regarding postoperative hematoma formation, male sex, the use of preoperative anticoagulant therapy or postoperative subcutaneous heparin, and the presence of RG (38 cases) were all significant predictors in a group of 6900 thyroidectomies[85]. Instead, RG was not a significant risk factor in another series of 5900 operations, including a total of 148 RGs (2.5%)[86]. Both series, unfortunately, did not provide a definition of RG nor how the extension was determined. On the contrary, another analysis of the aforementioned UK registry (n= 53838 entries) revealed in multivariable analysis that male sex, increasing age, redo surgery, RG (whenever having an "extension to the thoracic inlet or below"), and total thyroidectomy were all correlated with an increased risk of reoperation for bleeding; interestingly, surgeon monthly thyroidectomy rate correlated with a decreased risk[87].

The presence of RG is linked with a major risk of developing clinical symptoms of hypocalcemia (OR 10.26)[88]. A recent study published by Chen et al. provides evidence that there are predictive factors for this adverse event. This meta-analysis includes 23 studies and identifies twelve significant risk factors for postoperative hypocalcemia. In particular, hypoparathyroidism (OR 5.58), total thyroidectomy (OR 3.59), hypomagnesemia (OR 2.85), and preoperative vitamin D deficiency (OR 2.32), were those most associated with hypocalcemia[89]. In another observational study, RG and its extension beyond the carina showed a statistically significant higher risk for transient (less than one year) hypocalcemia (relative risk = 1.76) after total thyroidectomy[90].

Van Slycke and colleagues reported that the higher risk of postoperative complication is influenced by the surgical approach chosen: out of 95 thyroidectomies performed for RGs, eighty patients (84%) were operated by cervicotomy and 15 (16%) by cervicosternotomy. The latter group had a higher risk of temporary recurrent laryngeal nerve palsy (21%) compared to cervicotomy (4%) and standard thyroidectomy (3%); also, the risk of temporary hypocalcemia after cervicosternotomy was higher than with transcervical approaches [62]. In addition, another study highlights how postoperative complications associated with RG surgical removal are low in the hands of experienced, high-volume thyroid surgeons, regardless of transcervical or transthoracic approach[91]. Instead, the presence of RG was statistically significant for being an independent predictor of any complication (OR 2.1), when controlling for age, BMI, gender, and race[91].

Tracheomalacia remains the most dreadful complication in the case of large RGs, despite its incidence seems to be very low[92]. In a series of 40 patients subjected to thyroidectomy with sternotomy, tracheomalacia was reported in 3 cases, in absence of any patient- or thyroid-related factor significantly associated with its development: one patient required tracheal resection with anastomosis, and two patients required tracheostomy[92]. In another paper, 17 cases of tracheomalacia out of 106 cases were reported, probably caused by long-standing tracheal compression from RG: this study suggested that prolonged intubation was sufficient to resolve airways collapse without tracheal reconstruction in all cases[93]. Zuo et al. reported how tracheomalacia could be successfully managed intraoperatively by suspending the trachea to the overlying skin with Prolene stitches, despite the fact that they didn't exhibit either the exact number of patients affected or the long-term outcomes[94]. Despite all the aforementioned complications, RG was not considered a contraindication for outpatient surgery: in a recent national survey conducted by the American Association of Endocrine Surgeons, the diagnosis of RG had no or minimal effect on same-day discharge[95].

The main issue in the analysis of the complications of surgery for RGs remains the non-standard definitions and characterizations. For instance, postoperative vocal cord dysfunction may be diagnosed by using a mirror[52], flexible laryngoscopy[57], or a mixture of both[82]. The timing of what constitutes a "permanent" hypocalcemia changes (after 6[57], versus after 12 months[53]); the same is true for hematoma/seroma that should be considered only when needing revision surgery according to some but not all the authors. To overcome these limitations, the use of the Clavien-Dindo system may be a solution: proposed in 1992 and revised in 2004, it appears reliable as a compelling tool for quality assessment in surgery worldwide. This classification system was reported as simple, reproducible, logical, useful, and comprehensive[96] and it is beginning to be implemented also in thyroid surgery[97].

Conclusions

RG is not an uncommon encounter for head and neck surgeons. Its management requires a long-standing experience in the classical transcervical approach that may be sufficient in over 90% of treated cases. Despite a growing body of publications, we still have no shared definition of RG and this continues to bring in heterogeneity in the literature because it hampers a formal comparison and synthesis of the results. We believe that reaching an international consensus among head and neck and endocrine surgeons on the very definition and classification/grading of RG is a priority in order to seriously compare outcomes by data pooling and to increase the evidence in this field. A second priority is the definition of the natural course of this condition since it is likely in the near future that we will face more and more incidental RG as the use of neck imaging is becoming widespread.

REFERENCES

1. Rugiu MG, Piemonte M. Surgical approach to retrosternal goitre: do we still need sternotomy? *Acta Otorhinolaryngol Ital* . 2009;29(6):331-338.

2. Hanson MA, Shaha AR, Wu JX. Surgical approach to the substernal goiter. *Best Pract Res Clin Endocrinol Metab* . 2019;33(4):101312. doi:10.1016/j.beem.2019.101312

3. Simó R, Nixon IJ, Vander Poorten V, et al. Surgical management of intrathoracic goitres. *Eur Arch Otorhinolaryngol* . 2019;276(2):305-314. doi:10.1007/s00405-018-5213-z

4. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Int J Surg* . 2021;88:105906. doi:10.1016/j.ijsu.2021.105906

5. Unlu MT, Aygun N, Kostek M, Isgor A, Uludag M. Substernal Goiter: From Definitions to Treatment. *Sisli Etfal Hastan Tip Bul* . 2022;56(2):167-176. doi:10.14744/SEMB.2022.30806

6. Ríos A, Rodríguez 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):233-238. doi:10.1016/j.surg.2009.06.018

7. Patel KN, Yip L, Lubitz CC, et al. The American Association of Endocrine Surgeons Guidelines for the Definitive Surgical Management of Thyroid Disease in Adults. *Ann Surg* . 2020;271(3):e21-e93. doi:10.1097/SLA.0000000000003580

8. Liddy W, Netterville JL, Randolph GW. *Surgery of Cervical and Substernal Goiter.* Vol Surgery of the Thyroid and Parathyroid Glands. 3rd ed. Elsevier; 2021.

9. Zamora E, Ghandili S, Zamora MA, Chun KJ. Incidental Primary Intrathoracic Goiter: Dual-Isotope Scintigraphy and Early-MIBI SPECT/CT. *World J Nucl Med* . 2022;21(2):148-151. doi:10.1055/s-0042-1750337

10. Regal M, Kamel MM, Alyami H, Al-Osail EM. Mediastinal ectopic thyroid mass with normal thyroid function and location: Case report. *Int J Surg Case Rep* . 2018;52:5-7. doi:10.1016/j.ijscr.2018.09.033

11. Faroq Abdulrahman SM, Teksöz S, Ferahman S, Demiryas S, Bükey Y, Özyiğin A. Missed thyroid gland after total thyroidectomy. *Turk J Surg* . 2018;34(2):137-139. doi:10.5152/turkjsurg.2017.3206

12. Oh SL, Chia CLK, Ooi OC, Sonawane V, Rao AD, Singaporewalla R. A rare case of ectopic retrosternal goiter. *Clinical Case Reports* . 2021;9(4):1849-1852. doi:10.1002/ccr3.3610

13. Sohail AA, Shahabuddin S, Siddiqui MI. Ectopic Thyroid Mass Separately Present in Mediastinum and Not a Retrosternal Extension: A Report of Two Cases. *Case Reports in Surgery* . 2019;2019:e3821767. doi:10.1155/2019/3821767

14. Rico F, Lung J. Thyroid Embryonic Anomalies Involving the Medial and Lateral Anlagen: Two Surgical Case Reports. *Case Rep Surg* . 2019;2019:3174848. doi:10.1155/2019/3174848

15. Stumpf MAM, Marques AS, Kluthcovsky ACGC, Belonci CG da C. Presternal Goiter. *J Coll Physicians Surg Pak* . 2019;29(6):574-576. doi:10.29271/jcpsp.2019.06.574

16. Bakkar S, Hamdeh Q, Haddadin R, Donatini G, Papavramidis TS, Tawalbeh M. Retrosternal goiter masquerading as type II respiratory failure. A case report. *Int J Surg Case Rep* . 2022;94:107104. doi:10.1016/j.ijscr.2022.107104

17. Kristensen MH, Abrahamsen J, Thomsen HH. Intrathoracic Goiter Visualized on iodine-123 and technetium-99m Single-Photon Emission Computed Tomography/Computed Tomography. *World J Nucl Med* . 2021;20(4):377-378. doi:10.4103/wjnm.wjnm_90_21

18. Iriarte MB, Morales EI, Velásquez M, Zúñiga V, Sua LF, Fernández-Trujillo L. Giant Intrathoracic Goiter of Atypical Presentation: A Case Report. *Clin Pathol* . 2020;13:2632010X20916741. doi:10.1177/2632010X20916741

19. Kwak HV, Banks KC, Hsu DS, Debbaneh PM, Wang KH, Velotta JB. Incidental paratracheal lymph node lung adenocarcinoma in a patient with goiter: a case report. *AME Case Rep* . 2022;6:29. doi:10.21037/acr-22-23

20. Bianchi D, Scamporlino A, Costantini M, Cavallesco G, Morandi U, Stefani A. A case of cervico-mediastinal paraganglioma mimicking an ectopic goiter. *Int J Surg Case Rep* . 2021;86:106357. doi:10.1016/j.ijscr.2021.106357

21. Knobel M. An overview of retrosternal goiter. *J Endocrinol Invest* . 2021;44(4):679-691. doi:10.1007/s40618-020-01391-6

22. Crile G. Intrathoracic goiter. Cleve Clin Q 6:313-322, 1939.

23. Sigdel B, Neupane B, Pokhrel A, Nepali P. Giant multinodular goiter for 24 years; hidden in a village in Western Nepal. *Clin Case Rep* . 2022;10(7):e6041. doi:10.1002/ccr3.6041

24. Figueiredo AA, Simoes-Pereira J. Giant retrosternal goitre causing lung atelectasis. *Endokrynol Pol* . 2022;73(4):794-795. doi:10.5603/EP.a2022.0043

25. Efthymiou CA. Retrosternal goitre assumed to be asthma causing asphyxia in pregnancy: case report and literature review. *Ann R Coll Surg Engl* . 2021;103(10):e311-e313. doi:10.1308/rcsann.2021.0061

26. Loo GH, Wan Mat WR, Muhammad R, Azman M. Obstructive retrosternal goitre mimicking severe bronchial asthma in pregnancy. *BMJ Case Rep* . 2019;12(8):e229763. doi:10.1136/bcr-2019-229763

27. Liu SP, Chien HC, Chen CK, Hsieh CC, Huang CS. Critical airway compression caused by a large mediastinal tumour with spontaneous haemorrhage. *Respirology Case Reports* . 2018;6(3):e00300. doi:10.1002/rcr2.300

28. Dias T, Santos A, Mesquita C, Santos RM. Acute airway obstruction due to benign multinodular goitre. *BMJ Case Rep* . 2019;12(4):e228095. doi:10.1136/bcr-2018-228095

29. Cankar Dal H. Difficult airway management and emergency tracheostomy in a patient with giant goiter presenting with respiratory arrest: A case report. *Exp Ther Med* . 2022;24(2):499. doi:10.3892/etm.2022.11426

30. Koulouris C, Paraschou A, Manaki V, et al. Cardiopulmonary Arrest Caused by Large Substernal Goiter-Treatment with Combined Cervical Approach and Median Mini-Sternotomy: Report of a Case. *Medicina (Kaunas)* . 2021;57(4):303. doi:10.3390/medicina57040303

31. Shioya N, Inoue N, Kawashima N, et al. Enlargement of Intrathoracic Goiter with Unilateral Phrenic Nerve Paralysis Leading to Cardiopulmonary Arrest. *Intern Med* . 2021;60(1):91-97. doi:10.2169/internalmedicine.5075-20

32. Riaz B, Anwar SS. Isolated Posterior Mediastinal Thyroid Nodule Simulating Esophageal Pathology: A Multi-Modality Diagnosis.*Cureus* . 2022;14(6):e26241. doi:10.7759/cureus.26241

33. Alhedaithy AA, AlGhamdi AM, Abualhamayel TH, Aldabal NA. A retropharyngeal multinodular goiter: A case report and literature review. *Int J Surg Case Rep* . 2022;94:107122. doi:10.1016/j.ijscr.2022.107122

34. Ringrose T, Patel J, Ghasemi AA. Laryngeal varices: an atypical cause of globus. *BMJ Case Reports CP* . 2021;14(12):e246413. doi:10.1136/bcr-2021-246413

35. Daggett RLB, Farishta D, Cuellar H, Nathan CAO. Substernal goitre presenting with upper and lower extremity oedema. *BMJ Case Rep* . 2021;14(11):e245036. doi:10.1136/bcr-2021-245036

36. Pattashanee SK, Puri G, Kataria K, et al. Comparison of Modified Rose Method of Thyroid Palpation Versus Other Methods for the Detection of Retrosternal and Nodular Goitre. *J ASEAN Fed Endocr Soc* . 2022;37(1):4-13. doi:10.15605/jafes.037.01.02

37. Ziai H, Lebo NL, Kielar AZ, Odell MJ. Can Thyroid Ultrasonography Predict Substernal Extension or Tracheal Compression in Goiters?*Can Assoc Radiol J* . 2018;69(4):422-429. doi:10.1016/j.carj.2018.07.007

38. Yano T, Okada T, Sato H, Tomioka R, Tsukahara K. Preoperative Evaluation of Substernal Goiter by Computed Tomography in the Extended Neck Position. *Case Rep Oncol* . 2021;14(3):1353-1358. doi:10.1159/000518532

39. Uludag M, Kostek M, Unlu MT, Aygun N, Isgor A. Surgical Treatment of Substernal Goiter Part 1: Surgical Indications, Pre-Operative, and Peroperative Preparation. *Sisli Etfal Hastan Tip Bul* . 2022;56(3):303-310. doi:10.14744/SEMB.2022.52280

40. Sormaz İC, Uymaz DS, İşcan AY, et al. The Value of Preoperative Volumetric Analysis by Computerised Tomography of Retrosternal Goiter to Predict the Need for an Extra-Cervical Approach. *Balkan Med J* . 2018;35(1):36-42. doi:10.4274/balkanmedj.2017.0161

41. Mahajan S, L S, Kumar S. Airway Management in a Patient with Retrosternal Goiter: A Context-Sensitive Airway Management Strategy.*Indian J Otolaryngol Head Neck Surg* . 2022;74(Suppl 2):2214-2216. doi:10.1007/s12070-020-02083-6

42. Jeong YI, Jun IG, Ha SS, Kwon HJ, Lee YM. Extracorporeal membrane oxygenation for the anesthetic management of a patient with a massive intrathoracic goiter causing severe tracheal obstruction with positional symptoms: A case report. *Medicine (Baltimore)* . 2019;98(42):e17650. doi:10.1097/MD.0000000000017650

43. Lee PKG, Booth AWG, Lloyd BS. When Cardiopulmonary Bypass Is Not An Option-A Case of Massive Retrosternal Goiter With Severe Tracheal Compression in an Extremely Obese Patient. *J Cardiothorac Vasc Anesth* . 2018;32(2):956-959. doi:10.1053/j.jvca.2017.06.030

44. Pan Y, Chen C, Yu L, Zhu S, Zheng Y. Airway Management of Retrosternal Goiters in 22 Cases in a Tertiary Referral Center.*Ther Clin Risk Manag* . 2020;16:1267-1273. doi:10.2147/TCRM.S281709

45. Tasche KK, Dorneden AM, Swift WM, Boyd NH, Shonka DC, Pagedar NA. Airway Management in Substernal Goiter Surgery. *Ann Otol Rhinol Laryngol* . Published online May 25, 2021:34894211014794. doi:10.1177/00034894211014794

46. Cui R, Yu J, Han ZY, Liu FY, Yu XL, Liang P. Ultrasound-Guided Percutaneous Microwave Ablation for Substernal Goiter: Initial Experience. *J Ultrasound Med* . 2019;38(11):2883-2891. doi:10.1002/jum.14992

47. Li Y, Li X, Xiao J, et al. Ultrasound-guided microwave ablation combined with ethanol injection for the treatment of solitary nodular retrosternal goiter: a prospective study of 72 patients. *Eur Radiol* . 2023;33(2):752-762. doi:10.1007/s00330-022-09052-3

48. Chiang PL, Lin WC, Chen HL, et al. Efficacy and safety of single-session radiofrequency ablation for intrathoracic goiter: preliminary results and short-term evaluation. *Int J Hyperthermia* . 2021;38(1):976-984. doi:10.1080/02656736.2021.1942241

49. Tartaglia F, Sorrenti S, Maturo A, Ulisse S. Selective embolization of the thyroid arteries (SETA): Ten years' experience. *Asian J Surg* . 2019;42(8):847-848. doi:10.1016/j.asjsur.2019.05.008

50. Yilmaz S, Habibi HA, Yildiz A, Altunbas H. Thyroid Embolization for Nonsurgical Treatment of Nodular Goiter: A Single-Center Experience in 56 Consecutive Patients. *J Vasc Interv Radiol* . 2021;32(10):1449-1456. doi:10.1016/j.jvir.2021.06.025

51. Joll CA. The Indications for Surgical Treatment in Goitre.*Postgrad Med J* . 1932;8(81):262-265. doi:10.1136/pgmj.8.81.262

52. Vaiman M, Bekerman I, Basel J, Peer M. Surgical approach to the intrathoracic goiter. *Laryngoscope Investig Otolaryngol* . 2018;3(2):127-132. doi:10.1002/lio2.146

53. Wong WK, Shetty S, Morton RP, McIvor NP, Zheng T. Management of retrosternal goiter: Retrospective study of 72 patients at two secondary care centers. *Auris Nasus Larynx* . 2019;46(1):129-134. doi:10.1016/j.anl.2018.06.012

54. Aghajanzadeh M, Asgary MR, Mohammadi F, Darvishi H, Safarpour Y. An investigation into symptoms, diagnosis, treatment, and treatment complications in patients with retrosternal goiter. *J Family Med Prim Care* . 2018;7(1):224-229. doi:10.4103/jfmpc.jfmpc_286_17

55. Aygun N, Celayir MF, Isgor A, Uludag M. The effect of strap muscle transection on voice and swallowing changes after thyroidectomy in patients without laryngeal nerve injury. *Ann R Coll Surg Engl* . 2022;104(7):517-524. doi:10.1308/rcsann.2021.0225

56. Liddy W, Wu CW, Dionigi G, et al. Varied Recurrent Laryngeal Nerve Course Is Associated with Increased Risk of Nerve Dysfunction During Thyroidectomy: Results of the Surgical Anatomy of the Recurrent Laryngeal Nerve in Thyroid Surgery Study, an International Multicenter Prospective Anatomic and Electrophysiologic Study of 1000 Monitored Nerves at Risk from the International Neural Monitoring Study Group.*Thyroid* . 2021;31(11):1730-1740. doi:10.1089/thy.2021.0155

57. Ching HH, Kahane JB, Foggia MJ, Barber AE, Wang RC. Medial Approach for the Resection of Goiters with Suprahyoid, Retropharyngeal, or Substernal Extension. *World J Surg* . 2018;42(5):1415-1423. doi:10.1007/s00268-018-4576-z

58. Doulaptsi M, Karatzanis A, Prokopakis E, et al. Substernal goiter: Treatment and challenges. Twenty-two years of experience in diagnosis and management of substernal goiters. *Auris Nasus Larynx* . 2019;46(2):246-251. doi:10.1016/j.anl.2018.07.006

59. Dagan E, Kleid S. Obviating the need for sternotomy: Safety and effectiveness of microdebrider use for retrosternal goiter. *Head & Neck* . 2018;40(4):837-841. doi:10.1002/hed.25070

60. Chen YH, Kim HY, Anuwong A, Huang TS, Duh QY. Transoral robotic thyroidectomy versus transoral endoscopic thyroidectomy: a propensity-score-matched analysis of surgical outcomes. *Surg Endosc* . 2021;35(11):6179-6189. doi:10.1007/s00464-020-08114-1

61. Nakayama H, Goda M, Kohagura K, et al. A Large Substernal Goiter that Extended to Both Sides of the Thorax. *Case Rep Surg* . 2018;2018:6107982. doi:10.1155/2018/6107982

62. Van Slycke S, Simons AS, Van Den Heede K, et al. Combined cervicosternotomy and cervicotomy for true retrosternal goiters: a surgical cohort study. *Updates Surg* . 2021;73(4):1-10. doi:10.1007/s13304-021-01027-1

63. Ahuja K, Bhandari T, Banait-Deshmane S, Crowe DR, Sonavane SK. Incidentally detected ectopic thyroid in juxta cardiac location-Imaging and pathology. *Radiol Case Rep* . 2018;13(4):909-913. doi:10.1016/j.radcr.2018.06.004

64. Kocaman G, Yenigün BM, Çoruh AG, et al. Intrapericardial goiter. *Gen Thorac Cardiovasc Surg* . 2020;68(9):1051-1054. doi:10.1007/s11748-019-01211-6

65. Elhammady MS, Telischi FF, Morcos JJ. Retrosigmoid approach: indications, techniques, and results. *Otolaryngol Clin North Am* . 2012;45(2):375-397, ix. doi:10.1016/j.otc.2012.02.001

66. Tikka T, Nixon IJ, Harrison-Phipps K, Simo R. Predictors of the need for an extracervical approach to intrathoracic goitre. *BJS Open* . 2019;3(2):174-179. doi:10.1002/bjs5.50123

67. Casella C, Molfino S, Cappelli C, Salvoldi F, Benvenuti MR, Portolani N. Thyroiditis process as a predictive factor of sternotomy in the treatment of cervico-mediastinal goiter. *BMC Surg* . 2019;18(Suppl 1):20. doi:10.1186/s12893-019-0474-z

68. Linhares SM, Scola WH, Remer LF, Khan ZF, Nguyen DM, Lew JI. Depth of mediastinal extension can predict sternotomy need for substernal thyroid goiters. *Surgery* . 2022;172(5):1373-1378. doi:10.1016/j.surg.2022.06.026

69. Oukessou Y, Mennouni MA, Douimi L, et al. Cervical approach to cervico-mediastinal goiters: Experience of a Moroccan ENT tertiary center - Case series. *Ann Med Surg (Lond)* . 2021;62:353-357. doi:10.1016/j.amsu.2021.01.081

70. Haciyanli SG, Karaisli S, Acar N, Eygi B, Haciyanli M. Split Sternotomy in Retrosternal Thyroid and Mediastinal Parathyroid Pathologies. *Sisli Etfal Hastan Tip Bul* . 2021;55(3):318-324. doi:10.14744/SEMB.2021.76401

71. Abdullah AS, Bahjat AS, Mohammed AA. Huge toxic goiter extending to the posterior mediastinum; Case report with literature review. *Int J Surg Case Rep* . 2019;62:69-72. doi:10.1016/j.ijscr.2019.08.016

72. Machboua A, Thumerel M, Hustache-Castaing R, Jougon J. Cervicotomy using a hemi-clamshell approach for a rare enlarged substernal goitre. *Interactive CardioVascular and Thoracic Surgery* . 2022;35(1):ivac056. doi:10.1093/icvts/ivac056

73. Nesti C, Wohlfarth B, Borbély YM, Kaderli RM. Case Report: Modified Thoracoscopic-Assisted Cervical Resection for Retrosternal Goiter. *Front Surg* . 2021;8:695963. doi:10.3389/fsurg.2021.695963

74. Wang R, Li J, Jiang J, et al. Modified subxiphoid approach for surgical resection of a retrosternal goiter. *Frontiers in Surgery* . 2022;9. Accessed July 27, 2023. https://www.frontiersin.org/articles/10.3389/fsurg.2022.923389

75. Wadhavkar N, Kontopidis I, Bollig C. Transcervical and robotic-assisted thoracoscopic resection of a substernal goiter. *BMJ Case Rep* . 2022;15(10):e250953. doi:10.1136/bcr-2022-250953

76. Amore D, Cicalese M, Scaramuzzi R, Di Natale D, Curcio C. Antero mediastinal retrosternal goiter: surgical excision by combined cervical and hybrid robot-assisted approach. *J Thorac Dis* . 2018;10(3):E199-E202. doi:10.21037/jtd.2018.01.169

77. Nakamura R, Okuda K, Chiba K, et al. A large intrathoracic goiter with tracheal stenosis: Complete resection using a robot-assisted thoracoscopic approach. *Thorac Cancer* . 2022;13(12):1874-1877. doi:10.1111/1759-7714.14470

78. Saito Y, Ikeda Y, Takami H, et al. Combined thoracoscopic and axillary subcutaneous endoscopic thyroidectomy: a novel approach for cervicomediastinal goiters. *Langenbecks Arch Surg* . 2022;407(5):2169-2175. doi:10.1007/s00423-022-02579-5

79. Crudeli C, Reid L, Burg J, Shersher D. Minimally invasive combined approach robotic thymectomy and transcervical total thyroidectomy.*BMJ Case Rep* . 2022;15(4):e249292. doi:10.1136/bcr-2022-249292

80. Karsan RB, Nanjaiah P, Hogan J, Mehta D, Stetchman M. Concomitant aortic valve replacement and retrosternal goitre resection via mini-sternotomy: a novel case. *J Surg Case Rep* . 2020;2020(5):rjaa066. doi:10.1093/jscr/rjaa066

81. Testini M, Gurrado A, Avenia N, et al. Does mediastinal extension of the goiter increase morbidity of total thyroidectomy? A multicenter study of 19,662 patients. *Ann Surg Oncol* . 2011;18(8):2251-2259. doi:10.1245/s10434-011-1596-4

82. Głód M, Marciniak D, Kaliszewski K, et al. Analysis of Risk Factors for Phonation Disorders after Thyroid Surgery. *Biomedicines* . 2022;10(9):2280. doi:10.3390/biomedicines10092280

83. Abdelhamid A, Aspinall S. Intraoperative nerve monitoring in thyroid surgery: analysis of United Kingdom registry of endocrine and thyroid surgery database. *Br J Surg* . 2021;108(2):182-187. doi:10.1093/bjs/znaa081

84. Fiorelli RKA, Duarte AJV, de Quadros Teixeira A, et al. Anatomical and developmental aspects of iatrogenic injury to the right recurrent laryngeal nerve in surgical resections of substernal goiter. *Anat Rec (Hoboken)* . 2021;304(6):1242-1254. doi:10.1002/ar.24629

85. Tausanovic K, Zivaljevic V, Grujicic SS, Jovanovic K, Jovanovic V, Paunovic I. Case Control Study of Risk Factors for Occurrence of Postoperative Hematoma After Thyroid Surgery: Ten Year Analysis of 6938 Operations in a Tertiary Center in Serbia. *World J Surg* . 2022;46(10):2416-2422. doi:10.1007/s00268-022-06634-6

86. de Carvalho AY, Gomes CC, Chulam TC, et al. Risk Factors and Outcomes of Postoperative Neck Hematomas: An Analysis of 5,900 Thyroidectomies Performed at a Cancer Center. *Int Arch Otorhinolaryngol* . 2021;25(3):e421-e427. doi:10.1055/s-0040-1714129

87. Doran HE, Wiseman SM, Palazzo FF, Chadwick D, Aspinall S. Post-thyroidectomy bleeding: analysis of risk factors from a national registry. *Br J Surg* . 2021;108(7):851-857. doi:10.1093/bjs/znab015

88. Celik SU, Konca C, Genc V. A Cohort Study Assessing the Association Between Body Composition Parameters and Symptomatic Hypocalcemia After Total Thyroidectomy. *Am Surg* . 2021;87(8):1305-1312. doi:10.1177/0003134820979578

89. Chen Z, Zhao Q, Du J, et al. Risk factors for postoperative hypocalcaemia after thyroidectomy: A systematic review and meta-analysis. *J Int Med Res* . 2021;49(3):300060521996911. doi:10.1177/0300060521996911

90. Li W, Li H, Zhang S, Tao Y, Wang X, Cheng J. To explore the risk factors and preventive measures affecting the treatment of retrosternal goiter: An observational study. *Medicine (Baltimore)* . 2020;99(44):e23003. doi:10.1097/MD.0000000000023003

91. Linhares SM, Scola WH, Remer LF, Farrá JC, Lew JI. Morbidity Associated With Surgical Removal of Substernal Thyroid Goiters. *J Surg Res* . 2022;277:254-260. doi:10.1016/j.jss.2022.04.018

92. Sulaiman A, Lutfi A, Ikram M, et al. Tracheomalacia after thyroidectomy for retrosternal goitres requiring sternotomy- a myth or reality? *Ann R Coll Surg Engl* . 2021;103(7):504-507. doi:10.1308/rcsann.2021.0014

93. Ren W, Shang X, Fu H, Peng Z. Prolonged endotracheal intubation: a feasible option for tracheomalacia after retrosternal goitre surgery.*Ann Palliat Med* . 2020;9(4):1764-1769. doi:10.21037/apm-19-552

94. Zuo T, Gao Z, Chen Z, Wen B, Chen B, Zhang Z. Surgical Management of 48 Patients with Retrosternal Goiter and Tracheal Stenosis: A Retrospective Clinical Study from a Single Surgical Center. *Med Sci Monit* . 2022;28:e936637. doi:10.12659/MSM.936637

95. Hsu S, Melucci AD, Dave YA, et al. Outpatient endocrine surgery practice patterns are highly variable among US endocrine surgery fellowship programs. *Surgery* . 2023;173(1):76-83. doi:10.1016/j.surg.2022.05.004

96. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* . 2004;240(2):205-213. doi:10.1097/01.sla.0000133083.54934.ae

97. Bukarica S, Antić J, Fratrić I, Kravarušić D, Pajić M, Jokić R. Thyroid Surgery in Children: A 5-Year Retrospective Study at a Single Paediatric Surgical Center and Systematic Review. *Children (Basel)* . 2022;9(12):1818. doi:10.3390/children9121818

List of Figures

List of Tables

Hosted file

`Table1_outcomesRG.docx` available at https://authorea.com/users/675888/articles/673683-a-critical-update-on-the-management-of-retrosternal-goiter