World Journal of Surgery and Surgical Research

Review Article
Published: 20 Aug, 2021

# The Surgical Management of Retrosternal Goiter; an Ongoing Controversy

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## Abstract

The natural course of retrosternal goiters tend to be slow growing and most commonly present in patients in their fifth decade. There is a female preponderance in cases of RSG with a ratio of 3:1 and have a familial component in up to 30% of cases. Many different definitions of RSG exist in the literature, rendering it difficult to compare series and draw conclusions. Unquestionably, surgery is the optimal therapeutic option for surgically fit patients with compressive symptoms secondary to RSG. However, the role of thyroidectomy in the setting of asymptomatic RSG is less clear. Cervical goiters, in the absence of compressive symptoms or suspicion of malignancy, are managed expectantly. It seems plausible that a similar approach could be adopted for RSG especially as the natural course of RSG is slow and indolent. Several CT based classification systems have been devised to predict the need for sternotomy in surgery for retrosternal goiter. These classification systems are useful adjuncts when deciding the appropriate surgical approach and setting for RSG as high-risk cases should be consulted with thoracic surgery and performed in a setting where such services are available.

## Introduction

The role of surgical intervention in asymptomatic Retrosternal Goiters (RSG) remains controversial. The widespread adoption of cross-sectional imaging for indications other than thyroid disease has made this topic an interesting clinical conundrum. Whilst a non-operative approach is the standard of care for asymptomatic goiter in the absence of suspicious cytology, traditional surgical teaching recommends thyroidectomy for RSG in all surgically fit patients [1-3]. The natural course of retrosternal goiters tends to be slow growing and most commonly present in patients in their fifth decade [1]. Many different definitions of RSG exist in the literature, rendering it difficult to compare series and draw conclusions. Pre-operative investigations may help differentiate patients who require surgical resection to those who can be managed conservatively. Pre-operative Computed Tomography (CT) can visualize the anatomical relations between the RSG and each mediastinal component, the level of extension, and the presence or absence of tracheal or esophageal compression and exclude nodal disease [4,5]. Several CT based classification systems have been devised to predict the need for sternotomy in surgery for retrosternal goiter. These classification systems are useful adjuncts when deciding the appropriate surgical approach and setting for RSG as high-risk cases should be consulted with thoracic surgery and performed in a setting where such services are available [5-7]. Given the increased perioperative morbidity associated with manubriotomy and sternotomy, a cervical approach is recommended for RSG excision when pre-operative histological assessment and CT findings permit [8,9]. Advocates of surgical intervention for asymptomatic retrosternal goiter cite inevitable airway obstruction and an increased risk malignancy in RSG as clear rationale for primary operative management [10,11]. We aim to provide a review of the literature to determine the feasibility of non-operative expectant management of RSG.

## Incidence and Symptomology

The definition of a retrosternal goiter varies throughout the literature thus the incidence ranges from 0.2% to 45% of all goiters, depending on the definition used [12-15]. There is a female preponderance in cases of RSG with a ratio of 3:1 and have a familial component in up to 30% of cases [4,16]. Clinical signs and symptoms of retrosternal goiter depend on the size and location of the goiter. The mean duration of symptoms in a study by Doulaptsi et al. [17] was 23 months, suggesting that patients tend to seek treatment towards the latter course of the disease. An older study by Lahey and Swinton reported a much longer duration of symptoms, reporting

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**Received Date**: *26 Jul 2021*
**Accepted Date:** *16 Aug 2021*
**Published Date:** *20 Aug 2021*

***Citation:***
*Cullinane C, Evoy D, McDermott E, Prichard R. The Surgical Management of Retrosternal Goiter; an Ongoing Controversy. World J Surg Surgical Res. 2021; 4: 1328.*

between 13.04 years and 15.10 years depending on the grade of retrosternal goiter [18]. Common symptoms of RSG described in the literature include dyspnea (including positional dyspnea), orthopnea, dysphagia, dysphonia [19-21]. Rarely, compressive effects on neurovascular structures may also be observed and patients may develop superior vena cava syndrome [22]. Shen et al. [21] reported that 59% of their cohort with substernal goiters experienced dyspnea as a primary symptom, with 22% of this patient population also reporting symptoms of orthopnea. A study by Stang et al. found that positional dyspnea, defined as difficulty breathing improved by position change, was reported by 75.5% of patients with retrosternal goiters and strongly correlated with tracheal compression on cross sectional imaging [23]. Torchio et al. [24] examined the respiratory function sequela of orthopnea due to retrosternal goiters in 2003. Their analysis of 32 patients reported that intrathoracic goiters cause a reduction of end-expiratory lung volume and flow reserve in the tidal volume range, promoting respiratory flow limitation especially in supine position. Obesity was also identified as a significant factor that increases the risk of orthopnea in patients with goiter [24]. Dysphagia is the second most common symptom described by patients with retrosternal goiter after dyspnea [21]. Provided thyroidectomy is uncomplicated, patient self-reported swallowing scores improve dramatically post thyroid surgery [25]. Dysphonia or hoarseness is a symptom of Recurrent Laryngeal Nerve (RLN) compression; such involvement can often be indolent necessitating pre-operative visualization of vocal cord function [26].

## Clinical Examination Findings

Examination of retrosternal goiter is not always detectable clinically as in 20% to 30% of cases; the goiter is not palpable or is barely palpable in the neck, with most of the tumor bulk in the chest [27]. The presence of retrosternal goiter should be suspected when the inferior edge of the thyroid gland is not palpable and extends beyond the sternal notch on clinical examination with the neck in extension [17]. In patients with obesity, a short neck, kyphoscoliosis or inability to extend the neck fully it can be difficult to palpate the lower extent of the thyroid gland and these patients require cross sectional imaging to determine if inferior extension is present [19]. The presence of retrosternal goiters can sometimes be elicited via Pemberton's test. This test is positive if a patient hyperextend the neck whilst swallowing and raising both hands above their head and flushing of the skin, dilation of the external jugular veins or airway compromise occurs [4,28]. This position results in narrowing of the thoracic outlet and a large goiter will inhibit venous return, causing the patient's face to flush, which resolves when the arms are lowered. Some patients with superior vena cava syndrome will have obvious venous collaterals in the upper chest and neck [19]. Other clinical findings may include tracheal deviation and occasionally Horner's syndrome.

## Pre-Operative Investigations

The most important pre-operative radiological investigation in the evaluation of RSG is Computed Tomography (CT) [5]. Pre-operative CT scan can visualize the anatomical relations between the RSG and each mediastinal component, the level of extension, and the presence or absence of tracheal or esophageal compression and exclude nodal disease [4,5]. RSG calcifications detected on CT are of little significance as Page et al reported that 66% of their benign goiter cases had calcifications on CT and therefore cannot be considered a sign of malignancy [50]. Cross-sectional imaging using CT can also predict cases of RSG which may require an extra cervical approach (manubriotomy +/- sternotomy) [6,7]. Most retrosternal goiters can be resected *via* a Kocher cervical approach with the incidence of sternotomy in RSG ranging from 0% to 11% [2,51,52]. This wide range may be attributable to the variation in the definitions of RSG and an element of referral bias. Predicting patients who will likely require an extra-cervical approach is pivotal to ensure the presence of a multi-disciplinary team, also involving the thoracic surgeon, when necessary, and to correctly inform the patient about the approach which it may be necessary to adopt [53]. White et al. sought to identify factors associated with an extra-cervical approach and reported that expert endocrine surgeons require an extra-cervical approach in cases of primary RSG or when the thyroid mass is larger than the thoracic inlet [27]. Accurate measurement of thyroid extension in relation to the thoracic inlet is often difficult to do pre-operatively and a recent study by Sormaz et al. aimed to design such a CT protocol [54]. They aimed to define a pre-operative CT volumetric analysis of RSG to predict need for an extra-cervical approach *via* calculation of thyroid volume below the thoracic inlet using a volume-rendering tool [54]. Craniocaudal length (>66 mm), volume of mediastinal component (>162 $cm^3$) and previous thyroid operation were all significant factors in predicting extra-cervical approach for RSG [54]. Rugio et al. also reported that CT findings of a primary RSG, large thyroid gland volume as well as thyroid extension to the trachea carina are the most significant criteria for selecting patients requiring sternotomy [53]. Similarly, a grading system developed by Cho et al. is based on the percentage of thyroid gland in the mediastinum in relation to the neck and predicts that patients with grade II-IV RSG are likely to require an extra-cervical approach [38]. Huins et al. [30] reported that the majority of RSG definitions lack the anatomic clarity gained by referring to an intrathoracic landmark, such as the aortic arch. Their findings suggested that RSG should be graded according to its relation to the aortic arch and can guide the appropriate operative approach. Grade 1 refers to RSG above the level of the aortic arch which is suitable for a cervical approach. Grade II and III describe RSG extending from aortic arch to pericardium and below right atrium respectively and require additional surgical exposure techniques [30]. CT based classification systems to predict need for sternotomy in surgery for retrosternal goiter is an ongoing area of research. A Swedish study by Malvemy et al. [7] presented a series of 120 patients and discovered that RSG extension below the aortic arch concavity was confirmed as a significant risk factor for sternotomy, with a NPV for sternotomy of 97% for less extensive goiters. These findings were re-iterated by Coskun et al. as they reported that excision of goiter beyond the aortic arch is an absolute indication for median sternotomy [55]. This universal landmark provides a useful anatomic site to predict patients likely to require thoracic surgery input. The aortic arch was also adopted as a landmark to predict the requirement of an extra-cervical approach by Mercante et al. [6]. Their case series included 237 patients with RSG, 15 patients had an extra-cervical approach, and 17 patients were asymptomatic at the time of surgery [6]. In contrast to the classification system described by Huins et al. [30] which grades RSG according to its craniocaudal length in relation to the aortic arch, pericardium and right atrium, Mercante et al. [6] also incorporated an anteroposterior dimension. Retrosternal goiters were graded craniocaudally as: Grade 1 (above aortic arch), grade 2 (level of aortic arch), and grade 3 (below aortic arch); and in the anteroposterior dimension as type A (prevascular), type B (retrovascular-paratracheal), and type C (retrotracheal). Multiple logistic regression analysis identified grade 2, type C retrosternal goiter, and malignancy as risk factors for

**Table 1:** Definitions of retrosternal goiter in the literature.

| Definition | Clinical/Anatomical Finding |
|---|---|
| Hsu [30] | Goiter extends beyond the manubrium |
| Katlic[13] | 50% of the goiter is retrosternal |
| DeSouza [31] | 50% of the goiter extends below thoracic inlet |
| Kocher [32] | Some portion remains permanently retrosternal |
| Torre [1] | Some portion remains permanently retrosternal with neck in hyperextension |
| Eschapase [33] | Goiter located in the mediastinum that, in operating position, has its edge at least 3 cm below the sternal manubrium |
| Lahey [34] | Refers to any RSG that requires excision to be performed in the upper mediastinum |
| Lindskog [35] | Goiter extends to fourth thoracic vertebrae on X-ray imaging |
| Crile [36] | Goiter descending to the level of the aortic arch |
| Subcarinal [37] | RSG extending to the trachea carina |

RSG: Retrosternal Goiter

extra-cervical surgical approach [6]. Retrosternal goiter location in the posterior mediastinum was also recognized by McKenzie et al. as an independent risk factor for sternotomy [56]. They reported that a clinical history of goiter with retrosternal extension beyond 160 months and thyroid density on CT imaging are predictors of requiring an extra-cervical approach [56]. Thyroid tissue density was the strongest predictive factor and increased the risk of sternotomy 47-fold [56]. These classification systems and predictive factors are useful adjuncts when deciding the appropriate surgical approach and setting for RSG surgery as high-risk cases should be consulted with thoracic surgery and performed in a setting where such services are available.

## Definition and Classification

Many definitions of retrosternal goiter exist making it difficult to compare case series and draw conclusions. Terms such as retrosternal, substernal, intrathoracic and mediastinal are all used interchangeably to describe a goiter that extends beyond the thoracic inlet. Rios et al. recognized that having many definitions for the same clinical entity was counter-productive in 2010 and sought to determine the value of various definitions of retrosternal goiter in relation to post-operative morbidity [29]. Ten different definitions of Retrosternal Goiter (RSG) have been described (Table 1). Clinical retrosternal goiter was defined as a thyroid gland that had portion of the gland retrosternal without neck extension [29]. Hsu's definition of retrosternal goiter referred to thyroid goiter that extended beyond the manubrium (clinically or radiologically) [30]. The commonly adopted Katlic's definition describes RSG as at least 50% retrosternal [13]. This definition was echoed by deSouza et al. [31] who described RSG as one with at least 50% below the thoracic inlet. Likewise, Kocher and Torre's defined RSG in a similar manner. Kocher defined RSG as thyroid gland in which some portion remains permanently retrosternal [32] and Torres described RSG as a goiter with its lowest position remaining permanently below the sternal notch with the neck in hyperextension [1]. A more subjective definition adopted by Eschapase describes a goiter located in the mediastinum that, in operating position, has its edge at least 3 cm below the sternal manubrium [33]. Lahey refers to any RSG that requires excision to be performed in the upper mediastinum [34]. Lindskog defined RSG as growth up to fourth thoracic vertebrae on X-ray imaging [35]. Crile's definition referred to goiter descending to the level of the aortic arch [36]. Finally the subcarinal definition is self-explanatory describing RSG extending to the trachea carina [37]. There is obvious overlap between these definitions as Lindskog's definition incorporates many of the others. Rios et al. concluded that the clinical definition should be adopted due to its simplicity and can predict intubation difficulty at induction. The authors also reported that the Katlic definition on the other hand was a useful predictor of requiring sternotomy for excision of RSG [29]. It is imperative that clinicians subscribe to one definition to enable accurate recording of the clinical course of RSG and complications.

## Indications for Surgery

### Asymptomatic patients with retrosternal goiter do not appear to be at higher risk of developing airway compromise and complications in comparison to asymptomatic cervical goiters

Unquestionably, surgery is the optimal therapeutic option for surgically fit patients with compressive symptoms secondary to RSG [19]. However, the role of thyroidectomy in the setting of asymptomatic RSG is less clear as the traditional dogma of operating on all patients with RSG is based on historical, uncontrolled observational studies [3,38]. The rationale for performing surgery in an asymptomatic cohort of patients is that goiters do not tend to involute and will continue to grow until compression occurs on more rigid anatomic structures located in the thoracic inlet [17]. Similarly, advocates of a primary operative approach state that advancing age is associated with increased medical co-morbidity and an earlier operative approach may be associated with reduced complications relating to co-existing disease [40]. Cervical goiters also do not tend to involute and in the absence of compressive symptoms or suspicion of malignancy, they are managed expectantly [39]. It seems plausible that a similar approach could be adopted for RSG especially as the natural course of RSG is slow and indolent [34]. Pre-emptive surgery due to the possibility of developing morbidities in the future is a relatively loose indication for high-risk surgery. A study by Allo et al. [3] estimated that 1% to 3% of patients with RSG die of airway obstruction however this estimation was based on patients with severe airway compression due to RSG. Cho et al. [2] reported their results on 70 consecutive RSG surgeries and had a 4% rate of serious post-operative complications. Asymptomatic patients comprised 41% of the patient cohort. The inclusion of asymptomatic and symptomatic patients with RSG in studies makes it difficult to extrapolate the results to asymptomatic patients with RSG. Furthermore, Hardy et al. [40] suggested that in addition to chronic compressive symptoms, asymptomatic RSG can result in acute airway obstruction due to hemorrhage from within the thyroid gland or secondary to prolonged mechanical pressure with acute laryngeal edema and congestion. The incidence of such complications due to RSG is low with an incidence

of between 5% to 11% reported in the literature; however the authors state that the catastrophic consequences provide a clear rationale for thyroidectomy in patients with RSG [40]. It is important to note that this data was also deduced from studies including symptomatic patients with choking and dyspnea being the most common complaints and patients with tracheoesophageal compression on CT imaging due to RSG [10,41]. We argue that any difference in the management of cervical and retrosternal goiter is unfounded as they are variants of the same entity and there is no evidence that the natural history of asymptomatic cervical goiter is different to RSG.

The terms "symptomatic" and "asymptomatic" may carry different interpretations for the patient and clinician. Vadasz et al. reported several cases of RSG misdiagnosed as asthma and other airway obstructive disorders and advocated that once an accurate diagnosis of RSG is made, multimodal surgical approaches are required for safe removal [46]. For this reason, patients with radiological evidence of tracheal compression provide an indication for surgery due to the correlation between shortness of breath and tracheal compression which may not always be appreciated by patients [20].

### There is no convincing evidence of a higher incidence of incidental thyroid cancer in benign RSG compared to cervical goiter

An increased risk of malignancy is provided as another justification to manage RSG with prophylactic thyroidectomy. The reported incidence of malignancy between cervical and intrathoracic goiters differs in the literature. A study by Campbell et al. stated that substernal location was the only significant variable independently associated with an unexpected thyroid cancer on surgical pathology [OR: 2.360] [11]. The incidence of incidental thyroid cancer in the cervical goiter cohort was 6.3% compared to 13.7% in the RSG cohort. Patients with a cervical goiter in this study were more likely to have a pre-operative FNA performed (56% *vs.* 66%) [11]. On the other hand, White et al. performed a review of three large prospective studies and a large retrospective study in 2008 and concluded that limited level III-IV data suggests the incidence of cancer in RSG is similar to the incidence of cancer in cervical goiters [27,43-46]. Similarly, Landerholm et al. examined a cohort of 132 patients with goiter and there were no cases of unsuspected malignancy between the cervical and retrosternal goiter groups [47]. The disparity of findings may be attributed to pre-operative diagnostic difficulties with RSG. In contrast to cervical goiters that can undergo needle biopsy and ultrasonography examination, RSG's are more difficult to assess ultrasonographically due to artifact from surrounding body structure and not amenable to needle biopsy due to proximity to major vessels [40]. Incidental thyroid cancer in a multinodular cervical goiter specimen is not uncommon with incidences ranging from 3% to as high as 35% [42,43]. Advances in radiology and diagnostic technology will improve pre-operative diagnostics of RSG [44,45]. If there is a clinical suspicion of malignancy or diagnostic uncertainty RSG resection should be performed, however there is no convincing evidence that the incidence of malignancy is higher in this cohort and therefore should not be an indication for excision in an asymptomatic cohort with the absence of suspicious cytology.

Much of the literature on necessity of thyroidectomy for RSG dates to the 1980's when the incidence of asymptomatic RSG was low [2,31,33]. Recent increased societal demand for imaging has resulted in the incidence of thyroid incidentalomas increasing exponentially [46]. *Via* prolific use of ultrasonography, Computed Tomography (CT) and PET scanning for investigation of non-thyroid disease the incidence of asymptomatic RSG is increasing with up to 50% of cases diagnosed radiologically [21,40]. In endemic areas, the incidence of RSG is 25% in patients above 70 years of age where ultrasound screening of non-thyroid disease is common [47]. The recent surge of incidental RSG cases suggests that it is not feasible to perform thyroidectomies in all asymptomatic patients. Further understanding of the natural course of the condition is required to risk stratify patients who require early surgical intervention to prevent complications and reduce the risk of overtreatment [40].

## Surgical Approach to RSG and Complications

Complications arising from cervical thyroidectomy are low. A multicentre analysis of 14,934 patients reported a 1.7% rate of hypoparathyroidism, permanent palsy of the Recurrent Laryngeal Nerve (RLN) occurred in 1%, superior laryngeal nerve was damaged in 3.7%, dysphagia occurred in 1.4%, hemorrhage in 1.2% and wound infection in 0.3% [48]. Whether the choice of surgical incision influences the rate of complications is still uncertain. Several case series have reported higher incidence of surgical morbidity with extra-cervical approaches [8,9]. A series of 52 patients who had a sternotomy for RSG had a pulmonary complication rate of 21%, hypoparathyroidism in 4% and transient dysphonia in 6% of patients [49]. In contrast a Lebanese study examining the morbidity of RSG surgery using a cervical approach in a series of 127 patients reported a 5% rate of transient dysphonia and no cases of permanent hypoparathyroidism [50]. Similarly, a low incidence of complications was reported by Polistena et al. [51] who recently reviewed 1,767 cases of RSG. A cervical incision was used in 99% of cases and the rate of RLN palsy was 1.3% and permanent hypoparathyroidism was 4.1%. A shorter operating time was observed for surgery *via* the cervical approach in comparison to the sternotomy cohort [51]. Di Crescenzo et al. [22] sought to examine the complication rates between a cohort of patients with RSG who had a cervical approach (N=77) and an extra-cervical approach (N=22). The authors concluded that postoperative morbidity and mortality is very low, independent of surgical technique however the overall complication rate of sternotomy was 30.7% and mortality was 15.3% suggesting otherwise [22]. Although the rate of complications between the two surgical techniques did not reach statistical significance there was no explanation provided for such high morbidity and mortality numbers [22]. Comparing the two surgical techniques and the outcomes of patients in both groups is inherently biased as patients undergoing RSG surgery with an extra-cervical approach tend to be in the 10% cohort of patients with large, primary, descending, dense, retrotracheal goiters. Given the increased perioperative morbidity associated with manubriotomy and sternotomy, a cervical approach is recommended for RSG when pre-operative histological assessment and CT findings permit.

## Future Perspectives

There are several exciting breakthroughs in the diagnostic and therapeutic repertoires for RSG. One such diagnostic technique is Endobronchial Ultrasound Guided Transbronchial Needle Aspiration (EBUS-TBNA). Unlike cervical goiters, RSG are not amenable to ultrasound-guided fine needle aspiration due to the presence of the sternum and therefore open surgical techniques and surgical mediastinoscopy is required to obtain RSG tissue diagnosis [45]. EBUS-TBNA is a well-established technique used in the diagnosis and staging of non-small cell lung cancer and can be performed as an outpatient procedure with over 90% sensitivity and specificity

[45]. This technique was first described by Jeeban et al. [44] in 2009 who reported the first case of a posterior mediastinal intrathoracic goiter diagnosed with the aid of EBUS-TBNA. In cases of diagnostic uncertainty histological assessment may prevent asymptomatic patients from undergoing unnecessary surgery and select appropriate high risk retrosternal goiters for excision.

The incidence of RSG is highest in people in their fifth decade and the slow growing nature of the condition means that patients often present symptomatically at an older age [14]. Advancing age is associated with increased medical co-morbidities. Not all patients are suitable for thyroidectomy therefore alternative therapeutic options are required to treat RSG. In recent years, Microwave Ablation (MWA) therapy has been increasingly used to treat benign nodules and has proved to be an effective treatment option [52]. Due to the proximity of RSG to adjacent vessels and nerves, there was hesitancy to explore MWA as a therapy option. Liu et al. [52] reported the first 10 cases of RSG treated with ultrasound-guided percutaneous MWA in the literature. These preliminary results support the effectiveness and safety of MWA for local control of RSG [52]. In the future this technique could be applied to select patients with SSG who are ineligible for surgery. In an ever-aging society, a non-invasive treatment option for symptomatic relief of RSG is of utmost importance.

Open surgical techniques using a cervical and extra-cervical approach are well described in the literature [4]. These techniques result in permanent scars. Most patients presenting with thyroid disease in China are young females therefore laparoscopic thyroid surgery was introduced to minimize scarring and cosmetic sequela [53]. Laparoscopic thyroidectomies can be performed *via* the transoral and areolar approach with excellent results [54,55]. Wang et al. [53] through their accumulation of vast experience with laparoscopic thyroidectomy described a feasibility study of 15 cases of RSG treated with a laparoscopy *via* the areola approach. Whilst the conversion rate and morbidity rate were acceptable, this approach requires strict patient selection criteria and pre-operative 3D CT scan reconstruction to formulate surgical strategy to ensure feasibility [53].

## Conclusion

Despite being an established clinical entity since 1749, retrosternal goiters still pose several diagnostic and therapeutic quandaries. The lack of a universally accepted definition of RSG leads to difficulties capturing accurate data and extrapolating results. We propose that the original definition of RSG described by Haller himself should be adopted to describe any thyroid goiter extending beyond the sternal notch in the supine position either clinically or radiologically [12]. All symptomatic RSG require surgical thyroidectomy. Patients who are asymptomatic with RSG can be managed non-operatively provided there is no tracheal compression on CT imaging and no suspicion of malignancy. Well-conducted, prospective studies are required to understand the natural course of asymptomatic RSG and risk stratifies patients appropriately. Once a diagnosis is established, pre-operative CT is paramount to accurately grade disease and predict likely operative approach. High grade RSG with factors suggesting a high likelihood of requiring an extra-cervical approach should be identified pre-operatively and discussed with thoracic surgery.

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