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REVIEW ARTICLE

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Tracheomalacia in patients undergoing thyroid surgery—What is the true estimate: A systematic review and meta-analysis

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Abstract

Objectives: Tracheomalacia is defined as the weakening of the tracheal rings secondary to long-standing compression or inherent structural weakness, leading to stridor and airway compromise. The common etiological factor of tracheomalacia includes compression of the tracheal framework due to a large multinodular goiter. There are various management techniques described in the literature to manage a patient with tracheomalacia including tracheostomy, tracheal stenting, and tracheopexy. However, the evidence of tracheomalacia in the literature is conflicting. Therefore, a systematic review was conducted to estimate the incidence of tracheomalacia after thyroidectomy.

Methods: The systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A literature search was performed on PubMed, Web of Science, Cochrane library, and Elton B. Stephens Co. cumulative index to nursing and allied health literature plus to determine the incidence of tracheomalacia among patients undergoing thyroidectomy up till October 2021. The eligibility was assessed by two independent authors. A quality assessment of individual studies was performed using the National Institute of Health quality assessment tool. Outcomes were double data extracted and were analyzed using OpenMeta.

Results: The online search retrieved 214 papers, out of which 17 studies were included that fulfilled the eligibility criteria. The number of patients included in the systematic review who underwent thyroidectomy was 1108. The mean age was 55.8 ± 7.7 years, ranging from 48 to 75 years. Tracheomalacia was reported in 146 patients (1.4%). Sternotomy was performed in 102 patients to approach the goiters with retrosternal extension. The most common intervention to manage tracheomalacia was tracheostomy or prolonged intubation.

Conclusions: Tracheomalacia is a rare complication. In cases where tracheomalacia is encountered, common methods of management include tracheostomy or prolonged

endotracheal intubation. Prospective, long-term studies are required to accurately assess its true incidence and associated factors.

KEYWORDS
retrosternal goiter, stridor, thyroid surgery, thyroidectomy, total thyroidectomy, tracheomalacia

INTRODUCTION

Tracheomalacia is defined as a dynamic collapse of cartilaginous tracheal rings that are unable to maintain airway patency.[1,2] Tracheomalacia presents as an immediate airway compromise, presenting as stridor after extubation in a patient who has undergone thyroidectomy.[3] It is usually thought to arise from longstanding compression of tracheal rings, leading to loss of integrity and cartilage softening.[4,5] It may also be part of the reduced blood supply to the cartilaginous framework secondary to compression by an enlarged thyroid gland.

The etiology of multinodular goiter is multifactorial. Multinodular goiter develops commonly as a result of iodine deficiency.[6,7] Other factors such as smoking, age, and gender have also contributed to goiter development.[8] The reported prevalence of goiter ranges from 4% to 7% in developed countries.[9] Goiter is almost exclusively treated with surgical excision (thyroidectomy).[10,11] Indications for thyroidectomy are three Cs; Compressive symptoms, cancer, and cosmesis. Goiter can lead to compressive symptoms such as dysphagia, dyspnea, difficulty in lying flat, and a sensation of pressure in the neck.[12] They may also exhibit positive Pemberton's sign.[13] This is due to intermittent superior vena cava obstruction which is characterized by facial flushing, distention of neck veins, and inspiratory stridor when the patient is asked to raise their hands above head level.[13] Thyroid nodules can be benign or malignant. When diagnosed or suspected on fine needle aspiration cytology (FNAC) in a nodule, malignancy is a definitive indication for thyroidectomy. In underdeveloped countries, patients usually present late. An enlarged thyroid gland compresses the trachea and may lead to tracheomalacia.[5,14–17] Patients who present with retrosternal goiter also pose difficulty during intubation due to tracheal compression[9] and can lead to cardiopulmonary complications postextubation.[18]

There are various methods reported in the literature for the management of tracheomalacia.[19] Tracheostomy is the gold standard of care.[4,20] These patients are later decannulated following a careful tracheostomy rehabilitation. Other methods include tracheopexy, tracheal stenting, and positive pressure ventilation.[21,22] Mild forms of tracheomalacia are usually managed with conservative measures such as prolonged intubation.[23] Noninvasive positive pressure ventilation has also been shown to aid during this period.[24–27] Tracheomalacia, over time, improves, and no further intervention is required.[27] In case of a significant stridor right after extubation, a tracheostomy is performed to maintain the airway.

Tracheomalacia is an infrequent complication of thyroid surgery.[5] There is a conflicting argument in the literature as to whether tracheomalacia after thyroidectomy exists. Some have dubbed it a "myth" after presenting a large series of thyroidectomy patients with or without retrosternal extension without any case complicated with tracheomalacia.[5,28] On the contrary, there are reports and a series of patients diagnosed and treated for tracheomalacia after thyroidectomy.[3,4,9,11,19] Our systematic review aims to estimate the incidence of tracheomalacia in patients undergoing thyroidectomy. We also aim to review the management options considered for tracheomalacia.

METHODS

We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A literature search was performed on PubMed, Web of Science, Cochrane library, and Elton B. Stephens Co. cumulative index to nursing and allied health literature plus to identify tracheomalacia amongst patients undergoing thyroidectomy till October 2021. We used the medical subject heading (MeSH) and keywords for “Tracheomalacia,” “Thyroidectomy,” “thyroid enlargement,” “goiter,” “retrosternal goiter,” “sternotomy,” “tracheal compression” in various combinations. We included all study types in the English language only without any date restrictions. Furthermore, the inclusion criteria were all adult patients with goiter requiring thyroidectomy with postop tracheomalacia. Exclusion criteria were, 1. Any prophylactic procedure without confirming stridor 2. Case reports, 3. Peadiatric age-group, 4. Bilateral recurrent laryngeal nerve injury causing stridor.

Data extraction

Two authors (H. I. and S. K. G.) independently assessed the eligibility using apriori eligibility criteria and performed data extraction. Any discrepancies between the reviewers in either the decision of inclusion or exclusion of studies or in data extraction were resolved by a discussion aimed at reaching a consensus or contacting a third reviewer (S. A. A.). We extracted data on study ID, location, participants (country, sample size, age, inclusion and exclusion criteria), study design (retrospective chart review, case series, case reports), intervention (thyroidectomy, thyroid lobectomy, sternotomy), outcomes (tracheomalacia, management). We also performed a quality assessment of individual studies using the National Institute of Health quality assessment tool.[29]

TABLE 1 Main characteristics of 17 studies.

Author name (year)	Study duration (Months)	Mean age (Years)	Sample size	Number of thyroidectomies	Number of sternotomies	Type of sternotomy	Tracheomalacia	Histopathology	Intervention
Netterville (1998)[30]	120	59	23	23	0	0	0	Benign 19 Malignant 4	None
A. Abdel Rahim (1999)[31]	24	47	103	103	0	0	6	Benign 96 Malignant 7	Tracheostomy
Ajay Chauhan (2006)[11]	168	51.8	199	199	0	0	1	Benign 193 Malignant 5	Primary tracheal repair. Prolonged intubation.
Al Kadhim (2006)[32]	132	75	505	505	1	Cervical sternotomy	4	Malignant 67% Suspicious for malignancy 12% Thyrotoxicosis 21%	Tracheostomy Stenting Prolong intubation
Amit Agarwal (2007)[4]	180	51.4	900	900	0	0	28	Benign 12 Malignant 16	Tracheostomy Prolong intubation
ElHadi Mohammed ElBashier (2008)[33]	60	50	964	964	5	Median sternotomy	16	Recurrent Simple 16 (27%) Malignant 12 (20%) Toxic 8 (14%) Recurrent Malignant 2 (3%)	Tracheostomy
Gregory W. Randolph (2011)[34]	276	58.5	200	200	2	Cervical sternotomy	0	Benign 186 Malignant 14	None
Shun Yu-Chi (2011)[27]	60	Not mentioned	606	606	0	None	9	Benign 1 Malignant 5	Prolong intubation
J. M. Findlay (2011)[5]	30	Not mentioned	334	334	4	Median sternotomy	0	Benign 16 Malignant 2	Not applicable
Amit Agarwal (2012)[15]	168	41.5–45.7	813	813	12	Not mentioned	16	Benign 532 Malignant 281	Tracheostomy Prolong intubation No intervention
G. A. Dempsey (2013)[28]	53	65	19	19	0	0	0	Benign 18 Malignant 1	Not applicable
Bo Gao (2013)[35]	33	51	12	12	2	Median sternotomy	1	Benign 12 Malignant 0	Tracheostomy

(Continues)

TABLE 1 (Continued)

Author name (year)	Study duration (Months)	Mean age (Years)	Sample size	Number of thyroidectomies	Number of sternotomies	Type of sternotomy	Tracheomalacia	Histopathology	Intervention
Andrea Polistena (2014)[36]	336	60	1721	1721	25	Substernal sternotomy 21 Thoracotomy 04	37	Benign 1463 Malignant 258	Prolong intubation
N. Gilfillan (2014)[9]	268	52.4 (Nonretrosternal group) 59.7 (Retrosternal group)	4572	4572	03	Not mentioned	02	Not mentioned	Prolong intubation
Jesper Roed Sorenson (2017)[37]	17	55	65	65	0	0	0	Benign 65	Not applicable
Wai Keat Wong (2019)[38]	83	58.5	72	72	0	0	0	Benign 64 Malignant 8	Not applicable
A. Sulaiman (2021)[39]	109	48.7	40	40	40	Partial 24 Full 16	0	Benign 29 Malignant 11	Primary repair Tracheostomy

Note: Multiple means reported Gilfillan N, Ball CM, Myles PS, Serpell J, Johnson WR, Paul E. A cohort and database study of airway management in patients undergoing thyroidectomy for retrosternal goiter.

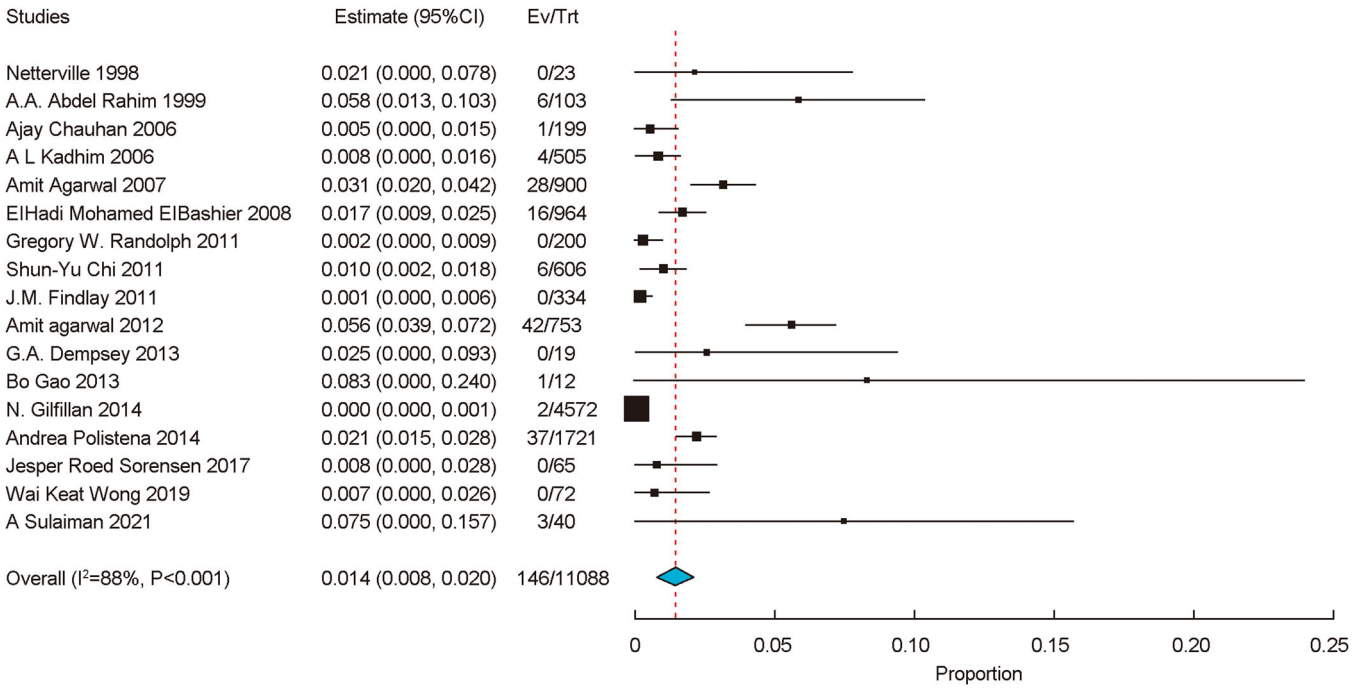

FIGURE 1 Forest plot showing the proportion of patients having developed tracheomalacia post thyroidectomy.

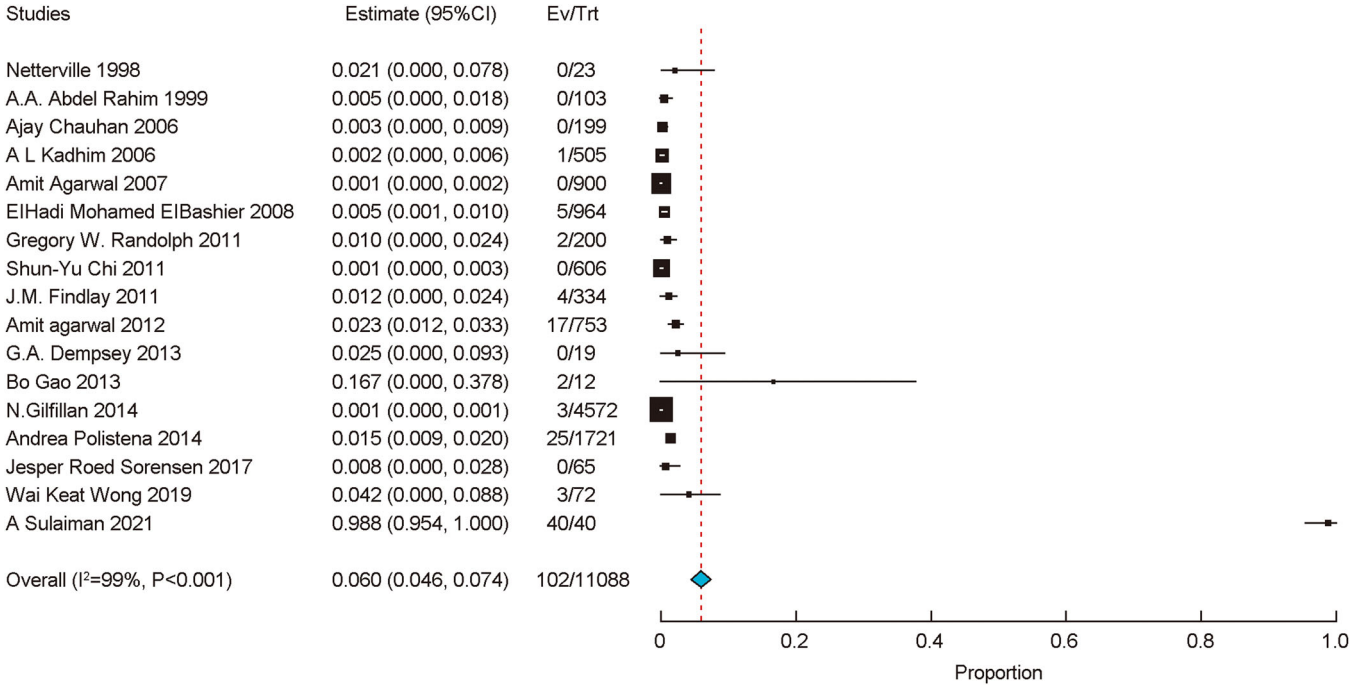

FIGURE 2 Forest plot showing the proportion of patients having undergone sternotomy concurrently with thyroidectomy.

Data analysis

Outcomes were double data extracted and were analyzed using OpenMeta. The weights given for each study were based on the inverse of the variance. Heterogeneity was quantified by χ^2 and I^2, which can be interpreted as the percentage of the total variation between studies that is attributable to heterogeneity rather than to chance, a low p value (less than 0.1), or a large χ^2 statistic relative to its degree of freedom and I^2 values greater than 50% were taken as substantial and high heterogeneity.

TABLE 2 Tracheomalacia patient characteristics.

Author name (year)	Patients	Age (Years)	Gender	Indication	Histopathology	Tracheal compression	Retrosternal extension	Intervention
A Abdel Rahim (1999)[31]	01	–	–	Collapsed trachea	–	Yes	The author does mention about the incidence of retrosternal extension in some patients who required tracheostomy, but does not specify the number. He hasn't mentioned how many patients among these 6 had retrosternal extensions, if any.	Tracheostomy
	02	–	–	Collapsed trachea	–	Yes		Tracheostomy
	03	–	–	Deformed trachea post thyroidectomy		Yes		Tracheostomy
	04	–	–	Deformed trachea post thyroidectomy	–	Yes		Tracheostomy
	05	–	–	Deformed trachea post thyroidectomy	–	Yes		Tracheostomy
	06	–	–	Deformed trachea post thyroidectomy	–	Yes		Steroid therapy
Ajay Chauhan (2006)[11]	01	56	F	Soft & compressed trachea	Multinodular goiter	Yes	Yes	Prolonged intubation for 24 h
	02	48	M	Narrow & deviated trachea	Multinodular goiter	Yes	Yes	Prolonged intubation for 48 h
Al Khadim (2006)[32]	01	–	–	Tracheomalacia	Multinodular goiter			Prolonged intubation for 48 h
	02	–	–	Tracheomalacia	Multinodular goiter	–	–	Endotracheal stenting
	03	–	–	Tracheomalacia	Multinodular goiter	–	–	Tracheostomy
	04	–	–	Tracheomalacia	Multinodular goiter	–	–	Tracheostomy
	Author has not given any particular definition of tracheomalacia.							
Amit Agarwal (2007)[4]	01	80	M	Tracheal softening	Poorly differentiated carcinoma	–	11 patients had retrosternal extension.	26 patients required tracheostomy.
	02	72	M	Postop stridor	Anaplastic carcinoma	–		
	03	60	F	Postop stridor	Papillary thyroid carcinoma	–		
	04	50	F	Respiratory distress	Papillary thyroid carcinoma	–		
	05	45	F	Respiratory distress	Follicular carcinoma	–		
	06	46	F	Tracheal softening	Follicular carcinoma	–		
	07	69	M	Postop stridor	Medullary thyroid carcinoma	–		

TABLE 2 (Continued)

Author name (year)	Patients	Age (Years)	Gender	Indication	Histopathology	Tracheal compression	Retrosternal extension	Intervention
	08	43	M	Postop stridor	Chronic lymphocytic thyroiditis	–		
	09	57	F	Tracheal narrowing	Poorly differentiated carcinoma	–		
	10	35	F	Postop stridor	Poorly differentiated carcinoma	–		
	11	41	M	Tracheal softening, Postop stridor	Adenomatous goiter	–		
	12	23	F	Tracheal softening	Amyloid goiter	–		
	13	38	F	Tracheal softening	Poorly differentiated carcinoma	–		
	14	51	M	Postop stridor	Adenomatous goiter	–		
	15	46	M	Tracheal softening	Multinodular goiter	–		
	16	41	M	Tracheal softening	Hurthle cell cancer	–		
	17	68	F	Tracheal softening	Adenomatous goiter	–		
	18	60	F	Tracheal softening	Hurthle cell cancer	–		
	19	55	F	Tracheal softening	Multinodular goiter	–		
	20	40	F	Tracheal softening	Multinodular goiter	–		
	21	55	M	Tracheal softening	Medullary thyroid carcinoma	–		
	22	30	M	Tracheal softening	Multinodular goiter	–		
	23	60	F	Tracheal softening	Follicular cancer	–		
	24	73	F	Tracheal softening	Follicular cancer	–		
	25	75	M	Tracheal softening	Follicular cancer	–		
	26	55	M	Tracheal softening	Multinodular goiter	–		
	27	47	F	Tracheal softening	Papillary cancer	–		
	28	41	F	Tracheal softening	Adenomatous goiter	–		

(Continues)

TABLE 2 (Continued)

Author name (year)	Patients	Age (Years)	Gender	Indication	Histopathology	Tracheal compression	Retrosternal extension	Intervention
ElHadi Mohamed ElBashier (2008)[33]	16 patients	50 (SD = 13)	–	Tracheal softening	Goiter (9 patients)	–	19 patients of the total sample size had retrosternal extension.	Tracheostomy
Shun Yu Chi (2011)[27]	01	58	F	Postop stridor	Goiter	Yes	–	Immediate reintubation, postextubation BiPAP
	02	82	F	Tracheal softening	Poorly differentiated carcinoma	Yes	–	Prolong intubation, postextubation BiPAP
	03	62	F	Postop stridor	Papillary thyroid carcinoma	Yes	–	Immediate reintubation, postextubation BiPAP
	04	70	F	Postop stridor	Follicular carcinoma	Yes	–	Immediate reintubation, postextubation BiPAP
	05	50	F	Tracheal softening	Poorly differentiated carcinoma	Yes	–	Prolong intubation, postextubation BiPAP
	06	53	F	Postop stridor	Papillary thyroid carcinoma	Yes	–	Immediate reintubation, postextubation BiPAP
Amit Agarwal (2012)[15]	42 patients	45.8	–	Tracheal injury Difficult extubation	281 patients of the total sample size had malignant thyroid nodule.	179 patients of the total sample size had tracheal compression.	106 patients of the total sample size had retrosternal extension.	Tracheostomy 32 patients Prolong intubation in 3 patients
Bo Gao (2013)[35]	01	–	–	Tracheal collapse	Goiter	Yes	Yes	Tracheostomy
N. Gilfillan (2014)[9]	01	–	–	–	–	–	Yes	Prolonged intubation
	02	–	–	–	–	–	–	Prolonged intubation
Andrea Polistena (2014)[36]	37	23 patients < 80	–	–	–	Yes	Yes	Prolong intubation

TABLE 2 (Continued)

Author name (year)	Patients	Age (Years)	Gender	Indication	Histopathology	Tracheal compression	Retrosternal extension	Intervention
A. Sulaiman (2021)[39]	01	48.73 ± 11.259	–	Tracheal softening	Goiter	Yes	Yes	Tracheal resection, end-to-end anastomosis
	02		–	Tracheal softening	Goiter	Yes	Yes	Tracheostomy
	03		–	Tracheal softening	Goiter	Yes	Yes	Tracheostomy

Abbreviation: –, not reported.

RESULTS

Eligible articles

Using the aforementioned key terms and eligibility criteria, the online search retrieved 214 papers. After removing duplicates and further screening, only 29 articles were assessed for full-text eligibility. After excluding a further of 12 studies not fulfilling the eligibility criteria, a total of 17 studies were included in the final evidence synthesis (Table 1).

Quantitative synthesis

The included articles were published from 1998 till October 2021 from multiple countries, such as the United States, Italy, China, Australia, and so on. A total of 11,088 patients who underwent thyroidectomy were included. The mean age was 55.8 ± 7.7 years, ranging from 48 to 75 years. The articles were reported as retrospective reviews ($n = 9$). In addition, there were retrospective cohorts ($n = 2$), prospective cohorts ($n = 2$), prospective descriptive studies ($n = 1$), prospective reviews ($n = 1$), longitudinal cohorts ($n = 1$), and a case series ($n = 1$).

The proportion of patients who had developed tracheomalacia was reported in 146 cases out of a total of 11,088 (1.4%) (Figure 1). The most common intervention for managing tracheomalacia was either tracheostomy or prolonged intubation (Table 1). Of a total of 11,088 patients who had undergone thyroidectomy, 102 (0.6%) sternotomies were performed, with the most common being total sternotomy (Figure 2). Other types of sternotomies included substernal, cervico-sternotomy, median, transcervical, and midline sternotomy. Tracheomalacia patient characteristics were shown in Table 2.

Study quality/qualitative assessment

The quality of the included articles was assessed independently by two authors (S. A. and S. K. G.) using the quality assessment tool developed by the National Heart Lung and Brain Institute (NHLBI). Disagreements were resolved by a third author (H. I.). Studies were scored out of 8 and categorized as good quality (score 6–8), fair quality (score 4–5), and poor quality (score<4) (Table 3).

DISCUSSION

Post-thyroidectomy tracheomalacia (PTTM) is a relatively uncommon occurrence treated with or without an invasive intervention.[1,21,22] Our meta-analysis reports an incidence of 1.4%, not making tracheomalacia a common complication following thyroid surgery.

PTTM is a distinct entity with an increased likelihood of being present in an endemic goiter region. Risk factors include goiter size, more than 5 years duration, and retro-sternal extension.[2,5] The clinical diagnosis of tracheomalacia, includes fiberoptic

TABLE 3 Qualitative synthesis using the quality assessment tool developed by the National Heart Lung and Brain Institute (NHLBI).

#	Author, year	Was the objective clearly stated?	Was the study population clearly and fully described, including a case definition?	Were the cases consecutive?	Were the subjects comparable?	Was the intervention clearly described?	Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Was the length of follow-up adequate?	Were the statistical methods well described?	Were the results well described?	Total	Level of evidence
1	Netterville, 1998[30]	Y	Y	Y	Y	Y	Y	N/R	N/A	Y	7	Good
2	Abdel Rahim, 1999[31]	Y	Y	Y	Y	Y	Y	N/R	Y	Y	8	Good
3	Chauhan, 2006[11]	Y	Y	Y	Y	Y	Y	N/R	N/A	Y	7	Good
4	Kadhim, 2006[32]	Y	N	Y	Y	Y	Y	N/R	N/A	Y	6	Good
5	Agarwal, 2007[4]	Y	Y	Y	Y	Y	Y	Y	N/A	Y	8	Good
6	El Bashier, 2008[33]	Y	Y	Y	Y	Y	Y	N/R	N/A	Y	7	Good
7	Randolph, 2011[34]	Y	Y	Y	Y	Y	Y	N/R	Y	Y	8	Good
8	Yu Chi, 2011[27]	Y	Y	Y	Y	Y	Y	N/R	N/A	Y	7	Good
9	Findlay, 2011[5]	Y	N	Y	Y	Y	Y	N/R	N/A	Y	6	Good
10	Agarwal, 2012[15]	Y	N	Y	Y	Y	Y	Y	Y	Y	8	Good
11	Dempsey, 2013[28]	Y	N	Y	Y	Y	Y	N/R	N/A	Y	6	Good
12	Gao, 2013[35]	Y	N	Y	Y	Y	Y	N/R	N/A	Y	6	Good
13	Gilfillan, 2014[9]	Y	N	Y	Y	Y	Y	N/R	Y	Y	7	Good
14	Polistena, 2014[36]	Y	N	Y	Y	Y	Y	N/R	Y	Y	7	Good
15	Sorensen, 2017[37]	Y	N	Y	Y	Y	Y	N/R	Y	Y	7	Good

TABLE 3 (Continued)

#	Author, year	Was the objective clearly stated?	Was the study population clearly and fully described, including a case definition?	Were the cases consecutive?	Were the subjects comparable?	Was the intervention clearly described?	Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Was the length of follow-up adequate?	Were the statistical methods well described?	Were the results well described?	Total	Level of evidence
16	Wong, 2019[38]	Y	N	Y	Y	Y	Y	N/R	C/D	N/A	5	Fair
17	Sulaiman, 2021[39]	Y	Y	Y	Y	Y	Y	N/R	Y	Y	8	Good

Abbreviations: CD, cannot determine; NA, not applicable; NR, not reported.

bronchoscopy (FOB) and confirming the presence of collapsing trachea.[3]

Retro-sternal goiters are a recognized condition, usually treated with thyroidectomy. The procedure has minimal surgical complications and incase of airway obstructions it can be managed by well-trained anesthetists.[9,11,12]

Our systematic review reveals a few cases of tracheomalacia even without retrosternal extension. This is a crucial finding as this requires further studies to determine the exact cause of tracheomalacia in these cases.

A study by Machado et al.[17] in 2011 reported several cases of PTTM in goiters weighing more than 500 g. This supports a study by Agarwal et al.[4] in 2007, which concluded that even in cases where the goiter is benign, patients are more likely to develop tracheomalacia.

On the contrary, Findlay et al.[5] reported no cases of PTTM, even in high-risk patients with significant tracheal compression. Furthermore, Shen and colleagues reported 60 patients with retrosternal goiter in a retrospective study done in 2004. Of them, 21 suffered tracheal compression to some extent; none experienced PTTM.[40]

Erbil and colleagues evaluated 170 cases of retrosternal goiter in 2004; 50 of these cases had either tracheal deviation, compression, or both; however, none had PTTM.[41] Only one retrospective analysis showed an incidence of tracheomalacia. Out of 199 thyroidectomies done for retrosternal goiter, 118 patients had some degree of tracheal compression. However, only two cases of tracheomalacia were reported.[11]

Excluding tracheostomies and stenting, several new effective techniques have emerged. Noninvasive positive pressure ventilation is sufficient and seems safe in managing stridor and airway compromise after early extubation in patients with PTTM.[24,26,27] Aortopexy is a popular surgical treatment for tracheomalacia in many centers. The method offers an anterior elevation of the aorta that is attached with sutures to the posterior wall of sternum.[42] This prevents the inwards collapse of the membranous rear wall of the trachea during inspiration.[43]

Strengths and limitations

Our review has several limitations. Even though we assessed a large population of 11,088 patients, our results showed a significantly high percentage of heterogeneity. This is attributed to the variation in the study population, heterogeneity in defining tracheomalacia and, the retrospective study designs of the included studies. Another limitation was including studies in the English language only, which might lead to under reporting of the incidence of tracheomalacia. Prospective, long-term, multi institutional cohort studies would be able to address the causes of tracheomalacia through regression analysis. Our review however highlights the estimated proportion of tracheomalacia following thyroidectomy. This number is close to 1%, making it an uncommon complication/sequalae of thyroid hypertrophy.

CONCLUSION

PTTM is a rare complication and hence unlikely to be seen in routine thyroidectomies. In most cases, it is managed by tracheostomy or prolonged endotracheal intubation. Novel research is being conducted on the utility of different treatment modalities for tracheomalacia, such as noninvasive positive pressure ventilation and aortopexy. Overall incidence remains low close to one percent according to the published data.

AUTHOR CONTRIBUTIONS

Eligibility criteria: Shayan Ansari, Mriganka De, Syed Akbar Abbas. *Data extraction*: Haissan Iftikhar, Shayan Khalid Ghaloo, Syed Akbar Abbas. *Quality assessment*: Syed Shabbir Afzal, Shayan Khalid Ghaloo, Haissan Iftikhar. *Data analysis*: Mriganka De, Haissan Iftikhar, Shayan Ansari. *Manuscript writing*: Syed Shabbir Afzal, Shayan Khalid Ghaloo, Haissan Iftikhar, Syed Akbar Abbas.

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The authors have nothing to report.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data will be provided upon request from the corresponding author.

ETHICS STATEMENT

The authors have nothing to report.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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