

Criteria for Using a Cervicothoracic Approach in Huge Retrosternal Goiter: Systematic Review and Meta-Analysis

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Abstract

Background: The definition of retrosternal goiter (RSG) is not uniform and varies among authors, some authors described retrosternal goiter as one that extends down to the aortic arch. Others defined retrosternal goiter as a lesion of the thyroid extending to the fourth thoracic vertebrae on chest X-ray.

Aim of Study: Perform a systematic review/meta-analysis to identify and assess factors that affect decision making in huge retrosternal goiter, whether sternotomy might be or might not be needed. And to assess the different tools used in decision making.

Material and Methods: This systematic review was conducted following the Cochrane Handbook for Systematic Reviews of Interventions. We also adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines during the design of our study. We conducted a literature search using PubMed, Scopus, Web of Science, and Cochrane Library. Clinical studies were conducted from January 2000 till August 2022 using MEDLINE/PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov., EMBASE, Web of Science, SCOPUS, and Grey Literature Searching, and journals related to the topic by using these keywords: huge goiter, retrosternal, total thyroidectomy, sternotomy, and cervicothoracic approach.

Results: We reported a total of 32 complications in cervical approach in form of tracheomalacia, hemorrhage, visceral injury, fistula, pneumothorax/pneumonia, Wound problems, and 9 complications in sternotomy in form of pleural effusion, hemorrhage, pneumothorax/pneumonia, tracheomalacia, wound problems. Three studies showed tracheal deviation/compression found significant higher among sternotomy procedure vs cervical. Pneumothorax/pneumonia and tracheomalacia were found insignificant differences between sternotomy procedure and cervical.

Conclusion: The cervical approach for patients with RSG extending to the aortic arch is an optimum, feasible and less invasive surgical approach that can be considered the appropriate choice in such cases and can be performed successfully by experienced specialized surgeons. Thoracic surgeon standby is required in a few selected cases which carry a chance that sternotomy might be needed.

Key Words: Cervicothoracic approach – Huge retrosternal goiter.

Introduction

THE definition of retrosternal goiter (RSG) is not uniform and varies among authors, some authors described retrosternal goiter as one that extends down to the aortic arch. Others defined retrosternal goiter as a lesion of the thyroid extending to the fourth thoracic vertebrae on chest X-ray [1].

Although it is estimated that >5% of the world population has goiter, the incidence of RSG varies considerably, ranging from 1% to 15% of thyroidectomies, depending on the defining criteria [2].

Ninety eight percent of the RSG were of the secondary type, and only 1.7% had a primary substernal so-called primary intrathoracic goiter that had developed from the growth of ectopic thyroid tissue present in the thorax that was not connected to the cervical thyroid gland [3].

Malignancy has been found in 3-20% of patients with RSG, and the types of carcinoma varied from follicular, papillary, Hurthle cell, medullary, anaplastic carcinoma to lymphoma [4].

The clinical manifestations of RSG are attributed to compression or displacement of the adjacent aero-digestive tract and mediastinal great vessels at the thoracic inlet, with dyspnea being by far the most frequent complaint. Although seldom seen, patients with RSG may develop acute airway obstruction which is usually attributed to intrathyroidal hemorrhage [5].

Computed tomographic scanning of the neck and chest permits identification of tissue planes of intrathoracic goitrous components and is the best proven diagnostic modality, reported 100% sensitivity with computed tomographic scanning, 77%

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with thyroid scanning, and 59% with chest radiography. Because most retrosternal thyroid tissue does not take up radioiodine ^{131}I , thyroid scan rarely alters management and often fails to define the intrathoracic mass [6].

Fine-needle aspiration cytology to exclude the presence of carcinoma is not recommended because intrathoracic goiters are not easily accessible and the procedure may lead to life-threatening complications [7].

The surgical team treating patients with RSG should be familiar with cervical thyroid surgery but should also have a thorough knowledge of mediastinal anatomy and specific operative techniques in order to achieve good results. As long as the inferior aspect of the gland can be reached through a cervical incision alone there is no indication for an intrathoracic approach. RSG that extend to and below the aortic arch cannot be delivered through a cervical incision and need adequate exposure through an intrathoracic approach [8].

The type of approach used in the surgical management of patients with RSG has necessitated the need of a standard definition and description of RSG. A proposed simple 3 grade classification system for RSG has been based on the relation to the aortic arch and right atrium: (1) Above the aortic arch; (2) From the arch to the pericardium; (3) Below the right atrium. The type of thoracic approach should be based on this classification [9].

Thyroidectomy for retrosternal goitre is usually carried out through a cervical incision. Around 4-12% of patients require an extracervical approach, usually by sternotomy which has two approaches open and thoracoscopic [10].

Aim of the work:

Perform a systematic review/meta-analysis to identify and assess factors that affect decision making in huge retrosternal goiter, whether sternotomy might be or might not be needed. And to assess the different tools used in decision making.

Material and Methods

We prepared this systematic review with a careful following of the Cochrane Handbook for Systematic Reviews of Interventions. We also adhered to The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines during the design of our study.

Literature search: We conducted a literature search using PubMed, Scopus, Web of Science,

and Cochrane Library. Clinical studies were conducted from January 2000 till August 2022 using MEDLINE/PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), Clinical Trials.gov, EMBASE, Web of Science, SCOPUS, and Grey Literature Searching, and journals related to the topic by using these keywords: Huge goiter, retrosternal, total thyroidectomy, sternotomy, and cervicothoracic approach.

Locating and selecting studies: Abstracts of articles identified by using our search strategy were reviewed, and articles that fulfill the inclusion criteria were fully retrieved in full data on at least one of the outcome measures must be included in the study. In case of doubt, a second reviewer assessed the article and a consensus was reached and the process was presented in a PRISMA flow chart, according to the PRISMA statement.

Data extraction: Two review authors independently extracted the data from eligible studies using a standardized data extraction form. Any duplicated data studies were removed. The "related articles" function was used to expand the search from each relevant study identified. Bibliographies of retrieved papers were further screened for any additional eligible studies. We searched for articles that were included in previous related systematic reviews. The identified citations were retrieved using Endnote X8 software package (Thompson Reuter, USA).

Eligibility criteria: We included studies that met our following inclusion criteria: Population: Adult patients aged 18: 70 years old who were candidates for total thyroidectomy with huge retrosternal goitre with huge retrosternal goitre. Intervention: Total thyroidectomy classical approach (transcervical) and combined cervicothoracic approach (with sternotomy partial or complete). Comparator: Different sternotomy approaches for management of huge retrosternal goiter. Study design: Clinical trials whether randomized or non-randomized prospective and retrospective comparative cohort studies. Outcomes: Operative data, surgical approach, operative data, disease characteristics, peri- and intraoperative complications as temporary hypocalcemia, tracheal deviation, compression, thyroid weight, hemorrhage, pneumothorax, pneumonia, tracheomalacia, temporary / permanent recurrent laryngeal nerve palsy, temporary hypoparathyroidism/hypocalcemia and disease characteristics.

We excluded animal studies, reviews, book chapters, thesis, editorial letters and papers with

overlapped dataset. Eligibility screening was conducted in a two step-wise manner (title/abstract screening and full-text screening). Each step was done by two reviewers independently according to the predetermined criteria.

There were no restrictions on language, race, sex, or age. The duplicated articles were removed primarily using Endnote X8 program (Thompson Reuter, USA) and manually using titles and abstracts screening.

Statistical considerations: Outcomes from included trials will be combined using The Review Manager Software. Data will be abstracted from each study in form of a risk estimate and its 95% Confidence Interval (CI). Pooled risk estimate will be obtained by weighing each study by the inverse variance of the effect measure on a logarithmic scale. When a risk estimate and its 95% Confidence Interval were not available from the article, unadjusted values from the published data of the article will be calculated, using SPSS ver. 20.0. This approach to pool the results assumes that the study populations being compared are similar and hence corresponds to a fixed effect analysis. The validity of pooling the risk estimates will be tested (Test of Homogeneity) using a Chi-square test. A violation of this test implies that the studies being grouped differ from one another. In the presence of significant heterogeneity of the effect measure among studies being compared, we will perform a random effect analysis that is based on the method described by Der Simonian and Laird (1986). The random effect analysis accounts for the interstudy variation. Because the test of homogeneity has low power.

Evidence of publication bias: The risk of bias for individual studies will be made according to the PRISMA Statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions.

Data extraction: Data were extracted by two independent authors and revised by another two independent authors. We extracted the characteristics of each study as following: Author, year of publication, baseline characteristics of study subjects such as age, gender besides incidence of retrosternal goiter and postoperative complications.

Statistical analysis: Continuous data were pooled as mean difference (MD) and 95% confidence interval, while dichotomous outcomes were pooled as odds ratio (OR) and 95% confidence interval. Revman software was used to pool studies. We estimated the change from baseline in each

outcome. We used I^2 square test to quantify the degree of heterogeneity across the studies.

Statistical analysis of the data: Data were fed to the computer and analyzed using MedCalc software package version 20.100 Confidence interval (CI) was established at 95% and p -values of less than or equal 0.05 were considered statistical significant. Statistical heterogeneity was assessed using I^2 (observed variance for heterogeneity) and Q (Total variance for heterogeneity). Qualitative Data are reported as total Number and number of event.

Results

The literature search revealed 10 published studies on Cervicothoracic Approach in Huge Retrosternal Goiter after excluding some studies.

Study characteristics: 10 studies were included 9 were retrospective and 1 were prospective study, 1094 cases were included with mean age was years 61.2 years as shown in Table (1).

Disease characteristics: Mean weight of thyroid was 156.3g, mediastinal extension was above AA (59), Below AA (13), at AA (17), Tracheal compression founded among 255 cases and previous thyroid surgery in 64 cases as shown in Table (2).

Operative data:

Mean operative time was 175.7, mean blood loss was 114.6 and as regard operative method Total thyroidectomy (35), Non-total thyroidectomy (178), final pathology was Benign (261), Malignant (44), mean hospital stay was 3 days as shown in Table (3).

Approach: Cervical approach used in 856 and sternotomy in 145 cases, 170 symptomatic/175 asymptomatic in cervical vs 9 symptomatic/22 asymptomatic in sternotomy, tracheal compression founded in 211/856 cervical vs 67/145 sternotomy, mean thyroid weight was 175.6 in cervical vs 249.6 in sternotomy as shown in Table (4).

Operative data: In 1 study operative method used was Total thyroidectomy (10), Non-total thyroidectomy (35) in cervical approach vs Total thyroidectomy (13), Non-total thyroidectomy (40) through sternotomy, mean surgical time 65 (24) min in cervical vs 142 (34) min in sternotomy, mean hospital stay was 3 days as shown in Table (5).

Disease characteristics: Mediastinal extension founded to be above AA (81), lateral extension (36), Below AA (39), Anterior mediastinal exten-

sion (46), Posterior mediastinal extension (1), Extension below carina (2) in cervical vs above AA (42), below AA (42), lateral extension (3), Anterior mediastinal extension (1), Posterior mediastinal extension (16), Extension below carina (15) in sternotomy.

Regarding final pathology was Benign (239), Malignant (35) in cervical vs Benign (67), Malignant (14) in sternotomy as shown in Table (6).

Perioperative complication: Recurrent laryngeal nerve palsy was Temporary (45), Permanent (6) in cervical vs Temporary (11), Permanent (2) in sternotomy, Hypoparathyroidism was Temporary (70) in cervical vs Temporary(5) in sternotomy, Hypocalcemia was Temporary (68), Permanent (2) in cervical vs Temporary (7), Permanent (2) in sternotomy as shown in Table (7).

Complications: 32 complications in cervical approach in form of Tracheomalacia, Hemorrhage, visceral injury, fistula, Pneumothorax/pneumonia, Wound problems, and 9 complications in sternotomy in form of Pleural effusion, Hemorrhage, Pneumothorax/pneumonia, Tracheomalacia, Wound problems as shown in Table (8).

Meta analysis:

Tracheal deviation/compression: 3 studies shows Tracheal deviation/compression found significant higher among sternotomy procedure vs cervical *p*-value <0.0001.

Thyroid weight: 3 studies shows Thyroid weight found significant higher among sternotomy procedure vs cervical *p*-value 0.0008.

Hemorrhage: 5 studies shows Hemorrhage found insignificant differences between sternotomy procedure and cervical *p*-value 0.46.

Pneumothorax/pneumonia: 3 studies shows Pneumothorax/pneumonia found insignificant differences between sternotomy procedure and cervical *p*-value 0.36.

Tracheomalacia: 2 studies shows Tracheomalacia found insignificant differences between sternotomy procedure and cervical *p*-value 0.711.

Asymptomatic: 3 studies shows Asymptomatic found insignificant differences between sternotomy procedure and cervical *p*-value 0.96.

Symptomatic: 4 studies shows symptomatic found significant higher among sternotomy procedure vs cervical *p*-value <0.0001.

Temporary recurrent laryngeal nerve palsy: 6 studies shows Temporary recurrent laryngeal nerve palsy found insignificant differences between sternotomy procedure and cervical *p*-value 0.9581.

Permanent recurrent laryngeal nerve palsy: 3 studies shows Permanent recurrent laryngeal nerve palsy found insignificant differences between sternotomy procedure and cervical *p*-value 0.2456.

Temporary Hypoparathyroidism: 3 studies shows Temporary Hypoparathyroidism found insignificant differences between sternotomy procedure and cervical *p*-value 1.00.

Temporary Hypocalcemia: 5 studies shows Temporary Hypocalcemia found significant higher among cervical procedure vs sternotomy *p*-value 0.0002.

Table (1): Study characteristics.

Author	Type of study	Number	Age	M/F
Wang X et al., [11]	Retrospective	115	52.29	21/94
Casella C et al., [12]	Retrospective	44	63	
Cvasciuc IT et al., [13]	Retrospective	98	55	29/69
Nankee L et al., [14]	Retrospective	220	56.25	65/155
Riffat F et al., [15]	Retrospective	97	66	44/53
SarS et al., [16]	Prospective	260		70/190
Sakkary MA et al., [17]	Retrospective	73	55.4	19/54
Rugiu MG et al., [18]	Retrospective	53	64	16/37
Cichon´ S et al., [19]	Retrospective	115	63	32/83
Hashmi SM et al., [20]	Retrospective	19	76.15	8/11

Table (2): Disease characteristics.

Author	Weight of thyroid (g)	Meditational extension	Tracheal compression	Previous thyroid surgery
Wang X et al., 2020			85	4
Casella C et al., 2019				
Cvasciuc IT et al., 2017	106		86	
Nankee L et al., 2015	171			18
Riffat F et al., 2013				
SarS et al., 2012				37
Sakkary MA et al., 2012		Above AA(59), Below AA(1), at AA(13)	46	
Rugiu MG et al., 2009	192	Below AA(12), Reaching C(4)	38	5
Cichon´ S et al., 2008				
Hashmi SM et al., 2006				

Table (3): Operative data.

Author	Operation time (min)	Blood loss (mL)	Operative method	Final pathology	Median length of hospital stay (day)
Wang X et al., 2020	115.11	54.43	Total thyroidectomy (12), Non-total thyroidectomy (103)	Benign (109), Malignant (6)	5.38
Casella C et al., 2019					
Cvasciuc IT et al., 2017			Total thyroidectomy (23), Non-total thyroidectomy (75)	Benign (75), Malignant (23)	
Nankee L et al., 2015	236.45	174.8			1.65
Riffat F et al., 2013					
SarS et al., 2012					
Sakkary MA et al., 2012				Benign (26), Malignant (13)	4.6
Rugiu MG et al., 2009				Benign (51), Malignant (2)	
Cichon´ S et al., 2008					
Hashmi SM et al., 2006					

Table (4): Approach.

Author	Approach	Number	Clinical presentation	Tracheal deviation/compression	Thyroid weight (g)
Wang X et al., 2020	Cervical	112			
	Sternotomy	3			
Casella C et al., 2019	Cervical	40	Asymptomatic (17), Symptomatic (23)		127.00±73.18
	Sternotomy	4	Asymptomatic (1), Symptomatic (3)		227.00±32.19
Cvasciuc IT et al., 2017	Cervical	45		44	127
	Sternotomy	53		42	227
Nankee L et al., 2015	Cervical	120			
	Sternotomy	7			
Riffat F et al., 2013	Cervical	80		40	
	Sternotomy	17		14	
SarS et al., 2012	Cervical	243	Asymptomatic (18), Symptomatic (3)	127	273 (142)
	Sternotomy	17	Asymptomatic (1), Symptomatic (16)	11	295 (114)
Sakkary MA et al., 2012	Cervical	66			
	Sternotomy	7			
Rugiu MG et al., 2009	Cervical	49	Asymptomatic (122), Symptomatic (12)		
	Sternotomy	4	Asymptomatic (1), Symptomatic (3)		
Cichon´ S et al., 2008	Cervical	88			
	Sternotomy	27			
Hashmi SM et al., 2006	Cervical	13	Symptomatic (13)		
	Sternotomy	6	Symptomatic (6)		

Table (5): Operative data.

Author	Approach	Number	Operative method	Surgical time (min)	Hospital stay (d)
Wang X et al., 2020	Cervical	112			
	Sternotomy	3			
Casella C et al., 2019	Cervical	40			
	Sternotomy	4			
Cvasciuc IT et al., 2017	Cervical	45	Total thyroidectomy (10), Non-total thyroidectomy (35)		
	Sternotomy	53	Total thyroidectomy (13), Non-total thyroidectomy (40)		
Nankee L et al., 2015	Cervical	120			
	Sternotomy	7			
Riffat F et al., 2013	Cervical	80			
	Sternotomy	17			
SarS et al., 2012	Cervical	243		65 (24)	1.6 (1.1)
	Sternotomy	17		142 (34)	7.3 (4)
Sakkary MA et al., 2012	Cervical	66			
	Sternotomy	7			
Rugiu MG et al., 2009	Cervical	49			
	Sternotomy	4			
Cichon´ S et al., 2008	Cervical	88			
	Sternotomy	27			
Hashmi SM et al., 2006	Cervical	13			
	Sternotomy	6			

Table (6): Disease characteristics.

Author	Approach	Number	Mediastinal extension	Final pathology
Wang X et al., 2020	Cervical	112		
	Sternotomy	3		
Casella C et al., 2019	Cervical	40	Above AA (40), lateral extension (36)	Benign (40), Malignant (15)
	Sternotomy	4	Above AA (1), below AA (3), lateral extension (3)	Benign (35), Malignant (8)
Cvasciuc IT et al., 2017	Cervical	45		Benign (34), Malignant (6)
	Sternotomy	53		Benign (3), Malignant (1)
Nankee L et al., 2015	Cervical	120		
	Sternotomy	7		
Riffat F et al., 2013	Cervical	80	Above AA (41), Below AA (39), Anterior mediastinal extension (46), Posterior mediastinal extension (1), Extension below carina (2)	Benign (51), Malignant (9)
	Sternotomy	17	Above AA(41), Below AA (39), Anterior mediastinal extension (1), Posterior mediastinal extension (16), Extension below carina (15)	Benign (38), Malignant (2)
SarS et al., 2012	Cervical	243		
	Sternotomy	17		
Sakkary MA et al., 2012	Cervical	66		
	Sternotomy	7		
Rugiu MG et al., 2009	Cervical	49		Benign (47), Malignant (2)
	Sternotomy	4		Benign (4), Malignant (0)
Cichon´ S et al., 2008	Cervical	88		Benign (86), Malignant (2)
	Sternotomy	27		Benign (4), Malignant (0)
Hashmi SM et al., 2006	Cervical	13		Benign (12), Malignant (1)
	Sternotomy	6		Benign (3), Malignant (3)

Table (9): Meta-analysis for Tracheal deviation/compression.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Cvasciuc IT et al., 2017	45	44	53	42	1.234	1.068 to 1.426
Riffat F et al., 2013	80	40	17	14	0.607	0.445 to 0.828
SarS et al., 2012	243	127	17	11	0.808	0.557 to 1.171
Total (fixed effects)					0.951	0.831 to 1.088
Total (random effects)					0.858	0.517 to 1.422
<i>Test for heterogeneity:</i>						
Q					21.1989	
DF					2	
Significance level					<0.0001*	
I ² (inconsistency)					90.57%	
95% CI for I ²					75.16 to 96.42	

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

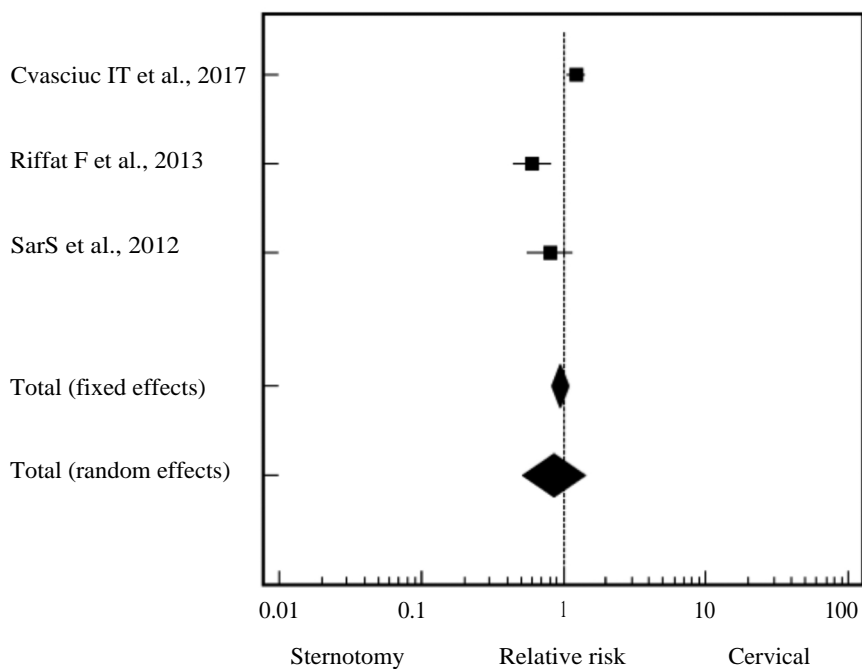


Fig. (1): Forest plot for Tracheal deviation/compression.

Table (10): Meta-analysis for Thyroid weight (g).

Study	Cervical		Sternotomy		SMD	SE	95% CI
	No.	Mean ± SD	No.	Mean ± SD			
Casella C et al., 2019	40	127±73.18	4	227±32.19	-1.382	0.536	-2.463 to -0.301
Cvasciuc IT et al., 2017	45	127±74.8	53	227±69.8	-1.375	0.224	-1.820 to -0.931
SarS et al., 2012	243	273±142	17	295±114	-0.156	0.25	-0.649 to 0.337
Total (fixed effects)					-0.882	0.159	-1.195 to -0.569
Total (random effects)					-0.934	0.468	-1.853 to -0.014

Test for heterogeneity:	
Q	14.1444
DF	2
Significance level	0.0008*
I ² (inconsistency)	85.86%
95% CI for I ²	58.82 to 95.14

Q : Total variance for heterogeneity.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).
 SMD: Standardized Mean Difference.

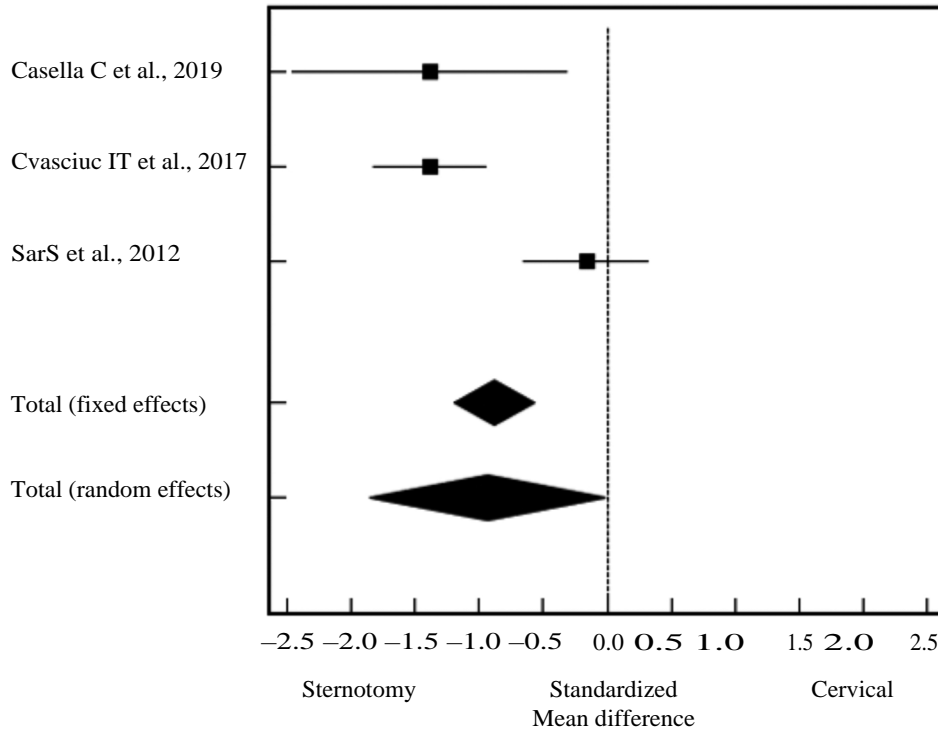


Fig. (2): Forest plot for Thyroid weight (g).

Table (11): Meta-analysis for Hemorrhage.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Wang X et al., 2020	112	0	3	0	–	
Nankee L et al., 2015	120	4	7	0	0.595	0.0350 to 10.112
Sakkary MA et al., 2012	66	1	7	1	0.106	0.00742 to 1.516
Rugiu MG et al., 2009	49	2	4	1	0.163	0.0186 to 1.435
Cichon´ S et al., 2008	88	2	27	0	1.573	0.0778 to 31.804
Total (fixed effects)					0.420	0.126 to 1.402
Total (random effects)					0.296	0.0805 to 1.092

Test for heterogeneity:

Q	2.5527
DF	3
Significance level	0.4658
I ² (inconsistency)	0.00%
95% CI for I ²	0.00 to 84.83

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

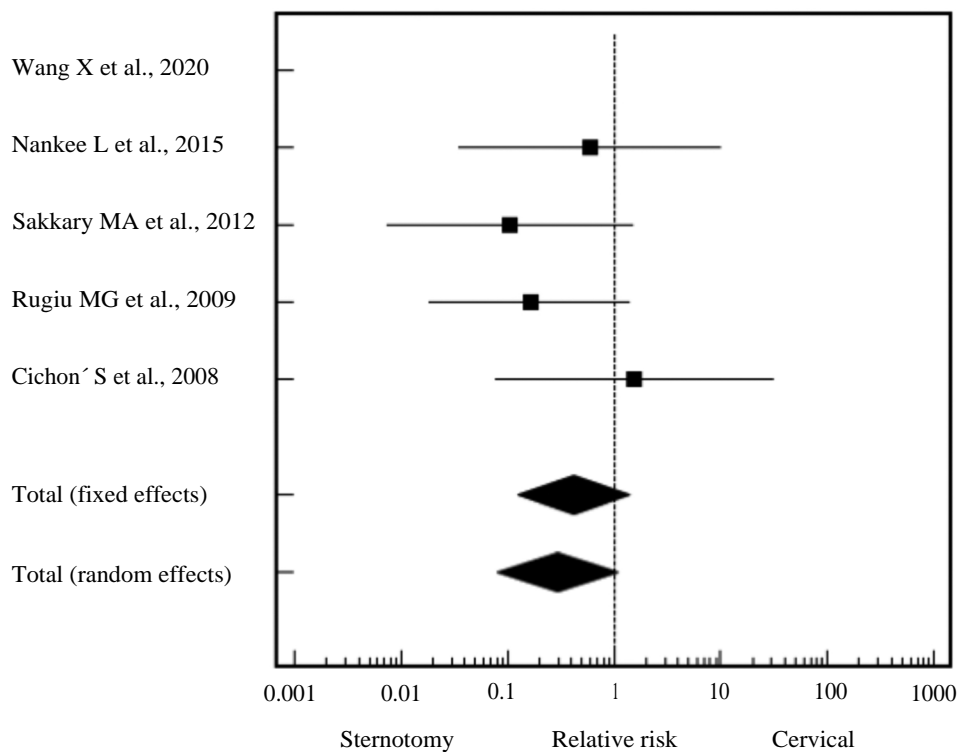


Fig. (3): Forest plot for Hemorrhage.

Table (12): Meta-analysis for Pneumothorax/pneumonia.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Wang X et al., 2020	112	0	3	0	–	
Sakkary MA et al., 2012	66	6	7	2	0.318	0.0786 to 1.288
RUGIU MG et al., 2009	49	1	4	1	0.0816	0.00620 to 1.075
Total (fixed effects)					0.238	0.0728 to 0.779
Total (random effects)					0.234	0.0684 to 0.798
<i>Test for heterogeneity:</i>						
Q					0.8278	
DF					1	
Significance level					0.3629	
I ² (inconsistency)					0.00%	
95% CI for I ²					0.00 to 0.00	

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

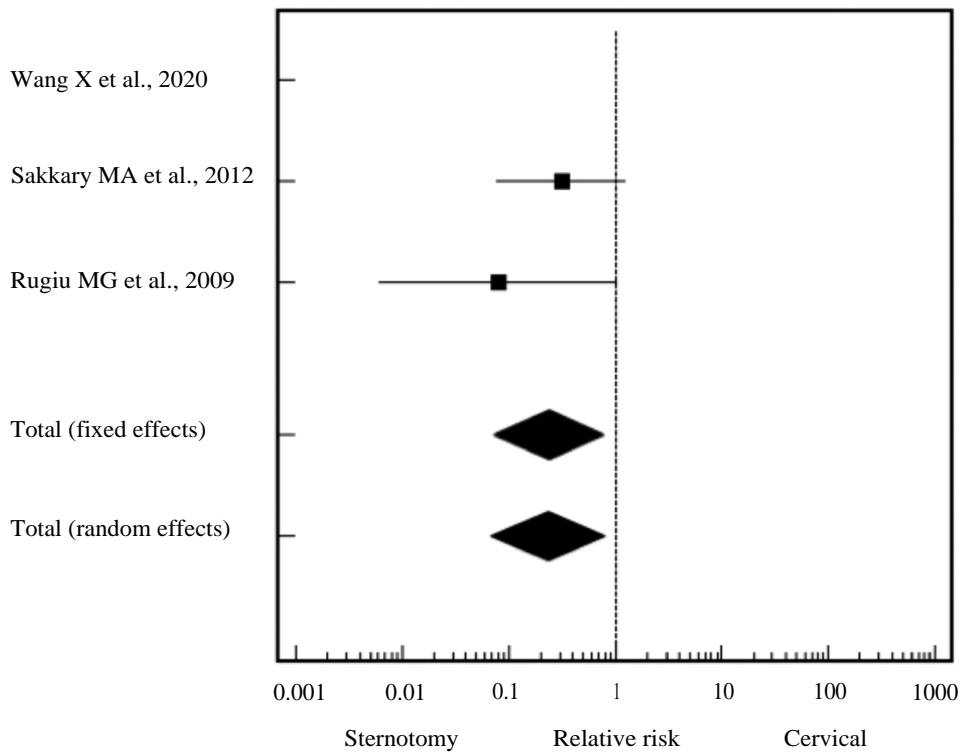


Fig. (4): Forest plot for Pneumothorax/pneumonia.

Table (13): Meta-analysis for Tracheomalacia.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Wang X et al., 2020	112	0	3	0	0.177	0.0101 to 3.115
Nankee L et al., 2012	66	6	7	2	0.321	0.0875 to 1.177
	49	1				
Total (fixed effects)					0.292	0.0898 to 0.946
Total (random effects)					0.29	0.0887 to 0.947
<i>Test for heterogeneity:</i>						
				0.1372		
Q				1		
DF				0.7111		
Significance level				0.00%		
I ² (inconsistency)				0.00 to 0.00		
95% CI for I ²						

Q : Total variance for heterogeneity.

RR: Relative Risk.

I² : Observed variance for heterogeneity.

CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

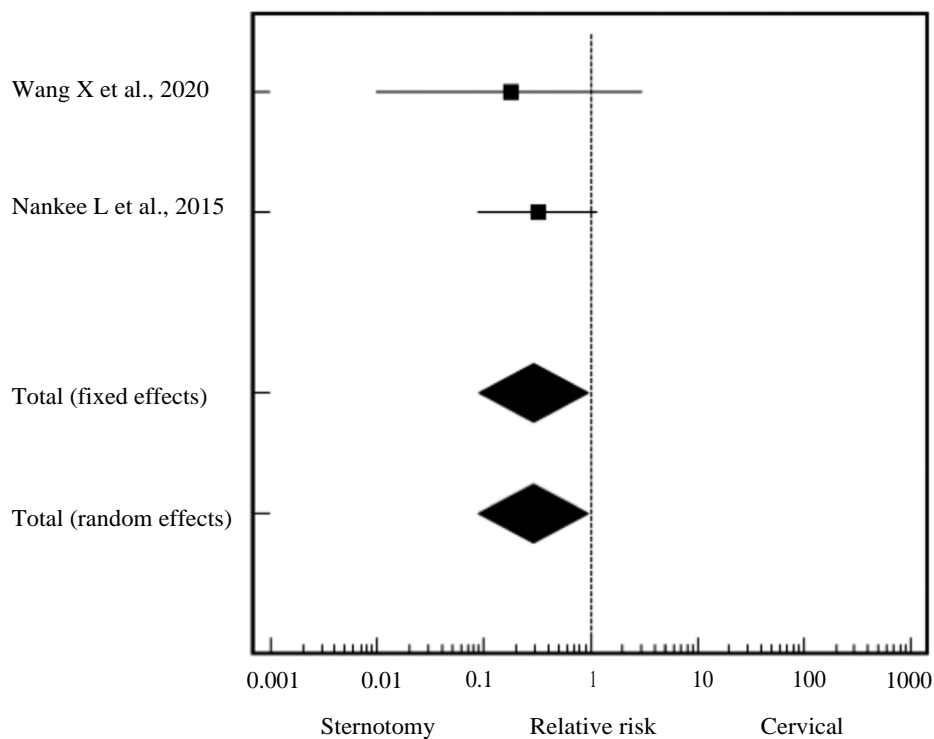


Fig. (5): Forest plot for Tracheomalacia.

Table (14): Meta-analysis for Asymptomatic.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Casella C et al., 2019	40	17	4	1	1.700	0.300 to 9.640
SarS et al., 2012	243	18	17	1	1.259	0.179 to 8.875
Rugiu MG et al., 2009	49	22	4	1	1.796	0.320 to 10.085
Total (fixed effects)					1.583	0.562 to 4.457
Total (random effects)					1.593	0.565 to 4.494
<i>Test for heterogeneity:</i>					0.07977	
Q					2	
DF					0.9609	
Significance level					0.00%	
I ² (inconsistency)					0.00 to 15.89	
95% CI for I ²						

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

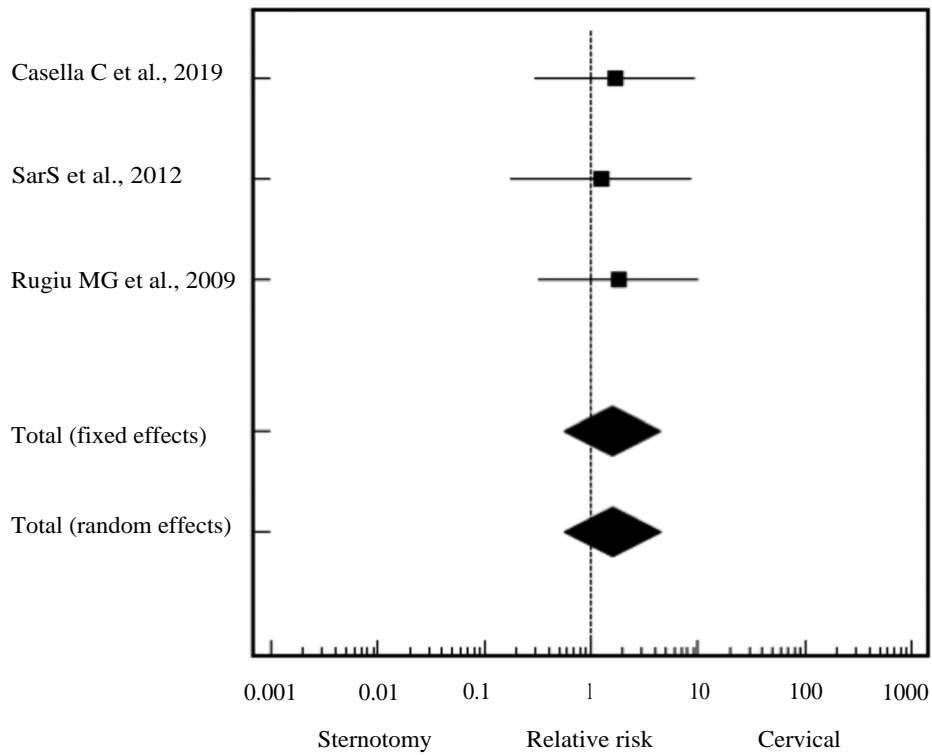


Fig. (6): Forest plot for Asymptomatic.

Table (15): Meta-analysis for symptomatic.

Study	Cervical		Sternotomy		RR	95 % CI
	Total	Event	Total	Event		
Casella C et al., 2019	40	23	4	3	0.767	0.410 to 1.433
SarS et al., 2012	243	31	17	16	0.136	0.0956 to 0.192
Rugiu MG et al., 2009	49	21	4	3	0.571	0.298 to 1.096
Hashmi SM et al., 2006	13	13	6	6	-	-
Total (fixed effects)					0.279	0.215 to 0.361
Total (random effects)					0.381	0.113 to 1.285
<i>Test for heterogeneity:</i>			31.0551			
Q			2			
DF			<0.0001 *			
Significance level			93.56%			
I ² (inconsistency)			84.56 to 97.31			
95% CI for I ²						

Q : Total variance for heterogeneity.

RR: Relative Risk.

I² : Observed variance for heterogeneity.

CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

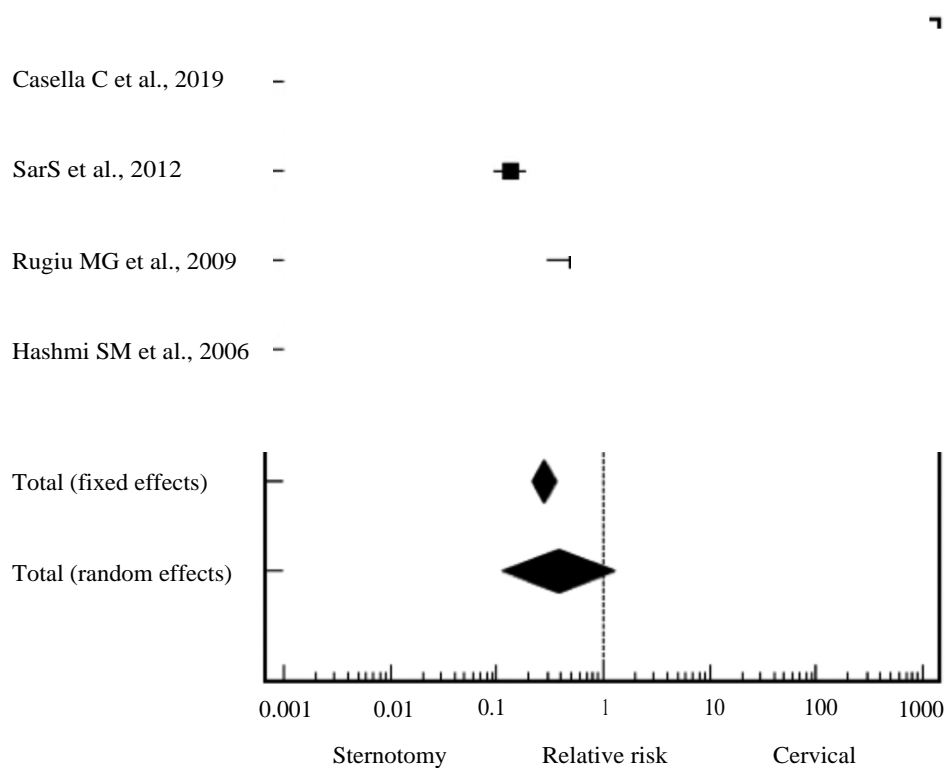


Fig. (7): Forest plot for symptomatic.

Table (16): Meta-analysis for temporary recurrent laryngeal nerve palsy.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Wang X et al., 2020	112	6	3	0	0.460	0.0310 to 6.834
SarS et al., 2012	243	11	17	1	0.770	0.105 to 5.614
Sakkary MA et al., 2012	66	8	7	0	2.030	0.129 to 31.955
Rugiu MG et al., 2009	49	1	4	0	0.300	0.0140 to 6.435
Cichon ´ S et al., 2008	88	16	27	8	0.614	0.295 to 1.275
Hashmi SM et al., 2006	13	3	6	2	0.692	0.154 to 3.119
Total (fixed effects)					0.682	0.381 to 1.222
Total (random effects)					0.646	0.361 to 1.158

Test for heterogeneity:

Q	1.0534
DF	5
Significance level	0.9581
I ² (inconsistency)	0.00%
95% CI for I ²	0.00 to 0.00

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

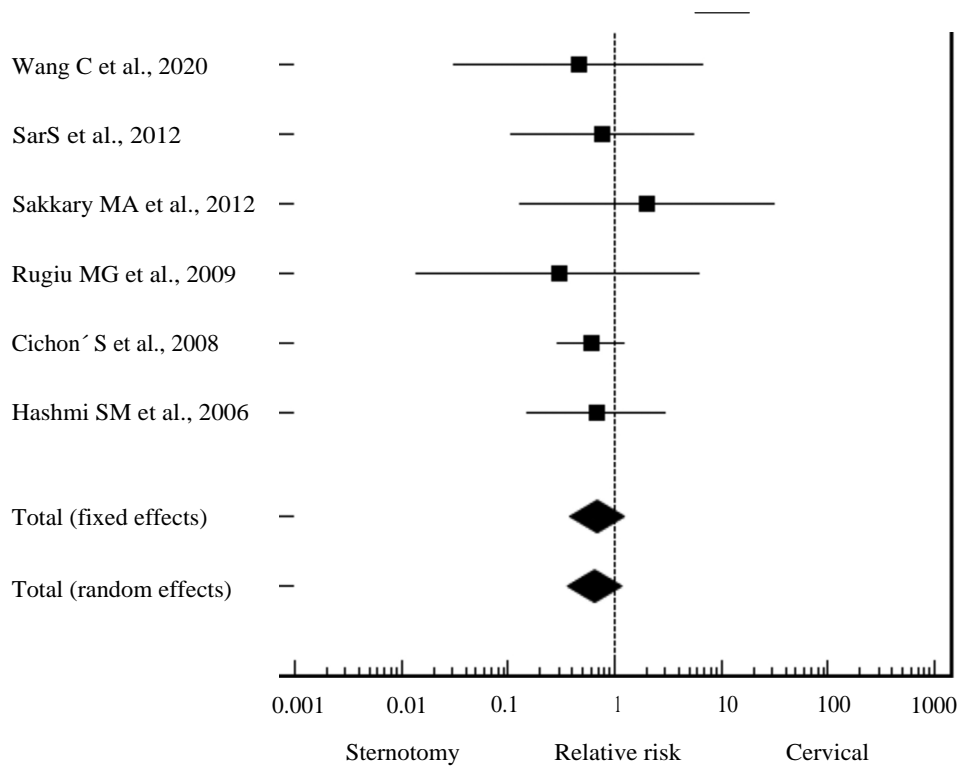


Fig. (8): Forest plot for temporary recurrent laryngeal nerve palsy.

Table (17): Meta-analysis for Permanent recurrent laryngeal nerve palsy.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Wang X et al., 2020	112	1	3	0	0.106	0.00507 to 2.223
Rugiu MG et al., 2009	49	0	4	0	–	–
Cichon´ S et al., 2008	88	5	27	2	0.767	0.158 to 3.732
Total (fixed effects)					0.609	0.152 to 2.429
Total (random effects)					0.435	0.0718 to 2.632

Test for heterogeneity:

Q	1.3480
DF	1
Significance level	0.2456
I ² (inconsistency)	25.82%
95% CI for I ²	0.00 to 0.00

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

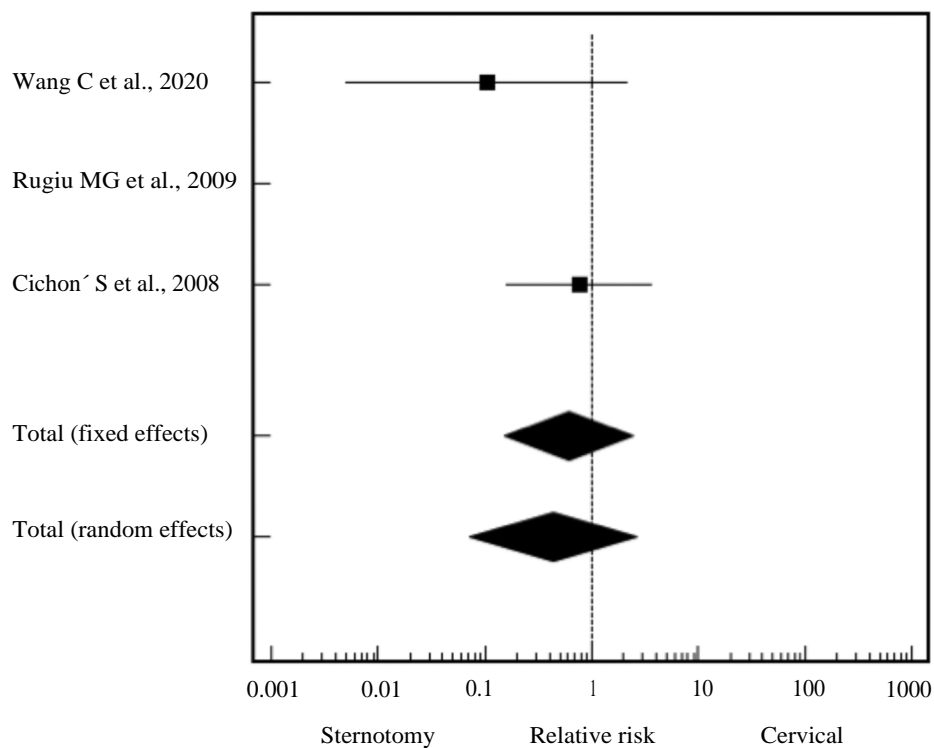


Fig. (9): Forest plot for Permanent recurrent laryngeal nerve palsy.

Table (18): Meta-analysis for Temporary Hypoparathyroidism.

Study	Cervical		Sternotomy		RR	95% CI
	Total	Event	Total	Event		
Wang X et al., 2020	112	16	3	10	0.0429	0.0429 to 0.0429
SarS et al., 2012	243	48	17	5	0.672	0.308 to 1.463
Cichon´ S et al., 2008	88	6	27	0	4.090	0.238 to 70.350
Total (fixed effects)					0.346	0.236 to 0.505
Total (random effects)					0.000	0.000 to 0.000

Test for heterogeneity:

Q	-
DF	2
Significance level	1.000
I ² (inconsistency)	-
95% CI for I ²	-

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

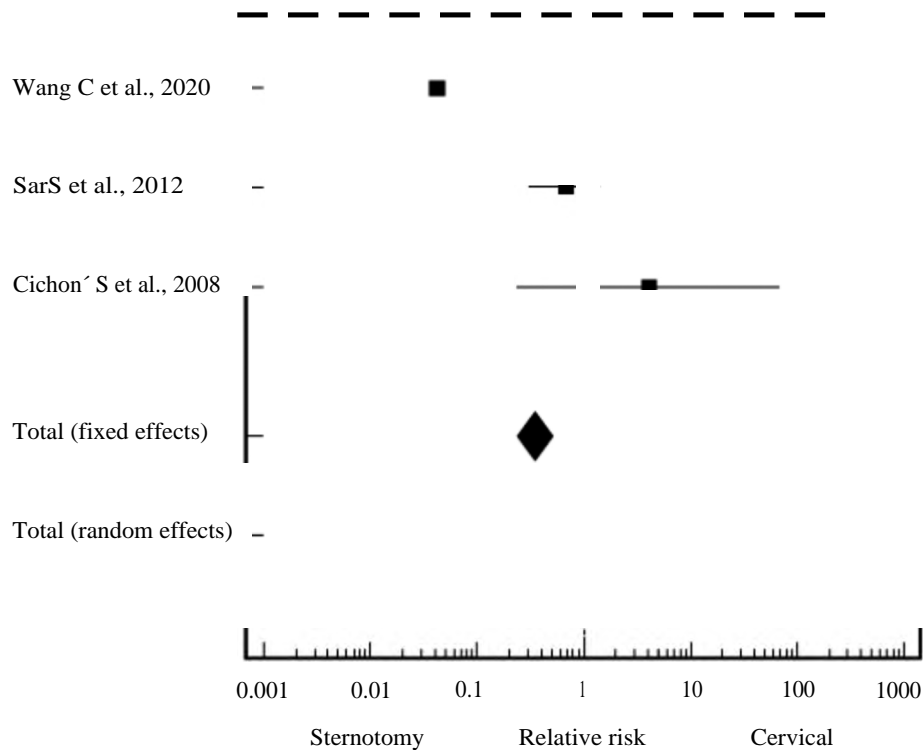


Fig. (10): Forest plot for Temporary Hypoparathyroidism.

Table (19): Meta-analysis for Temporary Hypocalcemia.

Study	Cervical		Sternotomy		RR	95 % CI
	Total	Event	Total	Event		
Wang X et al., 2020	112	23	3	2	0.308	0.128 to 0.742
Cvasciuc IT et al., 2017	45	9	53	1	10.600	1.396 to 80.505
Nankee L et al., 2015	120	11	7	0	1.521	0.0982 to 23.541
Sakkary MA et al., 2012	66	20	7	2	1.061	0.311 to 3.618
RUGIU MG et al., 2009	49	5	4	2	0.204	0.0565 to 0.737
Total (fixed effects)					1.297	0.722 to 2.330
Total (random effects)					0.871	0.190 to 3.996
<i>Test for heterogeneity:</i>						
Q					22.4772	
DF					4	
Significance level					0.0002*	
I ² (inconsistency)					82.20%	
95% CI for I ²					59.04 to 92.27	

Q : Total variance for heterogeneity.
 RR: Relative Risk.
 I² : Observed variance for heterogeneity.
 CI: Confidence interval (LL: Lower limit -UL: Upper Limit).

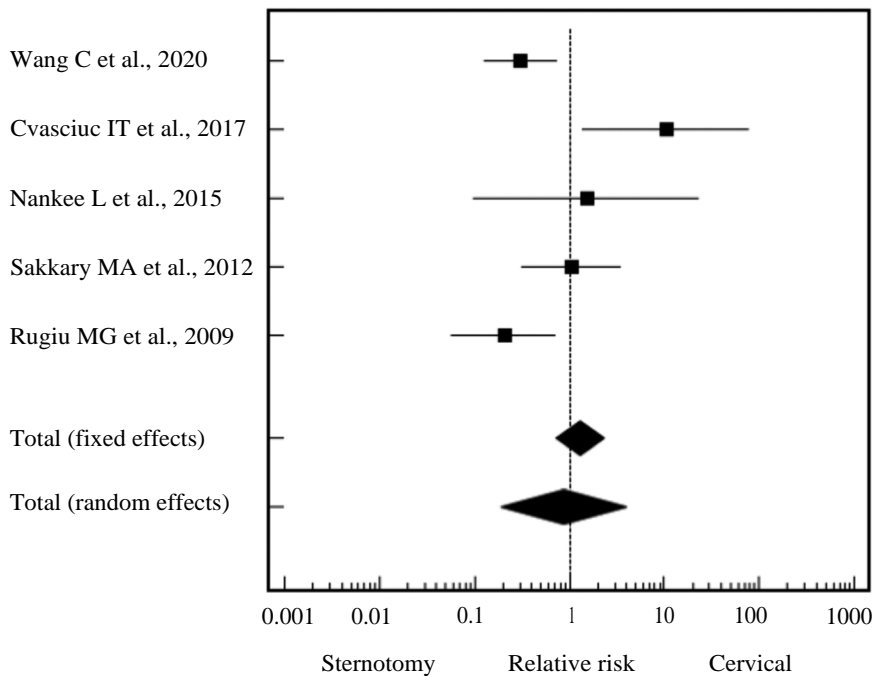


Fig. (11): Forest plot for Temporary Hypocalcemia.

Discussion

Thyroidectomy for retrosternal goitre is usually carried out through a cervical incision. Around 4-12% of patients require an extracervical approach, usually by sternotomy which has two approaches open and thoracoscopic [21].

Consequently, this study was conducted and aimed to perform a systematic review/meta-analysis to identify and assess factors that affect decision

making in huge retrosternal goiter, whether sternotomy might be or might not be needed. And to assess the different tools used in decision making.

This systematic review was conducted following the Cochrane Handbook for Systematic Reviews of Interventions. We also adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines during the design of our study. We conducted a literature search using PubMed, Scopus, Web of Science, and Cochrane

Library. Clinical studies were conducted from January 2000 till August 2022 using MEDLINE/PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov., EMBASE, Web of Science, SCOPUS, and Grey Literature Searching, and journals related to the topic by using these keywords: Huge goiter, retrosternal, total thyroidectomy, sternotomy, and cervicothoracic approach.

Mostafa et al., [22] concluded that the cervical approach for patients with RSG extending to the aortic arch is an optimum, feasible and less invasive surgical approach that can be considered the appropriate choice in such cases and can be performed successfully by experienced specialized surgeons. Thoracic surgeon standby is required in a few selected cases which carry a chance that sternotomy might be needed.

Cvasciuc et al., [13] reported that the shape and size of goitres is important in carefully planning surgery. CT imaging with cross-sectional reconstruction should be analysed before operation. The proposed classification helps treatment planning and allows comparison of outcomes by anatomical complexity. 847 thyroidectomies were performed with $n=98$ involving RSGs. Type A ($n=47$) are RSG with a shape of a "cone" or pyramid with the apex pointing down. Cervicotomy is the usual approach. Type B ($n=39$) are goitres with a shape of a "pyramid" with the apex pointing up, cervicotomy with \pm manubriectomy or sternotomy \pm thoracotomy maybe required. Type C ($n=6$) are thyroid enlargements in the mediastinum connected by a pedicle with the thyroid in the neck. A cervical approach \pm manubriectomy or sternotomy \pm thoracotomy is needed. Type D ($n=6$) are true intrathoracic or "forgotten" goitres. Sternotomy is indicated for thyroids in the anterior mediastinum though a thoracic approach for those located in the posterior mediastinum might be needed.

Nankee et al., [14] concluded that sternotomy for SSG is rare. All patients necessitating sternotomy had extension below the aortic arch and were more likely to present complaining of chest pressure and voice issues. Of the 220 patients, 127 patients (58%) had SSG, of whom 7 (5.5%) required sternotomy. All patients who underwent sternotomy underwent preoperative computed tomography scanning and were more likely to have preoperative symptoms of chest pressure and voice complaints and have extension of the thyroid gland below the aortic arch. Sternotomy took an average of 2 hours longer than a cervical incision, was associated with significantly more blood loss (600 versus 190mL,

$p=0.04$), and a longer length of stay (3.1 versus 1.8d, $p=0.03$) than cervical thyroidectomy.

10 studies were included 9 were retrospective and 1 were prospective study, 1094 cases were included with mean age was years 61.2 years.

Mean weight of thyroid was 156.3 g and thyroid weight was significant higher among sternotomy procedure vs cervical.

Meditational extension was above AA (59), Below AA (13), at AA (17), Tracheal compression founded among 255 cases and previous thyroid surgery in 64 cases.

Wang et al., [11] reported that retrosternal goiter surgery is challenging for surgeons. The best surgical approach for the patient should be based on CT scan evaluation. Based on preoperative CT imaging and in-operation evaluation, 50% of the tumor volume was located below the thoracic inlet and 50% of the tumor volume was located above the thoracic inlet in almost all of the patients. Both sections could be successfully removed via a cervical incision, and no obvious complications were observed during the perioperative period. With careful planning and execution before surgery and meticulous operation during surgery, most retrosternal goiters can be safely treated by cervical approach.

An average from 2 to 8% of substernal goiters require removal through a combined approach with cervicotomy and partial or total sternotomy [18].

Pata et al., [23] reported that sternotomy extends the operative field, facilitating dissection, decreasing the risk of recurrent nerve lesions and helping hemostasis in lesions of mediastinal goiter's vessels in case of occurrence.

Coskun et al., [6] reported that up today it is difficult to preoperatively identify the right surgical field extension and several Authors have highlighted how various factors may affect the choice of surgical treatment.

Sari et al., [24] concluded that it has been underlined that the presence in the mediastinum of a high density thyroid tissue evaluated by TAC is a highly indicative factor for the execution of an associated sternotomy.

For Riffat et al., [15] the indication to sternotomy depends on a few factors: The extension of the goiter below the hull, documented at the preoperative TAC, than the posterior mediastinal extension, the presence of ectopic nodules and the conical

shape of the goiter when it is compressed by a narrow thoracic higher isthmus.

According to Qureishi et al., [25] predictive factors of an associated surgical approach are: The extension under the aortic arch or in the posterior mediastinum, the handlebar form, the discrepancy between chest diameter and the one of the goiter.

Santini et al., [26] stated that a sternotomy is necessary when the goiter has an extension below the aortic arch with chest compression symptoms.

Di Crescenzo et al., [27] stated that a cervicotomic approach associated with sternotomy allows a safe resection of large thyroid masses in close proximity to mediastinal structures and it is also necessary in other cases, including the presence of thyroiditis.

Valerie et al., [28] also created a Difficulty Scale to identify predictors of difficult thyroidectomy. Among the factors that have been statistically associated with longer operating times and increased complications, there is the presence of anti-Tg Ab antibodies, therefore again in the context of thyroiditis.

The predictive factors for a “difficult thyroidectomy” and the consequent risks of surgical complications are well described in a large Italian multicentric series as regard Conzo et al., [29].

Gambardella et al., [30] reported that it is essential to predict, for example, the risk of a recurrent nerve injury, considering that it does not always depend on an error of the surgeon. Similarly, it is essential to predict the risk of any additional surgical access, such as sternotomy.

Mean operative time was 175.7, mean blood loss was 114.6 and hemorrhage was of insignificant differences between sternotomy procedure and cervical approach.

As regard operative method; total thyroidectomy (35), non-total thyroidectomy (178), final pathology was benign (261), and malignant (44), mean hospital stay was 3 days.

Cervical approach used in 856 and sternotomy in 145 cases, 170 symptomatic/175 asymptomatic in cervical vs 9 symptomatic/22 asymptomatic in sternotomy, tracheal compression founded in 211/856 cervical vs 67/145 sternotomy, mean thyroid weight was 175.6 in cervical vs 249.6 in sternotomy.

ITG can remain asymptomatic for many years until compression of the structures located in the thoracic inlet occurs. The most common symptoms are compressive ones: Compression of adjacent organs such as trachea, oesophagus and major vessels induces dyspnea, dysphagia, chronic cough, hoarseness, superior vena cava syndrome, and even haemoptysis. Otherwise, mechanical compression can be life-threatening because of the limited space below the thoracic inlet Rodrigues et al., [31].

Most of authors agree that medical treatment is ineffective for ITG and surgery is the treatment of choice especially in symptomatic forms. Even in the absence of clinical symptoms, surgery is a necessity considering the risks of malignancy and compression. But, surgical removal of ITG is a challenging procedure. The major problem is the adequate approach.

Cervical approach is sufficient in the vast majority even in patients with significant intrathoracic component. Whereas, extra cervical approach is required in 25% of thyroidectomies for ITG. Some authors have reported an incidence of sternotomy in 29% of cases, in patients in whom the gland cannot be safely resected through a cervical incision due to the volume of the tumor and the intimate contact with major vessels Wang et al. [11]; Cohen [32] and de Perrot et al. [33].

Several series have examined significant pre-operative predictive factors of the need for sternotomy. Most of authors recommended sternotomy for posterior mediastinal goiter with contra lateral extension, ectopic goiters with mediastinal blood supply, goiters causing superior vena cava syndrome, significant tracheal deviation, goiters extending below the aortic arch, when the diameter of the mediastinal nodule significantly exceeds the diameter of the thoracic inlet and revision surgery. Some authors stated that sternotomy is inevitable when a 70% of the goiter resides within the mediastinum Rolighed et al., [34] and Friedman et al., [35].

Other thoracic approaches such as posterolateral thoracotomy, anterior thoracotomy and thoracoscopic approach have been described for rare cases in which the goiter is predominantly intrathoracic Rolighed et al., [34] and Friedman et al., [35].

Posterolateral thoracotomy is rarely indicated, essentially in EITG or posterior goiters with superior vena cava syndrome. According to Merlier and Eschapasse, it is useless and very uncomfortable. Anterior thoracotomy in the 2nd or 3rd intercostal space in combination with cervi-

cotomy is uncommon, used essentially in right goiters in order to push up the lower pole Flati et al., [36].

It is easier to perform and aesthetically invisible especially for women. It does not oblige to change the position of the patient intraoperatively and gives a view of the superior mediastinum. Video-assisted thoracoscopy have rarely been described in the literature. In our study, VTS was used in a case of autonomous goiter. Robotic techniques have also been described recently Hajhosseini et al., [37].

An American study conducted in 2016 showed that patients operated for ITG had significantly more complications than patients operated on for cervical goiter. However, other authors were against Sancho et al. [38]; Christou and Mathonnet [39].

RLNP is the most common complication. Its mechanism corresponds to a stretching or even a section of the nerve during extraction maneuvers, especially at the right side. RLNP is seen mainly in voluminous goiters. It is usually unilateral and transient Hashmi et al. [20]; Pieracci and Fahey [40] and Hedayati and McHenry [41].

Both patients had large goiter (>9cm). There is relative agreement in the literature that the risk of RLNP seems to be higher with ITG surgery than in cervical goiter (2-10% versus 0.3-2%). Goudet et al., [42] made a comparative study between ITG and cervical ones. He found 3% of permanent RLNP in the thoracic group versus 0% in the cervical group but the difference was not significant ($p=0.06$). For Goudet and Yann-Sheng Li, sternotomy increases the likelihood of RLNP increases.

Hypoparathyroidism, another complication that seems to be more important in ITG surgery and which requires hormone replacement therapy. Some authors such as Erbil considered this risk to be higher in total thyroidectomy due to extracapsular dissection as regard Erbil et al., [43].

Recurrent laryngeal nerve palsy was temporary [45], permanent (6) in cervical vs temporary (11), permanent (2) in sternotomy.

Chandrasekhar et al., [44] reported that voice changes following thyroid surgery are common. Subjective changes in sound without significant nerve damage occur in 30% to 87% of patients.

Truong and Dickerson [45] noted that recurrent laryngeal nerve palsy suggests locally invasive thyroid malignancy. In contrast, recurrent laryngeal

nerve palsy caused by benign MNGs or ectopic thyroid tissue accounts for only 1% of cases.

When symptoms like voice (hoarseness) appear, the recurrent laryngeal nerve is considered to be damaged. Bilateral recurrent laryngeal nerve palsy can be associated with acute airway obstruction and the need for tracheostomy or other airway widening procedures as regard Chandrasekhar et al., [44].

Some of the main reasons for recurrent laryngeal nerve injury reasons are: (I) The normal route of the RLN has been altered by a space-occupying lesion, with a greater impact on the right side than on the left as reported by Lin et al., [8] and Shindo et al. [46]; (II) The recurrent laryngeal nerve has spread to the posterior surface of the goiter; or (III) bilateral cervical goiter as reported by Vaiman et al., [47].

The reported incidence of temporary and permanent RLN palsy after thyroid operations is 9.8% and 2.3%, respectively [48].

Hypoparathyroidism was temporary (70) in cervical vs temporary (5) in sternotomy, hypocalcemia was temporary (68), permanent (2) in cervical vs temporary (7), permanent (2) in sternotomy.

Edefe et al., [49] reported that hypoparathyroidism and hypocalcaemia are the most common complications following thyroid surgery. Surgery for retrosternal goiter means increasing the risk of hypocalcemia due to more difficulty in identifying the parathyroid glands.

Marcinkowska et al., [50] and Docimo et al., [51] reported that postoperative hypocalcemia is defined as serum calcium below 2.1mmol/L, and hypoparathyroidism is defined as a postoperative serum PTH below 14.5pg/mL. The incidences of temporary and permanent postoperative hypoparathyroidism range between 7% to 60% and 0% to 9%, respectively, and the incidence of postoperative hypocalcaemia is in the range of 1% to 50%.

Recent multicentric analysis conducted by Testini et al., [52] showed that the incidence rate of permanent hypocalcaemia was 2.1% and 2.9% when cervical and extracervical approaches were adopted, respectively. In patients who undergo secondary or even multiple surgery, which can increase adhesion to the surrounding tissue, the risk of hypocalcaemia it is perceived to be higher.

We reported a total of 32 complications in cervical approach in form of tracheomalacia, hemorrhage, visceral injury, fistula, pneumothorax/

pneumonia, Wound problems, and 9 complications in sternotomy in form of pleural effusion, hemorrhage, pneumothorax/pneumonia, tracheomalacia, wound problems. Three studies showed tracheal deviation/compression found significant higher among sternotomy procedure vs cervical. Pneumothorax/pneumonia and tracheomalacia were found insignificant differences between sternotomy procedure and cervical.

Conclusion:

The cervical approach for patients with RSG extending to the aortic arch is an optimum, feasible and less invasive surgical approach that can be considered the appropriate choice in such cases and can be performed successfully by experienced specialized surgeons. Thoracic surgeon standby is required in a few selected cases which carry a chance that sternotomy might be needed.

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معايير استخدام طريقة شق الرقبة والصدر في تضخم الغدة الدرقية الممتدة خلف عظمة القص : دراسة مرجعية

الخلفية: تختلف تعريفات الغدة الدرقية الممتدة خلف عظمة القص، حيث يصف بعض الغدة الدرقية الممتدة خلف عظمة القص عندما تمتد إلى قوس الأبهر، بينما يصف آخرون الغدة الدرقية الممتدة خلف عظمة القص على أنها ورم يمتد إلى الفقرات الصدرية الرابعة على صورة الأشعة السينية للصدر.

هدف الدراسة: إجراء استعراض منهجي تحليل / شامل لتحديد وتقييم العوامل التي تؤثر على عملية صنع القرار في حالة الغدة الدرقية الممتدة خلف عظمة القص الكبيرة، سواء كان من الممكن أو لم يكن من الممكن الاستغناء عن الجراحة بالفتح الصدرى. وتقييم الأدوات المختلفة المستخدمة في عملية صنع القرار.

المواد والطرق: تم إجراء هذا الاستعراض المنهجي وفقاً لكتيب كوكرين للمراجعات المنهجية للتدخلات. كما اتبعنا توجيهات تقارير المراجعات المنهجية والتحليلات الإحصائية (PRIMA) خلال تصميم الدراسة. أجرينا بحثاً في الأدبيات باستخدام قواعد البيانات الطبية الرئيسية، مثل PubMed و Scopus و Web of Science و Cochrane Library وتم البحث في الدراسات السريرية التي أجريت من يناير ٢٠٠٠ حتى أغسطس ٢٠٢٢ باستخدام MEDLINE/PubMed والتسجيل المركزى المراقب للتجارب السريرية (CENTRAL) و Trials.gov و Clinical و EMBASE و Web of Science و SCOPUS، وقمنا بالبحث في المجلات المتعلقة بالموضوع باستخدام الكلمات الرئيسية الآتية: cervicothoracic approach and sternotomy, total thyroidectomy, retrosternal, huge goiter.

النتائج: تم الإبلاغ عن مجموعة من مضاعفات نهج شق الرقبة بما في ذلك تشوه فى القصبة الهوائية، النزيف، الإصابة الحشوية، الهواء النافر، الالتهاب الرئوى، ومشاكل الجرح، وتم الإبلاغ عن تسعة مضاعفات فى نهج الشق الصدرى بما فى ذلك تجمع السائل البلورى فى الجنب، والنزيف، الهواء النافر، تشوه فى القصبة الهوائية، ومشاكل الجرح. أظهرت ثلاث دراسات تحول / ضغط فى القصبة الهوائية أكثر بشكل ملحوظ فى نهج الشق الصدرى مقارنة بنهج الشق الرقبى. ولكن لم يتم العثور على فروق ذات دلالة إحصائية بين نهج الشق الصدرى والشق الرقبى بشأن تشوه فى القصبة الهوائية أو الهواء النافر.

الاستنتاج: يعد الشق الرقبى للمرضى الذين يعانون من تضخم الغدة الدرقية وتمتد إلى الشريان الأبهرى نهجاً مثالياً وسهل الإجراء وأقل تدخلاً جراحياً ويمكن النظر فيه كخيار مناسب فى مثل هذه الحالات ويمكن تنفيذه بنجاح من قبل جراحين متخصصين وذوى خبرة. ومن المهم أن يكون جراح الصدر جاهزاً فى حالات معينة تحتم استخدام النهج الصدرى.