

Systematic Review

Supraglottoplasty for Laryngomalacia with Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis

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Objectives/Hypothesis: To determine if apnea-hypopnea index (AHI) and lowest oxygen saturation (LSAT) improve following isolated supraglottoplasty for laryngomalacia with obstructive sleep apnea (OSA) in children.

Study Design: Systematic review and meta-analysis.

Methods: Nine databases, including PubMed/MEDLINE, were searched through September 30, 2015.

Results: A total of 517 studies were screened; 57 were reviewed; and 13 met criteria. One hundred thirty-eight patients were included (age range: 1 month–12.6 years). Sixty-four patients had sleep exclusive laryngomalacia, and in these patients: 1) AHI decreased from a mean (M) \pm standard deviation (SD) of 14.0 ± 16.5 (95% confidence interval [CI] 10.0, 18.0) to 3.3 ± 4.0 (95% CI 2.4, 4.4) events/hour (relative reduction: 76.4% [95% CI 53.6, 106.4]); 2) LSAT improved from a M \pm SD of $84.8 \pm 8.4\%$ (95% CI 82.8, 86.8) to $87.6 \pm 4.4\%$ (95% CI 86.6, 88.8); 3) standardized mean differences (SMD) demonstrated a small effect for LSAT and a large effect for AHI; and 4) cure (AHI < 1 event/hour) was 10.5% (19 patients with individual data). Seventy-four patients had congenital laryngomalacia, and in these patients: 1) AHI decreased from a M \pm SD of 20.4 ± 23.9 (95% CI 12.8, 28.0) to 4.0 ± 4.5 (95% CI 2.6, 5.4) events/hour (relative reduction: 80.4% [95% CI 46.6, 107.4]); 2) LSAT improved from a M \pm SD of $74.5 \pm 11.9\%$ (95% CI 70.9, 78.1) to $88.4 \pm 6.6\%$ (95% CI 86.4, 90.4); 3) SMD demonstrated a large effect for both AHI and LSAT; and 4) cure was 26.5% (38 patients with individual data).

Conclusion: Supraglottoplasty has improved AHI and LSAT in children with OSA and either sleep exclusive laryngomalacia or congenital laryngomalacia; however, the majority of them are not cured.

Key Words: Obstructive sleep apnea, supraglottoplasty, laryngomalacia, systematic review, meta-analysis.

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INTRODUCTION

Pediatric sleep disordered breathing is a common problem. An epidemiological systematic review and meta-analysis¹ estimated that the prevalence of pediatric snoring is 7.45% (95% confidence interval [CI], 5.75%–9.61% based on

parent observations) and that the prevalence of pediatric obstructive sleep apnea (OSA) is 1% to 4%. Pediatric OSA severity is classified as: no OSA: apnea-hypopnea index (AHI) < 1 ; mild OSA: AHI 1 to < 5 ; moderate OSA: AHI 5 to < 10 ; and severe: AHI ≥ 10 events/hour.² In children, treatment options include adenotonsillectomy,³ myofunctional therapy,⁴ palate expansion,⁵ and allergy management. The success rate for adenotonsillectomy normalizing AHI (< 1 event/hour) was found to be between 59.8% and 82.9% based on two meta-analyses.^{3,6} There is a subset of children with OSA who additionally have laryngomalacia (a disorder in which supraglottic tissue collapses and subsequently obstructs normal airflow). The collapse of supraglottic structures can lead to inspiratory stridor, which may get worse a few months after birth.⁷ Triggers for stridor include upper respiratory infections, feeding, crying, agitation, and the supine position.⁷

In traditional (congenital) laryngomalacia, patients have symptoms during wakefulness and sleep; however, some patients have supraglottic collapse only during sleep, which we term *sleep exclusive laryngomalacia*. Typically, patients with congenital laryngomalacia present early given that there can be failure to thrive and significant respiratory distress at times with cyanosis, retractions, and/or witnessed apneic events.⁸ Sleep exclusive

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laryngomalacia has been described as occult laryngomalacia,² late-onset laryngomalacia,⁹ state-dependent laryngomalacia,¹⁰ and sleep-dependent laryngomalacia.¹¹ Sleep exclusive laryngomalacia patients can present in older children (2–18 years), has an estimated incidence of 3.9%, and can be diagnosed with drug-induced sleep endoscopy.¹² There have been studies reporting that supraglottoplasty has successfully treated or even cured OSA in patients with laryngomalacia; however, to our knowledge a systematic review of the literature with meta-analysis has not been performed. The primary objective was to determine whether the AHI and lowest oxygen saturation (LSAT) improve following isolated supraglottoplasty for both congenital and sleep exclusive laryngomalacia with obstructive sleep apnea in children. To complete the objective, a systematic review of the international literature was performed for polysomnography outcomes, as reported in children undergoing isolated supraglottoplasty as treatment for laryngomalacia with obstructive sleep apnea, and the data was used to perform a meta-analysis.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement was followed as much as possible during this study.¹³ As a systematic review of publically available articles, this study is exempted from institutional review board review.

Search Strategy

Four authors (M.C., B.D., J.S., R.G.) each independently searched initially on January 28, 2015, with an update through September 30, 2015 in Google Scholar, PubMed, Scopus, Embase, The Cochrane Library, Web of Science, Book Citation Index–Science, Cumulative Index to Nursing and Allied Health and Conference Proceedings Citation Index–Science from the inception of each database. Several terms, keywords, and phrases were searched. A PubMed search strategy is: (((supraglot*) AND (slee* OR snor* OR collapse OR apn* OR hypopn* OR oxygen)) OR ((supraglot* OR arytenoidectomy OR epiglottoplasty OR epiglottopexy OR Laryngomalacia/surgery* OR Glottis/surgery*) AND (laryngomalacia))) OR (“Laryngomalacia”[Mesh] AND (“Sleep Apnea Syndromes”[Mesh] OR sleep)).

Study Selection

Study inclusion criteria were as follows: 1) *patients*: children (< 18 years [y]) who have either congenital or sleep exclusive laryngomalacia and OSA; 2) *intervention*: isolated supraglottoplasty; 3) *comparison*: quantitative data pre- and postsupraglottoplasty; 4) *outcome*: polysomnography variables, general outcomes, and complications; and 5) *study design*: all designs were included in both published and unpublished forms and in all languages. Exclusion criteria were 1) studies with additional surgeries performed (unless individual patient data was reported for those undergoing isolated supraglottoplasties), 2) studies with qualitative outcomes only, and 3) patients with central sleep apnea.

Supraglottoplasty Surgeries

Based on the studies in this systematic review, the different kinds of supraglottoplasty surgeries performed specifically include: 1) unilateral aryepiglottic fold division, 2) bilateral aryepiglottic fold division, 3) bilateral aryepiglottic fold division

with unilateral removal of redundant arytenoid tissue, and 4) bilateral complete (bilateral aryepiglottic fold division and bilateral removal of redundant arytenoid tissues). In some patients, epiglottis surgery was also performed.

Study Quality Assessment

The National Institute for Health and Clinical Excellence (NICE) quality assessment tool¹⁴ was used to assess the quality of each individual study because it allows for assessment even when studies are the same level of evidence.

Statistics

The null hypothesis was that there is no difference in polysomnography outcomes pre- and post-supraglottoplasty. The IBM Statistical Package for Social Sciences software version 20.0 (Armonk, NY) was used for analyses. For two-tailed paired *t* tests, a *P* value < 0.05 was considered statistically significant. The Cochrane Collaboration's Review Manager Software (REVMAN) version 5.3 was used for the meta-analysis. REVMAN was used to calculate the mean differences (MD), standardized mean differences (SMD), and 95% CI. Cohen's guidelines¹⁵ were used for interpreting the SMD magnitude of effect (absolute value: small = 0.2, medium = 0.5, and large = 0.8). Inconsistency was evaluated with REVMAN's *I*² statistic, and the recommended cutoffs were followed (low inconsistency: 25%, moderate inconsistency: 50%, and high inconsistency: 75%).¹⁶ Heterogeneity between studies was evaluated by the Cochran *Q* statistic (*Q* statistic), and a *P* value ≤ 0.10 was considered to be statistically significant heterogeneity.¹⁷ If inconsistency and/or heterogeneity was present, REVMAN was used to perform a sensitivity analysis by removing one study at a time until inconsistency and/or heterogeneity no longer existed in order to identify which studies were the sources. If AHI and respiratory disturbance index (RDI) were reported in the study, the AHI was selected for statistical analysis. If RDI alone was reported in the study, the plan was to contact the authors to obtain the AHI. As recommended by the Cochrane Collaboration, a funnel plot assessment was performed if there were at least 10 studies evaluating any given variable. For individual patient data sub-analyses, the standard pediatric OSA severity classification was used: no OSA: AHI < 1, mild OSA: AHI 1 to < 5, moderate OSA: AHI 5 to < 10, and severe: AHI ≥ 10 events/hour.² Authors were contacted for studies that did not report enough data for meta-analysis to determine whether additional patient data could be obtained, which would allow inclusion in the analysis.

RESULTS

The searches yielded 517 studies, which were screened; 54 studies were reviewed in the full-text version; and after reviewing the references, another three studies were potentially relevant and were also reviewed (57 total).^{2,7–12,18–66} Thirteen studies met criteria for inclusion. Coauthor D.K.C. provided data from two studies (Chan (a) et al.²⁰ and Chan (b) et al.²) that excluded any duplicate patients and allowed for both studies to be included in the meta-analysis. After review of all the articles, only one article (Valera et al.⁶⁰) reported the RDI exclusively; the corresponding author was contacted, and upon review of the raw data the AHI and RDI were found to be the same. The corresponding author for the study by Tholpady et al.⁵⁹ was contacted to confirm whether any of the patients undergoing

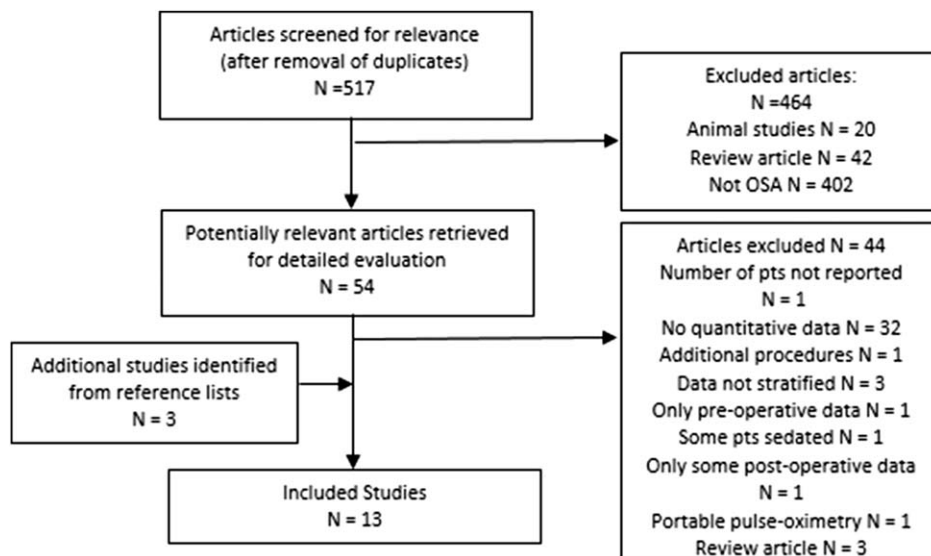


Fig. 1. Flow diagram for studies reporting polysomnographic data for patients undergoing isolated supraglottoplasty for laryngomalacia with OSA. N = number of studies; OSA = obstructive sleep apnea; pts = patients.

supraglottoplasty also underwent tonsillectomy, and the author replied that the patients did not; therefore, the study data could be included in the meta-analysis. Drs. Zafereo and Pereira confirmed that they always divide the aryepiglottic folds bilaterally, and then in 60% of the children in this study performed the unilateral supraglottoplasty, after that which consists of unilateral excision of the cuneiform cartilages and redundant mucosa. The corresponding author from Digoy et al.²³ was contacted twice in an attempt to obtain individual patient data; however, the attempts were unsuccessful. Figure 1 summarizes the study selection.

Forty-four studies were excluded for the following reasons: the number of patients undergoing polysomnography pre- and postsupraglottoplasty was not provided⁴³; no quantitative data for polysomnograms was provided^{12,18,21,22,24–26,28,29,32–39,41,42,44–46,49,51,53,54,56,58,61,64,66}; only adults were included¹⁹; procedure(s) were performed in addition to the supraglottoplasty with no stratification of data for those who underwent isolated supraglottoplasty^{27,50,63}; only preoperative data was available⁵⁵; some children were sedated with chloral hydrate⁴⁷; the postoperative data was only available for a fraction of patients³⁰; portable pulse-oximetry was used instead of formal polysomnography³¹; or they were review articles.^{40,52,62}

Overall, there were a total of 138 patients (ages 1 month–12.6 years) with quantitative polysomnographic data who underwent isolated supraglottoplasty. Sixty-four patients had sleep exclusive laryngomalacia, and 74 patients had congenital laryngomalacia.

Study Quality Assessment

Studies meeting criteria to be included in this review were case reports, case series studies, or case-control studies. The studies met three to six of the eight NICE quality-assessment tool criteria (see Table I).

Sleep Exclusive Laryngomalacia

Apnea-Hypopnea Index. Polysomnography outcomes for isolated supraglottoplasty demonstrated that the AHI decreased from a mean (M) ± standard deviation (SD) of 14.0 ± 16.5 (95% CI 10.0, 18.0) to 3.3 ± 4.0 (95% CI 2.4, 4.4) events/hour, see Table II. The MD was 10.7 events/hour (95% CI –14.9, –6.5). The relative reduction of the mean values was 76.4% (95% CI 53.6, 106.4%). A subanalysis using random effects modeling was performed for four studies (62 patients) in which M ± SD were reported, and the AHI MD was –9.38 events/hour (95% CI –12.67, –6.10), overall effect Z = 5.60, P value < 0.00001, Q statistic P value = 0.68 (no heterogeneity), I² = 0% (no inconsistency). The AHI SMD was –0.99 (95% CI –1.37, –0.62) (large magnitude of effect), overall effect Z = 5.17 P value < 0.00001, Q statistic P value = 0.91 (no heterogeneity), I² = 0% (no inconsistency).

Lowest Oxygen Saturation. The overall mean pre- and postsupraglottoplasty lowest oxygen saturation M ± SD were 84.8% ± 8.4% (95% CI 82.8, 86.8) and 87.6% ± 4.4% (95% CI 86.6, 88.8) (see Table II). A subanalysis with random effects modeling was performed for 62 patients in which M ± SD were reported, the MD was 1.79 points (95% CI –0.37, 3.96), overall effect Z = 1.62, P value = 0.10; Q statistic P value 0.29 (no heterogeneity) I² = 19% (low inconsistency). The sensitivity analysis demonstrated that after removal of the study by Chan (a) et al. there was no heterogeneity (Q statistic P value = 0.37) and no inconsistency (I² = 0%). The LSAT SMD was 0.40 (95% CI 0.04, 0.76) (small magnitude of effect), overall effect Z = 2.20 P value 0.03, Q statistic P value = 0.65 (no heterogeneity), and I² = 0% (no inconsistency).

Congenital Laryngomalacia

Apnea-Hypopnea Index. The AHI decreased from an M ± SD of 20.4 ± 23.9 (95% CI 12.8, 28.0) to 4.0 ± 4.5 (95% CI 2.6, 5.4) events/hour (38 patients) (see Table III). The MD was –16.4 events/hour (95% CI –21.9,

TABLE I.
General Characteristics and Quality Criteria of Included Studies.

Study's General Characteristics			Quality Assessment of Included Studies*										
Year, Study Authors, Design	Study Site	Ages	Evidence Level	Outcomes Analyzed	1	2	3	4	5	6	7	8	
2015, Mase et al., ¹¹ RCS	USA	17 mo (6–55)	4	AHI, MSAT, LSAT	no	yes	yes	yes	no	no	yes	yes	
2015, Tholpady et al., ⁵⁹ RCS	USA	NR	4	AHI	no	yes	yes	yes	no	no	yes	yes	
2013, Li et al., ⁶⁷ CC	China	1–21 mo	3	LSAT	no	yes	yes	no	no	no	yes	no	
2013, Oomen and Modi, ¹⁰ RCR	USA	5 mo	5	AHI, LSAT	NA	NA	NA	NA	NA	NA	NA	NA	
2012, Chan (a) et al., ²⁰ RCS	USA	6.8 ± 2.2 y	4	AHI, BMI, LSAT	no	yes	yes	yes	no	no	yes	yes	
2012, Chan (b) et al., ² RCS	USA	7.1 y	4	AHI	no	yes	yes	yes	no	no	yes	yes	
2012, Digoy et al., ²³ RCS	USA	1.2–12.6 y	4	AHI, LSAT	no	yes	yes	yes	no	yes	yes	yes	
2011, Powitzky et al., ⁸ RCS	USA	NR	4	AHI, LSAT	no	no	yes	yes	no	no	yes	yes	
2011, Revell and Clark, ⁹ RCS	USA	< 11.1 y	4	AHI	no	yes	yes	no	no	no	yes	no	
2009, O'Connor et al., ⁴⁸ RCS	Australia	2.3 mo (1–13)	4	AHI, LSAT	no	yes	yes	yes	no	no	yes	yes	
2009, Sesterhenn et al., ⁵⁷ RCS	Germany	2.4 ± 2.0 mo (1–7)	4	AHI, DI	no	yes	no	yes	no	no	yes	no	
2008, Zafereo et al., ⁶⁵ RCS	USA	4 ± 2.3 mo (1–9)	4	AHI, LSAT	no	yes	yes	yes	no	no	yes	yes	
2006, Valera et al., ⁶⁰ RCS	Brazil	7.1 mo (1–17)	4	AHI, LSAT	no	no	yes	yes	no	no	no	yes	

*Quality Assessment of cases series studies checklist from National Institute for Health and Clinical Excellence (NICE): 1) Was the case series collected in more than one center (i.e., multicenter study)? 2) Is the hypothesis/aim/objective of the study clearly described? 3) Are the inclusion and exclusion criteria (case definition) clearly reported? 4) Is there a clear definition of the outcomes reported? 5) Were data collected prospectively? 6) Is there an explicit statement that patients were recruited consecutively? 7) Are the main findings of the study clearly described? 8) Are outcomes stratified? (e.g., by abnormal results, disease stage, patient characteristics)?

A.H.I. = Apnea-Hypopnea index; BMI = body mass index; CC = case-control; DI = Desaturation index; LSAT = lowest oxygen saturation; mo = months; MSAT = mean oxygen saturation; NA = Not applicable; NR = Not reported; RCR = retrospective case report; RCS = retrospective case series; y = years.

–10.9), and the relative reduction was 80.4% (95% CI 46.6, 107.4%). A subanalysis with random effects modeling was performed for the six studies (38 patients) in which $M \pm SD$ were reported, and the AHI MD was –8.78 events/hour (95% CI –12.40, –5.17), overall effect $Z = 4.76$, P value < 0.00001, Q statistic P value = 0.19 (no heterogeneity), and $I^2 = 33\%$ (low inconsistency). The sensitivity analysis demonstrated that after removal of the study by O'Connor et al.,⁴⁸ there was no heterogeneity (Q statistic P value = 0.89) and no inconsistency ($I^2 = 0\%$). The AHI SMD was –1.21 (95% CI –1.83, –0.59) (large magnitude of effect), overall effect $Z = 3.84$, P value 0.0001, Q statistic P value = 0.91 (no heterogeneity), and $I^2 = 0\%$ (no inconsistency).

Lowest Oxygen Saturation. The overall mean pre- and postsupraglottoplasty lowest oxygen saturation was reported for 41 patients. The LSAT $M \pm SD$ were $74.5 \pm 11.9\%$ (95% CI 70.9, 78.1) and $88.4 \pm 6.6\%$ (95% CI 86.4, 90.4) (see Table III). A subanalysis with random effects modeling was performed for 41 patients in which $M \pm SD$ were reported: the MD was 12.18 points (95% CI 4.02, 20.34), overall effect $Z = 2.93$, P value = 0.003; Q statistic P value 0.006 (significant heterogeneity), and $I^2 = 76\%$ (high inconsistency). A sensitivity analysis demonstrated that after removal of the data from the study by Li et al.,⁶⁷ there was no heterogeneity (Q statistic P value = 0.31) and low inconsistency ($I^2 = 16\%$). The LSAT SMD was 1.31 (95% CI 0.32, 2.30) (large magnitude of effect), overall effect $Z = 2.60$, P value 0.009, Q statistic P value = 0.01 (significant heterogeneity), and $I^2 = 73\%$ (high inconsistency). The sensitivity analysis demonstrated that after removal of the study by Li et al.

there was no heterogeneity (Q statistic P value = 0.32) and low inconsistency ($I^2 = 12\%$).

The overall MDs, SMDs with the magnitude of effect based on Cohen's guidelines for AHI and LSAT are presented in Table IV.

Individual Patient Data Analysis

Nine studies^{9–11,20,48,57,59,60,65} provided individual patient data, whereas four studies did not.^{2,8,23,67} For patients with sleep exclusive laryngomalacia, cure (AHI < 1 event/hour) was observed in two out of 19 patients (10.5%). For patients with congenital laryngomalacia, cure was observed in 10 of 38 patients (26.5%).

Additional Outcomes

Studies reported several variables that improved after supraglottoplasty (see Table V). Mase et al. reported that the patients had increased postoperative weight for length percentile.¹¹ Li et al.,⁶⁷ Oomen and Modi,¹⁰ and Chan et al.² reported that the patients had no stridor after surgery. Li et al.⁶⁷ and Chan et al.² reported no feeding difficulties postoperatively. With regard to levels of stridor improvement, Zafereo et al.⁶⁵ noted mild improvement in 10% of patients, significant improvement in 70%, and complete resolution in 20%.

Complications

Digoy et al. reported that three of 36 children had a postoperative increase in coughing and throat clearing, and one had dysphagia for greater than 6 months.²³

TABLE II.
Sleep Exclusive Laryngomalacia.

Year, Study Authors	N	Pre-SG AHI	Post-SG AHI	Pre-SG Low O2	Post-SG Low O2
2015, Mase et al. ¹¹	9	23.5 ± 33.0 [1.9, 45.1]	4.8 ± 3.5 [2.5, 7.1]	82.7 ± 10.8 [75.6, 89.8]	88.3 ± 3.5 [86.0, 90.6]
2013, Oomen and Modi ¹⁰	1	10.2	2.4	88	89
2012, Chan (a) et al. ²⁰	8	12.4 ± 11.8 [4.2, 20.6]	5.0 ± 4.3 [2.0, 8.0]	89.8 ± 4.7 [86.5, 93.1]	89.3 ± 3.1 [87.1, 91.5]
2012, Chan (b) et al. ²	9	10.4 ± 8.8 [4.7, 16.2]	2.9 ± 3.2 [0.8, 5.0]	89.0 ± 4.0 [86.4, 91.6]	89.9 ± 2.8 [88.1, 91.7]
2012, Digoy et al. ²³	36	13.3 ± 12.9 [9.1, 17.5]	2.8 ± 4.3 [1.4, 4.2]	83.0 ± 8.6 [80.2, 85.8]	86.5 ± 4.9 [84.9, 88.1]
2011, Revell and Clark ⁹	1	2.5	0.3	-	-
<i>Total</i>	<i>64</i>	<i>14.0 ± 16.5 [10.0, 18.0]</i>	<i>3.3 ± 4.0 [2.4, 4.4]</i>	<i>84.8 ± 8.4 [82.8, 86.8]</i>	<i>87.6 ± 4.4 [86.6, 88.8]</i>

Demographic and polysomnographic data pre- and postsupraglottoplasty.

[] denotes lower and upper 95% confidence intervals, - denotes not reported.

AHI = apnea-hypopnea index; low O2 = lowest oxygen saturation; N = number; SG = supraglottoplasty.

Powitzky et al. reported that one of 20 patients required a revision supraglottoplasty, whereas five required an adenotonsillectomy to alleviate their OSA.⁸ O'Connor et al. reported that during surgery, one patient developed a collapse of a pulmonary lobe on the left side due to the endotracheal tube being in the right main bronchus.⁴⁸ In the study by Sesterhenn et al., a revision epiglottopexy was performed for suture dehiscence, and once the revision was performed the patient dramatically improved.⁵⁷ Four studies reported no significant or major complications (see Table V).

DISCUSSION

There are five main findings from this study. First, this review has demonstrated that sleep exclusive laryngomalacia and congenital laryngomalacia have different presentations and are comprised of distinct groups of patients. In the currently published studies, all children with sleep exclusive laryngomalacia have been diagnosed via drug-induced sleep endoscopy (DISE). Forty-eight of 62 (77.4%) of the children in this systematic review with sleep exclusive laryngomalacia were diagnosed after having failed adenotonsillectomy. Children with sleep exclusive laryngomalacia are typically diagnosed at an older age (around 2–12 years), with a few studies reporting the diagnosis in children under 2 years of age. On the other hand, congenital laryngomalacia, as the name implies, is identified soon after birth, and the children will classically present with stridor and respiratory difficulty. In all studies evaluating congenital laryngomalacia with OSA, flexible or awake laryngoscopy was used for diagnosis, and DISE was additionally performed in four of eight studies reporting supraglottoplasty outcomes.

Second, children with OSA and either sleep exclusive laryngomalacia or congenital laryngomalacia can have improvement in AHI after supraglottoplasty. In children with sleep exclusive laryngomalacia and OSA, supraglottoplasty decreased the AHI from a M ± SD of 14.0 ± 16.5 (95% CI 10.0, 18.0) to 3.3 ± 4.0 (95% CI 2.4, 4.4), and when evaluating the SMD, the magnitude of effect was large (Cohen's guidelines), with a value of -0.99 (-1.37, -0.62). In clinical practice, the diagnosis

of sleep exclusive laryngomalacia is made with DISE; therefore, in children who fail adenotonsillectomy, DISE could potentially help localize the site of obstruction (lingual tonsils, epiglottis, arytenoids, etc.). In children with congenital laryngomalacia and OSA, supraglottoplasty decreased AHI from a M ± SD of 20.4 ± 23.9 (95% CI 12.8, 28.0) to 4.0 ± 4.5 (95% CI 2.6, 5.4) events/hour, and the SMD for congenital laryngomalacia was -1.26 (-1.79, -0.73), which corresponds to a large effect.

Third, children with OSA and either sleep exclusive laryngomalacia or congenital laryngomalacia can have improvement in LSAT after supraglottoplasty. In children with sleep exclusive laryngomalacia and OSA, supraglottoplasty improved the LSAT from a M ± SD of 84.8 ± 8.4% (95% CI 82.8, 86.8) to 87.6 ± 4.4% (95% CI 86.6, 88.8), and the SMD demonstrated a small magnitude of effect overall. Two studies did not demonstrate a large improvement: the study by Chan (b)² et al. reported a 0.9 point increase in the LSAT in nine patients, and Chan (a)²⁰ et al. reported a 0.5 point decrease in the LSAT in eight patients after supraglottoplasty—and why this occurred is unclear. For congenital laryngomalacia, the LSAT improved from a M ± SD of 74.5 ± 11.9% (95% CI 70.9, 78.1) to 88.4 ± 6.6% (95% CI 86.4, 90.4), with the SMD demonstrating a large magnitude of effect. The most dramatic improvement in LSAT was reported in the study by Li et al.,⁶⁷ who reported a 21.5 point improvement in LSAT after surgery, which is likely secondary to the study specifically selecting infants with severe laryngomalacia. Overall, supraglottoplasty improved the lowest oxygen saturation by 2.8 points in sleep exclusive laryngomalacia patients (Table II) and by 13.9 points in congenital laryngomalacia patients (Table III).

Fourth, when the subanalyses were performed by using random effects modeling to evaluate if there was a study or a group of studies that stood apart from the rest as having better or worse than expected outcomes, there was no study with significant differences for AHI in sleep exclusive laryngomalacia and only one study (O'Connor et al.⁴⁸), with significant differences for AHI in the congenital laryngomalacia patients. With regard to the LSAT, there was statistically significant

TABLE III.
Congenital Laryngomalacia. Demographic and Polysomnographic Data Pre- and Post-Supraglottoplasty.

Year, Study Authors	N	Pre-SG AHI	Post-SG AHI	Pre-SG Low O2	Post-SG Low O2
2015, Tholpady et al. ⁵⁹	3	12.0 ± 1.9 [9.9, 14.2]	5.4 ± 4.7 [0.1, 10.7]	–	–
2013, Li et al. ⁶⁷	16	–	–	68.6 ± 10.6 [63.4, 73.8]	90.1 ± 4.1 [88.1, 92.1]
2011, Powitzky et al. ⁸	20	11.2 (4.9, 16.2)*	4.7 (3.2, 8.5)*	84.5 (77.0, 89.9)	86.6 (82.0, 90.0)
2011, Revell and Clark ⁹	2	9.6 ± 4.9 [1.1, 13.3]	1.7 ± 0.9 [0.1, 2.3]	–	–
2009, O'Connor et al. ⁴⁸	10	42.7 ± 37.3 [19.6, 65.8]	4.5 ± 4.8 [1.5, 7.5]	74.8 ± 10.9 [68.0, 81.6]	87.6 ± 4.0 [85.1, 90.1]
2009, Sesterhenn et al. ⁵⁷	8	15.6 ± 7.6 [10.3, 20.9]	4.5 ± 5.9 [0.4, 8.6]	–	–
2008, Zafereo et al. ⁶⁵	10	12.2 ± 11.6 [5.0, 19.4]	4.2 ± 4.8 [1.2, 7.2]	79.2 ± 12.3 [71.6, 86.8]	87.4 ± 11.1 [80.5, 94.3]
2006, Valera et al. ⁶⁰	5	9.5 ± 6.2 [4.1, 14.9]	2.2 ± 1.7 [0.7, 3.7]	83.2 ± 9.7 [74.7, 91.7]	86.4 ± 6.1 [81.1, 91.8]
<i>Total</i> [†]	74	20.4 ± 23.9 [12.8, 28.0]	4.0 ± 4.5 [2.6, 5.4]	74.5 ± 11.9 [70.9, 78.1]	88.4 ± 6.6 [86.4, 90.4]

*Denotes the median, with the 25th and 75th percentile values.

[†]Based on studies with means and standard deviations.

() denotes range; [] denotes lower and upper 95% confidence intervals; - denotes not reported; AHI = apnea-hypopnea index; low O2 = lowest oxygen saturation; N = number; SG = supraglottoplasty.

heterogeneity and low inconsistency for sleep exclusive laryngomalacia studies and significant heterogeneity and high inconsistency among the congenital laryngomalacia studies. To find inconsistency and heterogeneity with regard to the lowest oxygen saturation in this meta-analysis is not surprising given that infants (i.e., Li et al.⁶⁷) generally have worse oxygen desaturation before surgery secondary to lower oxygen reserves as compared to older children (Chan (a) et al.²⁰ and Chan (b) et al.).² In children with congenital laryngomalacia, the literature demonstrates the additional benefit of improvement in daytime symptoms such as stridor, feeding difficulties, and failure to thrive.

Fifth, additional research is needed. The earliest study we identified reporting polysomnography outcomes was by Marcus et al.⁴⁷ in 1990; however, the study was excluded because some of the patients were sedated with chloral hydrate during the polysomnogram, and there was no individual patient data for those not sedated. All of the studies identified in the literature with quantitative polysomnographic data meeting inclusion criteria were published within the past decade. One study was level 5 evidence (case report), 11 studies were level 4 (case series), and one study was level 3 (case-control); there was no cohort and no randomized trial encountered in the literature. It should be pointed out that a

major confounder is that patients with the most severe laryngomalacia may have significant obstruction (causing hypoxemia, cyanosis, acute life-threatening events, cor pulmonale, pulmonary hypertension, etc.); these patients generally undergo supraglottoplasty in a more urgent fashion, and in that case there may not be pre- and/or postoperative polysomnograms. Additionally, in considering patients with severe symptoms, it may not be possible to randomize them to either isolated supraglottoplasty or an observational control arm because the lack of an intervention may be unacceptable and unethical due to the risk of allowing ongoing, untreated severe obstructions, which can lead to repeated hypoxemia and associated complications. Therefore, if randomized trials were performed, they would likely include patients with mild to moderate disease. Additionally, in order to facilitate the use of a common language, we are recommending that common terminology be used by researchers. With regard to the type of patients included in the study, it should be clear whether the patients are those with congenital laryngomalacia, or if the patients are those with sleep exclusive laryngomalacia. It would be expected that patients with congenital laryngomalacia will present earlier given that they generally have more signs and symptoms than those who present when they are older children. With regard to outcomes data, if the

TABLE IV.

Meta-Analysis Data With Random Effects Modeling, Summarizing the Mean and Standardized Mean Differences With Magnitudes of Effect.

Variable	MD	MD 95% CI	SMD	SMD 95% CI	Cohen's Effect
Sleep exclusive laryngomalacia					
AHI	-9.38	[-12.7, -6.10]	-0.99	[-1.37, -0.62]	large
LSAT	1.79	[-0.37, 3.96]	0.40	[0.04, 0.76]	small
Congenital laryngomalacia					
AHI	-8.78	[-12.40, -5.17]	-1.26	[-1.79, -0.73]	large
LSAT	12.18	[4.02, 20.34]	1.31	[0.32, 2.30]	large

95% CI = 95% confidence interval; AHI = apnea-hypopnea index; Cohen's effect = magnitude of effect based on Cohen's guidelines; LSAT = lowest oxygen saturation; MD = mean difference; SMD = standardized mean difference.

TABLE V.
Description of Comorbidities, Polysomnography Criteria, Type of Surgery, Reported Complications, and Nonpolysomnographic Outcomes.

Year, Study Authors	Major Comorbidities	Prior T&A	Baseline Findings	Surgery Type	Outcomes/Complications
Sleep Exclusive Laryngomalacia 2015, Mase et al. ¹¹	AGCC (1/9), AUT (1/9), DMD (1/9), VCP (1/9)	Yes (44%)	DISE: Supraglottic structures noted to prolapse into the laryngeal introitus, obstruct respiratory flow and generate perturbation. DISE: Arytenoids prolapsed into airway during inspiration during sleep endoscopy	Bilateral. Divided AE folds, removed redundant arytenoid mucosa and sparing of interarytenoid groove mucosa. CO2 laser and/or cold steel. Bilateral. Divided AE folds and excised redundant mucosa over the cuneiform cartilages. Cold steel.	Increased post-operative weight for length percentile. Complications not reported.
2013, Oomen and Modi ¹⁰	None	No	DISE: Collapse of arytenoids into glottis during inspiration during sleep endoscopy	Bilateral. Divided AE folds and removed redundant mucosa from accessory cartilages. CO2 laser.	Complete resolution of sleep related inspiratory stridor. Follow-up PSG noted only central apneas.
2012, Chan (a) et al. ²⁰	CP (NS), DS (NS), NMD	Yes (100%)	DISE: Collapse of arytenoids into glottis during inspiration during sleep endoscopy	Bilateral. Divided AE folds and removed redundant mucosa from accessory cartilages. CO2 laser.	Post-operative AHI was significantly higher in those with co-morbidities (7.3/h) than those without (2.6/h). SG less successful in obese.
2012, Chan (b) et al. ²	NS	Yes (100%)	DISE: Collapse of arytenoids into glottis during inspiration during sleep endoscopy	Bilateral. Divided AE folds and removed redundant mucosa from accessory cartilages. CO2 laser.	No stridor, feeding difficulties or failure to thrive pre or post-SG. No major complications.
2012, Digoy et al. ²³	CH (1/43), CP (5/43), DG (2/43), DS (6/43)	Yes (74%)	DISE: Dynamic collapse of supraglottic structures into the glottis during sleep endoscopy	Bilateral. Divided AE folds with scissors, then used CO2 laser to remove redundant tissue.	Improved sleep: 91%, decreased or resolved snoring: 86%, happy their child had surgery: 94%. Transient or no dysphagia: 93%, three children had increase in coughing and throat clearing. One caregiver not satisfied with surgery (no improvement in patient's PSG).
Congenital Laryngomalacia 2015, Tholpady et al. ⁵⁹	CHD (4/11), DW (1/11), PRS (11/11), TC (1/11)	NR	Awake laryngoscopy and/or DISE: findings NR.	Unilateral. Partial excision of right AE fold. CO2 laser.	Infants with PRS and laryngomalacia were successfully treated with MDO and SG and helps avoid tracheostomy.
2013, Li et al. ⁶⁷	NR	NR	Awake laryngoscopy and clinical assessment: NR	Bilateral. Removed redundant mucosa from lateral aspects of arytenoid cartilage. Divided AE folds. CO2 laser ablation assisted epiglottopexy. CO2 laser.	No stridor. No breathing difficulties, no feeding difficulties. No failure to thrive. No major complications.
2011, Powitzky et al. ⁸	CT (1/20), DS (1/20), MG (1/20)	NR	Awake laryngoscopy and DISE: findings of moderate or severe laryngomalacia	Bilateral. Divided AE folds with scissors, removed redundant supraglottic mucosa along superior portion of cuneiform cartilage. CO2 laser.	35% required a second procedure to alleviate OSA: one patient required a revision SG, while five required TA.
2011, Revell and Clark ⁹	CHD (1/26)	NR	Awake laryngoscopy and DISE: findings of mild, moderate or severe laryngomalacia	Unspecified if unilateral vs. bilateral. Divided AE folds and removed redundant tissue with or without cuneiform cartilage. Cold steel.	Both subjective and objective improvement. No significant complications.

TABLE V.
(Continued)

Year, Study Authors	Major Comorbidities	Prior T&A	Baseline Findings	Surgery Type	Outcomes/Complications
2009, O'Connor et al. ⁴⁸	DS (2/10)	NR	Flexible fiberoptic nasopharyngoscopy: findings of moderate or severe laryngomalacia	Bilateral. Divided AE folds, resection of redundant arytenoid mucosa and four of ten patients had trimming of epiglottis or epiglottopexy. Cold steel.	One patient was intubated post-operatively for 24 hours and developed a collapse of the left lobe due to ETT being in right main bronchus.
2009, Sesterhenn et al. ⁵⁷	NR	NR	Awake laryngoscopy and DISE: findings of severe laryngomalacia	Bilateral. Divided AE folds, single spot application and/or epiglottopexy. CO2 laser.	No aspiration. Revision epiglottopexy performed for suture dehiscence.
2008, Zafero et al. ⁶⁵	UVFP (2/10), MSGS (1/10)	NR	Flexible endoscopy: findings of moderate laryngomalacia	Divided AE folds bilaterally either alone or with unilateral excision of redundant mucosa and the cuneiform cartilage. CO2 laser.	Mild improvement (10%), or complete resolution (20%) of stridor and nocturnal snoring. No complications.
2006, Valera et al. ⁶⁰	TM (1/7) PLM (2/7)	NR	Flexible fibroscopy: omega-shaped epiglottis, shortened AE fold, and redundant arytenoid mucosa	Bilateral. Divided AE folds with excision of redundant mucosa in the lateral arytenoid region. One patient underwent epiglottopexy. Cold steel.	Clinically there was partial to moderate improvement in all cases.

() represents the number of patients out of the total with the comorbidity; † = study included congenital (2 patients) and sleep exclusive (1 patient).

AGCC = agensis of the corpus colosum; AHI = apnea-hypopnea index; AUT = autism; CHD = congenital heart disease; CL = congenital laryngomalacia; CMF = craniomaxillofacial disorders; CO2 = carbon dioxide; CP = cerebral palsy; CT = chromosomal translocation (9 and 15); DISE = drug-induced sleep endoscopy; DMD = demyelination disorder; DS = Down Syndrome; DW = Dandy-Walker; ETT = endotracheal tube; MDO = mandibular distraction osteogenesis; MG = myasthenia gravis; MSGS = mild subglottic stenosis; NMD = neuromuscular disease; NR = not reported; NS = not stratified (comparison group vs supraglottoplasty group); SEL = sleep exclusive laryngomalacia; SG = supraglottoplasty; PLM = pharyngolaryngomalacia; PRS = Pierre Robin sequence; T&A = Adenotonsillectomy; TC = Treacher Collins; UVFP = unilateral vocal-fold paralysis; VCP = vocal cord paresis.

following variables were reported consistently and in a standardized fashion, it would significantly facilitate future research: 1) polysomnography scoring criteria used (e.g., 3% or 4% desaturations); 2) apnea-hypopnea index should be reported, this would not preclude authors from reporting other indices (i.e., RDI); 3) oxygen saturation variables, such as: a) the overall mean oxygen saturation (M O₂ sat), b) the oxygen desaturation index, c) the time (T) spent below specific oxygenation levels (i.e., 85% and 90% oxygen saturation [T < 85%] and [T < 90%], respectively), and d) lowest oxygen saturation); 4) details regarding the extent of surgery performed for the patients, with Ms and SDs; and 5) publication of the individual patient data when possible.

Limitations

As with any systematic review, it is possible that we missed studies in the literature despite our best efforts. Second, there may be differences in hypopnea scoring criteria between institutions; however, these differences were not specified by the articles in this review. Third, the studies were all retrospective in nature; therefore, the study authors were limited to the data available in the medical records.

CONCLUSION

Supraglottoplasty has improved AHI and LSAT in children with OSA and either sleep exclusive laryngomalacia or congenital laryngomalacia; however, the majority of them are not cured.

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