



Surgical outcomes and sleep endoscopy for children with sleep-disordered breathing and hypotonia



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ABSTRACT

Objective: To study the efficacy of surgical management for obstructive sleep apnea (OSA) syndrome in children with hypotonia, and to identify common anatomic sites of airway obstruction.

Methods: Retrospective chart review of polysomnographic parameters and quality of life instrument scores for seventy eight children with hypotonia who underwent surgical intervention for sleep-disordered breathing at two tertiary children's hospitals, and analysis of drug-induced sleep endoscopy data using a previously validated scoring system.

Results: Children undergoing surgical intervention had baseline severe OSA with a statistically significant improvement in apnea-hypopnea index from 23.6 to 11.1 after surgery, but persistent severe OSA. OSA-18 sleep-related quality of life measurement and overall quality of life score showed statistically and clinically significant improvements, from 72.0 to 43.4 and from 5.3 to 7.6 respectively. Sleep endoscopy showed an average obstructive score of 7.2/15 (n = 39), with multi-level obstruction in 49% of children. Greater than 50% obstruction was observed at the tongue base in 64% of patients, velum in 46%, lateral pharyngeal wall in 38%, supraglottis in 38%, and adenoid in 23%.

Conclusion: OSA syndrome is challenging to treat in hypotonic children. Severe residual OSA is common after surgical intervention, but improvement in quality of life is clinically and statistically significant. The tongue base is the most common site of persistent airway obstruction. Drug-induced sleep endoscopy can identify sites of airway obstruction and may aid in surgical planning for high-risk patients.

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1. Introduction

Childhood obstructive sleep apnea syndrome (OSAS) is characterized by partial or complete airway obstruction during sleep resulting in repetitive arousals and/or oxygen desaturations [1]. In most cases, this common condition, estimated to affect 1–4% of children, is effectively treated surgically in order to avert the neurocognitive, behavioral, cardiovascular, and inflammatory sequelae of untreated OSAS [1–6]. However, patients with certain risk factors are at high risk of disease refractory to surgery. In particular, a comorbid diagnosis such as asthma, obesity, or Down syndrome greatly increases the likelihood of severe refractory OSAS [5,7–11].

Hypotonia is considered a risk factor for relative surgical failure, but this has not been definitively shown [11], with a paucity of data in the literature describing the underlying pathophysiology and the efficacy of surgical management of OSAS in hypotonic children.

We present a retrospective cross-sectional analysis of children with hypotonia who were surgically managed for sleep-disordered breathing at two tertiary children's hospitals. We sought to describe treatment course and residual disease burden through evaluation of OSA symptoms and sleep-related quality of life, and to gain a better understanding of the pathophysiology and severity of airway obstruction at multiple anatomic levels utilizing a previously validated sleep endoscopy scoring system [12].

2. Methods

2.1. Patient selection and data collection

This study was approved by the institutional review boards of the University of California, San Francisco and Seattle Children's

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¹ Drs. Park and Chan had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Hospital. The investigators adhered to policies for protection of human subjects as prescribed in 45 CFR 46. Waiver of written informed consent was obtained and approved by both institutional review boards. Children with a clinical diagnosis of hypotonia who underwent surgical procedures for sleep-disordered breathing by attending pediatric otolaryngologists at the UCSF Benioff Children's Hospital from 2002 through 2014 and from Seattle Children's Hospital from 2011 to 2013 were collected in quality-improvement databases. Databases were queried retrospectively at the time of the study.

Primary inclusion criteria were documentation of a surgical procedure for treatment of sleep-disordered breathing and a diagnosis of hypotonia. During chart review, particular attention was taken to multidisciplinary evaluation by pediatricians, pediatric neurologists, and medical geneticists supporting a diagnosis of hypotonia on physical exam, thus selecting for children with syndromic and non-syndromic hypotonia and neuromuscular dysfunction. Patients were excluded if evaluation for sleep-disordered breathing had been conducted (including polysomnography, sleep endoscopy, or direct laryngoscopy and bronchoscopy), but no treatment procedure had been performed. No additional exclusion criteria were applied, in order to improve study generalizability.

During chart review for 78 included patients, demographic data, operative details, polysomnographic indices, drug-induced sleep endoscopy findings, and OSA-18 quality of life questionnaire data were collected.

2.2. OSA-18 questionnaire for sleep-related quality of life

The OSA-18 questionnaire is an 18-item seven point Likert scale survey measuring quality of life in five domains: sleep disturbance, physical suffering, emotional symptoms, daytime function, and caregiver concern [13]. The OSA-18 index, or summary score, is the sum of all item scores, with a minimum of 18 and a maximum of 126 points and a value of 60 or above considered abnormal. A visual analog scale item asking caregivers to rate the child's overall quality of life (scored 0–10 with 10 representing the best possible quality of life) was also on the questionnaire. The questionnaire was administered at clinic visits and scores recorded in the electronic medical record.

2.3. Pediatric polysomnography

Polysomnograms were performed at the sleep laboratory at Seattle Children's Hospital or at the UCSF Benioff Children's Hospital Pediatric Sleep Laboratory. These were scored according to standard American Academy of Sleep Medicine scoring criteria for pediatric polysomnography [14]. The apnea-hypopnea index (AHI) was defined as the total number of apneas and hypopneas averaged per hour of total sleep time. The oxygen saturation nadir was defined as the lowest oxygen saturation recorded during an obstructive event. AHI and oxygen saturation nadir values were obtained from the primary reports of polysomnograms. Obstructive sleep apnea syndrome was categorized by AHI as absent (<1), mild (1–5), moderate (5–10), or severe (>10).

2.4. Validated scoring system for drug-induced sleep endoscopy

Transnasal flexible fiber-optic drug-induced sleep endoscopy (DISE) was performed in the operating room with patients positioned supine and spontaneously ventilating under anesthesia. The standard regimen for DISE at both institutions is total IV anesthesia via propofol drip. As previously described, videos were evaluated for airway obstruction on a 0–3 scale at five anatomic sites:

adenoids, velum, lateral pharyngeal walls, tongue base, and supraglottis [12]. Higher total obstructive scores and multilevel obstruction – defined as significant obstruction (50–99%, score ≥ 2) within both the upper airway complex (adenoid, velum, or lateral pharyngeal wall) and the lower airway complex (tongue base or supraglottis) – are correlated with worsened polysomnographic parameters [12].

2.5. Statistical analysis

Comparisons of paired nonparametric data (including AHI and oxygen saturation nadir) were performed with the Wilcoxon rank-sum test. Unpaired nonparametric data were compared with the Mann-Whitney rank-sum test. Parametric data were compared with the *t*-test. Binomial data were compared with the Fisher exact test. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Patient population

78 patients with hypotonia underwent surgical procedures for sleep-disordered breathing. Study population characteristics are given in Table 1. The most common comorbidities were Down syndrome ($n = 24$, 31%), developmental delay ($n = 22$, 28%), and cerebral palsy ($n = 12$, 15%). Other comorbid diagnoses included Trisomy 13, partial Trisomy 18, chromosome 1q43q44 duplication, unspecified chromosomal abnormality, generalized muscle weakness, laryngomalacia, epilepsy, agenesis of the corpus callosum,

Table 1
Demographic and clinical characteristics of the study patients.^a

Characteristic		
Total patients, No.	78	
Age, y	5.3	(0.46; 4.4–6.2)
Pre-op AHI (N = 48)	20.1	(3.4; 13.2–27.0)
Pre-op O ₂ , % (N = 48)	80.5	(1.7; 77.0–84.0)
Post-op AHI (N = 38)	11.8	(2.8; 6.2–17.4)
Post-op O ₂ , % (N = 38)	83.9	(1.2; 81.5–86.3)
Pre-op OSA-18 (N = 23)	72.0	(5.2; 61.9–82.9)
Pre-op OSA-18 overall QOL (N = 23)	5.3	(0.42; 4.4–6.2)
Post-op OSA-18 (N = 14)	43.9	(6.0; 31.0–56.8)
Post-op OSA-18 overall QOL (N = 14)	7.6	(0.59; 6.3–8.9)
Mean# procedures per patient	1.7	(0.15; 1.4–2.0)
Patients with 1 procedure, No. (%)	56	(72)
Patients with 2 procedure, No. (%)	8	(10)
Patients with >2 procedures, No. (%)	14	(18)
Procedures received		
Adenotonsillectomy, No. (% of patients)	62	(80)
Supraglottoplasty, No. (% of patients)	14	(18)
Revision adenoidectomy, No. (% of patients)	10	(13)
Turbinate reduction, No. (% of patients)	10	(13)
Lingual tonsillectomy, No. (% of patients)	9	(12)
Adenoidectomy, No. (% of patients)	6	(8)
Tonsillectomy, No. (% of patients)	3	(4)
Revision tonsillectomy, No. (% of patients)	3	(4)
Genioglossus advancement, No. (% of patients)	3	(4)
Inter-arytenoid injection, No. (% of patients)	1	(1)
Palatoplasty, No. (% of patients)	1	(1)
Common comorbidities		
Down syndrome, No. (%)	24	(31)
Developmental delay, No. (%)	21	(27)
Cerebral palsy, No. (%)	12	(15)

Abbreviations: O₂, oxygen saturation; post-op, postoperative; pre-op, preoperative.
^a Unless otherwise indicated, data are reported as mean (SEM; 95% CI) values.

holoprosencephaly, Progressive Encephalopathy, IVH, Noonan syndrome, Duchenne's muscular dystrophy, Pierre-Robin sequence, Bohring-Opitz syndrome, William's syndrome, Beckwith-Wiedemann syndrome, Chiari I malformation, and Cri du Chat syndrome.

Most children underwent 1 individual surgical procedure, with an average of 1.7 procedures per child – 72% underwent one, 10% underwent two, and 18% underwent greater than two procedures. The most common procedure was adenotonsillectomy (n = 62, 80%), followed by supraglottoplasty (n = 14, 18%) and lingual tonsillectomy (n = 9, 11.5%). Additionally, 6 (8%) children underwent adenoidectomy without tonsillectomy, ten (13%) underwent revision adenoidectomy after prior adenotonsillectomy, 3 (4%) underwent tonsillectomy without adenoidectomy, and 3 (4%) underwent revision tonsillectomy. Ten children (13%) underwent inferior turbinate reduction and three (4%) genioglossus advancement.

3.2. Baseline polysomnography and improvement with surgical management

Polysomnographic AHI is the most commonly used objective measure of OSA severity. Forty eight children underwent polysomnography prior to surgical intervention. Average AHI was 20.1

(n = 48, 95% CI 13.2–27.0) for these children, signifying severe baseline OSA (Table 1 and Fig. 1A). OSA was absent or mild in 18.7%, moderate in 25.0% and severe in 56.3% of these children. Thirty eight children underwent polysomnography after surgical intervention. In these children, average AHI was 11.8 (n = 38, 95% CI 6.2–17.4), signifying severe residual OSA (Fig. 1A). Residual OSAS was absent or mild in 50.0%, moderate in 18.4%, and severe in 31.6% of these children. The difference in AHI between those children who underwent preoperative PSG and those who underwent postoperative PSG was statistically significantly different (p = 0.004).

We also performed paired statistical analysis on the 26 children for whom both preoperative and postoperative polysomnography data was available. In these children, average AHI improved from 23.6 (95% CI 12.4–34.7) to 11.1 (95% CI 4.2–17.9) (n = 26, p = 0.007) (Fig. 1B). Average O2 nadir rose from 77.7% (95% CI 71.7–83.7) to 83.4% (95% CI 80.2–86.5) (n = 26, p = 0.04) (Fig. 1B).

3.3. Baseline impairment of quality of life and improvement with surgical management

Alleviation of the negative impact of OSAS on sleep-related quality of life is an important treatment goal. We analyzed OSA-

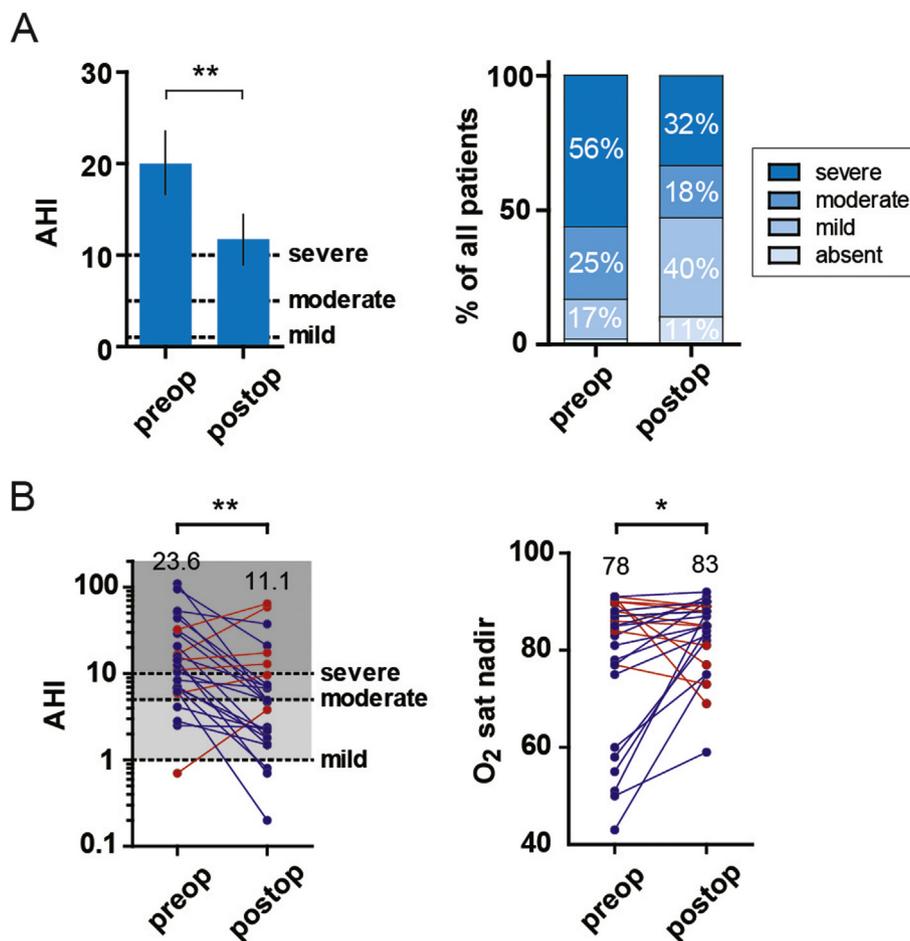


Fig. 1. Severe OSA is improved after surgical management. A) Mean AHI of study patients is lower postoperatively than preoperatively, though residual OSA remains in the severe range. (**, p < 0.01. Error bars indicate SEM). The percentage of patients with different degrees of severity of OSA preoperatively and postoperatively is shown. Severity is defined by AHI (absent: <1, mild 1–5, moderate 5–10, severe >10). B) Paired statistical analysis on the 24 children for whom both preoperative and postoperative polysomnography data was available shows statistically significant decrease in AHI. Lines represent preoperative and postoperative data for individual patients. Red lines and markers indicate an increase in AHI or decrease in O2 saturation nadir postoperatively; blue lines and markers indicate a decrease in AHI or increase in O2 saturation nadir. (*, p < 0.05. **, p < 0.01). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

18 data from 23 children who completed the survey preoperatively and 14 children who completed it postoperatively. Average OSA-18 index measurement was 72.0 (n = 23, 95% CI 61.1–82.9) and OSA-18 overall quality of life score was 5.3 (n = 23, 95% CI 4.4–6.2) preoperatively (Table 1 and Fig. 2A). For children who completed the survey postoperatively, average OSA-18 index was 43.4 (n = 14, 95% CI 31.0–56.8) and OSA-18 overall quality of life score was 7.6 (n = 14, 95% CI 6.3–8.8) (Table 1 and Fig. 2A). These differences in scores were statistically significant (p = 0.002 for OSA-18 index, p = 0.003 for quality of life score).

We also performed paired statistical analysis on the 11 children for whom both preoperative and postoperative OSA-18 data was available. In these children, the average OSA-18 index measurement improved from 75.0 (95% CI 58.9–91.1) to 43.9 (95% CI 28.0–59.8) (n = 11; p = 0.002) and OSA-18 overall quality of life score improved from 5.7 (95% CI 4.4–7.1) to 7.8 (95% CI 6.3–9.3) (n = 11; p = 0.04) (Fig. 2B).

3.4. Assessment of efficacy of individual isolated surgical procedures

The number of patients in this study was insufficient to assess the comparative efficacy of all individual surgical procedures. We analyzed the preoperative and postoperative AHI as well as OSA-18 quality of life scores for patients who underwent certain

procedures in isolation.

Preoperative AHI was 16.0 (n = 33, 95% CI 8.9–23.0) among patients who underwent only adenotonsillectomy, and postoperative AHI was 10.6 (n = 22, 95% CI 2.5–18.8) (p = 0.01). Average OSA-18 index measurement improved from 79.3 (n = 16, 95% CI 68.4–90.3) to 44.4 (n = 10, 95% CI 26.6–62.2) (p = 0.0007) and OSA-18 overall quality of life score improved from 4.8 (n = 16, 95% CI 3.7–5.8) to 7.6 (n = 10, 95% CI 6.0–9.2) (p = 0.003).

Among patients who underwent only supraglottoplasty, preoperative AHI was 17.2 (n = 4, 95% CI 2.4–32.0) and postoperative AHI was 5.4 (n = 4, 95% CI -3.3–14.1) (p = 0.11). Insufficient OSA-18 quality of life score data was available for this subset of patients.

3.5. Identification of sites of obstruction by sleep endoscopy

Thirty nine children underwent DISE to identify potential sites of airway obstruction – in 13 children to identify additional sites of airway obstruction given residual OSA after adenotonsillectomy (n = 10) or adenoidectomy (n = 3), in 25 children prior to any surgical intervention due to high clinical suspicion for multiple levels of obstruction given hypotonia or airway obstruction not expected to improve significantly with adenotonsillectomy alone (e.g. if tonsils were not large on in-office clinical exam), and in 1 child to evaluate for sites of obstruction after the child failed a tracheotomy capping trial (Table 2). Children underwent surgical interventions directed at sites of obstruction as listed in Table 2 based on the results of sleep endoscopy. Long-term follow-up data regarding the efficacy of these procedures is not available to date.

For the 10 children who had previously undergone past adenotonsillectomy, average DISE obstructive scores were 1.2 (95% CI 0.8–1.6) at adenoid, 1.5 (95% CI 0.8–2.2) at velum, 0.9 (95% CI 0.3–1.5) at lateral pharyngeal wall, 2.6 (95% CI 2.3–2.9) at tongue base, and 2.1 (95% CI 1.2–3.0) at supraglottis. The average total obstructive score was 8.3 (95% CI 6.9–9.7). Notably, 100% of children had significant obstruction (score ≥ 2 , corresponding to >50% collapse) at the tongue base, and 73% had significant obstruction at the supraglottis (Fig. 3A–B). Multi-level obstruction (within both the upper and lower airway complexes) was present in 64% of children; significant obstruction was present in only one of the upper and lower airway complexes in an additional 36% of children.

For the 25 children who had not undergone any prior surgical intervention for OSA, average DISE obstructive scores were 1.1 (95% CI 0.7–1.5) at adenoid, 1.5 (95% CI 1.1–1.9) at velum, 1.6 (95% CI 1.6–2.0) at lateral pharyngeal wall, 1.5 (95% CI 1.1–1.9) at tongue base, and 1.2 (95% CI 0.8–1.6) at supraglottis. The average total obstructive score was 6.9 (95% CI 5.9–7.9) (Fig. 3A–B). Multi-level obstruction (within both the upper and lower airway complexes) was present in 40% of children; significant obstruction was present in only one of the upper and lower airway complexes in an additional 44% of children.

In aggregate, the average total obstructive score for all children in this study who underwent DISE was 7.2/15 (n = 39; 95% CI 6.4–8.0). Average obstructive scores were 1.1 (95% CI 0.8–1.4) at adenoid, 1.5 (95% CI 1.2–1.8) at velum, 1.4 (95% CI 1.1–1.7) at lateral pharyngeal wall, 1.9 (95% CI 1.6–2.2) at tongue base, and 1.4 (95% CI 1.0–1.8) at supraglottis. Significant obstruction (50–99%, score ≥ 2) was observed most commonly at the tongue base (in 64% of patients). Obstruction was also significant at the velum in 46%, lateral pharyngeal wall in 38%, supraglottis in 38%, and adenoids in 23% of children (Fig. 3A–B). Multi-level obstruction (within both the upper and lower airway complexes) was present in 49% of children; significant obstruction was present in only one of the upper and lower airway complexes in an additional 41% of children (Fig. 3C).

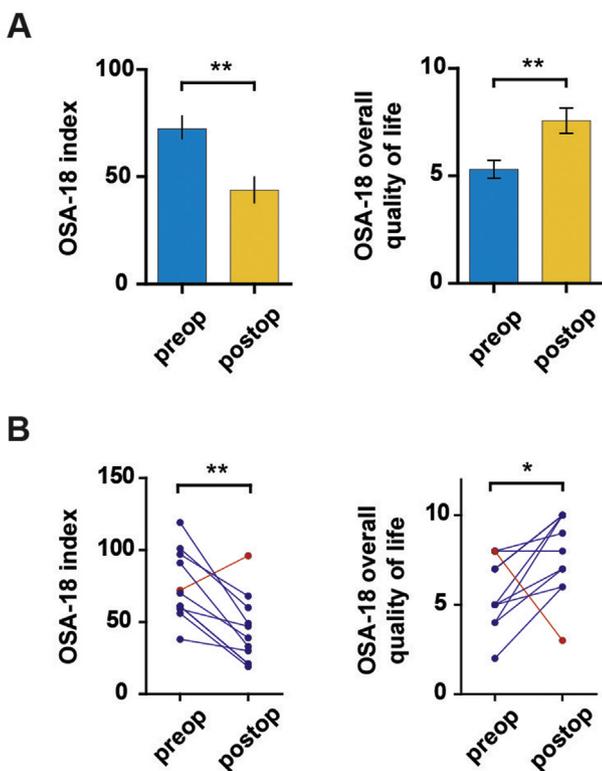


Fig. 2. Sleep-related quality of life is improved after surgical management. A) Comparison of average OSA-18 index and OSA-18 overall quality of life demonstrates improvement in both indices postoperatively. B) Paired statistical analysis on the 11 children for whom both preoperative and postoperative OSA-18 data was available shows statistically significant improvement in OSA-18 index and OSA-18 overall quality of life. Lines represent preoperative and postoperative data for individual patients. Red lines and markers indicate an increase in OSA-18 index or decrease in OSA-18 overall quality of life; blue lines and markers indicate a decrease in OSA-18 index or increase in OSA-18 overall quality of life. *, p < 0.05. **, p < 0.005. Error bars indicate SEM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Individual diagnoses, surgical procedures performed, and sleep endoscopy obstructive scores.

Diagnosis	Procedures before DISE	Procedures after DISE							DISE obstruction scores							
		T&A	T	A	LT	RFA	GGA	Turb	SGP	Other	A	V	L	T	S	Sum
1 Developmental delay, neuromuscular weakness	none	x									1.0	1.0	2.0	2.0	0.0	6.0
2 William's syndrome (possible), developmental delay	none	x									3.0	3.0	3.0	1.0	0.0	10.0
3 Cerebral palsy, hypotonia	none	x									2.0	2.0	3.0	3.0	1.0	11.0
4 Beckwith-Weidemann syndrome	none	x									0.0	0.0	1.0	2.0	0.0	3.0
5 Hypotonia	none	x									0.0	1.0	1.0	2.0	1.0	5.0
6 Chiari I malformation, hypotonia	none	x									1.0	0.0	2.5	0.0	0.8	4.3
7 Down syndrome, chronic lung disease, congenital heart dz	none	x									0.0	0.5	0.5	2.8	3.0	6.8
8 Intraventricular hemorrhage, hypotonia	none	x									2.8	2.8	3.0	0.8	1.5	10.8
9 Progressive encephalopathy, hypotonia	none	x									1.5	1.3	3.0	0.5	2.5	8.8
10 Chromosomal abnormality NOS, hypotonia, congenital hypothyroidism	none	x									1.8	1.0	0.3	1.3	0.0	4.3
11 Developmental delay, neuromuscular weakness	none	x									2.0	0.0	1.0	1.0	1.0	5.0
12 Developmental delay, neuromuscular weakness	none	x									1.0	1.0	1.0	1.0	1.0	5.0
13 Ohtahara syndrome, developmental delay, chronic lung disease, seizure disorder, spastic quadriplegia, hypotonia	none	x									1.0	2.0	2.0	2.0	2.0	9.0
14 Down syndrome	none	x									1.0	3.0	3.0	2.0	0.0	9.0
15 Developmental delay, hypotonia	none	x									2.0	2.0	2.0	0.0	0.0	6.0
16 Developmental delay, neuromuscular weakness	none	x								palatoplasty	1.0	1.0	1.0	3.0	0.0	6.0
17 Chromosomal abnormality NOS	none	x									1.0	1.8	2.0	0.5	2.3	7.5
18 Cri du chat, hypotonia	none	x								x	0.0	0.0	1.0	0.3	1.5	2.8
19 Holoprosencephaly	none				x					x	0.7	0.0	0.8	0.5	1.8	3.7
20 Trisomy 18 (partial), infantile spasm	none				x					x	0.3	2.8	1.0	1.0	1.8	6.8
21 Generalized muscle weakness	none										3.0	2.0	1.0	2.0	0.0	8.0
										inter-arytenoid injection						
22 Pierre-Robin seq, hypotonia	none									x	0.0	3.0	2.0	3.0	2.0	10.0
23 Bohring Opitz (possible), developmental delay, hypotonia, abnormal brain development, infantile spasms; grade 1 subglottic stenosis	none										2.0	3.0	3.0	2.0	1.0	11.0
24 Agenesis of the corpus colosum	none									x	0.0	2.0	0.5	0.8	2.8	6.0
25 Developmental delay, hypotonia, failure to thrive	none									x	0.0	1.5	0.0	2.8	2.8	7.0
26 Down syndrome	T&A				x	x				x	2.0	2.0	0.0	2.0	3.0	9.0
27 Down syndrome	T&A				x	x				x	1.0	3.0	1.0	3.0	3.0	11.0
28 Down syndrome	T&A				x	x				x	1.0	2.0	1.0	2.0	0.0	6.0
29 Down syndrome, obesity, cardiac defects, developmental delay	T&A				x	x				x	1.0	1.0	2.0	3.0	3.0	10.0
30 Developmental delay, neuromuscular weakness	T&A				x	x				x	2.0	0.0	1.0	2.0	0.0	5.0
31 Pierre-Robin sequence, developmental delay	T&A				x					x	1.0	3.0	3.0	2.0	2.0	11.0
32 Hypotonia	T&A				x						1.8	1.3	0.3	3.0	0.3	6.6
33 Down syndrome	T&A				x					x	1.0	1.0	1.0	3.0	3.0	9.0
34 Down syndrome	T&A				x	x				x	1.0	2.0	0.0	3.0	3.0	9.0
35 Down syndrome	T&A										1.0	1.0	1.0	3.0	3.0	9.0
36 Global developmental delay, agenesis of the corpus callosum, consanguinity, failure to thrive	adenoidectomy				x						0.0	3.0	1.0	0.0	4.0	8.0
37 Down syndrome	adenoidectomy				x	x					2.0	1.0	3.0	0.0	7.0	13.0
38 Developmental delay, neuromuscular weakness	adenoidectomy				x					x	2.0	1.0	3.0	0.0	7.0	13.0
39 Down syndrome	T&A, SGP, tracheotomy				x						0.0	0.0	0.0	3.0	3.0	6.0

3.6. Differential sites of obstruction in children with down syndrome

Nearly one-third of patients in the study had an underlying diagnosis of Down syndrome (Table 1). While it is known that Down syndrome puts children at higher risk for severe OSA, neither the pathophysiologic mechanisms underpinning this increased risk nor improved methods of treatment have been satisfactorily described [9,10,15]. We performed a subgroup analysis comparing those children with Down syndrome in our study to those with any other diagnosis to assess for differences in OSA severity or anatomic pathophysiology.

Preoperatively, AHI was no different between the groups (13.6, 95% CI 5.2–22.1, n = 10 with Down vs 21.8, 95% CI 13.3–30.3, n = 38 with other diagnoses; p = 0.65), nor was oxygen nadir (82.8%, 95% CI 74.1–91.5, n = 10 vs 79.7%, 95% CI 75.6–83.8, n = 37; p = 0.30). Preoperative OSA-18 indices were also no different in children with Down syndrome as compared to those with other diagnoses (59.4, 95% CI 35.4–83.5, n = 7 vs 77.6, 95% CI 65.1–90.0, n = 16; p = 0.11), nor was overall quality of life (6.0, 95% CI 4.4–7.6, n = 7 Down vs

5.0, 95% CI 3.9–6.1, n = 16 non-Down; p = 0.29). There was insufficient sample size for similar postoperative analysis.

Sleep endoscopy showed total obstructive scores in children with Down syndrome not statistically significantly different from those with other diagnoses (8.3, 95% CI 7.2–9.4, n = 11 Down vs 6.8, 95% CI 5.8–7.8, n = 28 non-Down; p = 0.07). Children with Down syndrome did exhibit higher obstructive scores at the tongue base (2.7, 95% CI 2.4–3.0 vs 1.5, 95% CI 1.2–1.9; p = 0.001) and at the supraglottis (2.2, 95% CI 1.2–3.1 vs 1.0, 95% CI 0.65–1.4; p = 0.007). Obstructive scores at the lateral pharyngeal walls was not statistically significantly different between the two groups (0.95, 95% CI 0.35–1.6 vs 1.6, 95% CI 1.2–2.0; p = 0.068) (Fig. 3D). 64% of Down syndrome and 43% of non-Down syndrome children exhibited multi-level obstruction, though the subgroup sample size was small and statistically underpowered.

4. Discussion

Children with hypotonia and sleep-disordered breathing present a special clinical challenge. Not only is OSAS common and

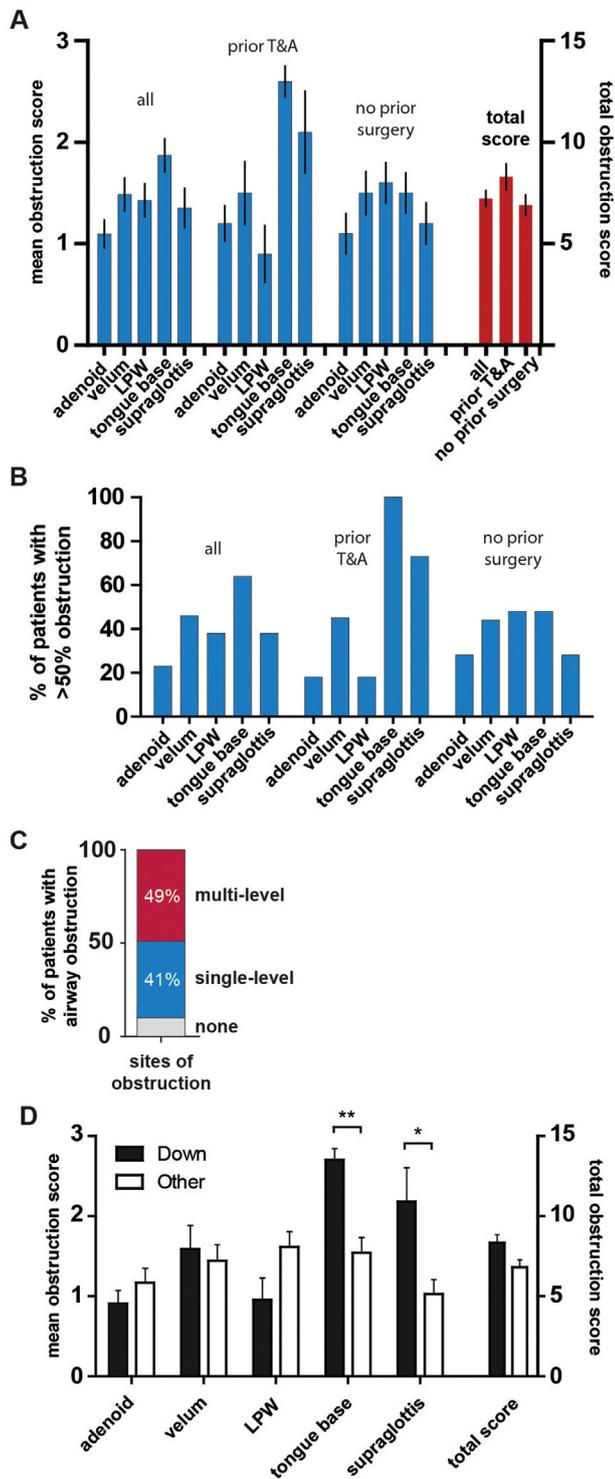


Fig. 3. Sleep endoscopy reveals sites and severity of airway obstruction and demonstrates differential sites of obstruction in children with Down syndrome. A) Mean obstruction scores at five anatomic sites on sleep endoscopy for all study patients (N = 39), children who had previously undergone adenotonsillectomy (N = 10), and children who had not had prior surgery for OSA (N = 25) (from left to right) (scale on left axis). Red, rightmost bars represent total obstruction score, which is the sum of individual site obstruction scores (scale on right axis). Error bars indicate SEM. B) Proportion of patients with significant obstruction, defined as 50–99% or obstructive score greater than or equal to 2, at five anatomic sites on sleep endoscopy. From left to right, all study patients (N = 39), children who had previously undergone adenotonsillectomy (N = 10), and children who had not had prior surgery for OSA (N = 25). C) Proportion of all study patients with no significant obstruction (no obstruction scores greater than or equal to 2), single-level obstruction (obstruction score greater

often severe in this population, symptoms are frequently refractory to surgical intervention [16]. Management often requires numerous procedures targeted at multiple levels of airway obstruction, though first-line treatment with adenotonsillectomy is often performed to lower the upper airway's contribution to total airway resistance and decrease dynamic airway collapse [16].

In this study, surgical management resulted in statistically and clinically significant improvements in OSA symptoms and sleep-related quality of life. Residual OSA was common, however – though 77% of children who underwent both preoperative and postoperative polysomnography showed improvement in AHI, an average postoperative AHI of 11.8 indicates severe residual OSA. Residual OSA was mild in 40%, moderate in 18%, and severe in 32% of study patients. For comparison, a broad cohort of children with OSAS in a large multicenter retrospective study had an average improvement in AHI from 18.2 to 4.1 after adenotonsillectomy, with normalization of AHI (less than 1) in 27.2% and moderate to severe residual OSA (AHI ≥ 5) in 21.6% of children postoperatively (Table 3) [7]. Further work remains to identify optimal methods of treating refractory OSA.

Our study also evaluated sites of airway obstruction using a previously validated sleep endoscopic scoring system. The most common site of significant obstruction in study children was the tongue base, followed by the velum, lateral pharyngeal wall, supraglottis, and adenoids. In about half of our children, endoscopy revealed multilevel obstruction – a finding previously correlated with worse polysomnographic indices [12] and perhaps indicative of patients who may require additional targeted procedures in addition to adenotonsillectomy. A simple, validated, and standardized method of scoring pediatric sleep endoscopic evaluations may facilitate more effective surgical interventions and improve ongoing outcomes research.

A future direction for our work is to determine whether patient subgroups – including those with specific high-risk comorbidities such as Down syndrome – exhibit particular patterns of airway obstruction. Such information could be useful in surgical planning. For example, we find it interesting that study children with Down syndrome had higher degrees of obstruction at the tongue base and supraglottis than other children despite no statistically significant difference in overall obstruction scores or AHI. However, a significant caveat lies in the non-uniform treatment of patients in this retrospective study. 73% of children with Down syndrome who underwent sleep endoscopy had undergone prior adenotonsillectomy, whereas only 21% with other diagnoses had done the same (p = 0.007 by Fisher's exact test). This disparity could underlie the differences between subgroups discovered in this study. Attempting to analyze only those patients who underwent adenotonsillectomy prior to sleep endoscopy yielded a small, statistically underpowered sample size of eight patients with Down syndrome and six patients with non-Down syndrome diagnoses. Comparison of only these patients did not yield any statistically significant differences in obstructive scores at any site, but did remain suggestive of some differences. Mean obstructive scores were: 2.8 (95% CI 2.4–3.1) Down vs. 2.2 (95% CI 1.4–3.0) non-Down at tongue base (p = 0.12); 2.6 (95% CI 1.7–3.5) Down vs. 1.5 (95% CI 0.3–2.8) non-

than or equal to 2 at sites within either the upper or lower airway complexes), and multi-level obstruction (obstruction score greater than or equal to 2 at sites within both the upper and lower airway complexes). D) Mean obstruction scores at five anatomic sites on sleep endoscopy for patients with Down syndrome (black bars) and other diagnoses (white bars), left axis. Rightmost bars show total obstruction scores, right axis. Children with Down syndrome exhibited significantly higher obstructive scores at the tongue base and supraglottis. *, p < 0.01, **, p = 0.001. Error bars indicate SEM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
Demographic and polysomnographic data as compared to results from a previously reported diverse multicenter cohort undergoing adenotonsillectomy.^a

Characteristic	Surgical management for hypotonic children (present study)	Adenotonsillectomy in diverse multicenter cohort ([7])
Number of patients	78	578
Mean age	5.3 ± 4.1	6.9 ± 3.8
Mean# procedures per patient	1.7 ± 1.3	1 (adenotonsillectomy)
AHI, pre-op (N = 48)	20.1 ± 23.8	18.2 ± 21.4
Adenotonsillectomy only (N = 33)	16.0 ± 19.8	
Supraglottoplasty only (N = 4)	17.2 ± 9.3	
AHI, post-op (N = 38)	11.8 ± 17.0	4.1 ± 6.4
Adenotonsillectomy only (N = 22)	10.6 ± 18.4	
Supraglottoplasty only (N = 4)	5.4 ± 5.5	
p-value, AHI pre- to post-op	0.004	<0.001
Adenotonsillectomy only subset	0.003	
O2 nadir, pre-op (N = 48)	80.5 ± 12.2	80.2 ± 13.1
O2 nadir, post-op (N = 36)	83.9 ± 7.3	86.2 ± 8.3
p-value, O2 nadir pre- to post-op	0.37	<0.001
% of patients with improved AHI	77%	90%
% of children with absent OSA post-op (AHI < 1)	10%	27%
% of children with mild OSA post-op (AHI between 1 and 5)	40%	51%
% of children with moderate to severe OSA post-op (AHI > 5)	50%	22%

Abbreviations: O₂, oxygen saturation; post-op, postoperative; pre-op, preoperative.

^a Unless otherwise indicated, values are reported as mean ± SD for direct comparison with data as presented in [7].

Down at supraglottis ($p = 0.11$), and 0.8 (95% CI 0.16–1.3) Down vs. 1.5 (95% CI 0.3–2.8) non-Down at lateral pharyngeal walls ($p = 0.19$). Well-controlled prospective studies would be valuable in the further study of individual patient subgroups.

A limitation of our study is that our patient population may be subject to selection bias. Patients present as a mixture of tertiary referrals and children seen originally in our clinic as primary referrals prior to adenotonsillectomy, which is not reflective of all practice situations. Another limitation is the study's retrospective nature and, accordingly, the non-uniform treatment of patients according to surgeon preference given a heterogeneous population. The inclusion of two sites and multiple surgeons serves to decrease bias to some extent. Children underwent a variety of surgical interventions including adenotonsillectomy (80%), supraglottoplasty (18%), lingual tonsillectomy (12%), turbinate reduction (13%), and genioglossus advancement (4%). Our analysis was designed to examine the outcomes of surgical management in aggregate, but not to assess the efficacy of specific procedures. This study's generalizability is supported by its broad inclusion criteria - all identified children with hypotonia who underwent surgical intervention for SDB/OSA were included in the analysis.

5. Conclusions

We present a retrospective cross-sectional analysis of children with hypotonia and SDB/OSA, providing a generalizable description of the severity of disease. We describe our experience treating these children - improvement with surgery, but severe residual disease - and show sleep endoscopy data examining patterns of airway obstruction. Multi-level obstruction is frequent and the tongue base is the most common site of obstruction. A prospective multi-institutional study with uniform follow-up and diagnostic evaluation including precise disease definitions for hypotonia and SDB/OSA would help definitively address questions surrounding the efficacy of specific interventions, usefulness of DISE in guiding surgical planning, and identification of correlations between underlying hypotonia diagnoses and patterns of airway obstruction. Our hope is that this work will guide future research and facilitate

counseling for the otolaryngologist presented with such a child in clinic.

Conflicts of interest

None to report.

Financial disclosures

None to report.

Previous presentation

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