Obstructive Sleep Apnea Pretreatment and Posttreatment in Symptomatic Children with Congenital Craniofacial Malformations

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Study Objectives: Obstructive sleep symptoms are common in children with craniofacial malformations (CFM). However objective data about obstructive sleep apnea (OSA) is still limited. The aims of this study were to investigate the frequency of OSA in symptomatic children with CFM and to determine improvement in severity of OSA after treatment.

Methods: Symptomatic children with CFM referred for a diagnostic polysomnogram (PSG) were identified. Obstructive sleep apnea was defined as an apnea/hypopnea index (AHI) ≥ 1 , with moderate/severe OSA as an AHI ≥ 5 .

Results: Overall, 151 symptomatic children were identified; 87% were diagnosed with OSA, of whom 24% had moderate-to-severe OSA. Children with syndromic CFM, compared to non-syndromic CFM, were more likely to have an AHI ≥ 5 (syndromic 33% vs. non-syndromic 15%, $p = 0.02$). Of the 131 children with OSA, 64 were treated and 32 returned for a posttreatment PSG, with 22 treated with either positive airway pressure (PAP) or adenotonsillectomy (AT). Children treated with PAP demonstrated a decrease in AHI from 6.2 to

3.5 ($p = 0.057$) and an increase in SpO₂ from 89.1% to 91.1% ($p = 0.091$). There were no significant improvements for those in the AT group for either AHI (2.5 to 1.8, $p = 0.19$) or SpO₂ (90.4% to 91.3%, $p = 0.46$). Normalization of the AHI (AHI < 1) occurred in only one child in each group (7% and 14% of the PAP and AT groups, respectively).

Conclusions: The vast majority of children with CFM referred for OSA evaluation are found to have objective evidence of OSA and a quarter of children have moderate-to-severe OSA. It is likely that many children with underlying OSA are not identified and referred for evaluation. Residual OSA after treatment is common in children with CFM.

Keywords: adenotonsillectomy, cleft, positive airway pressure, craniofacial malformations, polysomnography, obstructive sleep apnea, syndromes, treatment

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Since the first report by Guilleminault in 1976 of several cases of pediatric obstructive sleep apnea (OSA),¹ knowledge about prevalence, mode of presentation, and negative outcomes associated with untreated OSA has notably improved in the general pediatric population.^{2–4} The recurrent episodes of upper airway obstruction during sleep cause oxygen desaturation, hypercapnia, disruption of normal ventilation, and sleep fragmentation. Consequently, this results in multiple end-organ morbidities such as cardiovascular dysfunction and neurocognitive deficits due to local and systemic inflammation.⁵ Thus, diagnosis and treatment of pediatric OSA is important to ensure early treatment in order to prevent long-term morbidities.

In the general pediatric population it is well known that the frequency of OSA is up to 4% with a peak between 2–6 years of age when adenotonsillar size is largest relative to airway size.^{2,6} Previous studies suggest that the presence of craniofacial malformations (CFM) in children increases the risk for symptoms of sleep disordered breathing and OSA.^{7–11} Nevertheless, there are limited objective data about the prevalence of OSA in this pediatric population. Three retrospective studies, two in children with cleft lip and/or palate, and one in children with syndromic

BRIEF SUMMARY

Current Knowledge/Study Rationale: The presence of craniofacial anomalies in children is frequently associated with symptoms of sleep-disordered breathing yet, objective data regarding the presence of obstructive sleep apnea (OSA) in this population is lacking. The purpose of this study was to investigate the frequency of OSA and the impact of treatment in symptomatic children with CFM.

Study Impact: The vast majority of symptomatic children with CFM have objective evidence of OSA. Nonetheless, despite treatment, residual OSA is common in this population. We suggest that a posttreatment polysomnogram should be considered in symptomatic children with CFM.

cranosynostosis, have evaluated not only the presence of symptoms, but also the frequency of OSA.^{7–9} However, only two studies have prospectively investigated the frequency of OSA in children with CFM. The first one was conducted in children with syndromic craniosynostosis¹⁰ and the second in 50 infants with cleft lip and/or palate prior to any surgical procedure.¹¹ While these previous studies support an association between CFM and pediatric OSA, available data are limited to children with a specific CFM or to children in a particular age range. Moreover,

characteristics of OSA in this pediatric population, such as frequency and severity of OSA according to gender or race, are still unknown.

Treatment of OSA in children with CFM differs from that of the general pediatric population because of the multifactorial cause of upper airway obstruction in CFM and because this is a heterogeneous and complex pediatric population.¹² Indeed, while adenotonsillectomy (AT) is considered the standard treatment for OSA in the general pediatric population, AT has been associated with more postoperative complications and lower success in children with CFM.^{13,14} Although adenotonsillar hypertrophy is quite common in children with CFM, assessment of AT effectiveness based on polysomnographic outcomes in this pediatric population is limited.¹⁴ Children with CFM often have difficulties tolerating positive airway pressure (PAP) despite the fact that PAP is considered the first line treatment in these children.¹⁵ Thus, there remain few data regarding the impact of OSA treatment in children with CFM. The aim of this study was to investigate frequency of OSA in symptomatic children with CFM and to assess the impact of treatment. Our hypothesis was that OSA is common in children with CFM and that there would be a high frequency of residual OSA even after treatment.

METHODS

Subjects

Consecutive children with CFM from the Craniofacial Anomalies Program were identified if they were referred to the pediatric sleep clinic with suspicion of OSA. Inclusion criteria were: children ≥ 2 and < 19 years old with syndromic or non-syndromic congenital CFM who had an overnight diagnostic polysomnogram (PSG) at the University of Michigan between February 2003 and February 2013, and who had no previous treatment for OSA. Children with acquired craniofacial anomalies, those < 2 years or > 19 years, and those who had previous surgical procedures to improve upper airway obstruction were excluded. In addition, those whose first PSG was PAP or a titration with oxygen were excluded. This study was approved by the University of Michigan Institutional Review Board.

Demographic and anthropometric data obtained from the medical records included: gender, date of birth, age at the time of the PSG, racial background, height, and weight. Obesity and overweight were defined according to international standard definitions.¹⁶ The study population was divided into 3 age groups and 4 groups based on body mass index (BMI). The 3 age groups were as follows: toddlers/preschoolers (2.0–4.9 years), school-aged children (5.0–11.9 years) and adolescents (12.0–18.9 years). The 4 BMI groups were: underweight (BMI < 5 th percentile), normal weight (BMI ≥ 5 th percentile and < 85 th percentile), overweight (BMI ≥ 85 th percentile < 95 th percentile), and obese (≥ 95 th percentile). In addition, diagnosis, main characteristics of the congenital CFM, and management of OSA used in each case were also collected.

Polysomnography

The overnight diagnostic PSG monitoring included: electroencephalogram (EEG): frontal, central and occipital (F4-M1, C4-M1 and O2-M1; F3-M2, C3-M2 and O1-M2),

electro-oculogram (EOG): right and left; electromyogram (EMG): submental and right and left tibialis, electrocardiography (ECG), nasal pressure, oronasal airflow (thermistry), thoracic and abdominal inductance plethysmography, oxyhemoglobin saturation (SpO₂), snore sensor, and body position monitor. Esophageal pressure (Pes) and end-tidal CO₂ monitoring were also included in some cases to optimize diagnosis of upper airway resistance and hypoventilation, respectively. Sleep studies were scored by an experienced pediatric sleep technologist using the alternative rule recommended by the American Academy of Sleep Medicine (AASM).^{17,18} Respiratory events were distinguished as obstructive or central and apnea or hypopnea according to specific pediatric criteria recommendations of the AASM. Obstructive apneas were defined as respiratory events that lasted ≥ 2 breaths and were associated with a fall in amplitude of nasal pressure signal $\geq 90\%$, accompanied by inspiratory effort. Apneas not associated with inspiratory effort were defined as central apneas. Obstructive hypopneas were defined as a fall in amplitude $\geq 50\%$ with associated arousal, awakening, or $\geq 3\%$ desaturation. The apnea-hypopnea index (AHI), the main variable assessed, was calculated as the average of apneas and hypopneas per hour of sleep. Pediatric OSA was considered present with an AHI ≥ 1 . The study population was categorized into 3 severity groups of OSA: mild OSA (AHI 1–4.9), moderate OSA (AHI 5.0–9.9), and severe OSA (AHI ≥ 10). Positional apnea was defined as a total AHI ≥ 5 with a reduction $> 50\%$ in the AHI between supine and non-supine posture or AHI < 5 in the non-supine posture. Normalization of the AHI after treatment was considered in those cases with AHI posttreatment < 1 . The presence of periodic limb movements (PLMs) was also collected. PLMs were scored when they occurred in series of ≥ 4 repeated movements in the anterior tibialis muscle lasting between 0.5 to 5 seconds in intervals from 5 to 90 seconds.¹⁹ The periodic limb movement index was considered clinically significant if it was ≥ 5 .

Statistical Analyses

Statistical analyses were performed using SPSS 19.0 (IBM, Armonk, NY). The characteristics of the sample population were summarized using means $\pm$ standard deviations (SD) for normally distributed continuous variables, medians and interquartile ranges for non-normally distributed continuous variables, and counts and/or percentages for categorical variables. The χ^2 test was used to evaluate differences in the frequency of OSA between categories of the variables assessed such as gender, race, age groups, and BMI groups, syndromic and non-syndromic CFM, and with and without cleft palate. Student t-tests were used to compare differences in the means of normally distributed continuous variables such as age and BMI percentile, and nonparametric statistics were used to compare medians of the main polysomnographic variables assessed (total sleep time, sleep latency, REM latency, arousal per hour of sleep, NREM/REM stages, breathing events; AHI, obstructive apnea index [OAI], hypopnea index [HI], central apnea index [CAI], mean SpO₂, minimal SpO₂, PLM index during sleep, and PLM index during sleep accompanied by arousals). Differences in the AHI pre and posttreatment were analyzed using a paired t-test. A p-value < 0.05 was considered statistically significant for all tests.

Figure 1—Selection criteria.

RESULTS

Five hundred and seventy children with CFM followed at the Craniofacial Anomalies Program were identified. Of these, 183 underwent a nocturnal PSG at the University of Michigan between February 2003 and February 2013. Although some children underwent more than one PSG, for the current study only those children whose first PSG was a full-night diagnostic PSG without previous treatment were included. **Figure 1** shows the selection process. The final baseline sample size was 151. The mean age was 8.5 ± 4.2 years, 57% were boys, and 79% were Caucasian. Anthropometric data were available in the medical records for 129 children (85%). The frequency of obesity was 15%. Sixty-eight percent of children had non-syndromic CFM and 58% had cleft palate. Additional demographic, anthropometric, craniofacial, and polysomnographic data are shown in **Table 1**.

Medical records were reviewed to investigate the mode of presentation or main reasons for sleep consultation. These were available for 129 children. According to parents, referral forms, or physicians' notes, snoring was the most common symptom

associated with CFM (83%). In 32% of cases, snoring was reported as an isolated symptom, and in 29% of cases, snoring was associated with diurnal symptoms. Isolated diurnal symptoms were reported in only 5% of children (**Table 2**).

OSA Characteristics Pretreatment in Children with CFM

Obstructive sleep apnea ($AHI \geq 1$) was identified in 87% of the study population. Of these, 76% had mild OSA and 24% had moderate/severe OSA. Independent of the symptoms reported, the frequency of OSA was $> 80\%$ in the different symptomatic groups described in **Table 2**. Children whose parents reported nocturnal breathing symptoms and also diurnal symptoms had the greatest frequency of moderate/severe OSA (42%) compared with the other symptomatic groups (**Table 2**).

No significant differences were found in the frequency of OSA among genders, age groups, BMI groups, or race ($p = 0.48$, $p = 0.45$, $p = 0.60$, and $p = 0.25$, respectively; **Table 1**). Neither were statistically significant differences found in the frequency of OSA between children with and without syndromes, nor children with and without cleft palate ($p = 0.31$ and $p = 0.14$, respectively). In the subgroup of children with non-syndromic CFM, the frequency of OSA was as follows: 94% in children

Table 1—Demographic, anthropometric, craniofacial and polysomnographic characteristics.

Characteristics	Total Population N (%)	AHI ≥ 1 N (%)	AHI ≥ 5 N (%)
Age	n = 151	n = 131	n = 31
Toddlers/preschoolers	39 (26)	36 (28)	9 (29)
School age	77 (51)	66 (50)	13 (42)
Adolescents	35 (23)	29 (22)	9 (29)
Male (%)	86 (57)	73 (56)	14 (45)
Race	n = 151	n = 131	n = 31
Caucasian	119 (79)	106 (81)	25 (81)
Asian	12 (8)	10 (8)	2 (6)
African-American	7 (5)	6 (5)	2 (6)
Others	13 (9)	9 (7)	2 (6)
BMI percentile	n = 129	n = 109	n = 28
Underweight	15 (12)	11 (10)	4 (14)
Normal weight	76 (59)	65 (60)	19 (68)
Overweight	19 (15)	16 (15)	1 (4)
Obese	19 (15)	17 (16)	4 (14)
CFM	n = 151	n = 131	n = 31
Cleft palate	88 (58)	73 (56)	16 (52)
Non-cleft palate	63 (42)	58 (44)	15 (48)
Syndromes	48 (32)	44 (34)	16 (52)
Non-syndromes	103 (68)	87 (66)	15 (48)
PSG results (median, interquartile range)	n = 151	n = 131	n = 31
Total sleep time (min)	444 (52)	443 (58)	440 (47)
Sleep latency (min)	19 (32)	20 (32)	19 (36)
REM latency (min)	152 (89)	148 (88)	155 (82)
Arousal/hour sleep	9 (6)	9 (6)	12 (11)
Sleep efficiency (%)	88 (10)	88 (10)	89 (10)
Stages			
NREM I (%)	6 (6)	6 (6)	8 (8)
NREM II (%)	44 (20)	44 (20)	46 (14)
NREM III/IV (%)	32 (18)	32 (18)	29 (13)
REM (%)	17 (7)	17 (7)	16 (7)
Breathing events			
AHI	2 (3)	3 (3)	8 (10)
OAI	0 (0)	0 (0)	0 (2)
HI	1 (3)	2 (2)	5 (9)
CAI	1 (1)	1 (1)	2 (4)
Mean SpO ₂	97 (2)	97 (2)	97 (2)
Min SpO ₂	91 (6)	90 (5)	89 (6)
Positional apnea	3%	4%	16%
PLMs index in sleep	1 (4)	1 (4)	1 (5)
PLMs index + arousals in sleep	0 (1)	0 (1)	0 (0)

AHI, apnea hypopnea index; BMI, body mass index; CAI, central apnea index; HI, hypopnea index; OAI, obstructive apnea index; OSA, obstructive sleep apnea; PLMs, periodic limb movements; SpO₂, oxyhemoglobin saturation.

Figure 2

(top) Frequency and severity of obstructive sleep apnea in children with non-syndromic craniofacial malformations. (bottom) Frequency and severity of obstructive sleep apnea in children with syndromic craniofacial malformations. CLP, cleft lip and/or palate; CP, isolated cleft palate; CL, isolated cleft lip; VCF, velocardiofacial.

cleft lip and palate, and 71% in children with non-syndromic craniosynostosis. In the subgroup of children with syndromic CFM, the frequency of OSA was 100% in children with hemifacial microsomia and velocardiofacial or DiGeorge syndrome, 90% in children with Goldenhar syndrome, and 83% in children with syndromic craniosynostosis. Of the 131 children diagnosed with OSA, information about the velopharyngeal insufficiency repair was available in 78 children. However, no differences were found in the frequency of OSA between children who underwent sphincter pharyngoplasty compared to those who did not (86% vs. 79%, $p = 0.54$).

Characteristics of the study population according to the severity of OSA are shown in **Table 1**. Children with syndromic CFM were more likely to have an AHI ≥ 5 than children with non-syndromic CFM (33% vs. 15%, $p = 0.02$). In the subgroup of children with non-syndromic CFM, those with Robin sequence and isolated cleft palate were most likely to have an AHI ≥ 5 (29% and 22%, respectively). In the subgroup of children with syndromic CFM, those with hemifacial microsomia and velocardiofacial/DiGeorge syndrome were most likely to have an AHI ≥ 5

with isolated cleft lip, 89% in children with isolated cleft palate, 86% in children with Robin sequence, 81% in children with

Table 2—Summary of frequency and severity of OSA according to the presence of nocturnal and/or diurnal symptoms.

Symptoms	Total population N	AHI ≥ 1 N (%)	AHI ≥ 5 N (%)
Isolated snoring	41	35 (85)	4 (10)
Nocturnal breathing symptoms	15	13 (87)	5 (33)
Nocturnal breathing symptoms AND diurnal symptoms	38	35 (92)	16 (42)
Nocturnal breathing symptoms AND non-breathing symptoms	13	11 (85)	1 (8)
Nocturnal non-breathing symptoms	8	7 (88)	0 (0)
Nocturnal non-breathing symptoms AND diurnal symptoms	3	3 (100)	1 (33)
Diurnal symptoms	6	6 (100)	2 (33)
Presurgery evaluation	5	4 (80)	1 (20)

Nocturnal breathing symptoms included: snoring, apneas, gasping, and mouth breathing. Nocturnal non-breathing symptoms include: enuresis, parasomnias, night awakenings, poor sleep hygiene, and restless legs syndrome. Diurnal symptoms include: behavior problems, fatigue, and restless.

(50% and 40%, respectively; see **Figure 2**) No statistically significant differences were found in severity of OSA between children who underwent sphincter pharyngoplasty compared with those who did not (18% vs. 14%, $p = 0.71$).

Treatment Options and Polysomnographic Outcomes of OSA in Children with CFM

Of the 131 children diagnosed with OSA, 64 received treatment at our center. The mean age in the subgroup of treated children was 8.1 ± 4.3 years. The treatment options used were as follows: 3 (5%) children were treated with nasal steroids, 14 (22%) underwent AT, 38 (59%) were treated with PAP, 4 (6%) were treated with AT as well as PAP, and 5 (8%) were treated with combinations of treatment options including surgery. While PAP was the first line of treatment used in older school-aged children (mean age 8.7 ± 4.2 years) with moderate OSA, AT was the first line of treatment considered in young school-age children (mean age 6.2 ± 3.2 years) with mild OSA. The combination of AT together with PAP was the treatment used in preschool children (mean age 4.0 ± 1.9 years) with severe OSA. In order to investigate treatment options used according to the craniofacial diagnosis, those CFM diagnoses with a sample size ≥ 3 were selected. In the subgroup of children with non-syndromic CFM, PAP was the most common treatment used in children with isolated cleft palate, isolated cleft lip, and cleft lip and palate (70%, 67%, and 59%, respectively). While in the subgroup of children with syndromic CFM, PAP was the most common treatment used in children with syndromic craniosynostosis and Goldenhar syndrome (88% and 60%, respectively).

Of the 64 children who were treated at our center, a subsequent posttreatment PSG was performed in 32 children. It is assumed that the reason for the second PSG was the presence of residual symptoms after treatment. Of the 32 children, 2 (6%) were treated with nasal steroids, 7 (22%) underwent AT, 15 (47%) were treated with PAP, 4 (12.5%) with the combination of AT as well as PAP, and 4 (12.5%) with other treatment options. In children treated with PAP ($n = 15$), a 44% decrease of the AHI (from 6.2 to 3.5, $p = 0.057$) was found, and there was a tendency to increased minimal SpO_2 posttreatment (from 89.1% to 91.1%, $p = 0.091$). In children who underwent AT ($n = 7$), no significant difference in the AHI was found (from 2.5 to 1.8, $p = 0.19$), nor was there any significant increase in

Figure 3—Changes in the AHI in children treated with adenotonsillectomy, PAP, or the combination of adenotonsillectomy and PAP.

AHI pretreatment and posttreatment in the three main sub-groups of treatment: AT and PAP (combination of adenotonsillectomy and positive airflow pressure), PAP (positive airflow pressure) and AT (adenotonsillectomy). Horizontal lines indicate the different severity levels of pediatric OSA: mild OSA AHI 1–4.9, moderate OSA AHI 5.0–9.9, and severe OSA AHI ≥ 10 .

the minimal SpO_2 (from 90.4% to 91.3%, $p = 0.46$). Similarly, in children who received both AT as well as PAP ($n = 4$), the change in AHI was nonsignificant (from 11.6 to 4.9, $p = 0.33$), as was the change in minimal SpO_2 (from 86.0% to 89.7%, $p = 0.45$; see **Figure 3**). Nevertheless, while improvement of the AHI was found in the PAP and AT group, normalization of the AHI (< 1) was only achieved in one child from each of the PAP and AT groups (7% and 14%, respectively).

DISCUSSION

Results of this study show that the frequency of OSA in children with CFM referred to a sleep clinic due to the presence of symptoms was greater than 70% regardless of craniofacial anomaly diagnosis. It is widely recognized that the presence of craniofacial anomalies in a newborn can compromise the

morphology of the upper airway from birth, predisposing to sleep disordered breathing symptoms and OSA.^{7–11} Nevertheless, we found that even in “mild” non-syndromic CFM where the pharyngeal airway may not be involved, such as in isolated cleft lip, the presence of symptoms was associated with a frequency of OSA greater than 90%. It has been previously reported that children with syndromes are more likely to have symptoms and undergo PSG.⁷ Our findings further show that children with syndromic CFM were more likely to have an AHI ≥ 5 (syndromic 33% vs. non-syndromic 15%), particularly those children with hemifacial microsomia and velocardiofacial/DiGeorge syndrome (50% and 40%, respectively). The very high frequency of OSA among the studied children strongly suggests that there may also be many children who were not referred for PSG but who nevertheless had OSA—and may even have benefited from treatment. Thus, PSG assessment should be highly recommended in children with craniofacial anomalies and symptoms of OSA.

From a sleep perspective, a pediatric population with craniofacial anomalies is complex. This complexity lies not only the heterogeneity of these children, from cleft lip to severe syndromic craniosynostosis, but also in the limited objective data, lack of general knowledge, and even difficulties in getting access to sleep clinics. Consequently, increased knowledge of the relationship between OSA and CFM may aid sleep physicians, pediatricians, and general health providers to improve the diagnosis of this under-recognized, but common medical condition. A good medical history should be considered the first step in the diagnosis of OSA. Of note, we found that 80% of symptomatic children with CFM snore—the key symptom of OSA. Children who reported snoring or other nocturnal breathing symptoms, in addition to diurnal symptoms, had a high frequency and greater severity of OSA.

Children with CFM have long been believed to have an increased risk for OSA. Rose demonstrated that the upper airway in children with a cleft palate was more similar to the upper airway in children with OSA than to controls, even when no significant differences in AHI were found among groups.²⁰ Moreover, a recent study undertaken in 50 infants with cleft lip and/or palate concluded that the increased risk of sleep disordered breathing and obstructive events was present in all infants even before palate repair.¹¹ Nevertheless, other predisposing factors may play a role in the pathophysiology of OSA in children with CFM, such as genetic factors, ethnicity, or obesity.²¹ However, results from our study did not find differences in the frequency of OSA among racial backgrounds or BMI groups. This unexpected result, also found in a previous study by our team,²² might be due to a lower frequency of overweight/obesity in children with CFM, or perhaps because cephalometric anatomy may have a higher impact on upper airway obstruction during sleep in children with CFM compared to the impact of obesity.

To date, the limited literature on OSA in children with CFM has been focused on investigating the role of specific precipitating risk factors for OSA and on identifying those that are potentially modifiable. Precipitating factors are those factors that occur in a specific time and contribute to increases in the AHI such as inflammation of soft tissue (adenotonsillar hypertrophy) or surgeries undertaken to repair the congenital defect

or the velopharyngeal insufficiency. However, although adenotonsillar hypertrophy is common in children with CFM, the vast majority of studies performed in this population have investigated operative procedures as the main precipitating risk factor for OSA.^{23–27}

Half of the children diagnosed with OSA in our study were treated, and, of these, 50% had a subsequent posttreatment PSG. Treatment of OSA in children with CFM often differs compared to children without CFM.^{15,28} As expected, results of this study showed that PAP was considered the first line of treatment in children with CFM, particularly in older school-aged children. Nevertheless, AT or the combination of AT and PAP was considered the first line of treatment in younger children. While improvement of the AHI occurred in two-thirds of children treated with PAP and most children who underwent AT, normalization of the AHI posttreatment was not common and only occurred in one child in each group. These data demonstrate that residual OSA in children with CFM is remarkably common. Resolution of OSA appears to rarely occur. Further studies that include all children with CFM, rather than those just referred for a sleep evaluation, should be conducted in order to determine whether resolution of OSA is indeed rare.

The major strength of this study is that it provides objective data regarding characteristics of OSA pretreatment and posttreatment in a relatively large pediatric population with CFM. Second, this heterogeneous sample with a wide age range from a multidisciplinary clinic of a tertiary referral center is likely representative of craniofacial anomalies clinics. Third, while the impact of AT based on polysomnographic outcomes has been reported previously in children with syndromic craniosynostosis,^{14,29} the impact of PAP in children with CFM has not been previously documented.

Despite these strengths, there are several limitations. Firstly, this study is a retrospective chart review and is limited by the available data. Thus, access was limited to medical records of children who received treatment at our center. Nonetheless, we do not believe that our findings would be significantly altered if some children received treatment elsewhere. Secondly, the treatment options in this group of children are complex and we focused on the two main treatments, namely PAP and AT, since these treatments were the most common. Finally, only half of the treated children underwent a posttreatment PSG. It is possible that a repeat PSG was performed because of continued symptoms, and hence our finding of a high frequency of residual OSA is not surprising. However, even if all of the children who did not undergo a posttreatment PSG had their OSA successfully eliminated—which is highly unlikely—there would still be a high frequency of residual OSA in this population. Incomplete resolution of OSA has been reported in 23% to 75% of otherwise typically developing children,^{30–32} although in the latter populations the persistence of OSA is generally associated with obesity, which was uncommon in our CFM population.

In conclusion, the vast majority of symptomatic children with CFM have OSA regardless of the craniofacial diagnosis, and a quarter of these have moderate-to-severe OSA. Despite treatment, while some improvement in the AHI was observed, residual OSA is very common. It is likely that many children with underlying OSA are not identified and referred for evaluation. We suggest that a repeat PSG posttreatment should be

considered children with CFM. Prospective studies to better understand treatment response in this population are needed.

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