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22q11.2 Deletion syndrome and obstructive sleep apnea

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ABSTRACT

Otolaryngologic problems are common in the 22q11.2 deletion syndrome (DS) population. Structural anomalies and retrognathia may predispose these patients to obstructive sleep apnea (OSA). The current association of OSA in this population is not defined.

Objective: (1) Define the frequency of OSA in 22q11.2 DS patients referred for polysomnography (PSG). (2) Determine if OSA is present before and/or after surgery to correct velopharyngeal insufficiency (VPI). (3) Determine effect of prior adenotonsillectomy on OSA following VPI surgery.

Methods: Retrospective review of children treated from 2006 to 2013 in a tertiary care setting identified by ICD-9 758.32 (velocardiofacial syndrome) and 279.11 (DiGeorge syndrome). Surgical history and PSG data were abstracted from the identified records.

Results: We identified 323 patients with 22q11.2 DS; 57 (18%) were screened at any point in care using PSG and 15 patients had PSG at multiple time points in care. In most cases, indication for PSG was sleep disordered breathing or pre-operative planning. Overall, 33 patients met criteria for OSA on PSG, accounting for 10.2% of our study population; however, the percentage of patients with OSA was significantly higher within the group of 57 patients (58%) who were screened with PSG.

Twenty-one of the screened patients (54%) had PSG prior to any pharyngeal surgery and had mild to severe OSA (obstructive apnea/hypopnea index (AHI): median 5.1/h, range 1.9–25.6). Eighteen patients had PSG after adenotonsillectomy; 8 of these patients (44%) had mild to moderate OSA (median AHI 2.95/h, range 1.9–5.4). Seventeen patients had PSG after VPI surgery (palatopharyngeal flap (PPF) $n=16$, sphincteroplasty $n=1$). Nine of these patients (53%) had mild to severe OSA (median AHI 3/h, range 1.9–15). Patients who underwent adenotonsillectomy prior to VPI surgery had similar prevalence of OSA (50%, $n=12$) than those who did not (OSA: 60%, $n=5$, $p=0.70$). Most children had mild OSA.

Conclusion: Prevalence of OSA in this population of 22q11.2 DS patients is higher than expected in the general population. OSA risk is highest after VPI surgery, and may be decreased by adenotonsillectomy. Providers should have awareness of increased prevalence of OSA in patients with 22q11.2 DS. Close monitoring for OSA is warranted given the likelihood of subsequent surgical intervention that can worsen OSA.

1. Introduction

22q11.2 deletion syndrome (DS) occurs in approximately 1 in 4000 live births and is identified in most patients with DiGeorge, velocardiofacial, and conotruncal anomaly face syndromes [1]. In addition to the characteristic pattern of conotruncal cardiac anomalies, a significant number of common otolaryngologic problems are found within these syndromes [2]. Patients with 22q11.2 DS present with structural anomalies including retrognathia [3], which may predispose them to obstructive sleep apnea (OSA) [4–6]. The prevalence of OSA in this population has not previously been studied.

The majority of 22q11.2 DS patients have palatal anomalies, including palatal clefting and velopharyngeal insufficiency (VPI) in

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the absence of overt or submucous cleft palate [2,7]. Previous literature suggests that up to 37% of patients with cleft palate require surgery to correct VPI [8], generally through pharyngeal flap surgery or sphincter pharyngoplasty. Surgery to correct VPI carries a risk of causing or exacerbating OSA due to alteration of the naso/oro-pharynx which carries a potential for airway compromise [9]. In the 22q11.2 DS population, a wide posterior pharyngeal flap is often necessary due to the craniofacial dimensions and severity of the velopharyngeal dysfunction. Given the increased risk of OSA, some VPI treatment paradigms recommend that adenotonsillectomy be performed prior to pharyngeal flap surgery in order to minimize incidence of OSA postoperatively [10].

Little is known about OSA in the 22q11.2 DS population, with only one case report describing a child with 22q11.2 DS with both obstructive and central sleep apnea. Tonsillectomy benefited the patient by decreasing her respiratory disturbance index and improving nadir oxygen saturation [11]. It is well established that adenotonsillectomy is effective in treating OSA in nonsyndromic patients [12]. Surgeons may be reluctant to perform adenotonsillectomy in patients with 22q11.2 DS as adenotonsillectomy has been shown to uncover or worsen VPI [13].

It is important to define the baseline frequency of OSA in in 22q11.2 DS patients since many 22q11.2 DS patients have VPI and corrective surgery may cause or worsen OSA [14]. The current study sought to determine the prevalence of OSA in 22q11.2 DS patients referred for polysomnography (PSG) through a retrospective review of patients treated at the Children's Hospital of Philadelphia (CHOP) from 2006 to 2013. Secondary objectives evaluated presence of OSA before and/or after surgery to correct VPI, and the effect of adenotonsillectomy on OSA in this patient population.

2. Methods

After institutional review board approval was obtained, we conducted a retrospective chart review of consecutive patients seen between January 1, 2006 and July 1, 2013 at CHOP. Consent was waived for this retrospective study. Potential cases were identified by querying billing records for *International Classification of Diseases, Ninth Revision* (ICD-9) codes 758.32 (velocardiofacial syndrome) and 279.11 (DiGeorge syndrome). Inclusion criteria were male or female patients up to age 18 with documented 22q11.2 DS who were evaluated at CHOP. The following data were collected from patient medical records: age, gender, diagnosis, surgical history, pediatric sleep questionnaire (PSQ) [15] scores, and PSG dates and results, including obstructive apnea hypopnea index (AHI), nadir oxygen saturation, and peak end-tidal CO_2. PSG was performed and scored using American Academy of Sleep Medicine pediatric criteria [16]. PSG results were categorized by time point in care using the following designations: pre-surgical intervention, post-adenotonsillectomy, or post-surgical intervention for VPI. Surgical interventions for VPI were defined as posterior pharyngeal flap (PPF) surgery or sphincter pharyngoplasty. OSA was defined as AHI $\geq$ 1.5 [17,18]. Statistical significance was evaluated using a Kruskal–Wallis test for comparison of AHIs between pre-intervention, post-adenotonsillectomy, and post-VPI surgery cohorts. The Wilcoxon rank-sum test was used to evaluate the effect of prior adenotonsillectomy on OSA following VPI surgery. In both cases, a p value <0.05 was considered significant.

3. Results

The search of billing records for the diagnosis of velocardiofacial syndrome or DiGeorge syndrome yielded 323 total patients, of whom 57 (18%) were screened at any point in care using PSG. Table 1 shows the demographic and clinical characteristics of the screened population. In the cohort of patients not included in the study who had 22q11.2 DS but were not screened with PSG (n = 266), 40 (15%) had either adenotonsillectomy or adenoidectomy, 44 (17%) had palate surgery for VPI (38 PPF and 6 cleft palate repairs) and, 16 of the patients that had surgery for VPI (all PPF) had prior adenotonsillectomy or adenoid surgery.

Table 1
Clinical characteristics of screened patients.

Clinical characteristics of screened patients (n = 57)	
Male sex	25 (43.9%)
Age at first PSG (years)	6.4 (0.8–15.9)
Number of patients with multiple PSGs	15 (26.3%)
Number of PSGs	74
Number of patients who had PSG at various time points	
Pre-intervention	39 (52.7%)
Post-T and A	18 (24.3%)
Post-VPI surgery	17 (23.0%)
Number of patients who had OSA on any PSG	33 (58%)

Data displayed as n (%) or median (range).

Of our studied cohort of patients who had 22q11.2 DS and were screened with PSG (n = 57), 32 (56%) had either adenotonsillectomy or adenoidectomy, 22 (38.6%) had palate surgery for VPI (all PPF) and, 16 patients that had PPF had prior adenotonsillectomy or adenoid surgery. Twenty of the patients (35%) had completed a sleep questionnaire (PSQ). PSQ results did not correlate with AHI.

Fifteen (26%) of the patients screened received PSGs at multiple time points in care, and only two were screened at all three time points in care—prior to any pharyngeal surgery, after adenotonsillectomy, and after VPI surgery. Of the 57 patients screened by PSG, 33 (58%) met diagnostic criteria for OSA at some point in care (median AHI 4.2/h, range 1.9–25.6).

Overall, 39 (53%) of the screened patients had PSG prior to any pharyngeal surgery (pre-intervention). Indication for PSG was most often to evaluate sleep disordered breathing (n = 31), but also included preoperative planning for PPF surgery (n = 6). Indication for PSG was unavailable for 2 patients. Of this group, 21 (54%) had mild to severe OSA with a median AHI of 5.1/h (range, 1.9–25.6) (Fig. 1). The median nadir oxygen saturation for the patients with OSA was 86% (range, 67–92%) and median peak end-tidal CO_2 was 54 mm Hg (range 41–62). Patients with OSA from this cohort were managed with adenotonsillectomy or CPAP. In one case, VPI surgery was performed despite OSA (Fig. 2).

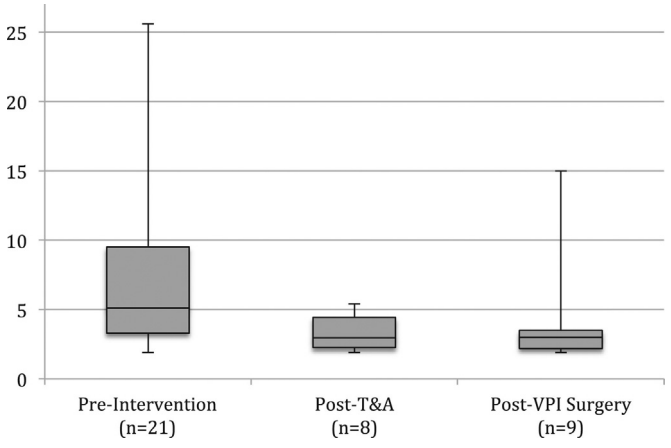

Fig. 1. Median apnea hypopnea index during polysomnography at point of intervention. n, number of patients in each category. Horizontal lines inside boxes represent the median; box edges show the lower and upper quartiles, and the whiskers denote the minimum and maximum.