Abstract: The purpose of this study was to analyze the prevalence, diagnosis, and management of velopharyngeal insufficiency (VPI) in patients with craniofacial microsomia (CFM).

Craniofacial microsomia patients 13 years of age and above treated at 2 centers from 1997 to 2019 were reviewed retrospectively for demographics, prevalence of VPI, and management of VPI. Patients with isolated microtia were excluded. Comparisons were made between patients with and without VPI using chi-square and independent samples t tests.

Among 68 patients with CFM (63.2% male, mean 20.7 years of age), VPI was diagnosed in 19 patients (27.9%) at an average age of 7.2 years old. Among the total cohort, 61 patients had isolated CFM, of which 12 (19.6%) were diagnosed with VPI. Of the patients with isolated CFM and VPI, 8 patients (66.7%) were recommended for nasoendoscopy, of which only 2 patients completed. Seven isolated CFM patients (58.3%) underwent speech therapy, whereas none received VPI surgery. In contrast, 7 patients were diagnosed with both CFM and cleft lip and/or palate (CL/P), all of whom had VPI and were recommended for nasoendoscopy, with 5 (71.4%) completing nasoendoscopy, 6 (85.7%) undergoing speech therapy, and 6 (85.7%) undergoing corrective VPI surgery. Overall, we demonstrated that VPI was present in 27.9% of all CFM patients. On subset analysis, VPI was diagnosed in 20% of patients with CFM and 100% of patients with CFM and CL/P. In addition, despite clinical diagnosis of VPI, a sizeable proportion of isolated CFM patients did not undergo therapy or surgical interventions.

Key Words: Craniofacial microsomia, Goldenhar syndrome, craniofacial microsomia, velopharyngeal insufficiency

Craniofacial microsomia (CFM), also called hemifacial microsomia, is the second most common congenital anomaly of the face, after cleft lip and/or palate (CL/P), and occurs in approximately 1 in every 5600 births. Craniofacial microsomia is defined by a spectrum of anomalous structures derived from the first and second branchial arches, including microtia, hypoplasia of the mandible, zygoma, and temporal bones, soft tissue hypoplasia, and facial nerve paralysis. Although not traditionally a central focus in the functional evaluation and treatment of patients with CFM, velopharyngeal insufficiency (VPI) has been observed and sparingly reported in the population.

Several anatomic reasons for VPI in CFM have been proposed in the literature. As a derivative of the first branchial arch, the tensor veli palatini muscle is involved in CFM, with its disruption possibly contributing to VPI. In his seminal 1965 review of 102 patients with first and second branchial arch-derived anomalies, Grabb observed that 5 out of 39 patients with mandibular involvement had unilateral underdevelopment and paralysis of the palatal muscles but no evidence of VPI. Subsequently, Luce et al noted that in their cohort of 18 patients with CFM, 14 patients had unilateral palatal paralysis and that one third of their total cohort demonstrated VPI. The combined finding of unilateral palatal paralysis and VPI in patients with CFM was later echoed by Funayama et al in a larger cohort. A different etiology was offered by Shprintzen and colleagues who suggested that unilateral hypoplasia of the pharyngeal constrictors may be at play as they observed that the pharynx was hypoplastic even at rest and movement of the lateral pharyngeal wall was deficient on the microsomic side in unilateral cases.

Interestingly, among the known reports, there has been disagreement in terms of the prevalence of VPI in patients with CFM. Shprintzen and colleagues evaluated 22 patients with CFM and found that 63% of their patients with isolated CFM had VPI and 33% of patients with CFM and cleft palate had VPI, whereas Luce et al noted that 33% of their cohort with CFM demonstrated VPI. On the other end of the spectrum, Funayama and colleagues demonstrated in a cohort of 48 patients with CFM that 50% of patients with CFM had a unilateral hypodynamic palate and 14.6% of their cohort had VPI. Due to the wide variance in prevalence and the limited literature on VPI in CFM, we sought to analyze the prevalence, diagnostic techniques, and therapeutic modalities used for VPI in patients with CFM in a multi-institutional study.
MATERIALS AND METHODS
This study was approved by the institutional review board at UCLA (IRB #11-000025).

Patient Selection
We performed a retrospective chart review of patients managed by a multidisciplinary team from the University of California, Los Angeles Craniofacial Clinic and the Craniofacial/Cleft Palate Program at the Orthopaedic Institute for Children in Los Angeles. Patients were diagnosed with CFM by physicians specialized in craniofacial conditions. All patients with CFM that were evaluated by a speech-language pathologist (SLP) between 1997 and 2019 were included. Patients younger than 13 years of age at time of the most recent evaluation and patients with isolated microtia were excluded. Demographics, presence of VPI, diagnostic methods, therapies, and surgical interventions were reviewed. Charts were reviewed beginning with the first speech pathology visit.

Statistical Analyses
All data were analyzed using SPSS software Version 25 (IBM, Chicago, IL). Descriptive statistics were performed for demographic variables. Descriptive statistics for categorical variables were performed using chi-square tests. Independent samples t tests were used to determine whether nonrandom associations existed between VPI demographics, various anomalies, and therapies. A P value less than 0.05 was considered significant.

RESULTS

Patient Characteristics
A total of 68 patients with CFM (43 male, 63.2%, mean age 20.7 ± 5.6 years) met inclusion criteria (Supplementary Digital Content, Table 1, http://links.lww.com/SCS/C910). Among the cohort, the most common clinical findings were mandibular hypoplasia (n = 60, 90.1%) and microtia (n = 58, 85.3%). A total 39.7% of patients were diagnosed with Goldenhar syndrome. Patients received their first speech evaluation at a mean age of 5.8 ± 4.9 years old and their last speech follow-up at an average age of 15.4 ± 3.6. 19 patients (27.9%) diagnosed with VPI. To account for patients who had surgeries that may have affected speech in the course of treatment of CFM, we reviewed surgical interventions involving the jaws. Among the cohort, 25 patients (36.7%) were treated with mandibular distraction and 18 patients (26.4%) received orthognathic surgery.

VPI Diagnosis and Treatment
Within the cohort, 19 patients (27.9%) were diagnosed with VPI at a mean age of 7.2 ± 5.0 years old during a multidisciplinary clinic visit by an SLP (Supplementary Digital Content, Table 2, http://links.lww.com/SCS/C910). Of the 19 VPI patients, 15 (78.9%) were recommended for nasoendoscopic evaluation, with 7 (36.8%) completing nasoendoscopy at an average age of 10.1 ± 4.6 years old. In terms of treatment, 13 VPI patients (68.4%) underwent speech therapy beginning at a mean age of 5.6 ± 3.6 years old with a total duration of 6.4 ± 4.2 years of therapy. Finally, 6 of these patients (31.6%) underwent surgery for VPI correction at an average age of 8.5 ± 3.6 years, with 5 undergoing pharyngoplasty and 1 receiving a posterior pharyngeal flap.

Findings and Treatment Differences Associated with VPI
Significant differences in clinical findings, including microtia, mandibular hypoplasia, facial nerve weakness, soft tissue deficiency, macrostomia, epibulbar dermoids, and spinal abnormalities were not found between patients with and without VPI (Supplementary Digital Content, Table 3, http://links.lww.com/SCS/C910). Similarly, no associations were found between mandibular distraction or orthognathic surgery and VPI.

A significantly higher proportion of patients with VPI underwent speech therapy (n = 13, 68.4%) compared to patients without VPI (n = 18, 37.5%, P = 0.022). Patients without VPI underwent speech therapy for speech delay or articulation errors, language skills, sibilant distortion, cognitive delay, hearing difficulties, and limited jaw opening. There was a mild tendency for patients with VPI to start speech therapy earlier and for a longer duration of time compared to patients without VPI, however this did not reach statistical significance.

VPI Diagnosis and Treatment in patients with CFM and CL/P
Within the 68 patient CFM cohort, 7 CFM patients (10.3%) were also born with CL/P (5 male, 71.4%). Two of these patients (26.6%) had isolated cleft palate, whereas 5 (71.4%) had cleft lip and palate. All patients had palatoplasties at infancy and all 7 CFM with CL/P patients (100.0%) were eventually diagnosed with VPI (Supplementary Digital Content, Table 4, http://links.lww.com/SCS/C910).

Compared to patients with isolated CFM, patients with both CFM and CL/P were more likely to be diagnosed with VPI (19.6% versus 100%, P < 0.001, respectively). Although no significant differences in starting age or duration of speech therapy were found between the 2 subsets, there was a tendency for more patients with both CFM and CL/P (n = 6, 85.7%) to undergo speech therapy than isolated CFM patients (n = 7, 58.3%). (Supplementary Digital Content, Table 5, http://links.lww.com/SCS/C910).

Among patients who were clinically diagnosed with VPI, 15 of the 19 were recommended for nasoendoscopy, of which 8 had isolated CFM and 7 had both CFM and CL/P. Although the majority of patients with CFM and CL/P recommended for nasoendoscopy ultimately underwent the procedure, only 2 of the 8 patients with isolated CFM completed nasoendoscopy despite referral (P = 0.017).

Similar to the differences in nasoendoscopy, patients with CFM and CL/P who were diagnosed with VPI were more frequently treated with surgery (6 out of 7 patients, 85.7%), whereas none of the patients with isolated CFM and VPI underwent corrective VPI surgery.

DISCUSSION
In this work, we sought to understand the prevalence and treatment of VPI in patients with CFM who were at least 13 years of age and above (mean 20.7 years, range of 13–34 years of age). We found that 27.9% of patients with CFM were clinically diagnosed with VPI in our multi-institutional cohort. Upon subset analysis, VPI was found in a fifth of patients with isolated CFM and all patients with...
both CFM and CL/P. In addition, subset analysis revealed VPI diagnosis and treatment differences between patients with isolated CFM versus patients with both CFM and CL/P. Although a majority of patients with CFM, CL/P, and VPI proceeded to receive speech therapy, only 58.3% of patients with isolated CFM and VPI did the same even though it is usually the first line of treatment to improve articulation errors associated with velopharyngeal function. Furthermore, despite a clinical diagnosis of VPI and referral for evaluation, completion of nasoendoscopy was particularly deficient in patients with isolated CFM compared to patients with both CFM and CL/P (P = 0.017). Similarly, whereas most patients with CFM, CL/P, and VPI underwent VPI surgery, none of the patients with isolated CFM and VPI had surgery. Our data suggests a few conclusions. First, the prevalence of VPI is relatively common in patients with CFM, particularly those with CL/P. Second, patients with isolated CFM had a tendency to receive less treatment for VPI when compared to patients with both CFM and CL/P and there appears to be a disconnect between those who completed and were referred for nasoendoscopy in isolated CFM patients. Lack of follow through with nasoendoscopy may explain why none of the isolated CFM patients proceeded to VPI surgery as surgical referral typically follows nasoendoscopy evaluation. Our findings suggest that compliance may be relatively low among isolated CFM patients, which could be a consideration for reinforcement during tertiary visits. In addition, findings point towards a greater severity of VPI in CFM CL/P patients that led to the increased emphasis and follow through of nasoendoscopy, speech therapy, and surgery in this population.

The 28% prevalence of VPI in our study population fell within the range previously published, as Funayama et al, reported a VPI prevalence of 15% in CFM and microtia patients without CL/P, whereas Luce et al, reported a 33% rate of VPI in all patients with CFM regardless of CL/P status.6,9 However, there are some differences between our current cohort and those reported in the literature. With respect to associations, Funayama and colleagues reported that the presence of VPI was highly correlated to the severity of mandibular hypoplasia and soft tissue deficiency, as well as presence of macrostomia and developmental delay.0,1 Additionally, CFM patients with CL/P were found to have worse speech results than those without CL/P. Although the latter 2 associations correlate with our cohort, we did not find a significant association between VPI and mandibular hypoplasia, soft tissue deficiencies, or macrostomia. Our cohort also included a large number of patients with Goldenhar syndrome (n = 27, 39.7%). Among the Goldenhar patients, 25.9% (7 out of 27) had VPI which was not significantly different compared to patients without Goldenhar syndrome.

The anatomic understanding of the causes of VPI in patients with CFM is unclear. An interesting discrepancy in the literature revolves around the embryologic origin of the levator veli palatini. Although Grabb in 1965 and Luce in 1977 attributed the embryologic origin of the levator veli palatini muscle to the second branchial arch,3,8 the levator veli palatini is actually innervated by the vagus nerve and a derivative of the fourth branchial arch.3,8 Hence, the question of how the levator veli palatini is affected in CFM, a condition involving the first and second branchial arch, remains uncertain. Although the tensor veli palatini is a derivative of the first branchial arch, it is unclear whether hypoplasia of the tensor veli palatini alone would be sufficient to cause the clinical findings of a unilateral hypodynamic palate in 50% of patients with CFM reported by Funayama and colleagues.9

Our current study suggested several areas for further study and potentially improvement in the care of patients with CFM. First, whereas VPI was clinically diagnosed in a significant number of patients, loss of follow through with objective diagnosis or further treatment was quite high. The reason for this phenomenon deserves further investigation. If the lack of treatment was secondary to patient or family wishes, it is possible that the severity of VPI was relatively mild and non-obtrusive for the patient. Alternatively, it is also possible that reinforcement from the multi-disciplinary clinical teams may be lower in patients with isolated CFM compared to patients with CFM and CL/P. Second, the anatomic etiology of VPI in CFM continues to be unclear. Further descriptions of the levator veli palatini muscles during surgery may assist in understanding whether or not the muscle is hypoplastic in CFM or if other abnormalities exist.

This study had several limitations. As a retrospective study, confounding variables were not available to be adequately measured and diagnostic techniques such as nasoendoscopies were not performed in all patients, preventing observation of all the velopharyngeal gaps and patterns of palatal motion. Furthermore, misdiagnosis and misinterpretation of clinical evaluation is possible. In addition, though our cohort size of CFM patients with VPI diagnoses is the largest in the current literature, our CL/P patient group was still quite small, introducing inherent variability.

CONCLUSIONS

In this study, we report the largest analysis of VPI in CFM and establish a 28% rate of VPI in the CFM population. Patients with CFM displayed a high prevalence of VPI, which increased five-fold in a subpopulation of patients with concomitant CL/P. Among patients with isolated CFM and a clinical diagnosis of VPI, a sizeable proportion of patients did not undergo speech therapy, nasoendoscopy, or surgical intervention. This suggests that VPI in isolated CFM patients may not be adequately managed by clinicians and that increased vigilance from the standpoint of the multidisciplinary team may be necessary to encourage compliance with VPI treatment in patients with CFM. Furthermore, as all CFM patients were diagnosed with VPI at a young age, this study demonstrates the importance of VPI screening in CFM patients, especially those with CL/P, at all stages of care to ensure best outcomes in affected patients.

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