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# Speech outcomes in children with 22q11.2 deletion syndrome following surgery for velopharyngeal insufficiency

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ABSTRACT

*Objective:* The purpose of this study was to identify prognostic factors associated with improved speech outcomes following surgical correction for velopharyngeal insufficiency (VPI) in pediatric patients with 22q11.2 deletion syndrome (22q11DS).
*Methods:* Eighteen patients were identified via retrospective chart review of patients with 22q11DS between 2005 and 2014. Patient characteristics, medical histories, associated comorbidities, surgical procedures, and pre- and postoperative perceptual hypernasality (subjectively rated 1–5 with 5 being the most severe) were gathered for each patient.
*Results:* 12 patients (67%) experienced improvement in hypernasality following corrective surgery for VPI. Higher severity of hypernasality preoperatively was found to be indicative of a lower chance of improvement with VPI surgery. Of 8 patients with a preoperative hypernasality score of 5, 3 (38%) showed improvement in hypernasality postoperatively, while 9 out of 10 (90%) of patients with a preoperative hypernasality score less than 5 showed postoperative improvement. Females were also found to have worse speech outcomes compared to males.
*Conclusion:* 22q11DS patients presenting with severely hypernasal speech preoperatively are less likely to show improvement in hypernasality following corrective surgery for VPI. Those patients with moderate hypernasality are most likely to benefit from surgery.


## 1. Introduction

The 22q11.2 deletion syndrome (22q11DS), known by many names including DiGeorge syndrome and velocardiofacial syndrome, is the most common human microdeletion syndrome, occurring between 1:6000 and 1:2000 live births [1–3]. The deletion results in hypoplasia of the branchial arches *in utero*, leading to abnormalities in the structures derived from them [4]. Consequently, 22q11DS is characterized as a highly variable constellation of findings including but not limited to congenital heart disease, hypoparathyroidism, immunodeficiency, neurocognitive disorders, cleft palate, and velopharyngeal insufficiency [5–8].

Velopharyngeal insufficiency (VPI) is very common in this population. The incidence of VPI has been reported to range widely from 30% to 80% of 22q11.2DS patients [9,10]. VPI is characterized by incomplete closure of the velopharynx during production of oral speech sounds, leading to hypernasality and/or nasal emission during speech production. This often affects speech intelligibility. In addition to velar abnormalities, generalized pharyngeal muscle hypotonia and cranial nerve abnormalities may play a role in the development of VPI in 22q11DS. Platybasia, or an abnormally obtuse cranial base angle, is also thought to contribute to VPI due to the corresponding increase in pharyngeal depth, but there are conflicting reports on whether this is clinically significant [11,12]. In addition, post-adenoidectomy VPI is common in children with this syndrome particularly because these patients depend more heavily on their adenoidal pads for velopharyngeal closure than do unaffected patients [5,13].

For patients with 22q11DS, many of whom suffer from

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neurocognitive disorders, it is important to correct VPI to encourage proper social and language development. Occurrence of VPI in this patient population is most commonly corrected surgically. The two most commonly discussed corrective surgical procedures for VPI in patients with 22q11DS are the superiorly based pharyngeal flap and the sphincter pharyngoplasty; however, others such as the Furlow pharyngoplasty, posterior pharyngeal augmentation, or any combination of these procedures are possible as well [14]. A systematic review by Spruijit et al. found no significant difference in speech outcomes across the various types of surgical procedures [15].

Even with surgical correction, as many as 45% of patients with 22q11DS will have persistent hypernasality post-operatively [16]. 22q11DS patients are three times more likely to have persistent VPI than their nonsyndromic counterparts, and 23–64% of these patients will require repeat surgery [17]. To date, no studies have successfully reported prognostic criteria that may predispose children to persistent VPI after surgical correction [16]. The purpose of this study was to identify pre-operative factors in patients with 22q11DS that correlate with speech outcomes following correctional surgery for VPI. Identification of preoperative predictive factors associated with successful VPI surgery would help guide patient selection and parents' expectations.

## 2. Methods

Approval for the study was obtained by an institutional review board. A retrospective chart review of patients with 22q11DS treated at the tertiary pediatric hospital between 2005 and 2014 was performed using an electronic medical record search. Inclusion criteria included all patients with velopharyngeal insufficiency under the age of 18 years at time of surgical intervention with confirmed 22q11DS by either fluorescence in situ hybridization or chromosomal microarray.

Information gathered included patient and family medical histories, associated comorbidities, age at presentation, and type of VPI corrective surgery. The primary outcome measure was preoperative and postoperative speech hypernasality. Each patient was evaluated by a single, senior speech language pathologist at our institution according to the protocol by Dailey et al. for hypernasality and scored on a 5-point scale as described by Bunton and Story (1 = mild, 2 = mild-moderate, 3 = moderate, 4 = moderate-severe, 5 = severe) [18–20]. A student's *t*-test was used to determine differences in pre- and postoperative hypernasality scores. A chi-squared test of independence was used to test differences in patient characteristics and comorbidities between improvement and non-improvement groups.

## 3. Results

Eighteen patients (7 male, 11 female) were identified based on the inclusion criteria. Patient characteristics and comorbidities are presented in Table 1. Of these 18 patients, the majority (72%) underwent pharyngeal flap surgery, the remainder undergoing either Furlow palatoplasty, sphincter pharyngoplasty, or a combination pharyngeal flap and sphincter pharyngoplasty. 67% of these patients experienced an improvement in their speech hypernasality, with the average pre- and postoperative hypernasality scores dropping from 3.9 ± 1.3 to 2.6 ± 1.9 ($p = 0.018$) (Fig. 1).

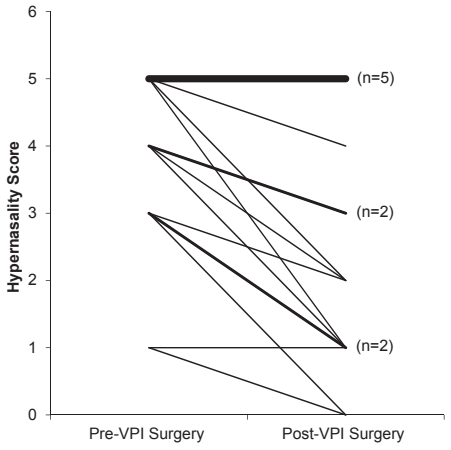
Characteristics of patients whose speech hypernasality improved after surgery are compared to those patients whose did not in Table 2. We did not identify any comorbidities that were predictive of postoperative hypernasality. However, patients who had a severe preoperative hypernasality score were less likely to improve. Of the 8 patients who had a preoperative hypernasality score of 5, only 3 of them (38%) showed any improvement in hypernasality following surgery. In comparison, 9 of the 10 patients (90%) with a preoperative hypernasality score of 4 or less showed improvement in speech outcomes with surgery ($p = 0.019$) (Fig. 2A). In addition, of the patients whose speech did improve with surgery, those with a preoperative score of 3 or 4 showed the greatest average amount of improvement (Fig. 2B).

We did observe difference in outcomes between sexes. Female patients had worse average pre- and postoperative hypernasality scores than their male counterparts. Preoperatively, male and female patients had hypernasality scores of 2.9 ± 1.5 and 4.5 ± 0.7 respectively ($p = 0.021$). Postoperatively, male and female patients had hypernasality scores of 1.3 ± 0.8 and 3.4 ± 1.9 respectively ($p = 0.015$) (Table 3).

**Table 1**
Patient characteristics and clinical findings.

| | |
|---|---|
| Patients requiring surgery | 18 |
| Male | 7 (39%) |
| Female | 11 (61%) |
| Age for VPI surgery (mean yrs ± stdev) | 6.4 ± 2.7 |
| Family history of 22q11DS | 2 (11%) |
| Cardiac disease | 11 (61%) |
| Normal | 7 (39%) |
| Mild[a] | 2 (11%) |
| Severe[b] | 9 (50%) |
| Developmental delay | 11 (61%) |
| Hearing loss | 10 (56%) |
| Hypocalcemia | 6 (33%) |
| Immunodeficiency | 1 (6%) |

[a] Mild - patent ductus arteriosus (PDA), patent foramen ovale (PFO), atrial septal defect (ASD), or ventricular septal defect (VSD).
[b] Severe - tetralogy of Fallot (TOF) or interrupted aortic arch (IAA).




Bolded lines indicate multiple patients with the same perioperative hypernasality scores. n=1 unless otherwise specified.

**Fig. 1.** Comparison of pre- and postoperative speech hypernasality.

## 4. Discussion

In this study, we sought to identify pre-operative factors associated with the presence and degree of speech improvement after surgical correction for VPI in patients with 22q11DS. The 18 patients identified in our study had similar characteristics and rates of comorbidities (Table 1) as those reported in previous population-based studies on patients with 22q11DS [2,5,16]. Consistent with prior research by Sprujit et al. and Losken et al., this study did not identify any comorbidities that predicted the persistence of