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What is This?
Predicting Surgical Intervention for Airway Obstruction in Micrognathic Infants

Sara C. Handley1, Nicholas S. Mader, PhD2, James D. Sidman, MD1,3, and Andrew R. Scott, MD4

Abstract
Objective. To determine which factors present in the neonatal period may predict subsequent need for surgical intervention in infants with micrognathia.

Study Design. Case series with chart review.

Setting. Two, urban, tertiary pediatric hospitals.

Subjects and Methods. The otolaryngology databases from 2 institutions were queried for the diagnosis of micrognathia over a 10-year period, and 123 infants were identified (101 with Pierre Robin sequence and 21 with micrognathia without cleft palate). The presence or absence of surgical airway intervention during the first year of life was noted, as were associated diagnoses. Univariate and multivariate analyses were performed to identify risk factors for requiring a definitive airway intervention.

Results. Forty-eight (39%) micrognathic children required definitive airway intervention during infancy in this series. These interventions came in the form of either tracheostomy (12 patients), mandibular distraction osteogenesis (MDO; 33 patients) or prolonged intubation prior to death (3 patients). Factors associated with a need for intervention included a history of intubation or tracheotomy in the first 24 hours of life (odds ratio [OR], 8.22; confidence interval [CI], 3.14-21.53), a history of intrauterine growth restriction (OR, 4.10; CI, 1.00-16.70), prematurity (<37 weeks of gestational age; OR, 2.38; CI, 1.02-5.56), and neurologic impairment (OR, 3.83; CI, 1.33-11.07). Those with isolated micrognathia without cleft palate were less likely to require intervention (OR, 0.20; CI, 0.05-0.71).

Conclusions. While it is understood that the need for MDO or tracheostomy should be determined on a case-by-case basis, this study identifies a number of factors that may predict which neonates with micrognathia are at increased risk for requiring early surgical intervention for respiratory and feeding problems.

Keywords
micrognahtia, Pierre Robin sequence, mandibular distraction osteogenesis, airway obstruction

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MICROGNATHIA, defined as a small and retrusive mandible in which the mandibular alveolus is significantly posterior to the maxillary alveolus, is a craniofacial condition that may have an immediate or long-term impact on management of the neonatal airway. Micrognahtia is often associated with Pierre Robin sequence (PRS), a constellation of findings including mandibular hypoplasia, glossoptosis, and a U-shaped cleft palate. Evans et al1 have proposed a basic protocol outlining clinical evaluation, medical and surgical management of neonates with PRS, identifying tongue-lip adhesion (TLA), mandibular distraction osteogenesis (MDO), and tracheostomy as surgical options for airway stabilization. However, the current literature, including this protocol, does not offer specific information to help physicians anticipate which neonates will be successfully managed medically and which are most likely to ultimately require surgical intervention. Such information, if available, could assist in counseling parents and in managing children in an efficient and timely fashion.

This study was designed to determine risk factors, both prenatal and postnatal, that might indicate which neonates are at most risk for requiring definitive surgical management of the airway in the first year of life. The airway interventions in this report varied from prolonged intubation (intubation until death) to delayed tracheostomy (after 24 hours of life) and MDO.

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Materials and Methods

After obtaining Institutional Review Board approval, a case series with chart review was performed. Infants with a diagnosis of micrognathia who were seen by the pediatric otolaryngology service between January 1, 2001, and September 30, 2011, at Children’s Hospitals and Clinics of Minnesota–Minneapolis, Minnesota, and the Floating Hospital for Children at Tufts Medical Center in Boston, Massachusetts, were included. The billing databases for each otolaryngology department were queried to identify children with micrognathia based on ICD-9 coding. The charts of these patients were then reviewed to confirm physical examination findings as noted by an attending pediatric otolaryngologist. For the purpose of this study, micrognathia was defined as a small mandible in which the inferior alveolus was positioned significantly posterior to the maxillary alveolus. This was a subjective call made by a pediatric otolaryngologist and corroborated by a geneticist who was a member of the respective institution’s multidisciplinary craniofacial team.

After chart review, 123 cases were identified. Patients’ charts were then reviewed for additional variables including gender; gestational age at time of delivery; amniotic fluid index; intraterine growth restriction (IUGR); abnormal heart, brain, renal, and limb findings on prenatal ultrasound; presence of a named syndrome; family history of micrognathia; and a history of airway intervention in the first 24 hours of life (intubation or tracheostomy). The outcome measure noted in this study was the occurrence of surgical intervention in the first year of life. These interventions included prolonged intubation (intubation until death), tracheostomy between 24 hours and 1 year of life, and MDO in the first year of life.

Statistical Analysis

Univariate and multivariate analyses were then performed to determine which of the above variables might be risk factors for airway intervention during infancy. Both univariate and multivariate analyses were run on an instance of STATA 12.0 on a Linux Server running the x86-64 instruction set, and asymptotic calculations of standard errors were reported. Variables that had \( P \) values of less than .10 in the univariate analysis were simultaneously controlled for in a binary logistic regression model (multivariate analysis) to determine those variables independently associated with intervention.

Results

The charts of 123 infants with micrognathia were reviewed; 101 children had PRS, and 22 infants had micrognathia without cleft palate. Forty-eight patients required long-term airway intervention, and these interventions occurred in the form of prolonged intubation prior to death (3 patients), tracheostomy (12 patients), and mandibular distraction osteogenesis (33 patients; Figure 1). There were 3 infant deaths within the first year that were not related to airway pathology but rather attributed to primary conditions including Trisomy 18, CHARGE syndrome with severe congenital heart disease, and Walker-Warburg syndrome. These fatalities occurred in the 3 children who underwent prolonged intubation until death. These subjects were included in the long-term intervention group, as they met criteria for surgical airway intervention, but surgery was deferred given their extensive comorbidities.

Significant risk factors for requiring surgical intervention in the first year of life in this series included prematurity (gestational age <37 weeks at time of birth), prenatal ultrasound findings of IUGR, evidence of neurologic impairment, and a history of intubation in the first 24 hours of life. Infants who required intubation within 24 hours of delivery were 8 times as likely to undergo airway surgery in the ﬁrst year of life (odds ratio [OR], 8.22; conﬁdence inter- val [CI], 3.14-21.53). Neurologic impairment demonstrated a nearly 4-fold increase in the odds of requiring surgery (OR, 3.83; CI, 1.33-11.07). Those with a history of IUGR were 4 times as likely to need surgery (OR, 4.10; CI, 1.00-16.70), and infants with prematurity (<37 weeks gestation) had an approximately 2-fold increase in the likelihood of an intervention (OR, 2.38; CI, 1.02-5.56).

Other variables reviewed that were not signiﬁcant, included gender; a family history of micrognathia; polyhydramnios; oligohydramnios; abnormal prenatal ultrasound ﬁndings associated with the brain, heart, kidney, or limb; and the diagnosis of any named syndrome. Infants with isolated PRS were just as likely to need definitive airway interventions as those with PRS and an additional syndrome diagnosis. Infants with isolated micrognathia without cleft palate were less likely to require intervention (OR, 0.20; CI, 0.05-0.71; Table 1).

Discussion

In many cases of micrognathia, there is upper airway obstruction owing to posterior positioning of the mandible leading to glossoptosis. Management of tongue base obstruction in infancy always starts with conservative measures (repositioning or prone positioning) and may progress to the use of an adjunctive airway device (nasopharyngeal airways and custom oral appliances). When less invasive measures fail, operative intervention may become necessary. Surgical options for managing tongue base obstruction in infants include glossectomy procedures, mandibular distraction osteogenesis, and...
Table 1. Summary of Risk Factors for Requiring Definitive Airway Intervention in the First Year of Life, Either with Mandibular Distraction Osteogenesis, Tracheotomy, or Prolonged Intubation until Death*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>n (% of Total Sample)</th>
<th>OR (95% CI)</th>
<th>P Value</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>71 (57.7)</td>
<td>0.79 [0.38, 1.64]</td>
<td>.523</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>iPRS</td>
<td>57 (46.3)</td>
<td>1.64 [0.79, 3.40]</td>
<td>.187</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Other syndrome</td>
<td>47 (38.2)</td>
<td>1.10 [0.52, 2.32]</td>
<td>.802</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>sPRS</td>
<td>44 (35.8)</td>
<td>1.23 [0.58, 2.61]</td>
<td>.581</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Prematurity (born &lt;37 weeks)</td>
<td>29 (23.6)</td>
<td>2.38 [1.02, 5.56]</td>
<td>.044</td>
<td>0.87 [0.28, 2.65]</td>
<td>.802</td>
</tr>
<tr>
<td>Micrognathia without cleft palate</td>
<td>22 (17.9)</td>
<td>0.20 [0.05, 0.71]</td>
<td>.013</td>
<td>0.19 [0.05, 0.83]</td>
<td>.027</td>
</tr>
<tr>
<td>Neurologically Impaired</td>
<td>18 (14.6)</td>
<td>3.83 [1.33, 11.07]</td>
<td>.013</td>
<td>3.94 [1.01, 15.34]</td>
<td>.048</td>
</tr>
<tr>
<td>FamHx of UAOS syn</td>
<td>13 (10.6)</td>
<td>0.67 [0.19, 2.30]</td>
<td>.522</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>IUGR</td>
<td>10 (8.1)</td>
<td>4.10 [1.00, 16.70]</td>
<td>.049</td>
<td>1.01 [0.20, 5.16]</td>
<td>.988</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>10 (8.1)</td>
<td>2.53 [0.68, 9.50]</td>
<td>.168</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Limb abnormality</td>
<td>10 (8.1)</td>
<td>0.65 [0.16, 2.64]</td>
<td>.544</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>8 (6.5)</td>
<td>0.93 [0.21, 4.10]</td>
<td>.927</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Stickler syndrome</td>
<td>8 (6.5)</td>
<td>0.93 [0.21, 4.10]</td>
<td>.927</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Heart defect</td>
<td>7 (5.7)</td>
<td>1.18 [0.25, 5.53]</td>
<td>.831</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Brain abnormality</td>
<td>7 (5.7)</td>
<td>1.18 [0.25, 5.53]</td>
<td>.831</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Arthrogryposis</td>
<td>6 (4.9)</td>
<td>1.60 [0.31, 8.27]</td>
<td>.575</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Renal abnormality</td>
<td>3 (2.4)</td>
<td>3.22 [0.28, 36.50]</td>
<td>.345</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; IUGR, intrauterine growth restriction; iPRS, isolated, nonsyndromic Pierre Robin sequence; FamHx of UAOS syn, family history of a syndrome associated with upper airway obstruction; OR, odds ratio; sPRS, syndromic Pierre Robin sequence.

*Bold values are statistically significant (P <.05). Multivariate regression analysis controlled for risk factors with P <.10 in univariate analysis.

Handley et al

tracheotomy. At the authors’ institutions, we attempt to manage all children conservatively, instituting use of a nasopharyngeal airway for relief of airway obstruction and feeding difficulty in those infants who are not responding to repositioning. Sleep studies are not reflexively performed as we feel that this may lead to an increased push toward intervention in those infants with only mild to moderate symptoms when awake. Instead, children are followed clinically with objective measures of continuous pulse oximetry, carbon dioxide levels on daily capillary blood gases (an indicator of chronic hyperventilation), and for the child’s ability to maintain adequate oral intake to meet nutritional needs. Using this approach to initial management, we are able to safely manage upward of 60% of patients without surgery. Our rate of surgical intervention is commensurate with other series reported2-4 but is lower than recent series in the craniofacial literature advocating for a more aggressive approach based on abnormal polysomnography results.5

When surgical intervention is required (for acute respiratory failure, for example), the authors prefer to manage children with either MDO or tracheotomy. It is our opinion that TLA procedures, even in the best of hands, offer an improvement in glossoptosis that comes at the expense of significant feeding impairment. Moreover, we feel that most children who will benefit from a TLA procedure alone are the same patients who can be managed successfully with a less invasive nasopharyngeal airway. Our shared philosophy is to manage neurologically normal children who are severely affected by micrognathia with early MDO, as this intervention consistently and definitively addresses both airway and feeding difficulties in this population.6-8 Conversely, those children with hypotonia, developmental delay, and neurological impairment do not always benefit from early MDO.6,9 We feel that these patients are better served with tracheotomy and gastrostomy placement since these interventions also effectively address conditions associated with neurologic impairment, such as poor coordination and chronic aspiration.

This approach to managing micrognathia seeks to establish a consistent and rational framework for addressing airway and feeding concerns in these infants in a stepwise fashion. Nevertheless, we cannot always predict which children will avoid invasive airway procedures and which ones will eventually come to require an intervention during their infancy. In the setting of micrognathia, these data support preterm gestational age, prenatal ultrasound findings of IUGR, evidence of neurologic impairment, and a history of intubation or tracheotomy in the first 24 hours of life as significant risk factors for requiring a surgical airway intervention in the first year of life. Such distinguishing risk factors have not been previously reported.

It should be noted that IUGR association is marginally significant at the 95% level and the statistically significant findings for IUGR and prematurity were not robust enough to allow for to multivariate adjustment of other conditions. Nevertheless, we would suggest that the results of both the
univariate and multivariate analysis in this study are clinically meaningful. The ORs reported from the univariate analysis reflect the total association (including both direct and indirect associations) of that condition with the need for surgical intervention. ORs from the multivariate analysis, reported in Table 1, reflect only the direct effect of that single variable in the scenario in which all other conditions are held constant. Multivariate analysis is generally preferable for determining causal associations between risk factors and the outcomes; by contrast, univariate ORs represent associations rather than causality. Since a child’s medical conditions rarely occur in isolation, the data from the univariate analysis still have value in counseling patients as to predicted risks on the basis of a given factor.

In children with micrognathia, the indication for surgical airway intervention during infancy is often multifactorial but is essentially driven by respiratory and nutritional status. Micrognathic infants are at a higher risk for airway obstruction, which can be constant or intermittent in nature, owing to varying degrees of tongue base obstruction. Some children are able to maintain a marginal airway and instead manifest their symptoms of obstruction by exhibiting significant feeding impairment. When micrognathia presents with cleft palate, feeding difficulties may be severe. Conversely, children with isolated glossoptosis without the additional factor of a cleft palate should not be as severely affected from a feeding standpoint, and this may explain the lower rate of intervention in these particular patients noted in this report.

Many of the risk factors identified by this study may be associated with respiratory and feeding deficits in their own right. The potential for requiring a surgical intervention for airway and feeding concerns seems to be further compounded when these risk factors exist as comorbidities complicating the underlying diagnosis of micrognathia.

Late preterm infants (34–37 weeks) have known feeding difficulties secondary to poor suck and swallow coordination, which is in part attributed to decreased oromotor tone. In addition, premature neonates have a higher rate of intubation than those born at term. Studies have shown that underweight infants, like those with IUGR, have increased morbidity and mortality. More specifically, underweight infants are at increased risk for respiratory failure and death compared with gestational-age–matched, appropriate-for-gestational-age–weight infants, even when adjusting for congenital abnormalities. This literature supports the idea that IUGR infants are more likely to require definitive airway management, regardless of craniofacial anomalies.

Many of the above comorbidities have already been shown to be associated with adverse airway and feeding outcomes in children with PRS. Rogers et al have already demonstrated that preoperative intubation and low birth weight are among a group of risk factors for failure of TLA surgery in infants with PRS. Their findings would support the notion that severe airway obstruction and prematurity merit more aggressive interventions.

The Rogers et al study also identifies syndrome diagnosis as a potential risk factor for failed TLA surgery. Other articles have suggested that children with syndromic PRS may have less favorable outcomes following mandibular distraction as well. In this series, we sought to distinguish between those children with a named syndrome (eg, Stickler syndrome, in which functional deficits are few) and those with neurological or functional impairment.

In neurologically impaired infants, hypotonia is often the underlying etiology of airway obstruction, which may manifest as obstructive sleep apnea with or without feeding difficulty. Micrognathia may exacerbate these issues, thus pushing these neonates toward the need for definitive airway intervention. Those infants with the highest risk airways are often the ones who rapidly deteriorate, requiring intubation within the first 24 hours of life. It is not surprising that these same children are more likely to require a surgical intervention for their airway problem than those who did not need intubation within the first day of life.

These data are biased, as they reflect infants with micrognathia concerning enough to warrant evaluation by the pediatric otolaryngology service, either prenatally or postnatally. In addition, it is possible that infants born at centers with pediatric otolaryngologists on site may undergo more aggressive airway management in the neonatal period. Nevertheless, the findings of this study may be applicable to most centers given that the ratio of isolated PRS to syndromic PRS in this report was similar to prior published series, as was the overall surgical intervention rate of 39%.

An additional limitation of this study is that certain syndromic forms of PRS with functional impairment (eg, Nager syndrome) are not represented in this cohort. Other diagnoses such as Treacher Collins syndrome and arthrogryposis multiplex congenita may be relatively overrepresented in our series. Conversely, the multiscalar, multi-institutional nature of this series is a relative strength of this study and further supports the likelihood that the risk factors for intervention identified in this article may not be unique to this series of patients.

Finally, the threshold for surgical intervention for airway and feeding deficits in micrognathic infants varies from institution to institution. There are still no standards or accepted criteria for surgery, despite an increased awareness for the need to select children for intervention based on objective measures. Management of these children is not an exact science. Polysomnography measures often vary between institutions, so sleep study results in infants are not always consistent. Moreover, surgeons’ philosophies with regard to the utility and merit of each specific surgical intervention remain controversial and differ between specialties (otolaryngology and plastics) and individual surgeons alike.

Conclusion

Previous literature has not provided patient-specific information to guide conversations about airway management in children with micrognathia or PRS. While it is understood that the need for MDO and tracheostomy are individual decisions, this study suggests that neonatal characteristics,
including prematurity, prenatal ultrasound findings of IUGR, signs of potential neurologic impairment, and a history of requiring airway intervention in the first 24 hours of life, may help identify those micrognathic neonates who are likely to require surgical airway intervention in the first year of life. A multivariate analysis would suggest that airway intervention in the first 24 hours of life and neurologic impairment are independent risk factors for requiring airway surgery during infancy. Likewise, infants with micrognathia without cleft palate seem to not require intervention at the same rate as their counterparts and may benefit from longer trials of respiratory and feeding support prior to surgery.

Author Contributions
Sara C. Handley, acquisition of data, analysis and interpretation of data, drafting of article; Nicholas S. Mader, conception and design, analysis and interpretation of data, revising article; James D. Sidman, acquisition of data, analysis and interpretation of data, revising article, final approval; Andrew R. Scott, conception and design, acquisition of data, analysis and interpretation of data, revising article, final approval.

Disclosures
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