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Clinical Paper
Craniofacial Anomalies

A comparison of airway interventions and gastrostomy tube placement in infants with Robin sequence

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Abstract. The purpose of this study was to evaluate feeding impairment following non-operative or operative management of airway obstruction in a large series of infants with Robin sequence (RS) by rate of G-tube placement. A retrospective study was conducted at Boston Children's Hospital including 225 patients (47.1% female) with RS treated between 1976 and 2018. Subjects were grouped by intervention required for successful management of airway obstruction: non-operative only ($n = 120$), tongue–lip adhesion (TLA, $n = 75$), mandibular distraction osteogenesis (MDO, $n = 21$), or tracheostomy ($n = 9$). The operative group had a higher rate of G-tube placement (58.1%) than the non-operative group (28.3%, $P < 0.0001$). Subjects in the TLA and tracheostomy groups had higher odds of G-tube placement than subjects in the MDO group: odds ratio (OR) 5.5 (95% confidence interval (CI) 1.8–17.3, $P = 0.004$) and OR 27.0 (95% CI 3.2–293.4, $P = 0.007$), respectively. Syndromic patients and those with gastrointestinal anomalies also had higher odds of G-tube placement: OR 3.5 (95% CI 1.7–7.2, $P = 0.001$) and OR 5.9 (95% CI 1.6–21.0, $P = 0.007$), respectively. Infants with RS who require an airway operation and those with a syndromic diagnosis or gastrointestinal anomalies are more likely to require placement of a G-tube. Of the operative groups, MDO was associated with the lowest G-tube rate, compared to TLA and tracheostomy.

Key words: Robin sequence; airway obstruction; mandibular distraction; tongue–lip adhesion; tracheostomy; feeding; failure-to-thrive; gastrostomy.

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Robin sequence (RS), defined as a triad of micrognathia, glossoptosis, and airway obstruction, affects 1:3000 to 1:14,000 live-born infants[1–7]. Airway obstruction and feeding impairment are typically present at birth. The airway obstruction can often be managed with prone or side positioning, supplemental oxygen, continuous positive pressure ventilation, and/or placement of a nasopharyngeal tube. Some patients will require an operation such as a tongue–lip adhesion (TLA),

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mandibular distraction osteogenesis (MDO), or tracheostomy. Airway outcomes for MDO are superior to those for TLA[8,9]. While tracheostomy is the most effective procedure for relieving airway obstruction, the associated morbidity and care burden typically relegate this operation to patients who are poor candidates for or have failed alternative operations[10].

Infants with RS often have difficulty with feeding and weight gain. Feeding impairment may manifest as prolonged feeding times, oxygen desaturation during feeding, dysphagia, gastroesophageal reflux, and/or aspiration[11,12]. In some patients, the high energy expenditure required to ventilate in the face of intermittent airway obstruction combined with insufficient caloric intake due to feeding impairment will cause failure-to-thrive. The mechanism of feeding impairment in infants with RS is unknown, but it is hypothesized to be a direct effect of breathing dysfunction. This is supported by reports of improvement in oral feeding and weight gain following resolution of airway obstruction[13–16]. Most infants with RS will receive caloric supplementation via nasogastric tube feeds for some period during early infancy. For those with prolonged oral feeding impairment, a gastrostomy tube (G-tube) is placed. G-tube placement requires an operation and exposes the patient to additional risk[17,18].

The aim of this study was to examine the rate of G-tube placement in infants with RS, and to determine whether this rate varies based on the type of airway management. As airway obstruction is theorized to be the direct cause of feeding impairment in infants with RS, it was hypothesized that the rate of G-tube placement would be higher in patients with obstruction severe enough to require an airway operation compared to those managed non-operatively. Furthermore, it was hypothesized that MDO, which relieves airway obstruction more predictably than TLA, would facilitate oral feeding and therefore be correlated with a lower rate of G-tube placement.

Materials and methods

Study design and sample

This was a retrospective study of patients who presented to Boston Children's Hospital (BCH) between 1976 and 2018 for the evaluation and management of RS. Inclusion criteria were (1) a diagnosis of RS (micrognathia, glossoptosis, and airway obstruction) by a member of the Craniofacial Center, and (2) complete records regarding airway obstruction and feeding during the first year of life. Exclusion criteria were (1) airway operation after the first year of life, (2) more than one airway operation, (3) death within the first year of life, and (4) insertion of a G-tube prior to an airway operation. All subjects received non-operative airway management such as prone or side positioning, supplemental oxygen, continuous positive airway pressure (CPAP), and/or insertion of a nasopharyngeal tube. Subjects were grouped according to the intervention(s) required during the first year of life for successful management of airway obstruction: non-operative management only ('no operation'), TLA, MDO, or tracheostomy. This study was approved by the Institutional Review Board of the Committee on Clinical Investigation at BCH (Protocol #P00023123).

Decisions regarding airway management were made by a multidisciplinary care team in collaboration with the families. In patients with persistent airway obstruction following non-operative interventions and demonstration of airway collapse primarily in the retroglossal area by endoscopic examination, either TLA or MDO was performed. TLA was used prior to 2014; from 2014 to 2018, MDO was used. This change was based on a review of TLA outcomes, which demonstrated unpredictable relief of airway obstruction with this operation[9]. The decision to use TLA vs. MDO was not based on severity of airway obstruction or other patient-specific factors. In patients with contraindications to TLA or MDO, multi-level airway collapse, and/or comorbidities requiring long-term ventilation and airway suctioning, tracheostomy was used.

Nasogastric tubes were inserted when the diagnosis of RS was made and were used either in lieu of oral feeding or for supplemental caloric intake. The feeding method, use of breast milk or formula, and caloric intake goals were determined by the neonatology and feeding teams with family input. In patients with a cleft palate, specialized feeding techniques were taught by a cleft-feeding nurse and specialty bottles were provided. The decision to place a G-tube was based on the expectation that non-oral feeding supplementation would be required beyond 3 months duration.

Study variables

The primary predictor variable was type of airway intervention. Secondary predictor variables included demographic data, presence of cleft palate, syndromic diagnosis, and neurological, cardiac, or gastrointestinal anomalies. The primary outcome variable was the rate of G-tube placement.

Statistical analysis

Descriptive statistics were calculated. The χ^2 test and Fisher's exact test were used to compare the rate of G-tube placement and categorical predictor variables between groups. One-way analysis of variance (ANOVA) was used to compare means of continuous variables. Binary logistic regression was applied to determine the effect of predictor variables on the primary outcome variables, and odds ratios (OR) with 95% confidence intervals (95% CI) were calculated. A P-value of <0.05 was considered significant.

Results

A total of 341 patients with RS during the study period were identified. Of these, 225 (47.1% female) met the criteria for inclusion in this study. A total of 105 (46.7%) subjects had an airway operation during the first year of life: MDO, $n=21$; TLA, $n=75$; tracheostomy, $n=9$.

A cleft palate was present in 214 (95.1%) subjects and was more prevalent in the non-syndromic infants (98.4%) than in the syndromic infants (91.2%, $P=0.013$). There were no other significant differences in predictor variables between groups (Table 1). A total of 102 (45.3%) patients had a clinical syndromic diagnosis, which was confirmed by genetic testing in 63 subjects (61.8% of those with a clinical syndromic diagnosis, 28.0% of the entire sample). Stickler syndrome was the most common syndromic diagnosis ($n=33$, 32.4%), followed by 22q11.2 deletion syndrome ($n=6$, 5.9%). Thirty-nine infants (38.2%) had multiple anomalies not consistent with a known syndrome. Seventy-one infants (31.6%) had extracraniofacial anomalies including cardiac anomalies ($n=47$, 20.9%), neurological anomalies ($n=33$, 14.7%), and gastrointestinal anomalies ($n=21$, 9.3%) (Table 2).

G-tube placement

A G-tube was placed in 95 subjects (42.2%). Of patients who had an airway operation, 61 (58.1%) underwent G-tube placement, compared to 34 (28.3%) in the no operation group ($P<0.0001$). Within the operative groups, the rates of G-tube placement were as follows: MDO, $n=7$

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Table 1. Demographic variables and operative data for all groups.

Variable	No operation ($n=120$)	MDO ($n=21$)	TLA ($n=75$)	Tracheostomy ($n=9$)	*P*-value
Female	54 (45%)	14 (67%)	34 (45%)	4 (44%)	0.318
Cleft palate	114 (95%)	17 (81%)	74 (99%)	9 (100%)	0.009
Additional anomalies	38 (32%)	5 (24%)	23 (31%)	5 (56%)	0.390
Cardiac anomalies	23	5	16	3	0.683
Neurological anomalies	22	2	6	3	0.061
Gastrointestinal anomalies	13	2	5	1	0.721
Syndrome	58 (48%)	12 (57%)	28 (37%)	4 (44%)	0.301
Age at airway operation (days), mean ± SD	–	64 ± 61	24 ± 37	16 ± 10	0.001
Age at gastrostomy (days), mean ± SD	81 ± 104	211 ± 131	42 ± 57	20 ± 15	<0.001
G-tube placement	34 (28%)	7 (33%)	46 (61%)	8 (89%)	<0.001
Concurrent	–	2	38	6	–
Postoperative	–	5	8	2	–

MDO, mandibular distraction osteogenesis; TLA, tongue–lip adhesion; SD, standard deviation. A *P*-value of <0.05 is considered significant.

Table 2. Frequency of syndromic diagnosis.

Syndromic diagnosis	Number	Percentage
No unifying diagnosis[a]	39	38.2%
Stickler syndrome	33	32.4%
22q11.2 deletion syndrome	6	5.9%
Craniofacial microsomia	2	2.0%
Fetal alcohol syndrome	2	2.0%
Mobius syndrome	2	2.0%
Treacher Collins syndrome	1	1.0%
Nager syndrome	1	1.0%
Cornelia de Lange syndrome	1	1.0%
Emanuel syndrome	1	1.0%
Van der Woude syndrome	1	1.0%
Other	13	12.7%

[a] Presence of multiple anomalies not consistent with a known syndrome.

(33.3%); TLA, $n=46$ (61.3%); tracheostomy, $n=8$ (88.9%). Compared to the MDO group, subjects in the TLA and tracheostomy groups had significantly higher odds for G-tube placement (OR 5.5, 95% CI 1.8–17.3, $P=0.004$ for MDO vs. TLA; OR 27.0, 95% CI 3.2–293.4, $P=0.007$ for MDO vs. tracheostomy) (Table 3).

Rates of G-tube placement for secondary predictor variables are shown in Table 4. Patients with a syndromic diagnosis had a higher rate of G-tube placement than non-syndromic patients for all groups (56.9% vs. 30.1%, $P<0.0001$) (Fig. 1). Binary logistic regression showed significantly higher odds for G-tube placement in syndromic compared to non-syndromic patients (OR 3.5, 95% CI 1.7–7.2, $P=0.001$). Those with gastrointestinal anomalies also had significantly higher odds of G-tube placement compared to subjects without such anomalies (OR 5.9, 95% CI 1.6–21.0, $P=0.007$) (Table 3).

Discussion

The results of this study affirmed both of the proposed hypotheses: the rate of G-tube placement was significantly higher in the operative groups than in the no operation group (58.1% vs. 28.3%, $P<0.0001$), and infants who had MDO required a G-tube less frequently than those who had a TLA (33.3% vs. 61.3%, $P=0.023$). Interestingly, infants who had a tracheostomy, which is the most effective operation to relieve airway obstruction, had the highest rate of G-tube placement. This could be due to institutional preference to place G-tubes in patients with a tracheostomy or may indicate that the subjects in the tracheostomy group had a more severe presentation of airway obstruction and feeding impairment than the other groups. The latter is supported by the prevalence of additional anomalies in the tracheostomy group, which were more common in this group than in the other groups, although statistical significance on this difference was not reached ($P=0.061$). Neurological anomalies were most common in this group and may have been associated with impaired swallowing function. Another explanation might be that the feeding impairment is primarily due to the impact of glossoptosis on pharyngeal swallowing, which is improved by TLA and MDO but not by tracheostomy.

The present study findings support the hypothesis that feeding impairment in infants with RS is a direct consequence of breathing dysfunction. Adequately addressing respiratory symptoms in these infants can lead to an improvement in nutritional and caloric intake. In parallel to other reports of feeding parameters, this study of G-tube rates is particularly informative given the more invasive nature of gastrostomies compared to other means of supplemental feeding and the comprehensive comparison of interventions[17,18]. Of the operative interventions, MDO was associated with the lowest G-tube rate. In addition to improved feeding parameters, its superiority over TLA and use as a means to avoid tracheostomy in the most severely affected infants indicate that MDO may represent the treatment of choice in those with an operative indication. The G-tube rates associated with each

Table 3. Binary logistic regression analysis for significant predictor variables and gastrostomy.

Variable	OR	95% CI	*P*-value
Cardiac anomalies	1.6	0.7–3.5	0.233
Neurological anomalies	1.4	0.5–3.9	0.494
Gastrointestinal anomalies	5.9	1.6–21.0	0.007
Syndrome	3.5	1.7–7.2	0.001
TLA[a]	5.5	1.8–17.3	0.004
Tracheostomy[a]	27.0	3.2–293.4	0.007

OR, odds ratio; CI, confidence interval; TLA, tongue–lip adhesion; MDO, mandibular distraction osteogenesis. A *P*-value of <0.05 is considered significant.

[a] TLA and tracheostomy were compared relative to the MDO group.

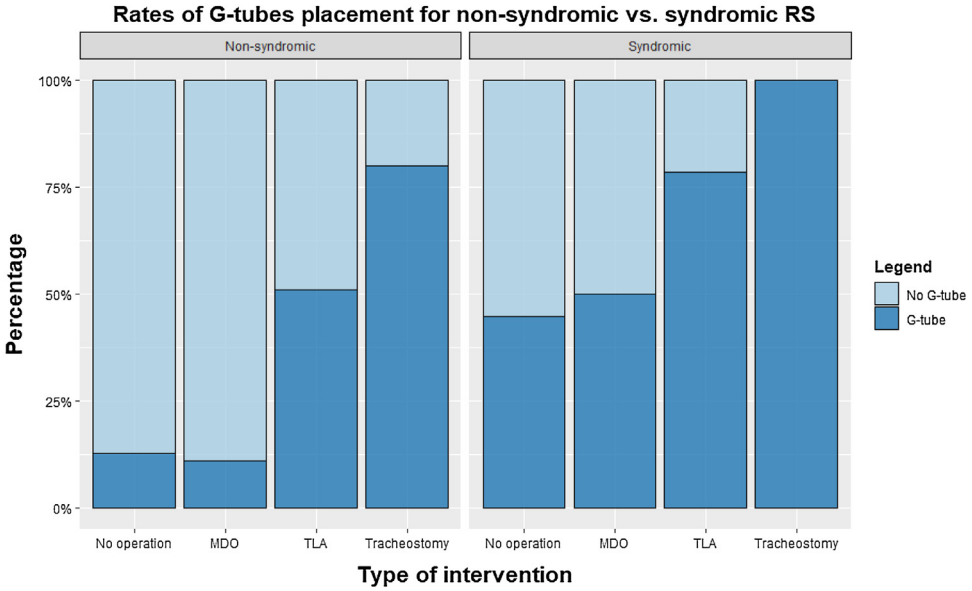

Fig. 1. Non-syndromic vs. syndromic Robin sequence. (Abbreviations: MDO, mandibular distraction osteogenesis; TLA, tongue–lip adhesion.).

Table 4. Rates of G-tube placement for secondary predictor variables.

Variable	Value	Number	Percentage with G-tube	*P*-value
Sex	Male	50	42.0%	0.947
	Female	45	42.5%	
Cleft palate	No	4	36.4%	0.687
	Yes	91	42.5%	
Cardiac anomalies	No	66	37.1%	0.002
	Yes	29	61.7%	
Neurological anomalies	No	73	38.0%	0.002
	Yes	22	66.7%	
Gastrointestinal anomalies	No	78	38.2%	<0.0001
	Yes	17	81.0%	
Syndrome	No	37	30.1%	<0.0001
	Yes	58	56.9%	

A *P*-value of <0.05 is considered significant.

respiratory treatment modality reported in this study highlight the need for concurrent consideration of both respiratory and feeding parameters and serve to inform management strategies for infants with RS.

The study results are consistent with those of other studies reported in the literature. In a literature review including 370 infants with RS who had MDO, Zhang et al.[19] reported improved oral feeding after the operation, with 87.0% of patients achieving full oral intake at the latest follow-up. Of the 157 patients treated with TLA, 70.0% achieved full oral intake. Susarla et al.[16] reported a lower rate of G-tube placement in 30 patients who had MDO (16.7%) compared to 31 patients after TLA (48.4%). The rates reported in the present study are higher for both MDO and TLA, highlighting institutional differences and discrepancies in the care of infants with RS.

Other studies also support the conclusion that a syndromic diagnosis is independently associated with a higher G-tube rate. Gary et al.[20] reported improved weight gain after MDO in non-syndromic patients only, with no postoperative feeding improvement in syndromic patients. In a systematic review of feeding outcomes in infants who had MDO for micrognathia, Breik et al.[21] reported full oral feeding in 93.7% of those with non-syndromic RS compared to 72.9% of those with syndromic RS. In terms of G-tube rates, the present study is novel in reporting this association for all infants with RS, including those who can be managed non-operatively. This finding underlines the importance of an early syndromic diagnosis, as it affects the management of airway obstruction as well as feeding.

Of note, the study sample showed a higher prevalence of cleft palate in the non-syndromic group than in the syndromic group (98.4% vs. 91.2%, $P=0.013$). The presence of a cleft palate was not associated with a higher G-tube rate (42.5% vs. 36.4%, $P=0.687$), likely indicating adequate management of feeding in the presence of a cleft palate for those patients who can tolerate oral feeding.

This study has several limitations. First, due to the retrospective study design, a causative relationship between airway obstruction and feeding impairment could not be determined. Also, the rate of G-tube insertion was used as a surrogate marker for feeding severity. The decision to insert a G-tube, however, was based on several factors including family and care team preferences; the assumption that insertion of a G-tube indicates severe feeding impairment may not always be accurate. Additionally, surgical intervention was used in this study to signify the severity of obstructive apnea, with the assumption that patients managed without an operation had less severe obstruction compared to those who had TLA or MDO, and that patients who had a tracheostomy had the most severe obstruction. A prospective study using objective measurements for feeding (caloric intake, weight gain) and airway obstruction (polysomnography) will further improve our understanding. Finally, Boston Children's Hospital is a tertiary referral hospital, which may have led to selection bias of more complicated patients.

In conclusion, infants with RS who required an airway operation, were syndromic, and/or had gastrointestinal anomalies were more likely to require

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placement of a G-tube for prolonged enteral feeding compared to those in whom the airway obstruction was managed non-operatively. Of those infants who had an airway operation, MDO was associated with the lowest rate of G-tube placement and tracheostomy was associated with the highest rate. The study findings underscore the relationship between feeding impairment and airway obstruction in RS.

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Competing interests

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Ethical approval

This study was approved by the Institutional Review Board of the Committee on Clinical Investigation at Boston Children's Hospital (Protocol #P00023123).

Patient consent

Patient consent was not required.

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