INTRODUCTION

Infants with Pierre Robin sequence (in the following called Robin sequence [RS], as it is unusual to include first names in a disease eponym) characteristically present with a small and/or retro-positioned mandible, glossoptosis, and upper airway obstruction (UAO). The latter becomes particularly prominent during sleep, manifesting as obstructive sleep apnea (OSA). Most patients also exhibit a cleft palate and failure to thrive, the latter resulting from feeding difficulties as well as from intermittent hypoxia (IH), OSA-related sleep fragmentation, and the increased work of breathing associated with increased airway resistance. Investigating the effectiveness of any intervention to overcome these problems requires monitoring via (repeated) sleep studies, as these are the only accepted modality to objectively diagnose sleep-disordered-breathing early in life. In addition, regular weight monitoring has proven a valuable tool to monitor treatment effectiveness. RS infants regularly develop somatic growth failure if their breathing and feeding problems are not addressed appropriately. Treatment should start early after birth, as frequent and prolonged IH early in life may result in cognitive impairments. Here, we will review the current evidence on the diagnosis and treatment of respiratory problems in RS infants.
with particular emphasis on sleep studies and growth trajectories as guides to intervention and outcomes.

1.1 Are sleep studies truly the only diagnostic tool to assess severity of in RS infants?

Clearly, in those with life-threatening UAO, a sleep study is not required to indicate the need for treatment. A large proportion of RS infants, however, exhibit more subtle clinical signs of UAO, often occurring only during sleep, and not necessarily leading to prominent oxygen desaturations (Figure 1). However, is full polysomnography (PSG) strictly necessary to assess OSA severity? More specifically, is IH the sole contributor to the occurrence of long-term clinical problems? If this were the case, then IH can be readily detected using pulse oximetry. However, as frequent obstructive respiratory events not resulting in IH are also important determinants of RS-associated morbidities, PSG or other relevant diagnostic approaches may be more appropriate. In a systematic review comparing the diagnostic accuracy of various simpler alternatives to PSG in diagnosing OSA, cardiorespiratory polygraphy, but not oximetry, emerged as a valid alternative to PSG. Of note, cardiorespiratory polygraphy is also the diagnostic tool that the first author employs in RS patients to guide treatment and monitor its effectiveness in the clinical setting at the University of Tuebingen in Germany, while the approach employed at the University of Missouri regularly utilizes PSG as the diagnostic tool. Notwithstanding, we should also allude to the fact that a recent American Academy of Sleep Medicine task force consensus failed to recommend the use of cardiorespiratory polygraphy as the gold standard, such that individual center discretion and multidisciplinary team preference is probably advisable. We should also remark that upon analysis of cardiorespiratory polygraphic studies, the focus is on the mixed-obstructive apnea index (MOAI), rather than the more commonly used obstructive apnea–hypopnea index (AHI), since the latter index requires the ability to detect electroencephalographic arousals, that is, requires a full PSG. Given that obstructive hypopneas are relatively uncommon in young infants, that is, are not substantial contributors to the obstructive AHI, we consider the MOAI a more appropriate parameter for assessing OSA severity in RS infants.

Several issues that remain to be addressed and merit future evaluation include whether alternative methodologies used to quantify the severity of IH, such as the hypoxic burden or autonomic probing using heart rate variability measures may provide better estimates of OSA severity, and also aid in treatment decisions. Of note, both of these measures would be available in either PSG or cardiorespiratory polygraphic recordings.

Would such an approach help in achieving a good long-term outcome? While not formally studied yet, we consider it encouraging that in a 7-year follow-up study of 34 consecutive children with isolated RS who had their postnatal airway obstruction identified and treated early and effectively (see below), we found an intelligence quotient (IQ) within the normal range, which is in contrast to other reports in RS patients showing impaired neurodevelopment in a significant proportion of patients. Similarly encouraging results are also reported from other programs employing a systematic approach to identifying and avoiding IH in RS infants.

Weight gain is the other measure of particular interest in RS infants. As stated above, poor weight gain is a frequent initial clinical manifestation in RS infants not requiring immediate intervention in the neonatal period, and is also a well-known complication of OSA. Failure to thrive is associated with impaired neurodevelopment, at least in preterm infants. Weight gain may thus be a valuable parameter to monitor overall treatment effectiveness.

Based on the aforementioned considerations, we will review data on sleep study findings and weight gain outcomes as they are related with current therapeutic approaches in the management of infants with RS, while purposefully differentiating between conservative and surgical treatment.

2 CONSERVATIVE MANAGEMENT OF RS

2.1 Prone positioning

This intervention was originally proposed by Robin himself, who hypothesized that the narrow pharyngeal space in RS can be corrected by gravity moving the mandible forward in infants sleeping prone. In some case series, 50%-80% of patients with RS were reported as being satisfactorily treated by prone positioning only. Furthermore, prone positioning was implemented by about 2/3 of the respondents in a recent survey focusing on interventions used in RS infants. Very few studies however, objectively documented the effectiveness of prone positioning. A recent PSG-study in 18 infants with RS (mean age, 1.5 months) found a significantly higher sleep efficiency in the prone position, but no significant reductions in OSA severity. Another study performed sleep studies in supine and non-supine position in 27 cleft infants with a mean age of 6 months, in whom 56% had RS. Again, no significant differences emerged between the infants’ positions regarding obstructive AHI or the nadir pulse oximeter saturation (SpO2). Given this apparent lack of effectiveness, combined with the fact that the prone sleep position is associated with a 14-times increased risk of sudden infant death, prone positioning cannot currently be recommended as an intervention aimed at improving breathing in RS infants.

2.2 Nasopharyngeal airway (NPA)

This simple device was first suggested by a British group and bridges the narrow pharyngeal space that characterizes RS infants by inserting an endotracheal tube into one of the nares so that its tip is placed immediately above the epiglottis (ascertained by endoscopy or x-rays). Of note, methods for estimating the required length of the tube without the need of endoscopy or x-rays, and securing it safely to the nose, have been described. Sleep study data on the
effectiveness of NPA are sparse. One study reported on 22 infants with RS (three syndromic), with 20 being managed with a NPA and high-calorie nasogastric tube feeding. Infants were gradually weaned from both tubes under SpO₂ monitoring. During a mean duration of hospital stay of 60 days (range 25–162), 18 infants were reported to grow along their birth percentiles for weight, but only three infants were fully bottle-fed at discharge. Also, only 10 infants maintained their weight centile until the time of cleft repair. Unfortunately, no sleep study results were provided. Another study reported weight gain in eight infants with a NPA (median age 50 days, range 15–180 days; four of these infants were also receiving supplemental oxygen). Their weight gain increased from 86 g/week before to 255 g/week with the NPA, but no data on weight gain beyond hospital discharge or PSG results were reported. The group that first described the use of a NPA also reported sleep study data on 63 infants managed with a NPA and indicated no residual UAO in 5, mild UAO in 39, and moderate UAO in 19 patients after use of the NPA for a median of 10 days; more detailed sleep study results, however, were not provided. An algorithm to RS treatment that also involved the NPA was recently reported by a surgical group. They based their treatment decisions on sleep study results, and treated those with moderate or severe OSA with a NPA. If a repeat sleep study showed improvement (true for 10 of their 20 patients), the NPA was continued or combined with noninvasive respiratory support; the remainder were deemed to reflect failure of the NPA and underwent laryngoscopy and then progressed to tracheostomy or one of the other surgical interventions discussed below. We should point out that a NPA exerts no stimulus on mandibular growth, nor does it favor the tongue to assume a more desirable horizontal position. Thus, while certainly valuable as a temporary measure, more data on NPA's long-term effectiveness are needed before recommending this approach as a routine treatment option in RS infants.

2.3 Pneumatic airway stenting using nasal continuous positive airway pressure (NCPAP) or intermittent positive pressure ventilation (NIPPV)

There are some case series on the use of NCPAP or NIPPV in RS. In a single-center analysis of 81 RS patients, 7 (9%) were treated using NIPPV, starting at a mean age of 2 months and lasting for a mean of 17 months. Reported benefits included a decrease in the proportion of time spent with SpO₂ less than 90% from a mean of 14% to 1% (at a mean airway pressure of 8 cm H₂O) and a decrease in mean transcutaneous CO₂ from 57 mmHg to 31 mmHg. All seven infants were discharged home with the device, which was used at home for an average of more than 8 h per day. No facial side effects were reported. The same group also reported on the successful use of CPAP in neonates with RS. Of 44 such neonates, nine were successfully managed with CPAP, four underwent tracheotomy, while the remaining received a recommendation of prone positioning. There is anecdotal evidence, however, that long-term NCPAP use in young children may result in mid-face hypoplasia. This is particularly relevant to RS patients who may suffer from a hypoplastic maxilla anyway, and yet this potential side effect has not yet been specifically studied systematically. Nonetheless, in our experience, CPAP is valuable as an intervention applied between admission and implementation of a more curative treatment.

2.4 Tuebingen palatal plate (TPP)

The TPP consists of a palatal base plate that covers the hard palate and the cleft, as well as the alveolar ridges, and supports a velar extension (spur) of individual length (approximately 3 cm) that ends just above the epiglottis and shifts the base of the tongue forward, thereby opening the airway and correcting the underlying glossop-tosis (Figure 2). Fitting of the TPP is controlled using fiberoptic nasopharyngoscopy without sedation. During the endoscopic procedure, which usually takes only 1–2 min, the tip of the velar extension is checked and its angle, responsible for the forward-shifting of the tongue base, is adjusted so that it pushes the latter sufficiently forward to erect the epiglottis, thereby widening the pharyngeal space. Effectiveness of the TPP is regularly ascertained using sleep studies, the first being performed immediately before treatment onset, and subsequently before discharge, and at least 3 and 6 months after initiating TPP therapy (Figure 1). The MOAI in these studies should be less than three events/h; if it is more than three events/h, the angle or length of the velar extension is modified. Treatment is usually discontinued around 6–8 months of age, depending on sleep study results (which should show a MOAI ≤ 1 event/h) and the facial profile at the time.

The TPP is the only device used to treat RS infants that was evaluated in a controlled study design, that is, versus a conventional palatal plate used as a sham procedure. After 48 h of treatment, the median MOAI had declined from 13.8 events/h to 3.9 events/h with...

**FIGURE 1** Representative 2-min sections of polygraphic recordings done (a) at admission and (b) after 2 weeks of treatment with a Tübingen Palatal Plate (TPP) in a baby girl with isolated Robin sequence admitted at 4 weeks of age. Shown are (from top to bottom) nasal pressure, thoracic and abdominal breathing movements, pulse oximeter saturation (SpO₂; in beat-to-beat mode), pulse waveforms, transcutaneous CO₂ and heart rate. The top segment shows 5 obstructive apneas of 2–7 s duration (grey bars; overall, the infant had a MOAI of 93/h in this recording). The bottom segment shows no respiratory event (the MOAI had fallen to 3/h). CO₂ was at 38–42 mmHg throughout. In parallel, oral intake in this infant had changed from 100% gavage feedings to 80% intake via bottle feeding (Playtex), weight from the 25th to the 40th centile. Note that no desaturations occurred in conjunction with the obstructive apneas; these events would have been missed by a simple recording of SpO₂ [Color figure can be viewed at wileyonlinelibrary.com]
the TPP ($p < .001$), while it remained unchanged at 14.8 events/h with the sham procedure.\textsuperscript{35} In an uncontrolled continuation of the study that involved 15 RS patients (median age at onset of treatment, 5 days), median MOAI fell from 17.2 events/h to 1.2 events/h after 3 months of treatment with the TPP. Notably, all infants had their feeding tubes removed before hospital discharge, and continued to gain weight at a mean rate of 24 g/day at discharge, and 19 g/day at the 3-month follow-up. All infants continued to be exclusively fed orally at follow-up.\textsuperscript{36} This beneficial effect of the TPP on feeding ability may be related to the fact that it not only opens the airway, but also corrects glossoptosis, thus helping the tongue to assume its normal, horizontal position. A normal tongue function, with a downward-movement of the tongue to a position below the nipple at the time of peak vacuum, is crucial to successful oral feeding,\textsuperscript{37} which may explain some of the feeding difficulties seen in RS infants.

To demonstrate that the TPP is also effective in more severe phenotypes of RS, the first author’s group compared the change in the MOAI before and during TPP treatment in 122 infants with isolated RS, including 55 infants with a MOAI of more than 10 events/h in their initial sleep study (median 29, interquartile range [IQR], 15–51). By the time of the 3-month follow-up, the MOAI had decreased to 0.2 events/h (0–1.3), which was very similar to the results found in infants with mild OSA, that is, an initial MOAI of 3–5 events/h.\textsuperscript{38} The remaining five patients did not tolerate TPP treatment, mostly related to problems with swallowing (e.g., in those with CHARGE association or Wiedemann–Beckwith syndrome). In contrast to those with isolated RS, the type of TPP used varied in these patients, with 23 using a plate with a perforated tube ($n = 20$) or a ring ($n = 3$) attached to the pharyngeal extension to prevent collapse of the lateral pharyngeal or laryngeal walls. Thus, syndromic RS patients showed an more than 80% reduction in the MOAI between admission and discharge. Also, in the 46 infants with complete data, Z-scores for weight at discharge were comparable to those documented at birth; that is, postnatal growth failure was avoided. Furthermore, the number of infants who were fed via nasogastric tube decreased from 23 to 7.\textsuperscript{39}

FIGURE 2  Tübingen Palatal Plate (TPP) production. Based on digital scanning of the oral cavity, a prototype is produced using CAD/CAM (left) and then assessed in the patient. If fitting is appropriate, the final plate is manufactured, and includes a strengthening wire inside the spur and extraoral bows for better retention of the plate when the TPP is in place [Color figure can be viewed at wileyonlinelibrary.com]

Of note, TPP treatment was also associated with mandibular catch-up growth, as evident from longitudinal measurements of the Jaw Index (JI), defined as the alveolar overjet (in mm) times maxillary arch/mandibular arch (also measured in mm).\textsuperscript{40} In 20 RS patients, the Tuebingen group determined the JI upon admission, discharge, and 3 months after discharge, and found a decrease from 8.8 (IQR, 6.3–11.3) on admission to 2.1 (2.0–4.0) at the 3-month follow-up ($p < .001$), which correspond to JI values similar to those found in healthy infants.\textsuperscript{41} The objectively determined data confirm the clinical impression of a rapid improvement in the facial profile occurring during TPP treatment (Figure 3), although it should be kept in mind that the JI has not yet been validated.

Of note, the TPP approach has also been adopted by others.\textsuperscript{42–44} For example, in a three-center study involving 49 consecutive RS infants, there was an overall decrease in median MOAI from 15.9 events/h (IQR, 6.3–31.5) on admission to 2.3 events/h (1.2–5.4) at discharge, thereby illustrating the similar outcomes to those initially reported in the authors’ center.\textsuperscript{45} Also, a group from Berlin reported
In another follow-up study, 10 of 11 RS patients required additional interventions for airway or feeding problems following TLA. Moreover, complications such as wound infections, adhesion dehiscence or scar formation of the lip and floor of the mouth were reported to occur in about 20%–25% of the patients. Thus, it remains unproven whether TLA can indeed be recommended as a good surgical approach for most children with RS.

3.2 Mandibular distraction osteogenesis (MDO)

This procedure aims at correcting the mandibular hypoplasia in RS by performing a bilateral vertical mandibular osteotomy, and placing pins for a multi-vector external (or internal) distractor. Beginning a few days after the operation, distraction is usually done at a rate of 1–2 mm/day until the patient has a Class III occlusion (see below for more details regarding the MDO procedure). This overcorrection is considered necessary to sustain an adequate airway in case a (partial) relapse occurs following distraction. Devices are usually removed 4–8 weeks after the end of the distraction period. Using an internal single-stage self-resorbable device is also possible.

Despite many studies reporting clinical success with the MDO technique, only a few have reported changes in weight gain. One study involving 10 patients even reported a decline in growth rate in seven patients in the first 12 months after MDO, despite continued tube feeding in three patients. This may be related to the fact that dysphagia, often seen in RS, is not corrected by the MDO procedure. A study in 17 infants reported full oral feeding being achieved in all infants by 3.5 months postoperatively, but provided no growth data. A Chinese group reported weight gain in a series of 41 RS infants after MDO. Mean weight percentile improved from 47 ± 18 g at the time of the initial surgical procedure to 74 ± 35 g at the time of distractor removal. Another group calculated standard deviation (Z-)scores for weight throughout the first year of life in 24 infants with RS, with 17 being treated by MDO. Their Z-scores changed from +0.1 and –0.8, respectively, in girls and boys at birth to a nadir of –1.6 at 5 months in girls, and –2.1 at 3 months in boys, translating in a mean weight deficit compared to the World Health Organisation standard of 1.7 and 1.4 kg at these time points. Catch-up growth following MDO onset has also been reported in a retrospective analysis from Yale, in parallel to an increase in the proportion of infants being fully orally fed from 50% pre-operatively to 73% at 6 months after surgery.

Several case series have reported PSG results before and after MDO. All noted improvements or normalization of the AHI or the respiratory disturbance index (RDI) in the majority of the patients, but only three of the studies provided detailed PSG results. One of the latter studies included seven patients, and reported a decrease in AHI from 60 ± 7.3 events/h before distraction to 1.6 ± 1.6 events/h at the end of the expander activation 6–8 weeks post-op. No longer-term follow-up data were reported. Another study reported a decrease in mean AHI from 10.6 events/h (range 0–43) to 2.2 events/h (0–12.9) in 13 infants undergoing MDO.

3 | SURGICAL INTERVENTIONS

3.1 Tongue-lip adhesion (TLA)

This surgical approach was first proposed by Shukowsky and subsequently reported to result in better survival rates. Success rates for this intervention, based on clinical criteria, vary and data on PSG results are scarce. Two studies compared sleep study results and clinical data in infants treated with TLA versus mandibular distraction osteogenesis (MDO; see below). Results showed that MDO was more effective in improving sleep study abnormalities, but MDO-treated patients were potentially also more prone to develop complications (e.g., wound infections; fracture of the bone anchoring the distractor).

FIGURE 3 Changes in the facial profile occurring over 3 years in a child with Robin sequence treated with the Tübingen Palatal Plate. Photos were taken by her father at age 6 weeks, 7 months, and 3 years. Note the normalization of the facial profile with attainment of normal oral functioning (photograph reproduced with parental permission) [Color figure can be viewed at wileyonlinelibrary.com]
while the third and largest study reported a decrease in AHI from a mean of 39.7 events/h (4.5–177) to 5.8 events/h (0–34) in a chart review of 28 infants in whom the MDO procedure was performed and changes in OSA documented by PSG. The authors describing the self-resorbable device mentioned above also reported resolution of UAO (i.e., an RDI less than 2.0 events/h) in all nine of their 14 nontracheostomized patients who were stable enough to tolerate a preoperative sleep study.

At the University of Missouri, mandibular distraction osteogenesis is performed using an internal device. Although resorbable devices were initially used to avoid secondary surgery to remove the hardware, the team has since moved to using metallic devices as the use of metallic, nonresorbable internal distractors was found to result in more effective and lasting mandibular advancement and resolution of OSA. An extensive conservative management protocol is used before MDO, including a craniofacial CT scan, laryngoscopy, PSG, and a swallow study. MDO is only considered if a trial of prone positioning and oxygen supplementation has failed. The proportion of referrals ultimately receiving MDO is less than 20% of those referred, and MDO is mainly pursued to avoid tracheostomy placement and facilitate feeding and weight gain.

Surgery is performed through bilateral submandibular external incisions (Figure 4). Oblique corticotomies of the mandible are made; the CT scans are used to position the osteotomies to avoid injury to...
the tooth buds. An oblique vector of distraction is chosen to achieve both anterior and vertical movement of the mandible, and the inferior alveolar nerve is preserved.

After a 48 h latency period, distraction proceeds at a rate of 2 mm/day with rhythm of 0.5 mm four times per day. After 10 mm of distraction, rate decreases to 1 mm/day at 0.5 mm twice per day. Distraction proceeds until overcorrection is achieved, which usually takes 2–3 weeks. After a further 8–12 weeks of consolidation, the hardware is removed.

Using this method, excellent success in avoiding tracheostomy, correcting OSA, and facilitating weight gain has been achieved. Complications have been minimal, primarily involving temporary marginal mandibular palsy. Patients are followed long term with clinical assessments and PSG.

In meta-analysis, however, complications such as pin site infections (18%), device failure (10%), persistent inferior alveolar nerve lesions (6%), and somewhat more rarely, damage to tooth buds resulting in long-term tooth loss, dentigerous cyst formation, or relapse of UAO symptoms and temporo-mandibular ankylosis were reported rather commonly. As previously mentioned, it is puzzling that MDO seems to be the treatment of choice in some countries, while it is hardly ever used in others, despite equally low tracheostomy rates.

### 3.3 Mandibular traction

This procedure, first described in 1937, involves fixation of a percutaneous parasymphysial circumferential wire to the mandible, with traction being applied by suspension weights (50–200 g), and is left in place for 4–6 weeks. Its effect on UAO is unknown, and it requires long-term immobilization of the patient during a critical developmental period. Also, a long-term follow-up study showed persistence of retrognathia on cephalometric x-rays. Therefore, based on the favorable outcomes using alternative interventions, this procedure is not currently recommended.

### 4 Conclusion

A review of the current management approaches for RS infants suggests that the TPP may be the conservative treatment of choice, and has a wide applicability in both isolated or syndromic cases as well as in those with mild to severe clinical manifestations. Importantly, the TPP procedure is associated with normal long-term development, at least in patients with isolated RS. When surgical interventions are adopted, MDO is currently the most frequent surgical procedure being conducted and appears to yield favorable outcomes, albeit in the absence of high quality evidence. Nonetheless, what is needed is a head-to-head comparison between conservative approaches such as CPAP, the NPA or the TPP and surgical treatments such as MDO or TLA, and an identification of unique phenotypic features that justify the selection of one approach versus the other. As randomized trials are difficult to realize in this rare condition, this may be the only realistic way to reaching agreement on these differing clinical management pathways. Independent of the treatment approach being selected, repeated serial PSG or cardiorespiratory polygraphic recordings and careful monitoring of weight gain are critical for correct clinical decisions to be implemented at every stage. Further refinements of the information provided by the multichannel recordings may assist in improving therapeutic and outcome targets in the near future.

### ACKNOWLEDGEMENT

We are grateful to the nursing and medical staff at our institutions for their dedication and support in caring for these babies, and to Wolfgang Buchenau, MD, for technical assistance in preparing this manuscript. Open Access funding enabled and organized by Projekt DEAL.

### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

### AUTHOR CONTRIBUTIONS

Christian F. Poets: conceptualization (lead); writing original draft (lead). Cornelia Wiechers: writing review & editing (supporting). Bernd Koo: resources (supporting); writing review & editing (supporting). David Gozal: writing review & editing (supporting).

### DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this manuscript.

### ORCID

Christian F. Poets https://orcid.org/0000-0002-1072-0066

### REFERENCES

1. Kaditis AG, Alonso Alvarez ML, Boudewyns A, et al. ERS statement on obstructive sleep disordered breathing in 1-to 23-month-old children. Eur Respir J. 2017;50:1591-1598.
2. Maas C, Poets CF. Initial treatment and early weight gain of children with Robin Sequence in Germany: a prospective epidemiological study. Arch Dis Child Fetal Neonatal Ed. 2014;99:F491-F494.
3. Poets CF, Roberts RS, Schmidt B, et al. Association between intermittent hypoxemia or bradycardia and late death or disability in extremely preterm infants. JAMA. 2015;314:595-603.
4. Brockmann PE, Schaefer C, Poets A, Poets CF, Urschitz MS. Diagnosis of obstructive sleep apnea in children: a systematic review. Sleep Med Rev. 2013;17:331-340.
5. Kirk V, Baughn J, D’Andrea L, et al. American Academy of Sleep Medicine position paper for the use of a home sleep apnea test for the diagnosis of OSA in children. J Clin Sleep Med. 2017;13:1199-1203.
6. Brockmann PE, Poets A, Poets CF. Reference values for respiratory events in overnight polygraphy from infants aged 1 and 3 months. Sleep Med. 2013;14:1323-1327.
7. Azarbarzin A, Sands SA, White DP, Redline S, Wellman A. The hypoxic burden: a novel sleep apnoea severity metric and a predictor of cardiovascular mortality-Reply to ‘The hypoxic burden: also known as the desaturation severity parameter’. Eur Heart J. 2019; 40:2994-2995.
8. Martín-Montero A, Gutiérrez-Tobal GC, Kheirandish-Gozal L et al. Heart rate variability spectrum characteristics in children with sleep apnea. Pediatr Res. 2020.

9. Drescher FD, Jotzo M, Goelz R, Meyer TD, Bacher M, Poets CF. Cognitive and psychosocial development of children with Pierre Robin sequence. Acta Paediatr. 2008;97:653-656.

10. Evans AK, Rahbar R, Rogers GF, Mul liken JB, Volk MS. Robin sequence: a retrospective review of 115 patients. Int J Pediatr Otorhinolaryngol. 2006;70:973-980.

11. Kapp-Simon KA, Krueckebaeger S. Mental development in infants with cleft lip and/or palate. Cleft Palate Craniofac J. 2000;37:65-70.

12. Alencar TRR, Marques IL, Bertucci A, Prado-Oliveira R. Neurological development of children with isolated Robin sequence treated with nasopharyngeal intubation in early infancy. Cleft Palate Craniofac J. 2017;54:256-261.

13. Thouvenin B, Djadi-Prat J, Chalouhi C, et al. Developmental outcome in Pierre Robin sequence: a longitudinal and prospective study of a consecutive series of severe phenotypes. Am J Med Genet A. 2013;161A:312-319.

14. Marques IL, Bettiol H, de Souza L, Barbieri MA, Bachega MI. Longitudinal study of the growth of infants with isolated Robin sequence considered being severe cases. Acta Paediatr. 2008;97:371-375.

15. Cozzi F, Totonelli G, Frediani S, Zani A, Spagnol L, Cozzi DA. The effect of glossopexy on weight velocity in infants with Pierre Robin syndrome. J Pediatr Surg. 2008;43:296-298.

16. Hsu CT, Chen CH, Lin MC, Wang TM, Hsu YC. Post-discharge body weight and neurodevelopmental outcomes among very low birth weight infants in Taiwan: a nationwide cohort study. PLoS One. 2018;13:13.

17. Robin P. Glossophtosis due to atresia and hypotrophy of the mandible. Am J Dis Child. 1934;48:541-547.

18. Caouette-Laberge L, Bayet B, Larocque Y. The Pierre Robin sequence: review of 125 cases and evolution of treatment modalities. Plast Reconstr Surg. 1994;93:934-942.

19. Kirschner RE, Low DW, Randall P, et al. Surgical airway management in Pierre Robin sequence: is there a role for tongue-lip adhesion? Cleft Palate Craniofac J. 2003;40:13-18.

20. van Lieshout MJS, Joosten KFM, Mathijssen IMJ, et al. Robin sequence: a European survey on current practice patterns. J Craniomaxillofac Surg. 2015;43:1626-1631.

21. Coutier L, Guyon A, Reix P, Franco P. Impact of prone positioning in infants with Pierre Robin sequence: a polysomnography study. Sleep Med. 2019;54:257-261.

22. Greenlee CJ, Scholes MA, Gao DX, Friedman NR. Obstructive sleep apnea and sleep position: does it matter for infants with a cleft palate? Cleft Palate Craniofac J. 2019;56:890-895.

23. Carpenter R, Irgens L, Blair P, et al. Sudden unexplained infant death in 20 regions in Europe: case control study. Lancet. 2004;363:185-191.

24. Heaf DP, Helms PJ, Dinwiddie R, Matthew DJ. Nasopharyngeal airways in Pierre Robin syndrome. J Pediatr. 1982;100:698-703.

25. Masters IB, Chang AB, Harris MO, Neil MC. Modified nasopharyngeal tube for upper airway obstruction. Arch Dis Child. 1999;80:186-187.

26. Wagener S, Rayatt SS, Tatman AJ, Gornall P, Slator R. Management of infants with Pierre Robin sequence. Cleft Palate Craniofac J. 2003;40:180-185.

27. Chang AB, Masters IB, Williams GR, Harris M, O’Neill MC. A modified nasopharyngeal tube to relieve high upper airway obstruction. Pediatr Pulmonol. 2000;29:299-306.

28. Abel F, Bajaj Y, Wyatt M, Wallis C. The successful use of the nasopharyngeal airway in Pierre Robin sequence: an 11-year experience. Arch Dis Child. 2012.
palatal plate prototype for newborns with Robin sequence. BMC Oral Health. 2020;20:171.

47. Poets CF, Koos B, Reinert S, Wiechers C. The Tubingen palatal plate approach to Robin sequence: summary of current evidence. J Craniofac Surg. 2019;47:1699-1705.

48. Shukowsky WP. Zur Ätiologie des Stridor inspiratorius congenitus. Jahrb Kinderheilk. 1911;73:459-474.

49. Douglas B. The treatment of micrognathia associated with obstruction by a plastic procedure. Plast Reconstr Surg. 1946;1946(1): 300-308.

50. Resnick CM, Calabrese CE, Sahdev R, Padwa BL. Is tongue-lip adhesion or mandibular distraction more effective in relieving obstructive apnea in infants with Robin sequence? J Oral Maxillofac Surg. 2019;77:591-600.

51. Flores RL, Tholpady SS, Sati S, et al. The surgical correction of Pierre Robin sequence: mandibular distraction osteogenesis versus tongue-lip adhesion. Plast Reconstr Surg. 2014;133:1433-1439.

52. Denny AD, Amm CA, Schafer RB. Outcomes of tongue-lip adhesion for neonatal respiratory distress caused by Pierre Robin sequence. J Craniofac Surg. 2004;15:819-823.

53. Bijnen CL, Don Griot PJ, Mulder WJ, Haumann TJ, Van Hagen AJ. Tongue-lip adhesion in the treatment of Pierre Robin sequence. J Craniofac Surg. 2009;20:315-320.

54. Sadakah AA, Elshali MA, Farhat AA. Bilateral intra-oral distraction osteogenesis for the management of severe congenital mandibular hypoplasia in early childhood. J Craniofac Surg. 2009;37:216-224.

55. Tibesar RJ, Scott AR, McNamara C, Sampson D, Lander TA, Sidman JD. Distraction osteogenesis of the mandible for airway obstruction in children: long-term results. Otolaryngol Head Neck Surg. 2010;143:90-96.

56. Burstein FD, Williams JK. Mandibular distraction osteogenesis in Pierre Robin sequence: application of a new internal single-stage resorbable device. Plast Reconstr Surg. 2005;115:61-67.

57. Spring MA, Mount DL. Pediatric feeding disorder and growth decline following mandibular distraction osteogenesis. Plast Reconstr Surg. 2006;118:476-482.

58. Pinheiro Neto CD, Alonso N, Sennes LU, Goldenberg DC, Santoro Pde P. Polysomnography evaluation and swallowing endoscopy of patients with Pierre Robin sequence. Braz J Otorhinolaryngol. 2009;75:852-856.

59. Looby JF, Schendel SA, Lorenz HP, Hopkins EM, Aizenbud D. Airway analysis with bilateral distraction of the infant mandible. J Craniofac Surg. 2009;20:1341-1346.

60. Luo D, Chen Y, Wang H, et al. The effect of mandibular distraction osteogenesis on weight velocity in infants with severe Pierre Robin syndrome. J Craniofac Surg. 2018;29:1851-1854.

61. Li L, Scott AR. Weight gain in infants with Pierre Robin sequence in the first year of life. Otolaryngol Head Neck Surg. 2020;163:1032-1037.

62. Gary CS, Marczewski S, Vitagliano PM, Sawh-Martinez R, Wu R, Steinbacher DM. A Quantitative analysis of weight gain following mandibular distraction osteogenesis in Robin sequence. J Craniofac Surg. 2018;29:676-682.

63. Monasterio FO, Drucker M, Molina F, Ysunza A. Distraction osteogenesis in Pierre Robin sequence and related respiratory problems in children. J Craniomaxillofac Surg. 2002;13:79-83.

64. Dauria D, Marsh JL. Mandibular distraction osteogenesis for Pierre Robin sequence: what percentage of neonates need it? J Craniofac Surg. 2008;19:1237-1243.

65. Hammoudah J, Bindingnavele V, Davis B, et al. Neonatal and infant mandibular distraction as an alternative to tracheostomy in severe obstructive sleep apnea. Cleft Palate Craniofac J. 2010.

66. Denny AD. Distraction osteogenesis in Pierre Robin sequence with tracheal obstruction. Clin Plast Surg. 2004;31:221-229.

67. Miller JJ, Kahn D, Lorenz HP, Schendel SA. Infant mandibular distraction with an internal curvilinear device. J Craniofac Surg. 2007;18:1403-1407.

68. Sahoo NK, Roy ID, Dalal S, Bhandari A. Distraction osteogenesis for management of severe OSA in Pierre Robin sequence: an approach to elude tracheostomy in infants. J Maxillofac Oral Surg. 2016;15:501-505.

69. Zhang RS, Hoppe IC, Taylor JA, Bartlett SP. Surgical management and outcomes of Pierre Robin sequence: a comparison of mandibular distraction osteogenesis and tongue-lip adhesion. Plast Reconstr Surg. 2018;142:480-509.

70. Grayson BH, McCormick S, Santiago PE, McCarthy JG. Vector of device placement and trajectory of mandibular distraction. J Craniofac Surg. 1997;8:473-480.

71. Breik O, Tivey D, Umapathysivam K, Anderson P. Does the rate of distraction or type of distractor affect the outcome of mandibular distraction in children with micrognathia? J Oral Maxillofac Surg. 2016;74:1441-1453.

72. Murage KP, Costa MA, Friel MT, Havlik RJ, Tholpady SS, Flores RL. Complications associated with neonatal mandibular distraction osteogenesis in the treatment of Robin sequence. J Craniofac Surg. 2014;25:383-387.

73. Ow A, Cheung JK. Skeletal stability and complications of bilateral sagittal split osteotomies and mandibular distraction osteogenesis: an evidence-based review. J Oral Maxillofac Surg. 2009;67:2344-2353.

74. Callister AC. Hypoplasia of the mandible (miokrgnathy) with cleft palate: treatment in early infancy by skeletal traction. Am J Dis Child. 1937;53:1057-1059.

75. Schettler D, Koch H. Growing jaw during and after orthopedic-surgical extension in children with congenital microgenia. Fortschr Kiefer Gesichtschir. 1974;18:166-169.