DOI: 10.4149/BLL_2024_006

Bratisl Med J 2024; 125 (1)
33 – 37

REVIEW

Comprehensive review of the timing of surgical management of macroglossia in Beckwith-Wiedemann syndrome

Peter KIZEK, Karolina Kamila GLINSKA, Marcel RIZNIC, Branislav BORZA, Vladimira SCHWARTZOVA, Zuzana KOTULICOVA

Department of Stomatology and Maxillofacial Surgery, PJ Safarik University and L Pasteur University Hospital in Kosice, Slovakia. **dr.riznic@gmail.com**

ABSTRACT
Beckwith-Wiedemann Syndrome (BWS) is a rare genetic disorder that causes developmental defects as well as an elevated risk of malignancies. Macroglossia, or an enlarged tongue, is a common symptom of BWS that may have a negative influence on a person‘s quality of life. The aim of this systematic review is to look at the present state of knowledge about the repercussions of macroglossia, as well as the influence of the timing of surgical resection, or glossectomy, in the treatment of severe cases of macroglossia *(Ref. 35)*. Text in PDF *www.elis.sk*
KEY WORDS: macroglossia, Beckwith-Wiedemann syndrome, glossectomy.

Introduction

Beckwith-Wiedemann Syndrome is a genetic illness that affects numerous organ systems, with varied phenotypic presentations. Due to that reason, in 2018, a consensus group (1) decided to classify it as Beckwith-Wiedemann spectrum (BWSp). BWSp is traditionally distinguished by macroglossia, macrosomia, abdominal wall abnormalities, and a greater risk of embryonal tumors (2–4). One of the distinctive physical aspects of BWSp is macroglossia, affecting 80–99 % of patients (1). Tongue reduction surgery (TRS) tries to decrease the size of the tongue, while retaining normal form and function (5). Surgical resection rate averages about 70 % (6–8). Due to the rarity of BWSp (1 in 10,000 births), there were a few studies debating the appropriate time of resection, but none were definitive or conducted on a large number of cases (2). This literature review provides a complete examination of the existing research to investigate the need for surgical resection in managing macroglossia associated with BWSp and optimal time of such intervention.

Methods

A systematic search was conducted in electronic databases, including Web of Science, PubMed, and Google Scholar, using keywords such as „Beckwith-Wiedemann Syndrome“ “optimal timing”, “timing” „macroglossia“ „ and „glossectomy“ “tongue reduction”. Relevant articles published in English were included, and their references were cross-checked to ensure comprehensive coverage.

Results

The literature review revealed that macroglossia is a frequent finding in individuals with BWSp (1) and can have significant effects on speech, food intake, and overall quality of life and are deemed as an indication for surgical resection (9). Depending on severity of the large tongue and impairment of the mention functions the surgical methods are chosen. Depending on the severity of the macroglossia, the ideal time and need of the treatment may be decided; partial glossectomy correction may be beneficial (8–10). In the majority of review articles, the age of the patients is not mentioned separately from the main reason of resection. A representation of this indications, possible complications post-surgery with the information about the age of the patients undergoing of the procedure have been described.

Food intake

Infants with BWSp frequently have feeding problems prior to surgery, which may put them at risk of chocking. This is due to the limited and altered tongue movements, as well as the inability to swallow food correctly. Alternative positioning, liquid diet, and low flow rate were proposed as compensatory feeding practices. However, the authors strongly recommend surgical resection because the issues were greatly reduced or eliminated after performing tongue resection surgery (11). Bulk of the tongue may also cause masticatory system dysfunction due to repeated damage to

Department of Stomatology and Maxillofacial Surgery, PJSafarik University and L Pasteur University Hospital in Kosice, Slovakia

Address for correspondence: Marcel RIZNIC, Department of Stomatology and Maxillofacial Surgery, PJ Safarik University and L Pasteur University Hospital, Rastislavova 43, SK-041 90 Kosice, Slovakia.
Phone: +421 908 027 585

its surface (12). The first comprehensive study of new-born feeding before and after surgical tongue resection in BWSp. Patients undergoing glossectomy in that study ranged in age from 4 to 12 months (11). A case of 16-month-old boy was described where the utilisation of with modified stellate/wedge surgical technique in order to combat the problem with drooling and food intake. The case mentions also respiratory issues such as noisy breathing and troubled breathing when laying. The case report doesn't mention postoperative difficulties (13).

Speech

Some authors suggest that for the influence of the appropriate speech development, surgical resection is ought to be performed before the stage of babbling begins. Overall, this enhances the probability of the infant acquiring speech patterns that are appropriate for their age, while also preventing the development of compensatory techniques and distortions (14). Number of authors have suggested that the surgery should be performed at age 2, in order to influence the speech when the development progresses quickly (15). The study group containing 35 participants, of which 12, undergone the procedure of TRS. No post operative complications were noted, and the age of patients with indication was unknown. In the evaluation of the surgical treatment of patients with BWSp, there was a big variation in the existence of speech delay in BWSp patients with macroglossia who had surgery versus non-surgical correction (16). In study conducted by Mass (4), where 18 patients the glossectomy. Majority of them had an issue with containment of the tongue inside of the oral cavity. Children operated on were aged 5 and older and had satisfactory outcome with the surgical correction.

Airway obstructions and sleep apnoea

Brioude et al suggest that in case of severe airway obstruction, surgical intervention (adenoid tonsillectomy with or without glossectomy) should be considered earlier than in 1yo. Furthermore, the Consensus Statement provided by cooperation of the specialist European Network for Congenital Imprinting Disorders in area of the BWSp suggest that in case the airway obstruction is suspected the team of specialist such as ORL and polysomnography should be performed (1). In the absence of respiratory obstruction, surgery is usually postponed until the child is at least 12 months old, when tongue size is more stable. If the indication for surgery is unclear, the child's progress should be monitored to see if new indications emerge (1). In study of 118 patients with sleep apnoea, the results have suggested that large tongue is not sole reason of this disturbance. In these patients adenotonsillectomy on its own or combined with TRS was performed. In this study, partial glossectomy was performed at a median age of 5 months and 10 months in patients who had sleep apnoea symptoms resolved after the procedure. At the median age of 2.5 years, two patients underwent concurrent tonsillectomy and partial glossectomy. On the other hand, the choice to conduct surgery should be decided on a case-by-case basis by a certified healthcare practitioner and was limited to only one facility (17).

Another retrospective study, based on a review of 391 patient records, suggests that resection be performed on an infant or an individual with deciduous dentition. The severity of the sleep apnoea and abnormal jaw relations were used to determine whether or not to operate in this study (10). In 2021 a case report of tongue reduction due to the breathing a swallowing was described, with no further complications on 2 year follow up. Authors consider the possible need for secondary surgery in the future (18). Rimmel based on experience of treating patients with macroglossia stated that although in infancy the upper airway obstruction is caused by the enlargement of the base of the tongue and in the reported cases was treated by tracheostomy, in the later years of child life this issue is caused by enlargement of adenoid gland and should be treated accordingly (6). This might be indicative of the early resolution of macroglossia, since conducting tracheostomy on a child of such a young age is unquestionably debateable.

Challenges of anaesthesia

If decided for the surgical resection the post operative oedema and complication may also be important of appropriate timing and procedure. As it is suggested in couple studies children after undergoing procedure have been in the intensive care unit and extubated on 5–6 days after procedure in order to mitigate the post operative swelling, in patients younger than a year, in children above that age the time shortens to 1 to 3 days (19). Nevertheless, some studies suggest successful extubating directly after the surgery (20, 21). Some authors suggest using new techniques such as harmonic scalpel the Ultrasonic Dissector (22) or CO_2 laser (23, 24) in order to control haemostasis and post operative swelling as well as reduce post operative pain and healing, but the sample reported on them is not big enough to state the effectiveness of this method. A study of 201 of intubated BWSp was performed by team of anaesthesiologists in order to examine the difficulty in intubation in children affected by the syndrome. Although the results of difficult intubation was only registered in 5.2 % of the participant, one of the factors influencing the difficult airways was age of under 1 (amongst macroglossia) (25).

In cases of tongue reduction, Najuokat et al (8) found that allegations of difficult intubation were exaggerated. As part of the procedure for post-operative care, children have been feed with nasogastric tubes. Only in severe instances of macroglossia, children younger than 12 months were operated on, according to the author. The rationale behind this remark cannot be determined. The youngest patient to have surgery was four months old. The research of 68 patients indicates that the effects of surgery regarding preservation of taste and enhancement of quality of life were observable and supports the notion of improved orthodontic outcomes since fewer individuals required treatment. Matsuda highlights the similarity between the site and nature of surgical performance in adenectomies and tonsillectomies in his review. This procedure is usually performed due to obstructive breathing (17). Due to issues arising after anaesthesia, such as the requirement for reintubation, the guidelines in this field propose a minimum age of 3 years for surgical procedures (26–28).

Orthognathic system

Study by Marsh et al in 2023 (10), based on retrospective study of individuals that underwent the procedure of tongue resection have noted a significant difference in occlusal relationship in anterior area in comparison of patients followed that has not undergone procedure. This theory was confirmed again by a Kawafuji (29) and Kim (30). Anterior open bite and wide dental arch has also been presented if macroglossia was left untreated (29). Some authors describe the combination of orthognathic and glossectomy procedure in order to compensate for the overgrowth of tongue. Studies have shown that both micrognathic mandible although rear was present in patients with BWSp (17). Opposing stance was presented in a couple studies, where authors conducted that the glossectomy does not improve the craniofacial and dentoskeletal features in young patients affected by BWSp (16).

Need for second stage debulking, or two stage surgery

Hettinger and Kucker reported the need for subsequent surgery. In Hettinger's report, repeat surgical resection was conducted 6 months after surgery, however the patient's age is not stated specifically (9, 23, 31). Choi et al proposed at 2-stage surgery on a study case of one patient which suffered from macroglossia not related to BWSp. The primary complaint was issues with swallowing and speech. The first surgery was performed at age and followed at 3 years of age and followed at age of 9. Whereas the first resection was planned to improve function, second was performed to reach a satisfactory aesthetics of the tongue. The author preposes two stage technique in order to reduce injury to neurovascular structures and prevent post-operative swelling. This technique considers a future need of debulking as this might be a challenge in growing children (32). In the research by Najuokat et al, 11 percent of patients required subsequent surgery, however the age of patients undergoing first surgery was not determined. This is a persuasive case for the two-stage operation proposal. The technique can be considered in children which were late advised to centre due to lessen macroglossia which was not absolute indication but still caused later issues (8). Controversy the need of this procedure is connected to avoidance of orthognathic discrepancies and prognathism. Operating at a young age, some studies have shown the necessity for subsequent surgery owing to the development of the tongue's growth, which might be interpreted as proof that operating at a young age is not optimal.

Discussion

Macroglossia associated with Beckwith–Wiedemann Syndrome can significantly impair oral function and impact quality of life. While conservative management approaches may provide limited relief surgical resection, or glossectomy, becomes a viable option for severe cases (8). In extreme circumstances, the justifications for surgical tongue reduction are undeniable and especially pertinent due to the critical indication. In early developing children, tongue excision has been claimed to be beneficial in dentoalveolar and functional development. There are several case reports or small cohorts of BWSp patients, but little is known about the long-term outcomes of a large patient group. In addition, natural resolution of macroglossia, as well as growth-related adaptation, have been documented some authors (6). Some authors recommend the combination of surgical treatment at a young age with physiotherapeutic and orthodontic treatment in order to obtain a stable results (32).

Often the timing is influenced by the macroglossia being moderate and other issues associated with the syndrome such as hypoglycemia, midline abdominal wall defect, large umbilical hernia, renal abnormalities, and tumors need the primary attention (16). In case of moderate macroglossia patients suffer from inability to contain the tongue inside of oral cavity which could alter their speech learning progression, but also affect their social status as this creates a look of their mental impairment or different from other children (33). As shown in the studies (age older) this kind of procedure can be still beneficial at older age (4). The complications associated with the macroglossia most definitely have been discussed to have secondary effect on the stomatognathic system (10, 29, 30) but also sleep apnea which is associated with this defect (17). The sleep apnea has been discussed to be cause of health issues such as attention deficit disorder, or thorax deformation, this might lead to belief that early treatment of even moderate cases of the macroglossia could be beneficial (34). The issue of normal speech foundation and practice has also been associated with the prognosis of the early timing of the surgery being beneficial to the leering process of the child (15). When looked upon the challenged of anaesthesia authors have noted that the procedure itself is straightforward and the process is often wrongly seen as overcomplicated (8). It must be for sure noted that the outcome of the surgery is difficult to predict as often difficulties with speech (31) and need for secondary surgery arise (9). Issue of the impact on the orthognathic system has been widely discussed having two opposing arguments of the macroglossia having effect on the mandibular growth. So far the conclusions have not been supported across a big cohort study, thus the effect on timing is disputable in this case (16, 19). Drooling which is most often associated with the inability to contain the tongue inside of the oral cavity is not only problematic from the dehydration point of view, reoccurring infections but also the social aspect as mentioned earlier. A multidisciplinary approach, involving various healthcare professionals, is crucial in the assessment, decision-making, and post-operative care to achieve the best outcomes for patients with BWSp and macroglossia in young age (19). Long-term functional results and quality of life after glossectomy in BWSp patients with macroglossia require more study. In each trial that followed patients, several criteria such as taste retention, aesthetics, and drooling were recorded. however, in order to definitively define the optimal time (of which arguably exist), it would be ideal if similar post-operative complications and unified tests describing tongue functionality, orthognathic system growth, polysomnography, were recorded.

Surgical options for patients with Beckwith-Wiedemann syndrome are very case-specific due to the influence of the afore-

mentioned clinical complicating factors. The fact that the need for surgical resection varies from case to case is consistent with the current personal medicine approach; Since our understanding of the efficacy of the early tongue reduction may change as we continue to watch these individuals, the timing of the therapy should be selected based on symptomatology rather than the patient‘s chronologic age.

References

1. Brioude F, Kalish JM, Mussa A, Foster AC, Bliek J, Ferrero GB et al. Expert consensus document: Clinical and molecular diagnosis, screening and management of Beckwith-Wiedemann syndrome: an international consensus statement. Nat Rev Endocrinol 2018; 14: 229–249. https://doi.org/10.1038/nrendo.2017.166.

2. Mussa A, Ferrero G, Ceoloni B, Basso E, Chiesa N, De Crescenzo A et al. Neonatal hepatoblastoma in a newborn with severe phenotype of Beckwith-Wiedemann syndrome. European J Pediatr 2011; 170: 1407–1411. https://doi.org/10.1007/s00431-011-1455-0.

3. Weksberg R, Shuman C, Beckwith JB. Beckwith-Wiedemann syndrome. Eur J Hum Genet 2010; 18: 8–14. https://doi.org/10.1038/ejhg.2009.106.

4. Maas SM, Kadouch DJ, Masselink A-CCM, Van Der Horst CMAM. Taste and speech following surgical tongue reduction in children with Beckwith-Wiedemann syndrome. J Craniomaxillofac Surg 2016; 44: 659–663. https://doi.org/10.1016/j.jcms.2016.02.010.

5. Heggie A a. C, Vujcich NJ, Portnof JE, Morgan AT. Tongue reduction for macroglossia in Beckwith Wiedemann syndrome: review and application of new technique. Internat J Oral Maxillofac Surg 2013; 42: 185–191. https://doi.org/10.1016/j.ijom.2012.09.003.

6. Rimell F, Shapiro A, Shoemaker D, Kenna M. Head and Neck Manifestations of Beckwith-Wiedemann Syndrome. Otolaryngol Head Neck Surg 1995; 113: 262–265. https://doi.org/10.1016/S0194-5998(95)70115-X.

7. Kadouch DJM, Maas SM, Dubois L, Horst CMAM van der. Surgical treatment of macroglossia in patients with Beckwith–Wiedemann syndrome: a 20-year experience and review of the literature. Internat J Oral Maxillofac Surg 2012; 41: 300–308. https://doi.org/10.1016/j.ijom.2011.10.021.

8. Naujokat H, Möller B, Terheyden H, Birkenfeld F, Caliebe D, Krause MF et al. Tongue reduction in Beckwith-Wiedemann syndrome: outcome and treatment algorithm. Internat J Oral Maxillofac Surg 2019; 48: 9–16. https://doi.org/10.1016/j.ijom.2018.07.008.

9. Hettinger PC, Denny AD. Double Stellate Tongue Reduction: A New Method of Treatment for Macroglossia in Patients With Beckwith-Wiedemann Syndrome. Ann Plast Surg 2011; 67: 240–244. https://doi.org/10.1097/SAP.0b013e3181f77a83.

10. Marsh JL, Perlyn CA. Beckwith-Widemann Macroglossia: The Role of Surgical Tongue Reduction. Cleft Palate-Craniofacal J 2023. https://doi.org/10.1177/10556656221148900.

11. Prendeville N, Sell D. Tongue Reduction Surgery and Feeding Difficulties in Infants With Beckwith Wiedemann Syndrome: A Case Series. Cleft Palate-Craniofacal J 2019; 56: 679–689. https://doi.org/10.1177/1055665618794070.

12. Perkins J. Overview of macroglossia and its treatment. Curr Opinion Otolaryngol Head Neck Surg 2009; 17: 460–465. https://doi.org/10.1097/MOO.0b013e3283317f89.

13. Irhamni B. Case report macroglossia: Review and application of tongue reduction technique. J Pediatr Surg Case Rep 2015; 3: 198–200. https://doi.org/10.1016/j.epsc.2015.03.009.

14. Van Lierde KM, Mortier G, Huysman E, Vermeersch H. Long-term impact of tongue reduction on speech intelligibility, articulation and oromyofunctional behaviour in a child with Beckwith–Wiedemann syndrome. Internat J Pediatr Otorhinolaryngol 2010; 74: 309–318. https://doi.org/10.1016/j.ijporl.2009.12.006.

15. Kveim M, Fisher JC, Jones KL, Gruer B. Early tongue resection for Beckwith-Wiedemann macroglossia. Ann Plast Surg 1985; 14: 142–144. https://doi.org/10.1097/00000637-198502000-00008.

16. Style CC, Cruz SM, Lau PE, Lee TC, Wesson DE, Olutoye OO. Surgical Outcomes of Patients with Beckwith-Wiedemann Syndrome. J Pediatr Surg 2018; 53: 1042–1045. https://doi.org/10.1016/j.jpedsurg.2018.02.041.

17. Follmar A, Dentino K, Abramowicz S, Padwa BL. Prevalence of sleep-disordered breathing in patients with Beckwith-Wiedemann syndrome. J Craniofac Surg 2014; 25: 1814–1817. https://doi.org/10.1097/SCS.0000000000000991.

18. Lamfoon S, Abuzinada S, Yamani A, Binmadi N. Beckwith-Wiedemann syndrome with macroglossia as the most significant manifestation: A case report. Clin Case Rep 2021; 9: e04479. https://doi.org/10.1002/ccr3.4479.

19. Cohen JL, Cielo CM, Kupa J, Duffy KA, Hathaway ER, Kalish JM et al. The Utility of Early Tongue Reduction Surgery for Macroglossia in Beckwith-Wiedemann Syndrome. Plast Reconstr Surg 2020; 145: 803e–13e. https://doi.org/10.1097/PRS.0000000000006673.

20. de la Varga O, Galve AI, Romera A. Perioperative anesthetic management of reductive glossoplasty in a patient with Beckwith-Wiedemann syndrome. Rev Esp Anestesiol Reanim 2021; 68: 156–160. https://doi.org/10.1016/j.redar.2020.02.009.

21. Geisler EL, Jeffers J, Salhi S, Perlyn CA. Reduction Glossectomy for Macroglossia in Beckwith-Wiedemann Syndrome: Is Post-Op Intubation Necessary? Cleft Palate-Craniofacal J 2022; 59: 126–131. https://doi.org/10.1177/1055665621991739.

22. Kittur MA, Padgett J, Drake D. Management of macroglossia in Beckwith-Wiedemann syndrome. Brit J Oral Maxillofac Surg 2013; 51: e6–8. https://doi.org/10.1016/j.bjoms.2012.01.015.

23. Kacker A, Honrado C, Martin D, Ward R. Tongue reduction in Beckwith-Weidemann syndrome. Internat J Pediatr Otorhinolaryngol 2000; 53: 1–7. https://doi.org/10.1016/S0165-5876(00)00280-9.

24. Yilmaz M, Mercan H, Karaman E, Kaytaz A. Tongue Reduction in Beckwith-Wiedemann Syndrome With CO2 Laser. J Craniofac Surg 2009; 20: 1202–1203. https://doi.org/10.1097/SCS.0b013e3181acdd72.

25. Sequera-Ramos L, Duffy K, Fiadjoe J, Garcia-Marcinkiewicz A, Zhang B, Perate A et al. The Prevalence of Difficult Airway in Children With Beckwith-Wiedemann Syndrome: A Retrospective Cohort Study. Anesthesia Analgesia 2021; 133: 1559–1567. https://doi.org/10.1213/ANE.0000000000005536.

26. Schneuer FJ, Bell KJ, Dalton C, Elshaug A, Nassar N. Adenotonsillectomy and adenoidectomy in children: The impact of timing of surgery and post-operative outcomes. J Paediatr Child Health 2022; 58: 1608–1615. https://doi.org/10.1111/jpc.16052.

27. Biavati MJ, Manning SC, Phillips DL. Predictive Factors for Respiratory Complications After Tonsillectomy and Adenoidectomy in Children. Arch Otolaryngol Head Neck Surg 1997; 123: 517–521. https://doi.org/10.1001/archotol.1997.01900050067009.

28. Lawlor CM, Riley CA, Carter JM, Rodriguez KH. Association Between Age and Weight as Risk Factors for Complication After Tonsillectomy in Healthy Children. JAMA Otolaryngol Head Neck Surg 2018; 144: 399–405. https://doi.org/10.1001/jamaoto.2017.3431.

29. Kawafuji A, Suda N, Ichikawa N, Kakara S, Suzuki T, Baba Y et al. Systemic and maxillofacial characteristics of patients with Beckwith-Wiedemann syndrome not treated with glossectomy. Am J Orthod Dentofacial Orthop 2011; 139: 517–525. https://doi.org/10.1016/j.ajodo.2009.07.021.

30. Kim D, Kim J, Huh G, Lee D, Kwon S. Tongue Reduction Surgery Improves Mandibular Prognathism in Beckwith-Wiedemann Syndrome without Compromising Tongue Function. Clin Exp Otorinolaryngol 2022. https://doi.org/10.21053/ceo.2022.00976.

31. Defabianis P, Ninivaggi R, Romano F. Dentoskeletal features and growth pattern in Beckwith-Wiedemann spectrum: is surgical tongue reduction always necessary? Clin Oral Invest 2023. https://doi.org/10.1007/s00784-023-05043-w.

32. Choi SH, Kang DY, Kim YH, Hwang CJ. Severe skeletal Class III malocclusion treated with 2-stage orthognathic surgery with a mandibular step osteotomy. Am J Orthod Dentofacial Orthop 2014; 145: p125–135. https://doi.org/10.1016/j.ajodo.2013.07.017.

33. Abeleira M, Seoane-Romero J, Outumuro M, Caamano F, Suarez D, Carmona I. Case report A multidisciplinary approach to the treatment of oral manifestations associated with Beckwith-Wiedemann syndrome A long-term case report. J Amer Dental Ass 2011; 142: 1357–1364. https://doi.org/10.14219/jada.archive.2011.0136.

34. Shipster C, Morgan A, Dunaway D. Psychosocial, Feeding, and Drooling Outcomes in Children with Beckwith Wiedemann Syndrome Following Tongue Reduction Surgery. Cleft Palate-Craniofacial J 2012; 49: E25–34. https://doi.org/10.1597/10-232.

35. Harada T, Yamanishi T, Kurimoto T, Nishio J. Improved Quality of Life for Children With Beckwith-Wiedemann Syndrome Following Tongue Reduction Surgery. J Craniofac Surg 2019; 30: 163–166. https://doi.org/10.1097/SCS.0000000000004823.

Received August 29, 2023.
Accepted August 30, 2023.