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Tongue reduction in Beckwith–Wiedemann syndrome: outcome and treatment algorithm

H. Naujokat[1], B. Möller[1], H. Terheyden[1], F. Birkenfeld[1], D. Caliebe[2], M. F. Krause[3], H. Fischer-Brandies[4], J. Wiltfang[1]

[1]Departments of Oral and Maxillofacial Surgery, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany; [2]Departments of Anesthesiology and Intensive Care Medicine, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany; [3]Departments of Pediatrics, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany; [4]Departments of Orthodontics, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

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Abstract. Beckwith–Wiedemann syndrome is a rare congenital overgrowth disorder with macroglossia being one of the cardinal symptoms. In pronounced cases, macroglossia can lead to airway obstruction, musculoskeletal alterations and functional deficits. Surgical tongue reduction is performed at varying ages and with different techniques. This study evaluated perioperative complications, as well as long-term aesthetic and functional outcomes, in a large cohort. A total of 68 patients, treated either surgically or conservatively, were included. Depending on the severity of macroglossia, patients were divided into three groups to determine the treatment algorithm. Complications after surgical tongue reduction were prolonged intubation and revision due to dehiscence or haematoma. In the long term, no patient suffered from impaired sense of taste or paresthesia, although the shape of the tongue was disproportional in 85%. With the present treatment algorithm, operative tongue reduction exerts a positive influence on skeletal, dentoalveolar and functional development with sufficient long-term outcome and high grade of satisfaction of the patients. Supportive therapy in an interdisciplinary centre is of fundamental importance for both surgical and conservative treatment.

Key words: Beckwith–Wiedemann syndrome; macroglossia; tongue reduction; treatment algorithm.

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Beckwith–Wiedemann syndrome (BWS) is a congenital overgrowth disorder with an estimated incidence of 1 in 13,700 births[1]. BWS is the most common overgrowth syndrome in infancy, affecting females and males with equal frequency[2]. The clinical manifestations can be highly variable and may show varying degrees of asymmetries. Additional features can be neonatal hypoglycaemia, abdominal wall defects, anomalies of the ear, midface hypoplasia and prominent occiput. Varying organ abnormalities of liver, spleen and kidney have been described, as well as an increased risk of developing malignant tumours during early childhood[3–6]. The genetic alterations underlying BWS are complex and have not been fully elucidated[7]. In 75–80% of cases, genotypic abnormalities of the imprinted region of chromosome 11p (11p15.5) have been

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identified. Most cases occur sporadically, and only 15% show familial transmission[8–10].

Therapy of BWS is undertaken in a symptom-orientated manner, depending on the presented organ manifestations. Macroglossia is reported in 80–99% of BWS patients. Macroglossia can lead to airway obstruction and respiratory insufficiency in severe cases[4,11,12] (Fig. 1). Therefore, tongue-reduction procedures can be of major importance in early childhood. In cases without immediate vital risk, tongue reduction should be delayed until after the first year of life because of potential perioperative complications[13]. Additional symptoms and disabilities associated with macroglossia can be an indication for surgical tongue reduction. Functional deficits, including dysphagia, drooling and pronunciation difficulties can occur, as well as musculoskeletal and dentoalveolar alteration (anterior open-bite, malocclusion, prognathism, diastema and proclination of the incisors) because of increased pressure of the tongue[14]. In addition, aesthetic and psychological aspects need to be considered for surgical indication. The clinical picture with protrusion of the tongue may provide an incorrect appearance of mental deficiency, whereas these patients usually have normal intelligence. Thus, studies have shown a negative impact on psychological health and quality of life[4,11,15].

Various surgical techniques for tongue reduction have been proposed. Most of these techniques include resection of the tip of the tongue. The aim is to achieve a nearly normal size such that the tongue remains behind the incisors with sufficient mobility to moisturize the lips[15,16]. The most popular techniques have been described by Egyedi and Obwegeser and by Schwenzer and are both performed at our department. Egyedi and Obwegeser suggest a resection of the central body and the tip of the tongue. This technique is a symmetric resection and is particularly indicated for bilateral macroglossia[17]. The technique of Schwenzer preserves the tip of the tongue but the body is reduced centrally in combination with a lateral wedge resection. An indication for this technique is given especially by unilateral macroglossia (Fig. 2). In cases with less pronounced macroglossia, conservative therapy is recommended with orofacial regulation therapy according to Castillo–Morales with the help of oral stimulation plates (Fig. 3) and speech therapy[15,18]. Conservative treatment is also used pre- and postoperatively as supportive therapy. Furthermore, orthodontics and orthognathic surgery may be required in the course of growth as an adjuvant therapy[14,19,20].

The purpose of this study was to evaluate clinical long-term results and to detect health impairments or permanent side-effects in patients with BWS who underwent either a conservative or an operative macroglossia therapy.

Materials and Methods

This study was a retrospective, cross-sectional, single-centre study of BWS patients with macroglossia who were treated conservatively or operatively from 1987 until 2016 at the Department of Oral and Maxillofacial Surgery of the University Hospital Schleswig-Holstein, Kiel, Germany. Approval from the ethics committee of the medical faculty of the Christian-Albrechts-University of Kiel was obtained (D 447/11) and all patients had provided informed written consent for participation in the study. The applied therapeutic concept and the chronological sequence of surgical and supportive treatment are described in Table 1. The indication for surgical tongue reduction was determined in an interdisciplinary team consisting of an oral- and maxillofacial surgeon, a paediatrician, a speech therapist and an orthodontist, depending on the severity of macroglossia and the degree of impairment. Surgical intervention at an age younger than 12 months was performed only in cases of vital danger (airway obstruction, swallowing problems with failure to thrive). The decision regarding surgical technique was made depending on symmetric or asymmetric macroglossia. All interventions occurred under general anaesthesia with nasotracheal intubation. Preoperatively, 5 mg prednisolone/kg body weight was administered as prophylaxis for swelling. The resected tongue tissue was quantified in a volumetric flask. Postoperatively, the patients were mechanically ventilated and sedated on the paediatric intensive care unit. A nasogastric feeding tube was administered to ensure postoperative nutrition and to protect the wound.

Data collection

Data collection consisted of two parts: retrospective evaluation of patient data and cross-sectional analysis on the basis of patient survey and follow-up examinations. All

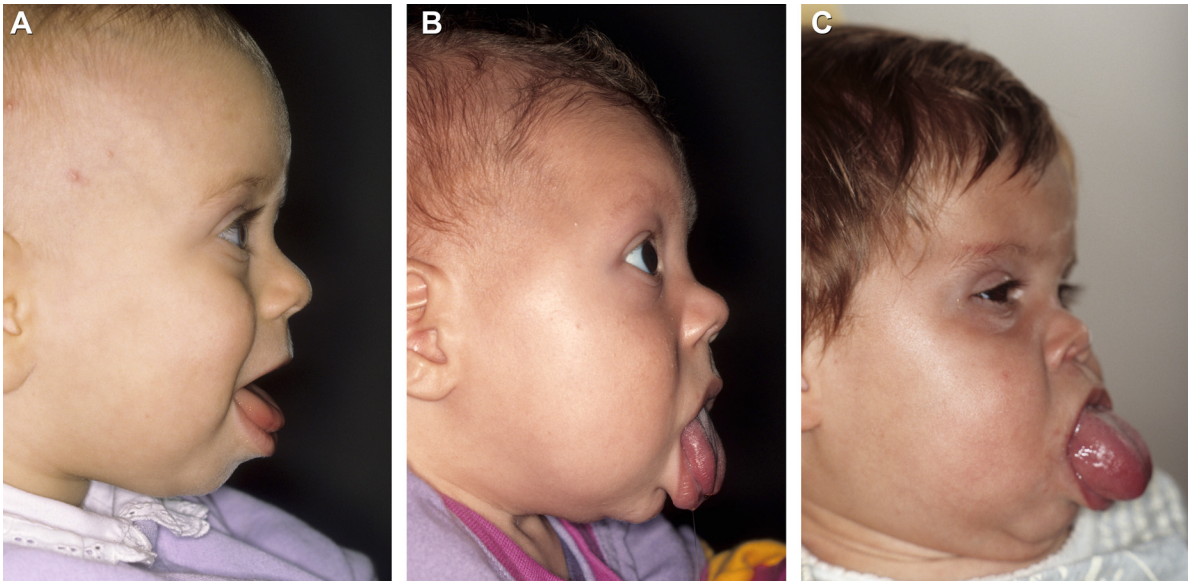

Fig. 1. Various manifestations of macroglossia in Beckwith–Wiedemann syndrome with mild (A), moderate (B) and strong (C) expression.

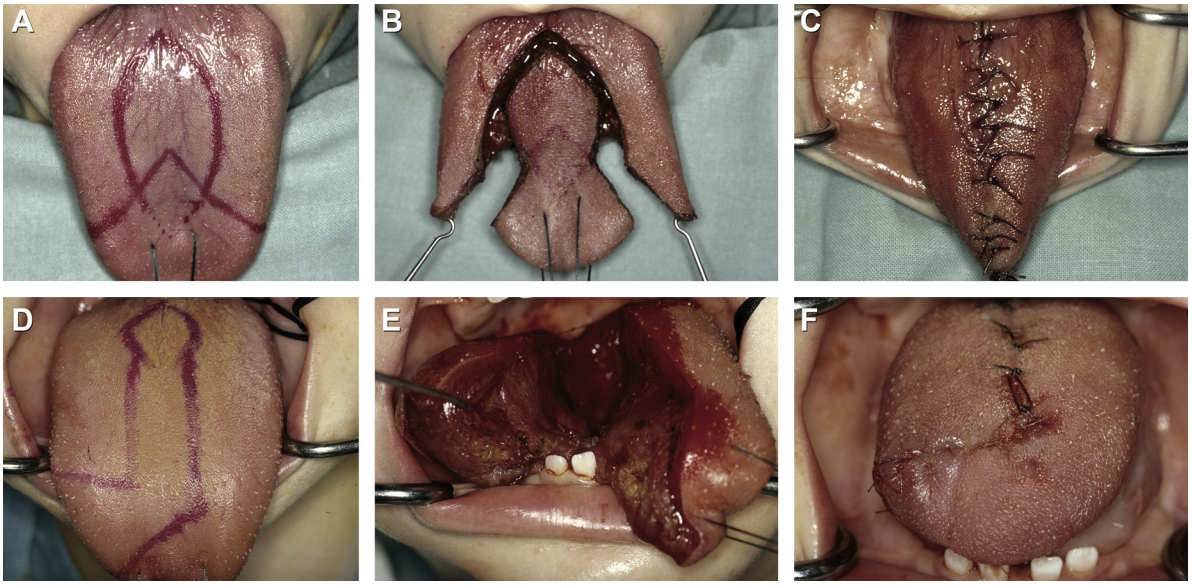

Fig. 2. Technique of partial glossectomy. (A–C) The method by Egyedi and Obwegeser; (D–F) the method introduced by Schwenzer.

Fig. 3. Oral stimulation devices: A plate with a small wheel for the upper jaw (A), a plate with small balls for the upper jaw (B) and a historical method with spikes on the incisors of the mandible (C).

Table 1. Chronological sequence of surgical and supportive therapy of Beckwith–Wiedemann syndrome patients.

Preoperative treatment	Orofacial regulation therapy (Castillo–Morales)
	Oral stimulation plate
	Speech therapy
Surgical tongue reduction	Operation technique by Egyedi and Obwegeser
	Operation technique by Schwenzer
Postoperative treatment	Orofacial regulation therapy (Castillo-Morales)
	Speech therapy
	Orthodontics
	Combined orthodontic/jaw surgery treatment

patient data, surgical parameters, direct postoperative results and complications were collected by chart review. In addition, photographic documentation of every patient taken from preoperative, postoperative and follow-up visits were reviewed and included in the data pool. To evaluate long-term results, first a patient survey was conducted using a multiple-choice questionnaire including 47 items. The questionnaire was structured into general medical history (four items) and BWS history, including postoperative course (13 items). For evaluation of function and patient satisfaction, the survey was structured into appearance (two items), breathing (one item), swallowing (one item), taste (two items), sensitivity (one item), mobility (five items), dentoalveolar misalignment and dysgnathia (seven items), physical therapy and speech therapy (five items), pronunciation and speech development (four items), snoring/sleep apnea (one item) and an item for further notes. The patients who consented to additional follow-up examination were investigated regarding appearance and mobility of the tongue, sensitivity, speech, dentoalveolar malposition and the need for orthodontic treatment. A taste test was performed using solvents of 10% glucose, 7.5 and 15% NaCl, 5 and 10% citric acid and 1 and 5% quinine at various test sites on the tongue.

Results

Study population and treatment modality

A total of 68 patients with BWS and macroglossia that were treated from 1987 to 2016 were included. The patients were treated according to the above-mentioned therapeutic concept, and severity of macroglossia was determined. In 24 patients, the macroglossia was mildly distinct with only slight impact on function and musculoskeletal structure. These patients received conservative therapy. In 44 patients, the macroglossia was moderately or strongly pronounced, and indication for tongue reduction procedure was proposed. The youngest child was 3.5 months old at the time of surgery, and

the oldest was 8 years old. The average age was 2.5 years. Twenty-two patients were treated according to the technique of Egyedi and Obwegeser, and 22 patients were treated according to the technique of Schwenzer. The average resected volume was $10.2 \pm 3.4\ cm^3$ (range from 6 to $22\ cm^3$). Mean duration of surgical procedure was 76 ± 20 min (Table 2).

In 15 patients, at least one postoperative complication was documented. Eight types of complications occurred, including wound dehiscence, bleeding, haematoma and necrosis of the tip of the tongue. In five cases, the complication had to be treated by surgical revision. Three patients suffered from respiratory disorder and required intubation and mechanical ventilation for more than 3 days. Six patients were extubated during the second or third postoperative day. All other children were extubated either immediately after surgery or within 24 h. The oral diet usually started on the seventh day after surgery, depending on the swelling of the tongue. Longest duration of nasogastric feeding was 11 days in one case. The oral load consisted of a liquid-soft diet until complete wound healing was achieved. In three children, a second stage resection was necessary due to insufficient results of the initial surgery. In two cases, the second resection was performed 3 years later, and in one case, it was performed 5.5 years later. Unfortunately, one child suffered from myocardial failure based on a virus-myocarditis and passed away on the third postoperative day (Table 3).

Long-term outcome

Long-term data from 36 patients were collected by questionnaire (26 treated surgically and 10 treated conservatively), and 20 of them took part in a follow-up examination (13 surgical, seven conservative). The mean duration between surgery and follow-up visits was 15 years (range 2.2–29 years). Mean age of the patients was then 18 years. The oldest patient was 36 years old, and the youngest was 4.5 years old. Out of the 26 patients subjected to surgical tongue reduction, 85% described a disproportional shape of the tongue, and 19% showed unsightly scars. In most cases (88%), the tongue was thicker than normal, and only 12% had an overly short tip of the tongue. There were no cases in which sense of taste or sensitivity was impaired. Good results were achieved with respect to mobility of the tongue. A deviation during protrusion of the tongue was observed in 38% of the cases (Table 4). 30% of the patients treated conservatively and 50% of the patients treated by tongue reduction reported an impairment of phonation. However, a delay in development of speech was reported by 40% and 50%, respectively. In the group of surgical tongue reduction, 81% were satisfied with the shape of the tongue and 92% were satisfied with pronunciation. Patients with milder forms of macroglossia and without indications for tongue reduction were satisfied with pronunciation and appearance of the tongue in 90% of cases. Dentoalveolar and musculoskeletal malformations occurred in both groups to almost the same extent: malpositioned teeth in 62% (surgical) and 80% (conservative), anterior open bite in 58% (operative) and 70% (non-operative). Mandibular prognathism was observed exclusively in patients who had undergone

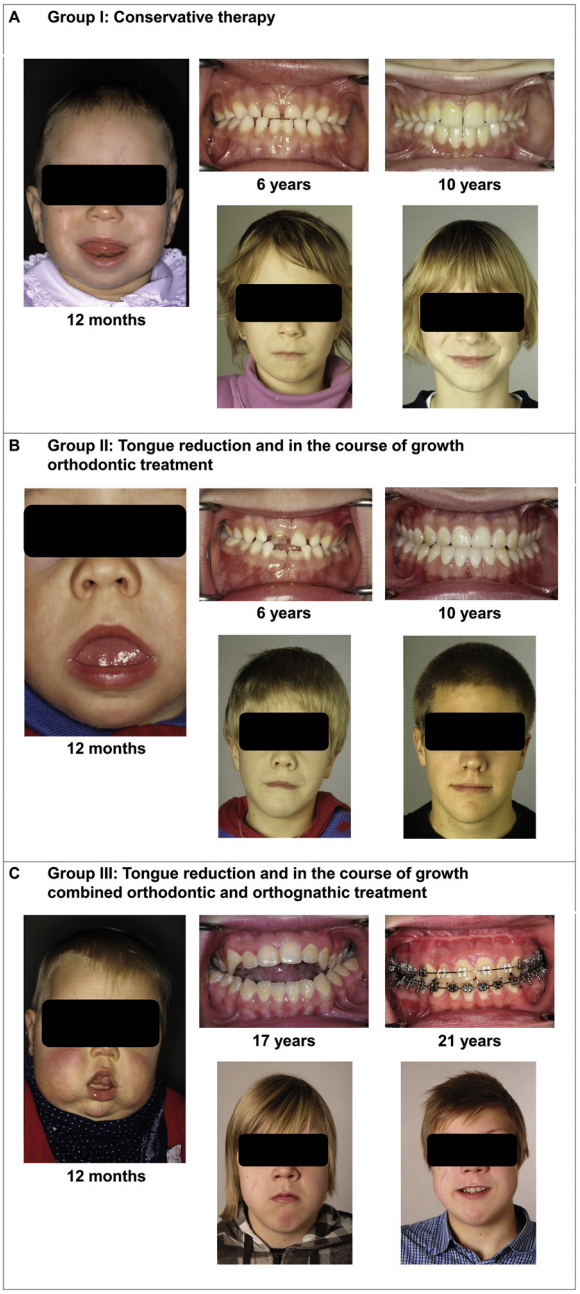

Fig. 4. Allocation of the patients to three groups according to the manifestation of macroglossia and need for adjuvant therapy in the course of growth. Group I: conservative therapy with supportive therapy including orofacial regulation therapy, oral stimulation plate and/or speech therapy (A). Group II: surgical tongue reduction, supportive therapy and orthodontic treatment in the course of growth (B). Group III: surgical tongue reduction, supportive therapy and combined orthodontic/orthognathic surgical treatment in the course of growth (C).

surgical treatment due to advanced macroglossia. Evaluation of supportive therapy in both the surgical and non-surgical groups showed that every patient of the surgical treatment group, as well as the conservative treatment group, underwent at least one supportive therapy modality. In the tongue-reduction group, 42% received orthodontic treatment in the course of time, and 8% required combined orthodontic–orthognathic interventions. Patients treated conservatively required orthodontics up to 50%, but none needed orthognathic surgery (Tables 5 and 6).

Discussion

Several authors describe tongue reduction in cases of macroglossia in BWS patients as an effective treatment[4,15,21]. The indications for surgical tongue reduction in severe cases are indisputable and particularly relevant by reason of the vital indication. Tongue resection performed in the young growing child leads to positive influence on musculoskeletal, dentoalveolar and functional development. There are many case reports or small cohorts with BWS patients; however, up until now only little is known regarding the long-term results of a large patient group[22–24]. The patients included in the present study presented with a wide range of macroglossia, extending from mild to strongly pronounced and from symmetric or asymmetric growth. Although every single patient was referred to our hospital with the intention of surgical therapy, we only treated 44 of 68 by partial glossectomy. The patient cohort could be divided into three groups depending on the manifestation of the macroglossia (Fig. 4). This grouping was an important treatment planning, as allocation leads to reliable treatment algorithms and predictable treatment planning, such as performing orthodontic treatment or combined orthodontic–surgical corrections after tongue reduction. Conservative therapy, including the orofacial regulation therapy as well as oral stimulation plates and speech therapy, showed adequate and satisfactory outcome for mild expression of macroglossia. In surgical cases, we adhered to the described therapeutic concept, which was performed in every case in an interdisciplinary manner. Depending on the asymmetry of the tongue, one of the techniques described above was preferred. The present results indicated that the chosen techniques were effective treatments for macroglossia. The techniques have negligible consequences regarding late complications for speech and taste. In the long term, we did not observe any limitations of speech intelligibility. Despite scar formation, patients and parents showed a high degree of satisfaction with the treatment. Several authors investigated the impact of surgical tongue reduction on these issues[11,15,18]. Although the investigations are difficult to compare because of various surgical techniques and investigation methods, the conclusions were similar. In our opinion, the most important issue is maintenance and quality of taste and sensitivity after tongue reduction. In our study, none of the patients complained of reduced taste or hypoesthesia, independently of the administered surgical technique. This result is accordance with the findings of other investigations demonstrating that the anterior wedge technique was a simple, effective and safe technique[11]. In addition, investigations of taste after partial glossectomy showed that taste perception was not disturbed in children[15]. These results might be surprising, as it is traditionally taught that there is a mapping of taste-modalities at different areas on the tongue and that surgical procedures done for tongue reduction would adversely affect perception of certain taste-modalities[25]. Recent research hints that the previously accepted tongue maps are incorrect and that the four tastes are perceived on all loci with taste receptors. Breslin et al. believe that receptor expression zones heavily overlap in most regions of the mouth[26,27]. In addition, van der Horst et al. developed a test for the evaluation of taste perception after tongue reduction and reported that there are no specific tasting areas[28]. This leads us to conclude that surgical technique should be chosen on the basis of the morphology of macroglossia and not under the aspect of future taste perception. According to skeletal changes, previous studies have shown that one major effect of macroglossia is a protrusion of dentoalveolar structures resulting in proclined frontal teeth, protruding mandible, anterior open bite, abnormally obtuse jaw angle and increased mandibular length[29]. Our data showed a strong association between the various manifestations of macroglossia and the expression of dentoalveolar and basal mandibular alterations. Patients treated conservatively because they were assigned to Group I (mild expression of macroglossia) had no need for orthognathic surgery, as the dentoalveolar changes did not affect the mandibular basis and could only be treated orthodontically. In Groups II and III, defined as moderate and extensive expression of macroglossia, mandibular prognathism occurred in 19% of cases and a total of 8% underwent surgical intervention for combined orthodontic–orthognathic therapy. It is difficult to determine whether the prognathism of the mandibular basis arises from macroglossia and dentoalveolar changes, or is genetically driven. Kawafuji et al. examined BWS patients not treated by glossectomy and point out that they suffered from a wide dental arch, a long facial height, as well as an enlarged anterior cranial base and mandibular body[30]. Zou et al. investigated patients with severe skeletal Class III dysgnathism and concluded that there is a moderate-to-high correlation between the dental and basal bone arch forms[31]. Macroglossia is certainly a growth stimulus for mandibular growth. However, whether this is the only

Table 2. Characteristics of study population.

	Number of patients $n = 68$	Percentage
Gender (male:female)	36:32	53%:47%
Mean age at investigation (years)	18.7 ± 7.2 (4.5–36.9)	
Surgery indication	44	65%
• Egyedi and Obwegeser	22	32%
• Schwenzer	22	32%
No surgery indication	24	35%
Mean age at surgery	2.5 ± 2.1 (0.3–8.1) years	
Mean resected volume	10.23 ± 3.37 (6–22) cm^3	
Mean duration of surgery	76 ± 20 min	
Mean period in between surgery and follow up investigation	15 ± 7.1 (2.2–29) years	

Table 3. Postoperative complications due to tongue reduction.

	Number of patients $n = 44$	Percentage
No complication	29	66%
Surgical complications	8	18%
Dehiscence	4	9%
Bleeding	2	5%
Hematoma	1	2%
Necrosis tip of tongue	1	2%
Re-operation due to complications	5	11%
General complications	10	23%
Respiratory disorder (intubation >3 days)	3	7%
Withdrawal symptoms	2	5%
Pneumonia	1	2%
Sinus tachycardia	1	2%
Epileptic seizure	1	2%
Hindered food intake	1	2%
Death by myocardial failure	1	2%

Table 4. Functional outcome after tongue reduction procedure.

Shape	Disproportional shape	85%
	Unsightly scars	19%
	Tongue thicker than normal	88%
	Overly short tip of the tongue	12%
Sensors	Impaired sense of taste	0%
	Paresthesia	0%
Mobility	Inability to moisten lips	4%
	Inability to reach posterior palate	0%
	Inability to reach vestibular surfaces	8%
	Repeated biting on tongue	12%
	Lateral deviation during protrusion	38%

Table 5. Supportive therapy modalities in the surgical and conservative group.

	Operative treatment $n = 26$	Conservative treatment $n = 10$
Supportive therapy	100%	100%
Oral stimulation plate	77%	90%
Orofacial regulation therapy	85%	100%
Speech therapy	96%	90%
Orthodontic	42%	50%
Orthognathic surgery	8%	0%

trigger for prognathism or whether genetic effects play an additional role, remains unclear. An early intervention by tongue reduction, early functional treatment of the stomatognathic system, or both are recommended in order to reduce the risk of developing both mandibular prognathism and anterior open bite[32]. In the mild form, conservative functional treatment can prevent dental and skeletal malformations and lead to regular craniofacial physiognomics. Although most patients showed an anterior open bite due to macroglossia, the functional treatment in combination with tongue reduction leads to improved outcome in adolescence and adulthood. Our study showed that 50% of non-operated and 42% of operated patients needed orthodontic treatment.

Our study emphasizes for the first time in a large study group the importance of functional and surgical therapy in BWS, depending on the manifestation of the macroglossia as well as the positive outcomes and satisfaction of the patients. Surgical intervention showed only a small number of complications, and the estimated risk of airway management in BWS patients might be overestimated. Nevertheless, the surgical procedure should be performed in an interdisciplinary centre with experienced specialists. Postoperative oedema and swelling may lead to severe airway obstruction, requiring prolonged postoperative intubation and mechanical ventilation[13]. In many cases, extubation was possible immediately after or within the first 24h after surgery. The optimal age for surgical intervention is not clear to date. It is recommended to perform tongue reduction after the age of 1 year to reduce the risk of perioperative complication, if there is no vital indication by the enlarged tongue. Perhaps the cephalad position of the larynx in the young child plays an essential role in the development of airway complications. Parameters such as the resected volume of the

Table 6. Long-term results of Beckwith–Wiedemann syndrome patient treatment.

		Operative treatment $n = 26$	Conservative treatment $n = 10$
Patient satisfaction	Satisfied with shape of the tongue	81%	90%
	Satisfied with pronunciation	92%	90%
Speech	Impairment in phonation	50%	30%
	Delayed development of speech	50%	40%
Dentoalveolar/musculoskeletal malformations	Tooth misalignment	62%	80%
	Anterior open bite	58%	70%
	Prognathism	19%	0%
	Difficulties with lip closure	19%	30%

tongue or surgery time had no influence on the risk of developing a respiratory insufficiency. Whether there is a specific risk to the affected tissues of developing excessive oedema in BWS patients cannot be determined from our investigation.

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No funding was secured for this study.

Competing interests

The authors have no conflicts of interest to disclose.

Ethical approval

Ethical approval was obtained from the ethics committee of the medical faculty of the Christian-Albrechts-University of Kiel. Reference number: D447/11.

Patient consent

Written patient consent was been obtained to publish clinical photographs.

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Address:
Hendrik Naujokat
Department of Oral and Maxillofacial Surgery
University Hospital Schleswig-Holstein
Campus Kiel
Arnold-Heller-Straße 3
24105 Kiel
Germany
Tel.: +49 431 50026140
Fax: +49 431 50026006
E-mail: naujokat@mkg.uni-kiel.de