Reconstruction of the alveolar process in cleft patients

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Abstract
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Background. The treatment of patients born with cleft lip and palate has been gradually modified over the years as the surgical procedures have developed and improved. Multidisciplinary team care has evolved and provided improved care with enhanced results. Clefts in the alveolus can be reconstructed by alveolar bone grafting or by periosteoplasty. The main goal is to repair and close the alveolar cleft and create a continuous alveolar processes so that the teeth can erupt.

   Aims. This thesis has several aims: to investigate the impact of dental status and initial cleft width on the outcome of Secondary alveolar bone grafting (SABG) in patients born with unilateral cleft lip and palate (UCLP) at the 10-year follow-up (Studies I and II); to compare the outcomes of primary periosteoplasty (PPP) with those of SABG in patients born with unilateral cleft lip and alveolus (CLA) (Study III); to evaluate clinical and radiographic conditions and identify factors important for the final treatment outcomes after SABG (Study IV); to evaluate two radiographic methods, i.e. occlusal radiographs and cone beam tomography (CBCT)) for assessing alveolar bone height (study IV).

   Results. In UCLP patients, SABG achieved excellent results in terms of bone height; tended to reduce with time, correlated with dental status and dental restoration factors. Occlusal radiographs correspond well with the CBCT, for evaluating alveolar bone height in cleft area. The width of the initial cleft does not seem to affect the success of SABG. Finally, patients with CLA treated with PPP at the time of lip repair have inferior bone formation outcomes in the cleft area compared with patients treated with SABG at the time of mixed dentition.

   Conclusion. Poor dental status and malpositioning negatively affect the long-term survival of bone in the alveolar cleft. The initial cleft width affects certain dental status factors. In adults with UCLP, the alveolar bone height in the cleft was correlated to the presence of gingival inflammation and restorations at 20 years follow-up. Specially designed maintenance therapy is beneficial, after complex dental restorations in the cleft area. SABG is preferred to PPP for the reconstruction of alveolar clefts.

Keywords: alveolar bone grafting, dental status, initial cleft size, dental restoration, unilateral cleft lip and palate, cleft lip and alveolus, primary periosteoplasty, facial growth

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List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I   Jabbari F, Skoog V, Reiser E, Hakelius M, Nowinski D. Optimization of dental status improves long-term outcome after alveolar bone grafting in unilateral cleft lip and palate. *The Cleft Palate-Craniofacial Journal* 2015; 52:210-218.

II Jabbari F, Reiser E, Thor A, Hakelius M, Nowinski D. Correlations between initial cleft size and dental anomalies in unilateral cleft lip and palate patients after alveolar bone grafting. *Upsala Journal of Medical Sciences* 2016; 121(1):33-37.

III Jabbari F, Thor A, Skoog V, Reiser E, Hakelius M, Nowinski D. Skoog primary periosteoplasty versus secondary alveolar bone grafting in unilateral cleft lip and alveolus: long-term effects on alveolar bone formation and maxillary growth. Submitted

IV Jabbari F, Thor A, Reiser E, Hakelius M, Nowinski D. Secondary alveolar bone grafting in patients born with unilateral cleft lip and palate: a 20-year follow-up. Submitted.

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Contents

Abbreviations

BI	Bergland index
BOP	Bleeding on probing
CBCT	Cone beam computed tomography
CEJ	Cemento–enamel junction
CLP	Cleft lip and palate
CL	Cleft lip
CP	Cleft palate
2D	Two-dimensional
3D	Three-dimensional
mBI	Modified Bergland index
GPP	Gingivoperiosteoplasty
PPP	Primary periosteoplasty
ICC	Intra-class correlation coefficient
mm	Millimetres
OP	Operation
OR	Odds ratio
SABG	Secondary alveolar bone grafting
SD	Standard deviation

Additional abbreviations are defined in the associated text or figures.

Introduction

Cleft lip and palate (CLP), a major congenital structural anomaly with a complex aetiology, is caused by abnormal facial development during gestation. Clefting is associated with a wide array of complex symptoms and difficulties, that vary from patient to patient and between different time-points in life. Cleft of the palate impairs breast-feeding during infancy as well as the subsequent development of intelligible speech. Clefts involving the maxilla and hard palate may lead to midfacial growth disturbances that in turn produce nasal airway obstruction and malocclusion. Furthermore, clefts that involve the maxilla are frequently associated with various dental problems, such as malpositioning, hypoplasia, and aplasia. Cleft-lip and cleft-palate deformities may be associated with a significant appearance handicap. This complex of symptoms and the required treatment can be highly challenging to the patient and may lead to psychosocial difficulties.

Management of the CLP patient from birth to completion of treatment requires an expert multidisciplinary team consisting primarily of plastic surgery, orthodontics, speech pathology, otorhinolaryngology, maxillofacial surgery, and psychology. Psychological support should be included as part of the overall treatment planning. The worldwide prevalence of CLP is often cited as 1 in 700 live births,[1] with considerable regional variability. Various efforts have been made to understand the aetiology of CLP. In recent years, advances in genetics and molecular biology have started to reveal the mechanisms of craniofacial development, and several genes associated with CLP have been identified.

Embryology

Knowledge of the complexities of normal embryological development is fundamental to understanding congenital pathology. The pattern of gene expression regulates cellular behaviour during early embryonic development. Gene products may be grossly divided into structural, regulatory, or enzymatic proteins. Development of the lip and palate involves a complex series of events that require close coordination of the programs for cell migration, proliferation, differentiation, and apoptosis. From the fourth to eight weeks, the embryonic period, most of the facial structures are formed, but it takes another three weeks until the palate is completed. In the fourth week of

embryonic growth, migrating neural crest cells from the anterior neural tube combine with mesodermal cells to establish five different facial prominences, i.e., the paired maxillary, paired mandibular, and single frontonasal prominences, which surround the primitive oral cavity.[2, 3] Formation of the nasal placodes by the end of the fourth week from the ectoderm around the primitive oral cavity divides the lower part of frontonasal prominences into paired medial and lateral nasal prominences. The medial nasal prominences and the area above the primitive mouth continue to grow and merge with each other to form a vertical groove in the middle of the upper lip, the philtrum. During the eighth week of development, the maxillary processes on both sides of the mouth grow forward and fuse with the lower edges of the lateral nasal prominences. They merge with the upper lip's groove, building a continuous ridge above the mouth to form the upper lip.

The upper lip groove is filled gradually by proliferating and migrating mesodermal tissue from the first brachial arch. If this process is delayed or absent, a cleft lip (CL) will develop. If the maxillary prominence on the affected side fails to merge with the merged nasal prominence, a unilateral cleft involving the alveolus will result.

The palate begins to form during the fifth week of gestation and development continues until week twelve, with the most critical time between weeks six and nine of gestation.[4] The first sign of development is seen when the maxillary prominences merge with the medial nasal prominences, forming a wedge-shaped mass of mesenchymal tissue. As this tissue grows, it separates from the upper lip and becomes the primary palate. The primary palate is thus located behind the gum line and extends to the incisive foramen.[5]

Development of the secondary palate begins during the sixth week of embryogenesis when two folds of mesenchymal tissue known as lateral palatal shelves grow from the lateral walls of the primitive mouth. Initially, they lie vertically on each side of the developing tongue. Development of the jaws results in a relatively smaller tongue, which moves inferiorly, allowing the palatal shelves to grow toward each other and elevate to a horizontal position. The palatal shelves fuse with the nasal septum and the primary palate. By 12 weeks, palatal fusion is complete and the palate is formed.[2] Although CL and CP often occur together, they have different embryological origins. CL results from failed merging of the maxillary and medial nasal elevation. Cleft palate (CP) results from failure of the lateral palatine processes to meet and fuse with each other.

Organ development is characterized by interaction between epithelial and mesenchymal tissues. Teeth are typical examples of epithelial and mesenchymal organs.[6] Teeth develop from pharyngeal epithelium and underlying neural crest-derived mesenchymal cells in a similar way to skin derivatives such as hairs. The first sign of individual tooth development occurs as a thickening of the oral epithelium, the dental lamina, at the sites of the future

dental arches of the maxilla and the mandible. The mineralized components of teeth, i.e., dentin and enamel, are formed by the odontoblasts and ameloblasts, differentiated from the mesenchyme and epithelium, respectively.

Aetiology

The complex embryology of the lip and palate renders this anatomical region vulnerable to various factors with a capacity to disturb development. Most orofacial clefts are not associated with a syndrome and their aetiology is multifactorial, with several factors acting in concert. Several causative factors have been linked to the aetiology of CLP and CP, including genetic factors, teratogen exposure, other environmental factors, and maternal age. Recent literature has also revealed wide ethnic and racial variations in the occurrence of cleft lip and/or palate.

Most research has focused on the contribution of genes. An inherited component of clefts was first recognized by Fogh-Andersen in 1942.[7] Although genetic linkage and association analyses of CLP have been limited by insufficient numbers of families, several studies have used candidate genes or loci. Studies based on 1–40 families have suggested loci for clefts on chromosomes 1, 2, 4, 6, 14, 17, and 19.[8, 9] However, linkages have been excluded at these same loci in other studies, which may reflect the limited number of families and/or locus heterogeneity. One locus, on 6P, has consistently shown linkage to CLP and was first reported in studies from Denmark[10] and Italy.[11] Additionally, several growth and signalling factors, such as the transforming growth factor alpha (TGFA),[12] interferon regulatory factor 6 (IRF6),[13] bone morphogenetic protein 4 (BMP4),[14] MSH homeobox 1(MSX1), fibroblast growth factor receptor 1(FGFR1), and methylenetetrahydrofolate reductase (MTHFR),[15] have been linked to CLP or CP. Ardingar et al. (1989) were the first to report that transforming growth factor alpha contributed to CLP.[15]

Several environmental factors have been demonstrated to be associated with the aetiology of CLP. Wyszynski et al. (1996) associated nutritional deficiencies with CP.[16] Other identified factors are maternal smoking, alcohol intake, some drugs, and maternal folic acid deficiencies. Studies considering a possible role of folic acid in preventing clefting have, however, produced conflicting results.[17-21]

Epidemiology

CLP is the most common congenital facial malformation and the fourth most common congenital malformation in humans.[22] It can either be an isolated event or one of several manifestations in a malformation syndrome. The

proportion of individuals with additional malformations varies greatly between studies, though the frequency of associated malformations is found to be greatest for isolated cleft palate and least for CL.[23, 24] In a European study of 4000 cases of isolated CP, 55% were isolated, 18% were associated with other anomalies, and 27% were part of recognized syndromes.[25] For CL with or without CP in more than 5000 patients, 71% were isolated cases and 29% were associated with other anomalies.[26] The worldwide incidence of CLP has been estimated to range from 0.3 to 3.6 cases per 1000 live births[27] depending on geographic origin,[28] racial and ethnic background,[29] and socioeconomic status.[30] The highest incidence, 3.6/1000, has been found among American Indians and the lowest, 0.3/1000, in African Americans.[28] In Sweden, the incidence of CLP is 1.7–2.0 per 1000 live births; for CL alone the incidence is 0.4, for CLA it is 0.2, and for CLP and CP it is 0.7 per 1000 live births.[27] The sex distribution for all clefts combined is somewhat higher among males than females. However, CP is more common in females: in female foetuses the palatal shelves take a week longer to fuse than in male foetuses, leaving more time for exposure to factors that can cause failure of fusion.[2, 31] In both genders, clefts of the lip and primary palate are more common on the left side.[32]

Classification and anatomy

Cleft types are classified according to their size and location and are determined during facial embryogenesis.[33] Aetiologically and clinically, clefts vary greatly, so it is important to classify them in order to understand their pathology and facilitate clinical description and communication. A cleft may be incomplete (meaning that some tissues bridge the cleft) or complete, unilateral, bilateral, or median. Several classification systems are used to describe clefts. In 1931, Veau suggested a simple classification based on the degree of deformity, using a numerical scale from 1 to 4: 1) cleft of soft palate only, 2) cleft of soft and hard palate, 3) complete unilateral CLP (UCLP), 4) complete bilateral CLP.[34] Fogh-Andersen (1942) described a morphological classification of different types of CLP based on embryology and genetics: 1) CL including cleft lip and alveolus (CLA) (primary palate); 2) CLP including unilateral and bilateral CLP; and 3) isolated CP with cleft up to the foramen incisivum.[7] In 1958, Kernahan and Stark reduced the classification to two groups on an embryological basis, describing clefts of the palate relative to the incisive foramen. They classified clefts anterior to the incisive foramen as clefts of the primary palate corresponding to CL and CLP and posterior to the incisive foramen as clefts of the secondary palate.[35] Kernahan (1971) modified this classification into "the striped Y" symbolic classification, which allows a separate description of the lip, alveolus, and palate.[36] Based on this concept, a further modification called the RPL system

was made by Schwartz et al. in 1993 entailing a three-digit numerical system: 1) the right side, 2) palate in the centre, and 3) the left side.[37] The striped Y concept is used for the classification and registration of patients at Uppsala University Hospital.

The extent and shape of clefts in the palate vary. Submucous clefts are typically characterized by a bifid uvula and split posterior nasal spine. Clefts may engage the soft palate only or extend into the hard palate to varying degrees. Palatal clefts may be grouped into: group 1 (soft palate), group 2 (one-third of hard palate), group 3 (more than one-third of hard palate), and group 4 (total). Cleft types can be distributed depending on the anatomical locations as follows: CL 34%, CLP 39%, and CP 27%. Left-sided clefts are more common (52%) than are right-sided (24%) and bilateral clefts.[32]

Complete UCLP involves the lip, nose, and alveolus, and continues into the palatal part of the maxilla. Incomplete forms occur when there is a soft tissue connection in the lip and an osseous bridge in the alveolar process. In complete bilateral CLP, the maxillary complex is divided into three separate segments. The nasal septum is seen with a bulbous lower border between the two lateral jaw segments. Protrusion of the premaxilla is the most characteristic feature of these patients. The musculature in the premaxilla is poorly developed and the columella is short. Examples of different clefts types are presented below.
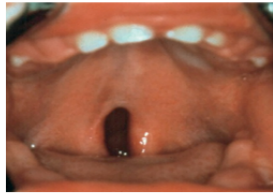
A; right sided cleft lip, **B**; double sided partial cleft lip **C**; right sided partial cleft lip, **D**; left sided unilateral cleft lip and palate (UCLP), **E**: right sided UCLP, **F** and **G**; Bilateral cleft lip and palate, **H,I, J**; Different type of cleft palate.

Management of clefts

Treatment of patients with CLP requires a prolonged multidisciplinary approach for optimal functional and aesthetic outcomes. The Uppsala University Hospital is one of six regional centres in Sweden for the treatment of patients with CLP. The catchment area includes the Örebro region and contains approximately 2.0 million inhabitants with an incidence of approximately 40 new cleft cases each year. The multidisciplinary team was founded in the early 1960s and has evolved over time. Today it consists of orthodontists, plastic surgeons, otorhinolaryngologist, maxillofacial surgeons, speech pathologists, psychologist, and a team-coordinating nurse. Patient data have been recorded over the years according to strict protocols.

Facial growth

Over the years, the dynamics of facial growth in patients born with CLP have been studied and compared with those of non-cleft individuals.[38] In cleft patients, the disturbances in mid-facial growth could be due to a combination of factors, such as intrinsic growth deficiency, and to the effects of various treatment methods, mostly related to surgical repair.[39] The most important deviations in facial development in these patients are deficient anterior growth of the maxilla as well as posterior growth rotation of the mandible relative to the anterior cranial base. As a consequence of the above deviations, the decreased vertical height of maxilla and increased mandibular plane angle result in a more obtuse gonial angle and increased lower facial height.[40-42] Surgical repair of the lip and palate causes growth disturbances, especially maxillary retrusion, as documented by various studies of unoperated adult cleft patients.[39, 43, 44] The data from inter-centre studies indicate different craniofacial morphologies associated with the surgical protocols applied.[45]

The maxilla grows both by apposition of bone at the surface and by sutural growth. The maxilla thereby assumes a forward-downward growth direction in relation to the cranial base.[46] Sagittal growth is mediated by the apposition of bone to the maxillary tuberosity, transverse palatine suture, and vomero-premaxillary suture.[47] Vertical growth occurs by apposition of bone to the alveolar process in combination with tooth eruption and the downward displacement by growth at the sutures and the nasal septum.[48] In CP surgery, the palatal repair and the extent of scar tissue contribute to the reduced length of the maxilla and to the forward displacement of the basal maxilla and, as a consequence, to a poor anteroposterior jaw relationship.[49] Maxillary growth was also found to be more unfavourable in children treated with early bone grafting or preoperative orthopaedics in combination with gingivoperiosteoplasty (GPP).[50, 51]

Surgeon skill, cleft width, and type of surgical technique all have an impact on the results and can inhibit the growth and development of the facial structures involved.[52, 53]

Facial growth is usually assessed radiographically by means of cephalometry. Lateral radiographs are obtained using standard settings. The head is positioned in a cephalostat ensuring that the sagittal plane is perpendicular to the x-ray beam. Standard anatomical landmarks are used to measure distances and angles on the radiographic films, and tracing is performed using

commercially available software. Cephalometric analysis allows for assessment of the dimensions and relations that reflect the growth status of the facial skeleton.

Dental anomalies

Dental anomalies occur more frequently in cleft patients.[33] The abnormal development of the alveolar process at the cleft area often leads to distorted dentition adjacent to the cleft.[54] The prevalence of dental anomalies also seems to be related to the severity of the deformity.[55] Anomalies can be numerical[56] and/or morphological.[33] Even eruptive problems, such as dental rotation and dental retention, are more frequent in cleft patients.[33] The congenital absence of the cleft-side permanent lateral incisor is the most common finding with frequencies of 43.6–58.6%.[57] A supernumerary tooth as in cleft side permanent lateral incisor is the second most common anomaly with frequencies of 14.9–20%.[58] Morphological anomalies (e.g., abnormally sized and shaped teeth), especially found in the lateral incisor, are found with frequencies of 35.0–49.5%.[59] The adjacent central incisor could also be malformed, rotated mesio-palatally and tilted towards the cleft. Enamel defects or malformations, called enamel hypoplasias, are classified according to the developmental defects and may be caused by disturbances in enamel formation during dental formation. This is a quantitative alteration secondary to a deficiency in enamel formation resulting from the absence of the enamel surface.[60] Enamel opacities, on the other hand, represent qualitative alterations of the enamel with yellow or brown coloration, though with an intact enamel surface. These are caused by developmental disturbances during amelogenesis or by mechanical trauma during enamel maturation.[61] Such opacities occur with high prevalence in both deciduous and permanent dentition in complete CL patients and are most frequent in upper anterior teeth in the permanent dentition.[62] These may have aesthetic implications and constitute an additional risk factor for plaque accumulation and dental caries.

Canine impaction occurs more frequently in patients with cleft alveolus than in non-cleft patients.[63, 64] The timing of alveolar bone grafting and canine inclination influence the risk of retention.[65, 66]

Intra-oral radiographs of central, lateral, and canine teeth on the cleft side are commonly used to determine the tooth status index, i.e., to determine the prevalence and degree of dental anomalies.[67] The tooth status index is used to rate tooth quality, based on the evaluation of tooth status in the cleft area, where 0) represents normal teeth, I) teeth requiring minor restorations, II) teeth requiring major restorations and peg-shaped laterals, III) teeth malformed to the extent of extraction, and IV) missing teeth. As secondary alveolar bone grafting (SABG) is performed to provide bone for the lateral or

canine teeth, evaluation of the presence of teeth and of their status, location, and development in the cleft area is important in planning the timing of SABG.

Oral health

Achieving optimal dental health in children born with clefts may be difficult due to the anatomy of the cleft area, misaligned and hypoplastic teeth, residual scar tissue, and immobility of the lip as consequences of surgical repair.[68]

A literature review reveals conflicting reports on oral and dental health in children born with clefts. Epidemiological data on the oral health of CLP children generally suffer from methodological problems such as inadequate sample size and difficulties finding appropriate control groups. Several studies have found that children with clefts have a higher risk of developing caries and gingival inflammation in the deciduous dentition, most markedly in the maxillary anterior teeth, than do children of the same age without congenital malformation.[69-72] At the same time, an early study of permanent dentition in CLP children found that the caries prevalence did not differ significantly from that of non-cleft children.[73] However, this finding was later contradicted by another study from Japan.[74] A systematic review of literature on the prevalence of caries in cleft lip and/or palate children, conducted by a Swedish group, revealed that caries in these children did not differ from those of non-cleft children.[75] A similar finding was reported by Lucas et al. in 2000.[76]

Stec-Slonicz et al. (2007), on the other hand, found that the caries index and plaque index were much higher among cleft patients than in the general population.[77]

Sundell et al. (2015) studied the prevalence of dental caries and enamel hypoplasia in 5- and 10-year-old Swedish children born with cleft lip and/or palate and compared it with those of matched non-cleft controls. They found that the prevalence of caries and enamel hypoplasia was higher in the primary dentition in children with cleft lip and/or palate[78].

Brägger et al. (1985) examined 80 children with clefts and found that the percentage of tooth surfaces covered by plaque was high in all cleft groups.[79] Parapanision et al. (2009) examined 41 Greek children with clefts and found that the oral hygiene of these children was inferior to that of the control group.[80]

Brägger et al. (1992) evaluated the progression of periodontal disease at sites adjacent to clefts in young adults born with various types of CLP. The results of this study indicated poorer oral hygiene and the manifestation of initial signs of periodontal disease to a slightly higher extent than in non-cleft individuals of a similar age.[81] However, due to the absence of a well-

matched control group, this study cannot demonstrate that CLP patients really have a higher risk of developing periodontal disease than do non-cleft subjects.

At the same time, Teja et al. (1992) found that teeth adjacent to clefts showed signs of gingivitis but not periodontitis. They claimed that anatomical defects, tooth eruption patterns, orthodontic treatment, and the presence of restorations all seemed to contribute to the reduced bone level due to a higher prevalence of gingivitis.[82] However, another study comparing data from the cleft and non-cleft sites of CLP patients suggested that the anatomical variation due to the presence of clefts is not a determining factor in the development of periodontal disease. Periodontal problems instead occur because of prosthodontic restorations in cleft areas.[83, 84] A recent study of the progression of periodontal disease in cleft patients over 25 years of follow-up demonstrated that individuals with clefts rehabilitated with fixed or removable dental prostheses are at high risk of periodontal disease progression.[85]

The review of available literature does not conclusively find that cleft patients have a higher risk of developing periodontal disease than do the non-cleft population, although they may have more gingivitis.

Surgical treatment of UCLP

Over the last half century, a range of fundamental principles for the treatment of clefts has gradually evolved and been commonly adopted by most treatment centres. However, the surgical techniques and timing of the procedures still differ between centres. The treatment protocol specifies the techniques, sequence, and timing of the surgical procedures. A CL is usually repaired as early as possible, at 3–5 months of age, to reduce the social stigma for the child and parents. The reconstructed lip also serves to mould the maxillary segments into a more favourable position. Closure of the CP can be done in one or two stages and in different sequences. Generally, the cleft in the palate should be closed as early as possible to facilitate speech. However, early complete palatal reconstruction may inhibit maxillary growth. The two-stage principle of palatal closure has evolved as a strategy to optimize the conditions for speech development with as little growth disturbance as possible. Either the soft palate is closed first followed by closure of the residual cleft in the hard palate, or the hard palate is closed at the time of lipplasty, followed by closure of the soft palate in a second sequence. The optimal age for palatal closure is still a matter of discussion and investigation.[86]

In Uppsala University Hospital, lip closure in UCLP is performed at three months of age using the technique described by Tord Skoog.[87] Until 1977, the CP was closed in one stage using the Veau-Wardill-Killner technique at the age of 18–24 months.[87] Thereafter, the surgical treatment protocol was changed to a two-stage protocol. The interval between the two operations was gradually decreased between 1977 and 1985, when the currently practiced timing was introduced with soft palate closure at the age of six months and closure of the residual cleft in the hard palate at 24 months. There are two fundamentally different strategies for bony reconstruction of the alveolar cleft, periosteoplasty and bone grafting.

Skoog was the first to describe primary periosteoplasty (PPP) performed at the time of lipplasty. In PPP, periosteal flaps were raised and used to form a periosteal tunnel across the cleft in the alveolus. The idea was that, with time, bone would form within the periosteal tunnel, obviating the need for later bone grafting. This technique was discontinued in Uppsala in 1976, due to clinical observations that not enough bone was formed to support permanent dentition. Furthermore, concerns were raised that the early periosteoplasty procedure could disturb maxillary growth. The concept of primary

periosteal reconstruction has, however, been advanced by other groups and techniques similar to that described by Skoog have been popularized in some centres in more recent years.

Secondary alveolar bone grafting (SABG) was first described in the 1970s.[88] The principle is to time the grafting of cancellous bone so that the permanent dentition in the cleft is supported. Bone is usually harvested from the iliac crest, and raising palatal mucoperiosteal flaps and gingivoperiosteal flaps in the oral vestibulum exposes the cleft in the alveolus. This procedure serves to reconstruct the alveolus, support permanent dentition, close any remaining anterior palatal fistulae, and support the alar base and lip on the cleft side. Re-establishing maxillary integrity is also beneficial if future orthognathic surgery is required.

Reconstruction of the alveolus

The main function of the alveolar process is to host the dentition. It is therefore essential that clefts in the alveolus be closed. Two surgical methods are used: bonegrafting and periosteoplasty. The main goal of bone grafting or periosteoplasty in CL/CLP patients is to repair and close the alveolar cleft and create a continuous alveolar process so that teeth can erupt and be moved by means of orthodontics. The reconstruction also serves to unify the maxillary segments and prevent their collapse. Bone grafting to alveolar clefts was first introduced in the late 1950s. The main difference between the treatment protocols of different treatment centres has been in the timing of the bone grafting.[89] The primary bone grafting introduced by Nordin and Johansson in 1955 served to reconstruct the cleft as early as infancy or early childhood.[90] Due to frequent reports of midfacial growth disturbances and less successful bone formation this method was gradually replaced by primary periosteoplaty.[91] In the 1960s, Tord Skoog introduced infant periosteoplasty at the same time as primary lipplasty.[92] In the strategy of "boneless bone grafting", local periosteal flaps covering the defect in the alveolar process at the time of lip repair obtained continuity between the maxillary segments. However, in many centres, this technique was discontinued due to accumulating experience and data on insufficient bone formation to support the teeth adjacent to the cleft.[93, 94] Furthermore, concerns were raised that the periosteal elevation required for the periosteoplasty procedure may harm skeletal growth when performed in infancy or early childhood. The answer to these shortcomings of both primary bone grafting and periosteoplasty came from the concept of grafting cancellous bone to the cleft alveolus at the time of mixed dentition, before the eruption of the permanent canine, in so-called secondary bone grafting.[95] Bone grafting performed during permanent dentition after completion of orthodontic treatment is called tertiary or late grafting.[96] Tertiary grafts are performed to allow prosthodontic and periodontal rehabilitation and to close persistent bucconasal fistulae. Tertiary or late bone grafting cannot replace bone loss affecting teeth adjacent to the cleft.[97]

Secondary bone grafting of the alveolar cleft, first described by Boyne and Sands in 1972, is now a common procedure.[98] It is performed at the stage of transitional dentition in conjunction with orthodontic treatment.[99] The optimal age is 8–11 years[99] when the root of the canine is between half and three-quarters formed.[100] The procedure allows proper eruption of the

canine through the cleft segment, provides bony support for teeth adjacent to the cleft, supports the arch width, and stabilizes the maxillary arch. It also serves to eliminate any remaining oronasal fistula and may improve facial symmetry by providing some alar base support and nasolabial contour

In 1990, Millard and Latham introduced a variant of periosteoplasty in combination with active presurgical orthopaedic treatment.[101, 102] So-called gingivoperiosteoplasty (GPP) is performed on alveolar segments that are in direct apposition as a result of the presurgical orthopaedics. Millard and Latham stressed that their method differs technically from that practiced by Skoog, in that minimally designed and invasive local flaps are used to cover the size-reduced alveolar defect. However, long-term follow-up studies performed by Berkowitz et al. revealed a retardation of growth in adolescence.[51]

Matic et al. evaluated the success of Millard-Latham type GPP versus SABG in patients with unilateral and bilateral clefts using a radiographic grading scale. They found that bone quality was inferior in patients treated with GPP and that most patients required additional bone grafting.[103]

In the further evolution of presurgical orthopaedic techniques, Grayson et al. presented nasoalveolar moulding in combination with GPP in 1999.[104] Their modifications of the technology for presurgical orthopaedics attempt to address the nasal deformity in addition to passively moulding the alveolar segments. As in Millard's concept, they advocate early union of the maxillary dental arch in conjunction with lip repair and primary GPP to reduce the need for future SABG.[105] The results of various studies of nasoalveolar moulding are inconsistent regarding changes in nasal symmetry.[106] Studies comparing outcomes of primary GPP and SABG have contradictory results. Wang et al. (2015) recently compared GPP with SABG and found that the clinical success was higher with SABG than with primary GPP.[107]

Radiographic assessment of the outcomes of secondary alveolar bone grafting (SABG)

Various clinical methods have been applied to evaluate the outcomes of SABG. Eruption of the teeth adjacent to the cleft site,[108] periodontal parameters for tooth support,[109] and facial aesthetic results have been analysed.[110] Radiographic diagnostic imaging is essential for treatment planning and for assessing outcomes for individual patients. It is used to evaluate the size of the alveolar cleft, level of bone around adjacent teeth, and presence of supernumerary teeth.

After bone grafting, radiographic imaging evaluates the outcome of the procedure, changes in the structural pattern of the bone graft with time, and eruption status of the lateral incisor or canine adjacent to the cleft.[99]

Various radiographic scales have been developed to evaluate the integration of the graft and to determine the success of SABG as a means to provide bony support for teeth adjacent to the cleft.[67, 99, 111, 112] Two-dimensional (2D) radiographs including panoramic, occlusal, and periapical films are generally used.

Occlusal radiography is the most frequently applied method to assess alveolar bone height in the cleft before and after grafting.

Bone height is usually graded according to the Bergland index (BI): Type I is normal alveolar bone height, Type II is more than three quarters of normal bone height, Type III is less than three quarters of normal bone height, and Type IV is failure with no continuous bridge achieved in the cleft area.[113]

There are drawbacks to 2D imaging, including difficulties assessing the bone graft in the bucco–palatine dimension, morphology, and bony structure. Moreover, the projection of occlusal radiographs may be difficult to standardize for maximal reproducibility. Consequently, several authors have started to use three-dimensional (3D) imaging in the form of computed tomography (CT) scanning to evaluate bone stock after alveolar bone grafting.

Radiation doses have been reduced with more recent cone beam CT technology. CT scanning may be used to accurately analyse the volume of the retained bone after bone grafting and the spatial position of adjacent or erupting teeth and to assess the extent of bony consolidation with surrounding bone. There are clear limits to the routine use of CBCT related to radiation exposure, cost, and accessibility for the treatment of patients with clefts.

CBCT is of value as an adjunct in difficult clinical cases in which additional information to supplement conventional radiographic imaging is desirable for further treatment planning. However, it is unclear if CBCT is superior to occlusal radiographs in the routine assessment of SABG outcomes.

Background to the present studies

The treatment of patients with CLP has been gradually modified over the years as surgical procedures have developed and improved. Multidisciplinary team care has evolved and provided improved care with enhanced results. SABG in conjunction with orthodontic treatment, first described in the 1970s, has become integral to the overall management of patients with CLP in most centres. Successful bone grafting creates the necessary conditions for orthodontic treatment, allowing orthodontic tooth movement into the previous cleft area.[114] Other secondary goals of this procedure are to close any remaining fistulae and to augment the hypoplastic paranasal maxilla.[88] The donor site used in most centres is the iliac crest[89] followed by the tibial tuberosity.[115] Regardless of the donor site, the SABG method relies on grafting cancellous bone into the exposed cleft space.[116]

Cancellous bone is preferred over cortical bone due to the rapid revascularization and abundance of osteogenic cells covering the surface of the trabeculae – conditions that promote osteoconduction through the process of creeping substitution as well as osteoinduction. With time, the graft has the capacity for complete integration with the surrounding bone of the maxillary alveolus.[111]

Several factors are believed to influence the outcomes of SABG and there has been considerable interest in evaluating the impact of these factors. Several studies have demonstrated that dental development at the time of grafting is important.[99] The best results are achieved when the bone grafting is performed at the end of mixed dentition, prior to canine eruption. The experience and skill of the surgeon is another factor influencing the results. It has been demonstrated that surgeons with greater experience of SABG have higher success rates than do less experienced surgeons.[117]

The abnormal development of the alveolar process in the cleft area may cause hypodontia, supernumerary teeth, peg-shaped teeth, crown and root malformation, and delay in tooth formation and eruption.[33, 57, 118, 119] It is generally accepted that these dental anomalies should be addressed in connection with the SABG procedure. However, the impact of dental anomalies as well as other dental irregularities, such as dental retention, rotation/inclination, enamel status, and oral hygiene, on the outcome of SABG is unknown.

Cleft width at birth is highly variable in the CLP deformity.[120] The general clinical opinion is that the availability of tissue and the position of the

maxillary segments, expressed as the cleft width, are essential variables influencing the treatment outcome. The impact of the initial cleft width on various treatment outcomes has been studied to some extent. Wide clefts, reflecting a more severe initial deformity, are generally associated with increased difficulty of primary surgical repair and the formation of postoperative palatal fistulae.[121] Greater initial cleft width is also correlated with increased transverse dental arch dimensions and less crossbite occlusion in the primary dentition.[122] Peltomäki et al. found an association between initial cleft width and inhibited maxillary growth in children with UCLP.[52] However, it has also been demonstrated that maxillary development is mainly dependent on the actual treatment performed rather than on the severity of the initial clefts.[123]

The impact of initial cleft size on dental status adjacent to the cleft and on SABG outcomes has not been investigated.

Evaluation of outcomes after SABG in adult patients born with UCLP and of factors that might influence the final treatment outcomes is important for optimizing the overall long-term stability of the bone graft. Prosthetic restorations are normally inserted at the end of facial growth and are expected to function throughout life. The sites adjacent to cleft areas are usually restored by means of various dental restorations due to lateral incisor absence or malformed enamel. Following completion of comprehensive oral rehabilitation, including the incorporation of fixed dental restorations, patients are usually not enrolled in regular maintenance care. The impacts of certain oral health factors, such as gingival inflammations and dental restorations in the cleft area, and final treatment outcomes have not previously been investigated.

Comparative results between Skoog type PPP and SABG in patients with unilateral CLA have not been reported to date.

Aims of the thesis

The overall aim of the thesis was to study the long-term outcome after secondary alveolar bone grafting and subsequently to compare it with the outcomes of other methods used to reconstruct the alveolar cleft in UCLP and CLA patients treated by the Cleft Lip and Palate Team, at the Craniofacial Center, Uppsala University Hospital, Uppsala, Sweden.

The specific aims of the research were as follows:

I   To study the long-term outcome of SABG and investigate the impact of dental anomalies in the cleft area on the outcome of SABG

II   To study the impact of initial cleft size on the outcome of SABG and on dental status in the cleft area in UCLP

III To study the impact of PPP on bone formation and facial growth in patients born with CLA

IV   To study the impact of oral health and dental restoration procedures on the final outcome of SABG in adults born with UCLP

Materials and methods

Studies I, II, and IV

Ninety-four consecutive cleft patients born with UCLP who underwent SABG between 1987 and 1997 were recruited from the database of the Cleft Lip and Palate Team, Craniofacial Center, Uppsala University Hospital. The material refers to a regional population of approximately 1.5 million people for whom the Cleft Lip and Palate Team in Uppsala was responsible for all types of cleft surgery. The inclusion criteria were complete UCLP, Caucasian ethnicity, non-syndromic diagnosis, treated according to the Uppsala protocol (Table 1), and operated on by the same surgeon (Valdemar Skoog) (Figure 1).

A total of 67 patients met these criteria for study I. The medical records from the Department of Plastic and maxillofacial surgery and the availability of dental study casts, panoramic radiographs, and anterior occlusal radiographs were thoroughly checked. Eleven patients had used a quad-helix expansion device for the upper arch prior to SABG, 10 patients had used a fixed appliance to align the rotated and inclined central incisor adjacent to the cleft, and two patients had received both expansion of the upper jaw and a fixed appliance. The remaining 44 patients did not receive any presurgical orthodontics. The mean age at the time of SABG was 10.0 years (range 8.5–12.0 years).

Depending on the investigation aims in studies II and IV, the number of subjects varied. One patient was excluded from study II due to the lack of a dental cast at the primary lipplasty.

For study IV, the same cohort of patients was asked to participate in a follow-up study via a letter of invitation containing information about the study. This was followed up by a telephone call within two weeks providing further information and setting the appointment. Five patients were deceased. Eight patients did not respond to the request. Four patients declined participation and 10 patients who did accept did not show up for their planned appointments. The remaining 40 examined patients had a mean age of 34 years (range 28–40 years). Fifteen were women and 25 were men.
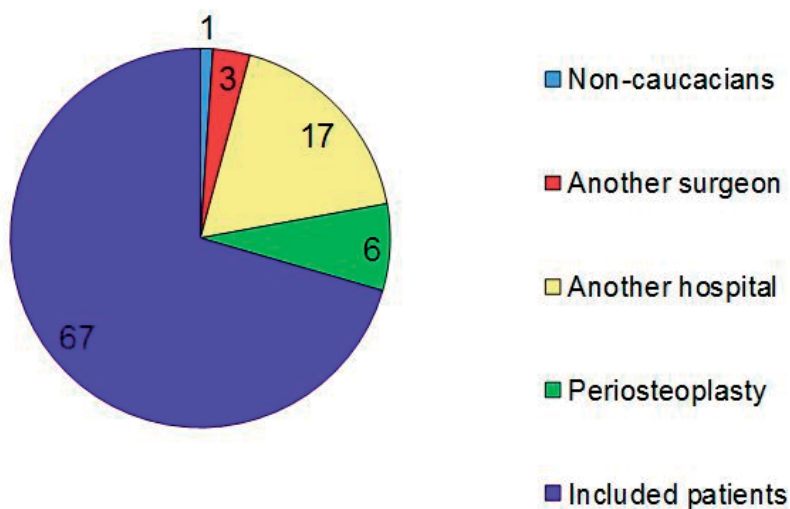
Figure 1. Distribution of patients with unilateral complete CLP.

Table 1. Surgical protocol of UCL/P in Uppsala

| Age	Surgery
3 months	Primary lipplasty according to Skoog
6 months	Soft palatoplasty
2 years	Two layer hard palate closure
8-10 years	Secondary alveolar bone grafting

Study III

Sixty-five consecutive patients born with unilateral CLA, all receiving Skoog-type primary lipplasty between 1960 and 1998, were recruited from the database of the Cleft Lip and Palate Team, Uppsala University Hospital, Uppsala, Sweden. The inclusion criteria were unilateral CLA, Caucasian ethnicity, non-syndromic diagnosis, and age above 18 years.

Eight patients were excluded: four patients had delayed periosteoplasty and in four patients SABG was not performed due to small cleft size. The remaining 57 patients were included in the study and grouped according to the surgical procedure used to reconstruct the alveolar cleft. Twenty-eight patients were treated using PPP at the time of lipplasty and 29 were treated using primary lipplasty and later SABG (Figure 2, Table 2). SABG was performed at a mean age of 10 years (range 8–10 years) from 1988 to 1998. All children received orthodontic treatment with removable appliances during early mixed dentition before bone grafting. Fixed appliances were used later to correct crossbite and negative overjet.

Table 2. Summary of patient baseline characteristics, mean (min–max).

Groups	PPP/ PPP+SABG	SABG
Partial	10	19
Complete	18	7
Simonart's band	–	3
Female	16	13
Male	12	16
Age at primary lipplasty	3.5 months (3-4)	4 months(2.5-5.5)
Age at Bone grafting	13 years (10-17)	9 years (8-10)
Weight at primary lipplasty	4 kg (3.5-4.5)	5 kg (4.5-5.5)
Weight at births	3 kg (3.4-2.6)	3.2 kg (3.7-2.7)
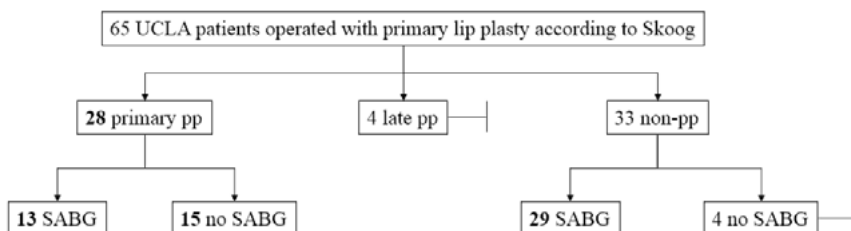
Figure 2. **Flow diagram of inclusion and exclusion. UCLA:** unilateral cleft lip alveolus; **PPP:** primary periosteoplasty; **SABG:** secondary alveolar bone grafting

Surgical procedures

The surgical protocol for studies I, II, and IV included lipplasty closure according to Skoog at three to four months, two-stage palatal closure with soft palate at six months, and closure of residual cleft in hard palate at 24 months.

Secondary bone grafting was performed at mixed dentition, with respect to the eruption of the permanent lateral and canines.

In both groups, the surgical protocol for study III included lipplasty according to Skoog at three to four months.[87] In the PPP group, periosteoplasty was performed at the time of lipplasty.[124] In the SABG group, SABG was performed as described earlier.[125]

Secondary alveolar bone grafting

The alveolar cleft was exposed by raising vestibular and palatal mucoperiosteal flaps. Deciduous teeth projecting into the cleft space were extracted. After sharp separation of the oral and nasal layers and excision of scar tissue and mucosal hyperplasias, the nasal floor was meticulously closed with multifilament resorbable sutures. Cancellous bone was harvested from the ilium by raising a cortical lid on the inner aspect of the iliac ala. The bone was grafted to fill the entire cleft space back to the incisive foramen. The flaps were advanced for tension-free closure and sutured with 4/0 multifilament sutures. Sutures were removed 14–21 days after surgery in the outpatient clinic (Figure 3).
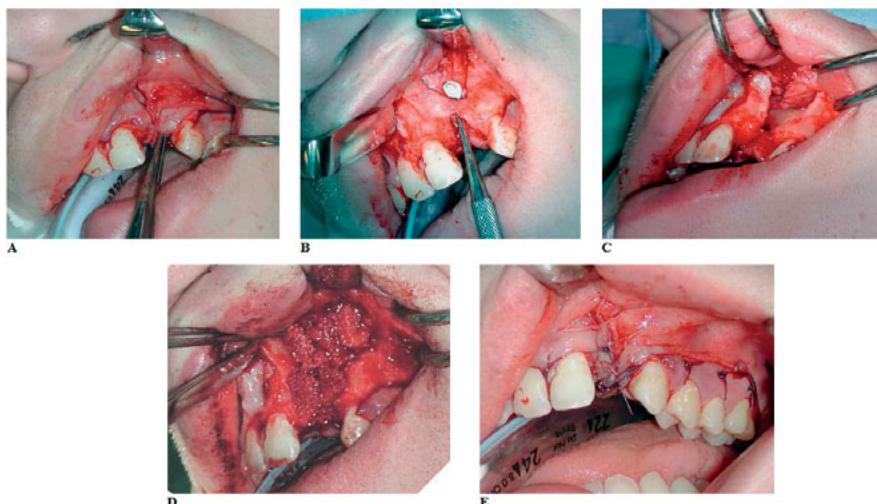
Figure 3. **Secondary alveolar bone grafting in patient treated with primary periosteoplasty. A:** Flaps raised to expose the alveolar cleft; **B**: periosteum induced bony bridge in the exposed cleft; **C:** periosteum is further elevated, bony bridge removed and nasal floor sutured; **D:** the cleft is filled with cancellous bone graft; **E:** flaps sutured in place to cover the bone graft.

Primary periosteoplasty

Infant primary periosteoplasty was performed at the time of primary lipplasty at three to four months of age. A mucoperiosteal tunnel was created across the alveolar cleft. For the inner lining of the cleft space, i.e., the nasal floor layer, the mucoperiosteum was raised and mobilized from the alveolar cleft edges. Closure was performed in two rows with catgut and resorbable sutures. The outer lining of the periosteal tunnel was constructed from a medially based periosteal flap, harvested from the anterior surface of the maxilla up to the infraorbital foramen. This flap was rotated more than 90 degrees and sutured to the premaxilla with 5/0 catgut (Figure 4).
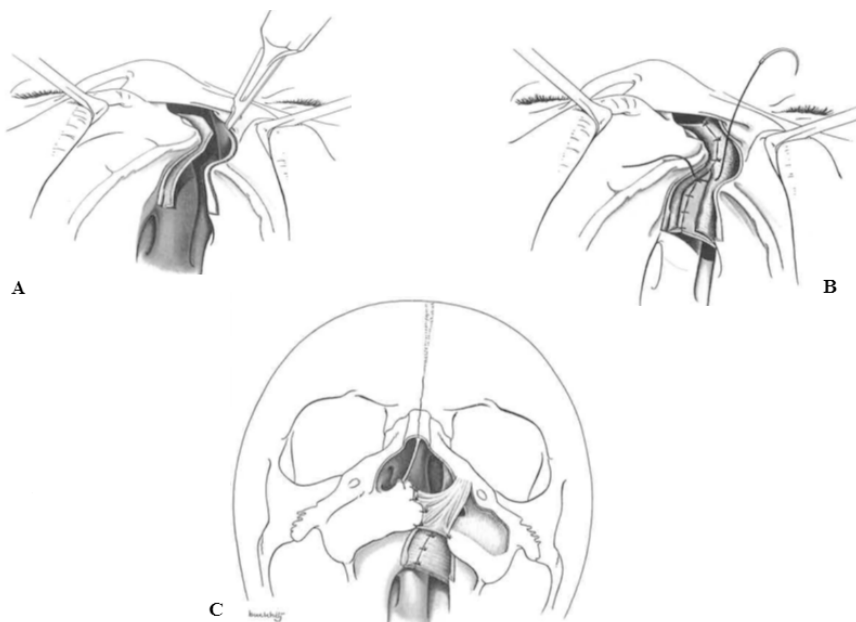
Figure 4. **Primary periosteoplasty**. Schematic drawings from Tord Skoog´s text-book Plastic Surgery (rights belong to the estate). **A**: The lateral border of the cleft is incised; **B**: periosteal sutures placed for reconstruction of nasal floor; **C**: The parana-sally based periosteal flap sutured to the premaxilla

Methods

Studies I and II

Alveolar bone height according to the Bergland index

Anterior occlusal radiographs were available for analysis of the alveolar bone height prior to SABG, one year postoperatively and at the ten-year follow-up. The bone formation in the grafted area was assessed according to the modified Bergland index (mBI), which measures the height of the inter-dental septum adjacent to the erupted canine as described by Bergland and in addition the basal level of bone graft.[99, 126]

Tooth Status

Intraoral radiographs obtained prior to surgery were used to determine the tooth status of the central incisor in the cleft area according to the tooth sta-tus index (Figure 5).[67] Furthermore, the presence or absence of the perma-nent lateral incisor was evaluated and scored as follows: Grade 0, hypodon-tia; Grade 1, extraction at the time of SABG; Grade 2, late extraction (>2 years post SABG); and Grade 3, persistent lateral incisor.
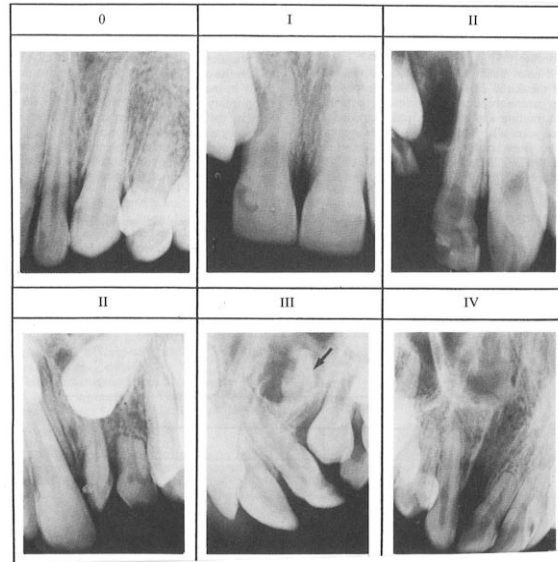
Figure 5. Tooth status index according to Brattström: 0, normal teeth; I, teeth requiring minor restorations; II, teeth requiring major restorations and peg-shaped laterals; III, teeth malformed to the extent of extraction; and IV, missing teeth.

Canine inclination

Inclination of the canine in the cleft area was evaluated from panoramic radiographs obtained at eight years of age and scored according to a scale previously described by Tortora et al.[127] In the present investigation, the inclination was scored as follows: Grade 0, canine inclination 0–15 degrees perpendicular to the occlusal plane; Grade 1, canine inclination 15–45 degrees; and Grade 2, canine inclination >45 degrees.

Central incisor inclination

Inclination of the central incisor on the cleft side in relation to a line perpendicular to the occlusal plane was measured on panoramic radiographs at eight years of age (Figure 6). The patients were scored as follows: Grade 0, incisor inclination 0–30 degrees; Grade 1, incisor inclination 30–50 degrees; and Grade 2, incisor inclination >50 degrees.
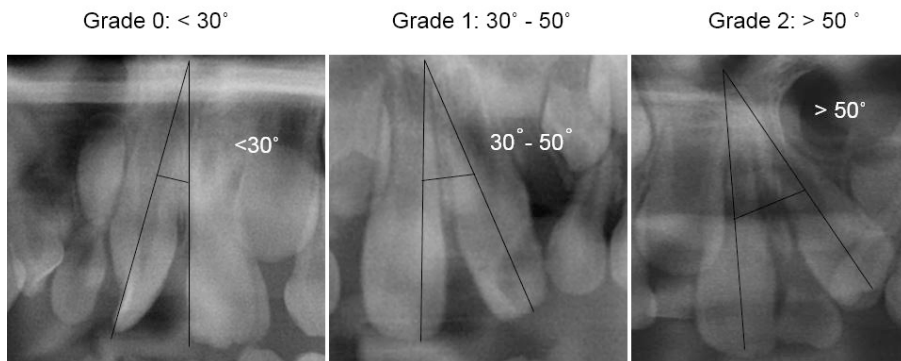
Figure 6. Incisor inclination assessed from panoramic radiographs.

Central incisor rotation

Rotation of the central incisor adjacent to the cleft was measured on dental casts at eight years of age (Figure 7). A paper was superimposed on the dental casts. A first transverse line was drawn between the first molars. A second line was drawn from a point between the central incisors, intersecting the first line at a 90 degree angle. A third line was drawn at a tangent to the central incisor edge, meeting the second line at the measured rotation angle. Three different scores were assigned: Grade 0, incisor rotation 0–30 degrees; Grade 1, incisor rotation 30–50 degrees; and Grade 2, incisor rotation >50 degrees.
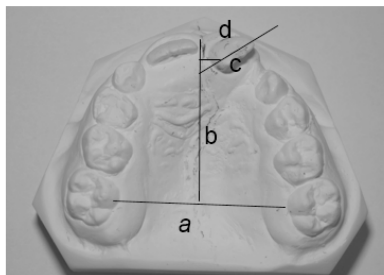
Figure 7. Incisor rotation was assessed on dental casts by constructing following lines: a) transverse line; b) mid-line, c) tangent to incisor, and d) rotation angle. "Grade 1: 30–50°".

Oral Hygiene

All patients were categorized into two groups, good and poor, with respect to their oral hygiene prior to SABG. The categorization was performed by studying comments in patient charts, clinical observation, and intraoral photographs (Figure 8). Patients with minor or no signs of gingival inflammation were categorized as having good oral hygiene.

Figure 8. Intraoral view of a left-sided UCLP, from patient charts.

Study II

Cleft width

Cleft size was measured on dental study casts obtained in connection with the primary lipplasty at three to four months of age. The reference points and linear measurements used in this study have been described in previous studies and in a previous thesis from our group.[122, 128, 129]

After initial inter-rater calibration of the landmarks between the two authors F.J. and E.R., F.J. performed all measurements and scorings. Distances were measured to the nearest 0.01 mm using a digital caliper (Figure 9). Alveolar bone height according to the BI,[99] canine inclination,[127] and central incisor inclination and rotation were as reported in our previous study.[130]

Tooth status

Intra-oral radiographs obtained prior to SABG were assessed for the tooth status of the central incisor in the cleft area according to a previously described tooth status index.[67]

Lateral incisor status

Lateral incisor status was dichotomized into presence (group 1) or absence (group 2) of the lateral incisor (hypodontia).
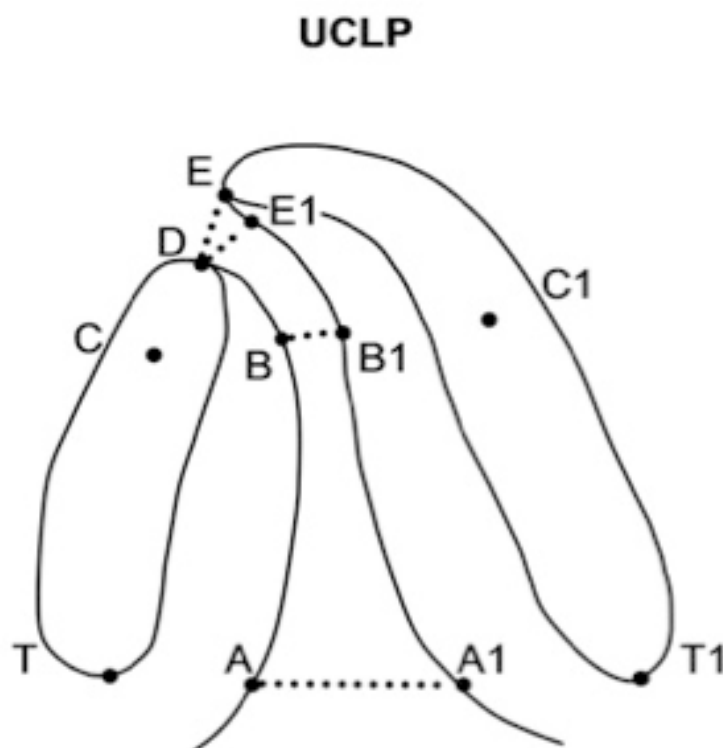
Figure 9. Schematic of a maxillary dental cast of an infant with UCLP showing landmarks and distances used in the linear measurements: D–E = cleft width at the level of the alveolar processes, anteriorly; D–E1 = smallest cleft width at the level of the alveolar processes, anteriorly; T–T1 = posterior width of the alveolar arch in the tuberosity area; A–A1 = width of the cleft at the T–T1 level; B–B1 = width of the cleft at the C–C1 level; B–B1/C–C1 = ratio of the cleft width related to the total alveolar arch width anteriorly at the canine point level; and A–A1/T–T1 = ratio of the cleft width related to the total alveolar arch width posteriorly at the tuberosity point level.

Study III

**Alveolar bone height according to the Bergland index**

Anterior occlusal radiographs were available for all patients at 10 and 16 years of age and were analysed for alveolar bone height and graded according to the BI as described above.[99]

Cephalometric

Lateral cephalometric radiographs obtained at 5, 10, and 18 years of age as part of the routine follow-up protocol were analysed to study longitudinal facial growth. The anteroposterior and vertical skeletal jaw relationships were analysed using the cephalometric tracing program FACD 3.0 (Ilexis

AB, Linköping, Sweden). The reference points and lines used for cephalo-metric analysis are shown in Figure 10.
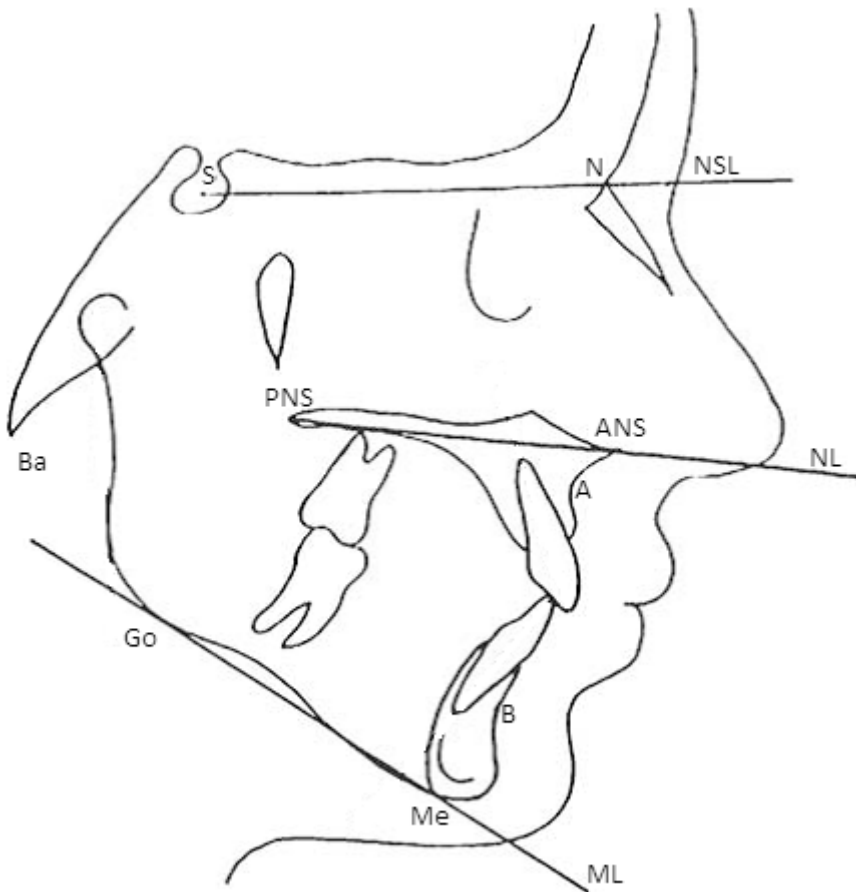
Figure 10. Cephalometric reference points and lines used in the study. *Reference points:* A = deepest point on the anterior contour of the upper alveolar process; ANS = anterior nasal spine; PNS = intersection between the nasal floor and the posterior contour of the maxilla; B = deepest point on the anterior contour of the lower alveo-lar process; Me = most inferior point on the mandibular symphysis; Go = mid-plane point at the gonial angle of the mandible; N = most anterior point on the nasofrontal suture; and S = centre of the sella turcica. *Reference lines:* ML = mandibular line, the tangent to the lower boundary of the mandible through Go and Me; NL = nasal line, the line through ANS and PNS; and NSL = nasion-sella line, the line through N and S.

Study IV

Clinical examination

The clinical examination entailed registration of: a) presence and condition of lateral incisor in the cleft area; b) occurrence of dental implants, crowns, and other dental restorations; c) gingival bleeding on probing (BOP) on four sites per tooth according to the gingival bleeding index (GBI);[131] and d) the pocket probing depth (PPD) in millimetres on four sites per tooth.[132]

The gingival condition was expressed as the percent of bleeding gingival units on probing. The gingival pocket depth was determined by measuring the distance from the gingival margin to the base of the pocket with a calibrated periodontal probe on four sites per tooth. The mean probing depth from the mesial, buccal, and lingual sites was subsequently calculated for each tooth.

Radiographic examination

All studied patients were examined with cone beam computed tomography (CBCT) (Accuitomo, Morita) according to the standard examination protocol for the maxilla. Anterior occlusal radiographs in three projections, i.e., through the cleft site, the midline, and non-cleft site, were acquired in a single session. Occlusal radiographs were analysed according to the BI.[99] The images from CBCT examinations in the axial, coronal, and sagittal views were used to analyse and measure alveolar bone height according to the same principles as described for the BI on occlusal radiographs. First, the marginal bone level was identified in the axial view. Next, we measured the distance between the cemento–enamel junction (CEJ) and the marginal alveolar bone height in the coronal view (bone loss). The distance between the CEJ and the apex was measured in the sagittal view (root length). The ratio between bone loss and root length was graded in a manner similar to the Bergland index (Figure 11). The bone level was also measured as the linear distance from the CEJ to the alveolar crest in the images of the sagittal views adjacent to the first molars of the upper jaw.
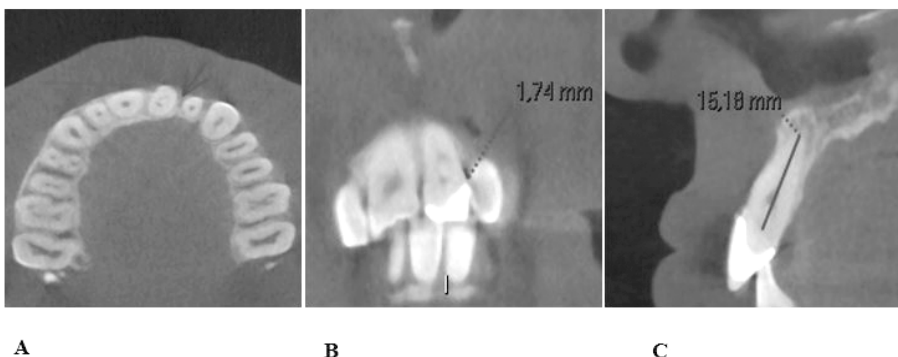
Figure 11. Cone beam computed tomography of the alveolar cleft: A) axial view for identification of the marginal bone level (indicated with arrow); B) coronal view showing the measured distance between the cemento–enamel junction (CEJ) and the marginal alveolar bone height (bone loss); and C) sagittal view showing the measured distance between the CEJ and the apex (root length).

Reproducibility of recording

Studies I and II

The reliability and intra-operator reproducibility of the measurements/scorings were determined from randomized duplicate recordings of 20 UCLP patients. Weighted kappa coefficients were calculated; they ranged from 0.59 to 0.90, indicating moderate to excellent agreement of repeated measurements.

For the dental cast measurements, intra-class correlation coefficients (ICCs) were calculated for intra-rater reliability, agreement of repeated measurements. The intra-rater reliability was considered excellent at 0.96–0.97.

Study III

The reliability and intra-rater reproducibility of the measurements/scorings were determined from randomized duplicate recordings of 20 CLA patients made six months apart. Bland-Altman plots were created and ICCs were calculated to determine intra-rater reliability. The values were 0.93–1.00 except for the intermaxillary relationship (ANB) at five years, which was 0.86. Taken together, the values were considered excellent. Weighted kappa coefficients were calculated; the kappa coefficient for the BI score was very good at 0.89.

Study IV

All bone height measurements performed on occlusal radiographs agreed with the scores obtained using CBCT. The kappa coefficient for agreement between the two methods was therefore 1.

Statistical analyses

Study I

Descriptive statistics (i.e., mean, standard deviation, median, and range) were calculated for all parameters. The relations between preoperative scoring of enamel hypoplasia, oral hygiene, inclination of the canine, and inclination and rotation of the central incisor adjacent to the cleft and BI scores 10 years postoperatively were analysed using Spearman rank correlation. The relation between cleft-side lateral incisor status and the BI score 10 years postoperatively was analysed using a chi-square test. A p-value <0.05 denoted statistical significance. All statistical analyses were performed using SAS v 9.4 (SAS Institute, Cary, NC, USA).

Study II

Descriptive statistics (i.e., mean, standard deviation, median, and range) were calculated for all parameters. The relations between cleft widths at different levels as well as ratios were analysed using Spearman rank correlation. Multivariate analysis was not suitable due to the non-parametric nature of the data.

Study III

Continuous growth variables were presented as means (standard errors) and categorical bone height variables were presented as counts and percentages. The Mann-Whitney U-test was used to assess growth differences between treatment groups at ages 5, 10, and 18 years, and to assess changes between 10 and 5 years, 18 and 5 years, and 18 and 10 years. The Wilcoxon matched-paired signed-rank test was used to evaluate the significance of changes between ages within groups. Fisher's exact test was employed to determine the association between treatment groups and the BI score, and to assess difference in proportion of partial and complete clefts between the groups. We used a proportional logistic regression model for comparison of Bergland scores between groups adjusted for complete/partial clefts.

Study IV

Data are presented as frequencies and percentages. The changes in BI scores on anterior occlusal radiographs from 10 to 20 years of age in the total material and by groups, with and without dental restoration, were tested using Wilcoxon's matched-pairs signed rank test. The BI score according to CBCT at age 20 was compared with the BI score at age 10 using the Kruskal-Wallis test. BI scores at age 20 were compared with the scores for pocket probing depth and gingival index at age 20 in the total material and by groups, with and without dental restoration, using Spearman's rank correlation.

Results

Dental status and alveolar bone height 10 years after SABG

Study I

One year after surgery, 97% of the patients had modified Bergland index (mBI) Grade I and the remaining 3% had mBI Grade II. Ten years after surgery, the share of patients with mBI Grade I had decreased to 43%, whereas 55% had mBI Grade II and 2% had mBI Grade III (Figure 12).

The degree of dental anomalies in the cleft area, such as enamel hypoplasia, incisor rotation, incisor inclination, and canine inclination, and poor oral hygiene registered preoperatively, were all negatively correlated with the BI 10 years after surgery. Enamel hypoplasia ($r = 0.70195$, $P < .0001$), followed by canine inclination ($r = 0.55429$, $P < .0001$), were the most strongly correlated with reduced intra-dental bone height in the cleft area (Figures 13–17).

Poor oral hygiene was correlated with reduced bone height as assessed by mBI at the 10-year follow-up ($r = .41965$, $P < .0004$) (Figure 15). Tables 3 and 4 summarize the statistical analysis of the correlation between the above parameters and the bone height 10 years after SABG.
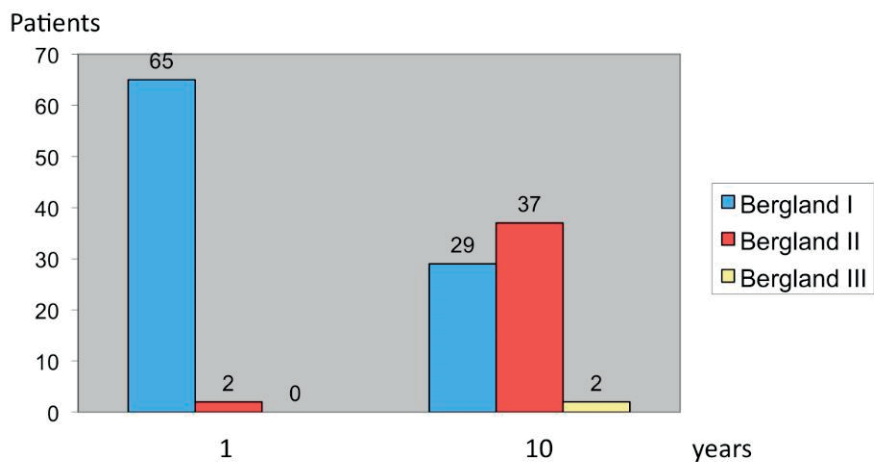

Figure 12. Alveolar bone height according to the Bergland index one and 10 years after SABG.
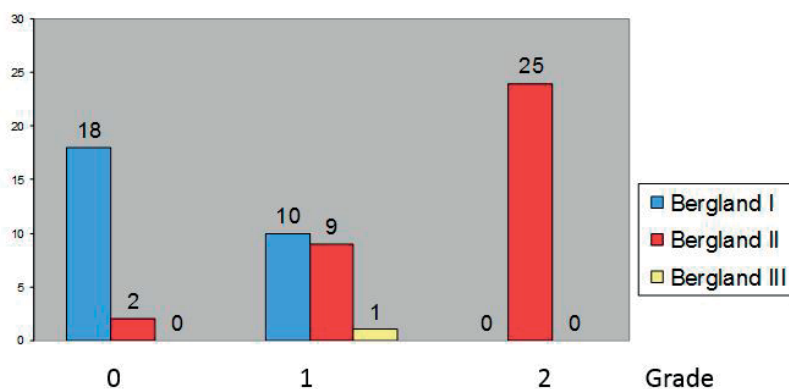
Patients

Figure 13. Enamel hypoplasia of the central incisor in the cleft area and degree of alveolar bone height according to the Bergland index at the 10-year follow-up.
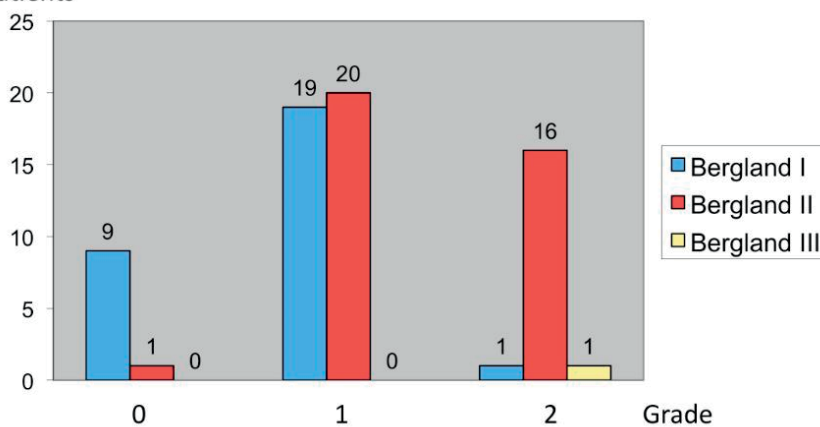
Patients

Figure 14. Inclination of the canine in the cleft area and degree of alveolar bone height according to the Bergland index at the 10-year follow-up.
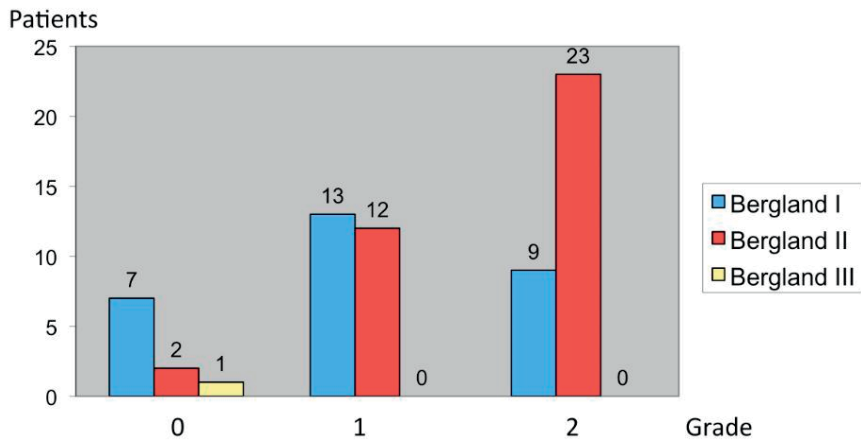
Figure 15. Rotation of the incisor in the cleft area and degree of alveolar bone height according to the Bergland index at the 10-year follow-up.
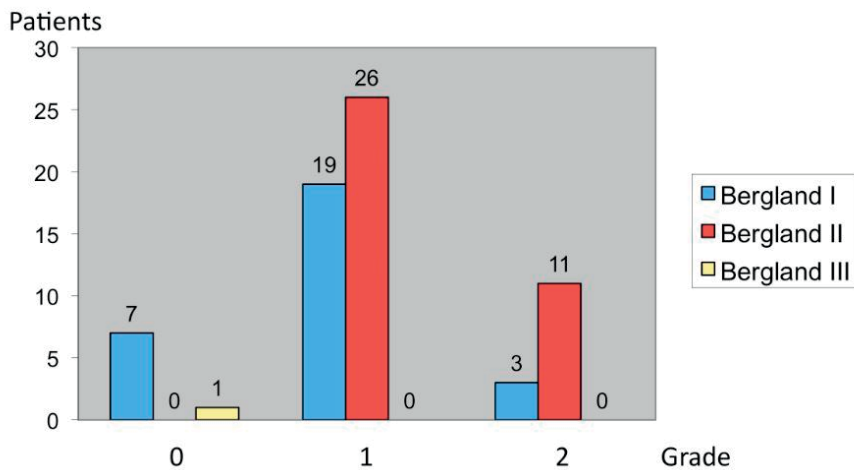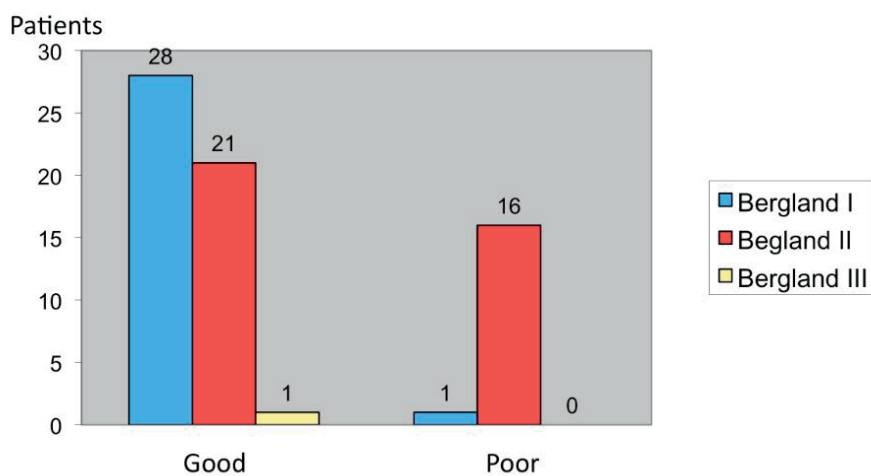

Figure 16. Inclination of the incisor in the cleft area and degree of alveolar bone height according to the Bergland index at the 10-year follow-up.

Figure 17. Oral hygiene and degree of alveolar bone height according to the Bergland index at the 10-year follow-up.

Table 3. Data from the scoring of bone height and dental status parameters.

Variable	N	Mean	SD	Max	Median	Min
Modified Bergland Index	67	1.58	0.53	3.00	2.00	1.00
Enamel hypoplasia	67	1.06	0.83	2.00	1.00	0.00
Oral hygiene	67	0.51	0.88	2.00	0.00	0.00
Canine inclination	67	1.12	0.64	2.00	1.00	0.00
Incisor inclination	67	37.09	13.00	70.00	40.00	0.00
Incisor rotation	67	60,82	29.27	90.00	45.00	0.00

Table 4. Coefficients of correlation between the various parameters of dental status and bone height 10 years after SABG.

	Correlation Cofficient	Lower 95% Confidence Limit	Upper 95% Confidence Limit	P
Enamel hypoplasia	0.70	0.55	0.80	<0.0001
Oral hygiene	0.42	0.20	0.60	<0.0004
Canine inclination	0.55	0.36	0.70	<0.0001
Incisor inclination	0.29	0.05	0.50	<0.0156
Incisor rotation	0.29	0.05	0.50	<0.0168

Correlation between initial cleft size, dental status, and the success of alveolar bone grafting

Study II

There was a wide inter-individual range in cleft dimensions in infancy. The median separation between the alveolar processes anteriorly (D–E) was 6.22 mm (mean 6.40, range 1.20–11.83 mm). The median anterior cleft width (B–B1) was 6.26 mm (mean 6.49, range 1.37–15.06 mm). The median posterior cleft width (A–A1) was 7.56 mm (mean 7.61, range 3.11–13.20 mm) (Table 5). There was no significant correlation between initial cleft width and alveolar bone height at either the 1- or 10-year follow-up (Table 5).

Enamel hypoplasia of the central incisor adjacent to the cleft area was found in 46 patients (69%). The degree of enamel hypoplasia was positively correlated with the relative anterior cleft width (B–B/C–C1) ($r = 0.24$, $P = 0.0498$) (Figure 18). There was no correlation between enamel hypoplasia and posterior cleft width. Central incisor rotation was positively correlated with relative anterior cleft width (B–B/C–C1) ($r = 0.25$, $P = 0.042$) (Figure
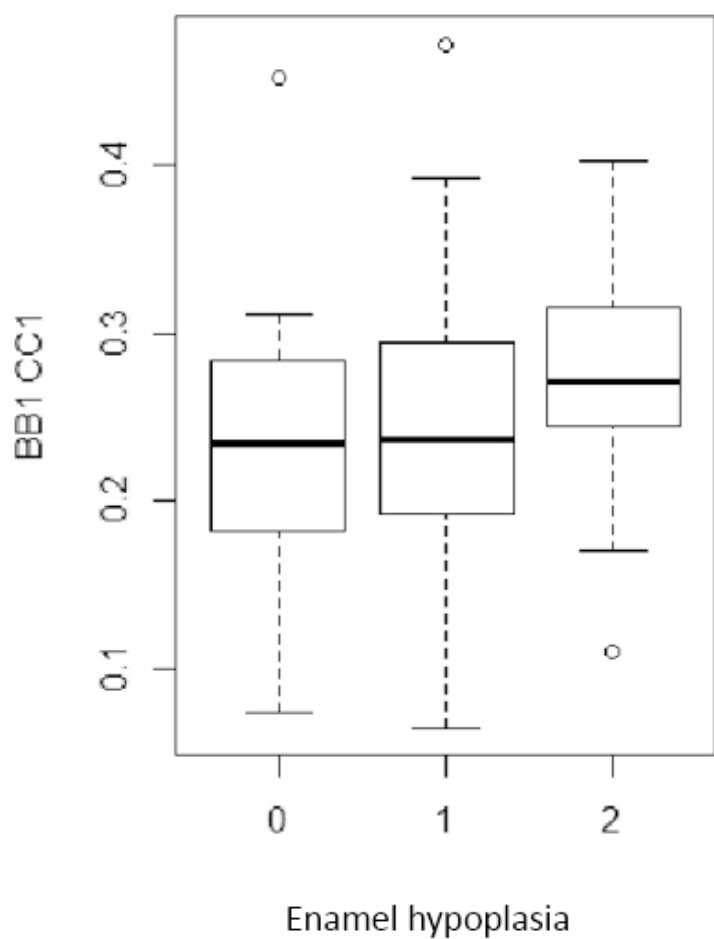
19), with cleft width at the level of the alveolar processes anteriorly (D–E) (r = 0.32, P = 0.0074) (Figure 20), and with the smallest cleft width at the level of the alveolar processes (D–E1) (r = 0.29, P = 0.0168) (Figure 21). There was no correlation between cleft width and the inclination of either the central incisor or canine adjacent to cleft area.

Table 5. Descriptive statics with mean, standard deviation, minimum, median, and maximum for cleft size measurements in millimetres (mm), cleft size ratios, degrees of dental anomalies, and modified Bergland index.

Variable	N	Mean	SD Dev	Minimum	Median	Maximum
Incisor inclination	67	37.09	13.00	0.00	40.00	70.00
Incisor rotation	67	60.82	29.27	0.00	45.00	90.00
Modified Bergland grad 1-4	67	1.03	0.17	1.00	1.00	2.00
Enamel hypoplasia	67	1.06	0.83	0.00	1.00	2.00
Canine inclination	67	1.12	0.64	0.00	1.00	2.00
MB, "10 year follow-up"	67	1.58	0.53	1.00	2.00	3.00
D_E	66	6.40	2.68	1.20	6.22	11.83
D_E1	66	3.10	2.58	0.00	2.41	10.31
C_C1	66	25.18	2.87	18.99	24.62	33.83
B_B1	66	6.49	2.65	1.37	6.26	15.06
BB1_CC1	66	0.25	0.08	0.06	0.26	0.47
T_T1	66	30.39	2.82	24.56	30.10	36.94
A_A1	66	7.61	2.45	3.11	7.56	13.20
AA1_TT1	66	0.25	0.06	0.12	0.25	0.37

Table 6. Spearman correlation between initial cleft width and alveolar bone height.

	MB_10_years_follow_upp	Modifierad_Bergland__grad_1_4_
AA1_TT1	0.05509 0.6604 66	-0.19858 0.1099 66
A_A1	0.11919 0.3405 66	-0.20509 0.0985 66
BB1_CC1	0.21202 0.0874 66	-0.12045 0.3354 66
B_B1	0.18771 0.1312 66	-0.15301 0.2200 66
C_C1	0.09007 0.4720 66	-0.17906 0.1503 66
D_E	0.18749 0.1317 66	0.04558 0.7163 66
D_E1	0.09605 0.4430 66	-0.15301 0.2200 66
T_T1	0.15272 0.2209 66	-0.10093 0.4201 66

Figure 18. Enamel hypoplasia of central incisor in the cleft area versus relative ante-rior cleft width (B–B ratio = B–B1/C–C1) as measured on dental cast obtained in connection with the primary lipplasty.
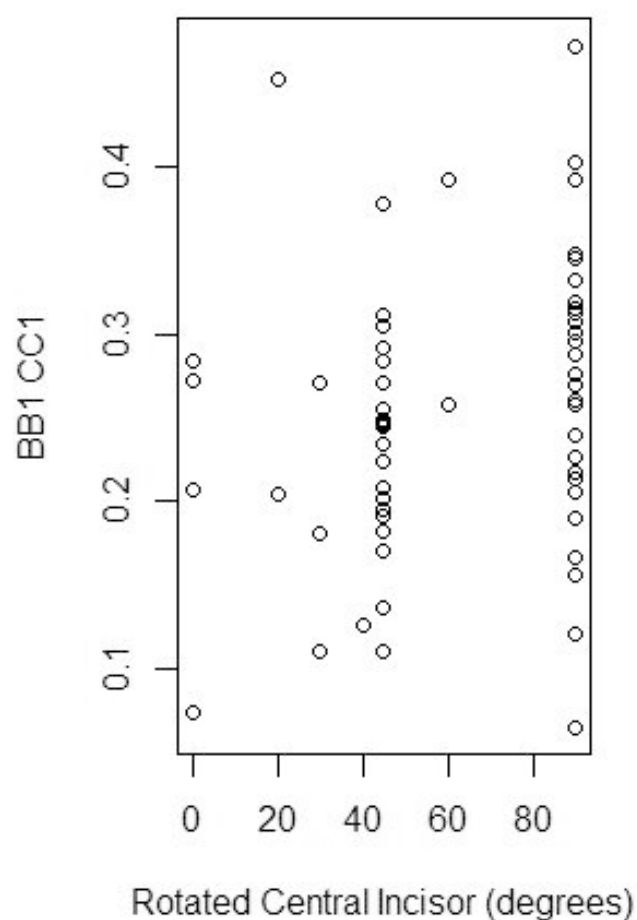
Figure 19. Rotation of the central incisor (degrees) in the cleft area versus relative anterior cleft width (B–B ratio = B–B1/C–C1) as measured on dental cast obtained in connection with the primary lipplasty.
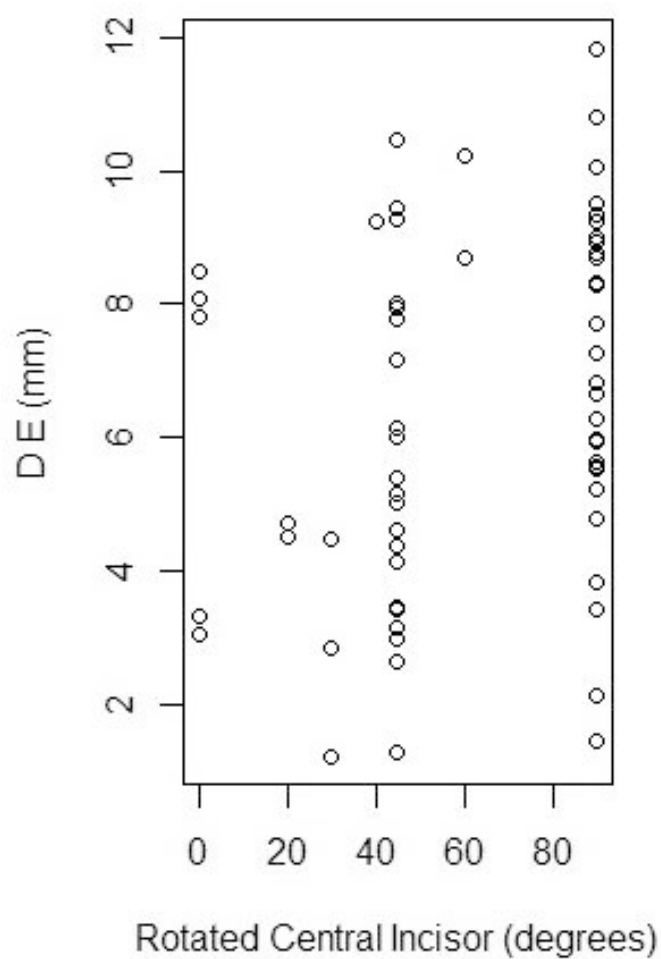
Figure 20. Rotation of the central incisor (degrees) in the cleft area versus cleft width at the level of the alveolar processes, anteriorly D–E (mm).
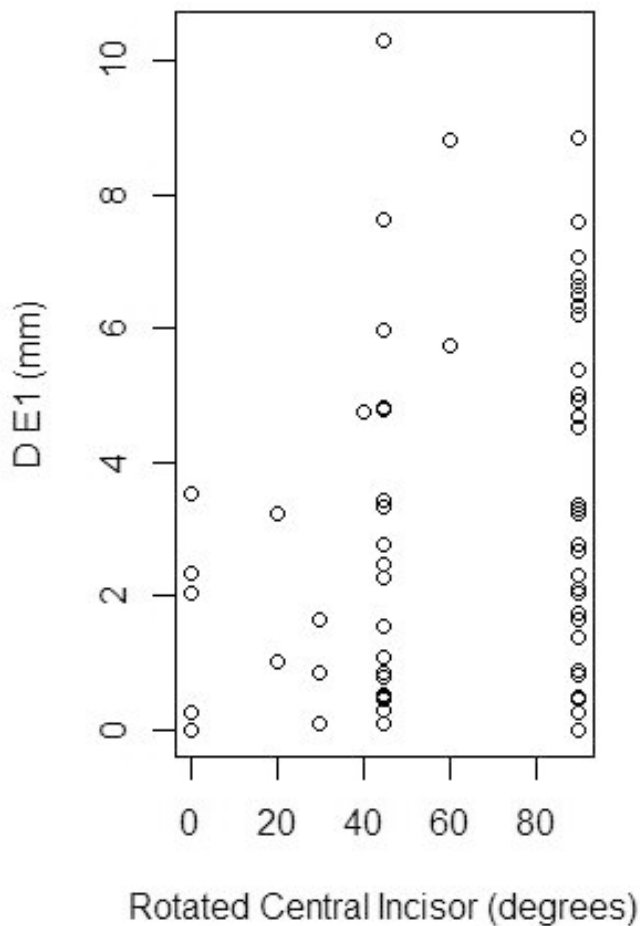
Figure 21. Rotation of the central incisor (degrees) in the cleft area versus smallest cleft width at the level of the alveolar processes, anteriorly D–E1 (mm).

Long-term effects on alveolar bone height and maxillary growth

Study III

The bone height in patients treated with PPP was significantly lower than in patients in the SABG group ($P < .0001$; Table 7). No patient in the PPP group had BI Grade I. In patients treated with PPP and later with SABG, the bone height was notably improved.

Groups	Bergland Grade I		Bergland Grade II		Bergland Grade III		Total
	%	n	%	n	%	n	
PPP	–	0	27	4	73	11	15
SABG	76	22	17	5	7	2	29
PPP/SABG	38.5	5	38.5	5	23	3	13
Total		27		14		16	57

Table 7. Height of the interalveolar septum according to the BI; number and frequency of patients in each treatment group. PPP = primary periosteoplasty, SABG = secondary alveolar bone grafting, PPP/SABG = both treatments.

Between 5 and 18 years of age, the maxilla position relative to the cranial base (SNA) becomes more retruded in both groups (Figure 22). The magnitude of this change in SNA was significantly greater in the PPP group at age 5–10 years ($P = 0.025$). The mandible position relative to the cranial base (SNB) increased between 5 and 18 years of age in both groups (Figure 23). Mandibular protrusion was greater in the SABG group, differing significantly at age 10 years ($P = 0.044$) and nearly significantly at age 18 years ($P = 0.08$).

The ANB angle, describing the sagittal interrelationship of the maxilla and mandible, decreased from 5 to 18 years in both groups, reflecting parallel trends toward maxillary retrusion (Figure 24). The ANB was significantly greater in the PPP group at 5 years of age ($P = 0.036$). There were no significant differences in maxillary and mandibular inclination relative to the cranial base (NL/NSL and ML/NSL) or in the vertical maxillary–mandibular relationship between groups (Figures 25–27).

Representative intraoral occlusal radiographs obtained at different times, showing pre- versus postoperative changes in both groups, appear in Figures 28 and 29.
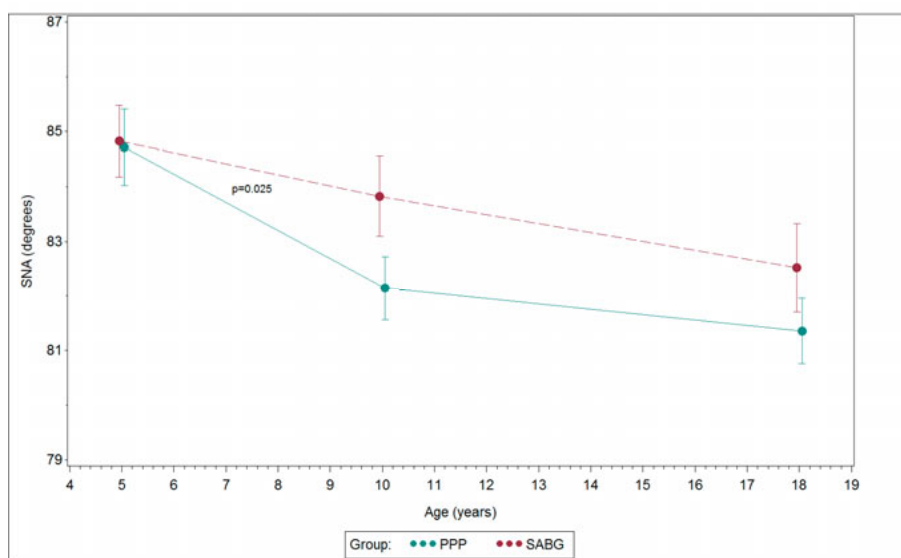
Figure 22. **SNA** versus age for PPP and SABG groups: **PPP** = primary periosteo-plasty, **SABG** = secondary alveolar bone grafting.
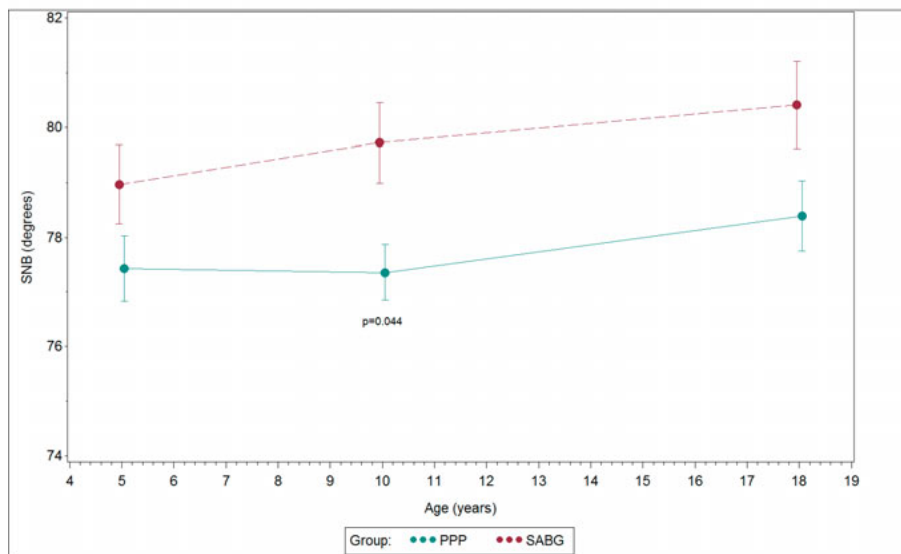
Figure 23. **SNB** versus age for PPP and SABG groups: **PPP** = primary periosteo-plasty, **SABG** = secondary alveolar bone grafting.
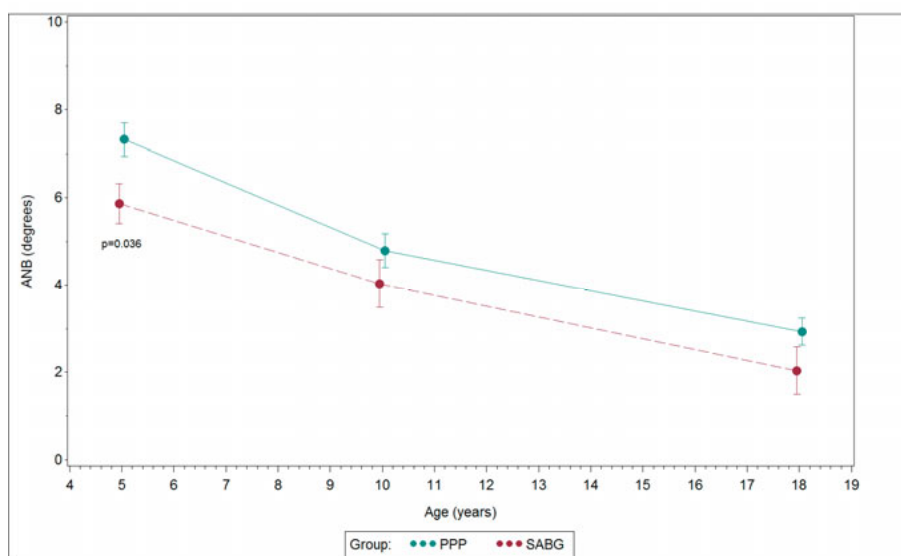
Figure 24. **ANB** versus age for PPP and SABG groups: **PPP** = primary periosteo-
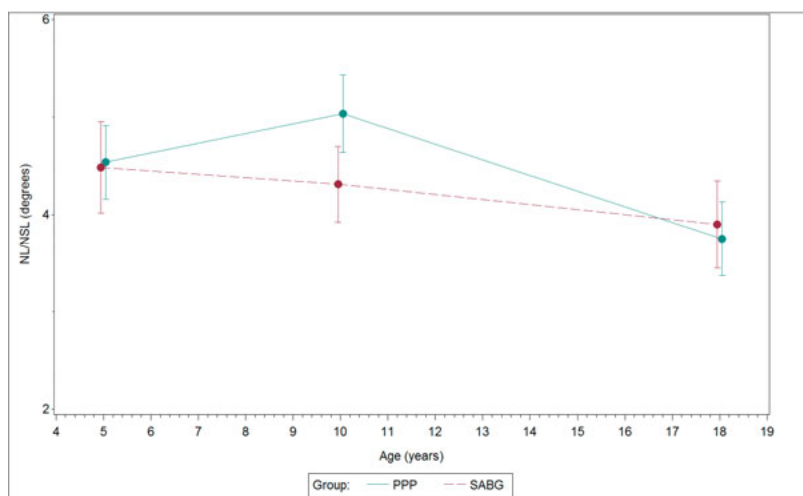plasty, **SABG** = secondary alveolar bone grafting.

Figure 25. **NL/NSL** versus age for PPP and SABG groups: **PPP** = primary perioste-
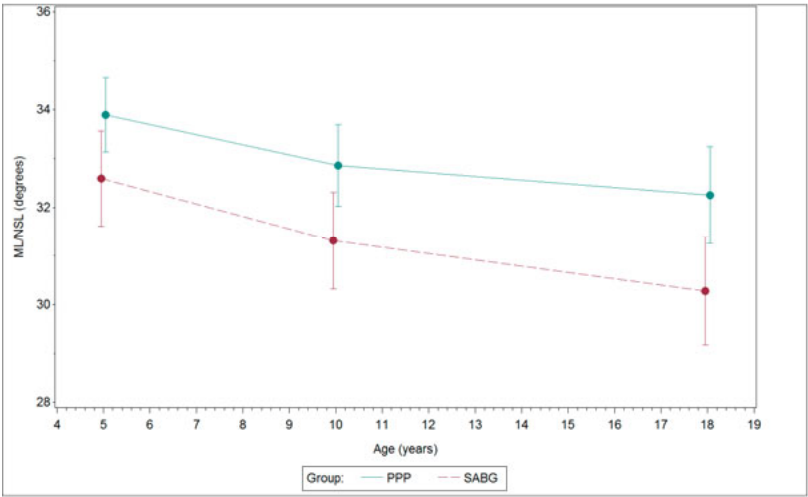oplasty, **SABG** = secondary alveolar bone grafting.

Figure 26. **ML/NSL** versus age for PPP and SABG groups: **PPP** = primary periosteoplasty, **SABG** = secondary alveolar bone grafting.
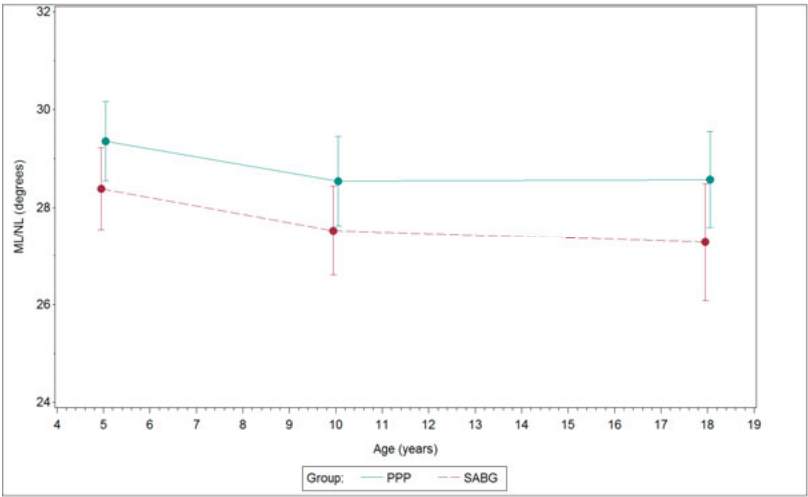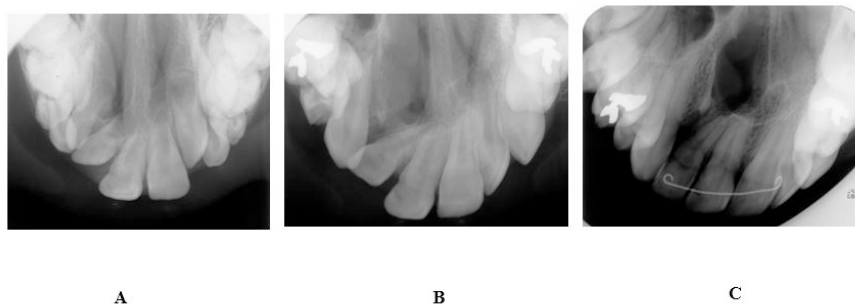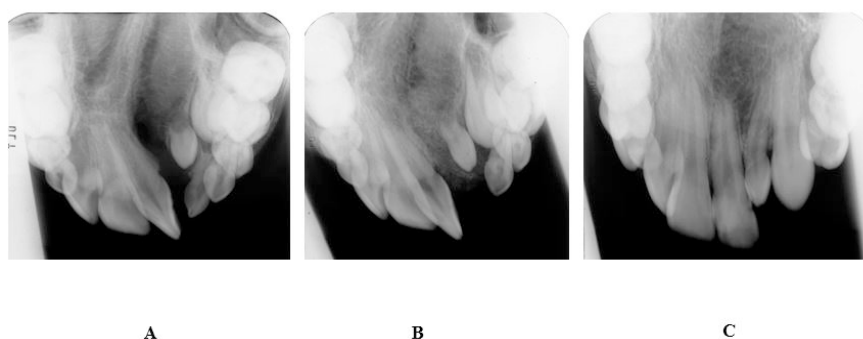

Figure 27. **ML/NL** versus age for PPP and SABG groups: **PPP** = primary periosteoplasty, **SABG** = secondary alveolar bone grafting.

60

Figure 28. **Occlusal radiographs from patient with unilateral cleft lip alveolus treated with primary periosetoplasty. A:** 8 years of age; **B:** 10 years of age; **C:** 16 years of age

Figure 29. **Occlusal radiographs from patient with unilateral cleft lip alveolus treated with secondary alveolar bone grafting. A:** Presurgical at 8 years of age; **B:** postsurgical at 10 years of age; **C:** postsurgical at 16 years of age

Oral status and alveolar bone height at 20-year follow-up

Study IV

Bone height at the 20-year follow-up after SABG was compared with the previous data obtained at the 10-year follow-up (presented in Study I). The percentage of patients with BI I declined from 40% to 32.5% and with BI II from 60% to 52.5%. The percentage of patients with BI III increased from 0% to 15% (Figure 30, Tables 8 and 9). The scores obtained from occlusal radiographs and CBCT were identical.

This reduction in alveolar bone height between 10 and 20 years was statistically significant in the total material ($P = 0.045$) and in patients with dental restorations in the cleft area ($P = 0.078$) (Tables 10 and 11).

There was a positive correlation between the bleeding index and the reduction in bone height (*r=0.51, p=0.0008*). There was also a positive correlation between the BI and the presence of dental restorations ($r = 0.69$, $P =$

0.0125). The general loss of alveolar bone as assessed by the pocket probing index was unrelated to the observed reduction of bone in the cleft area.
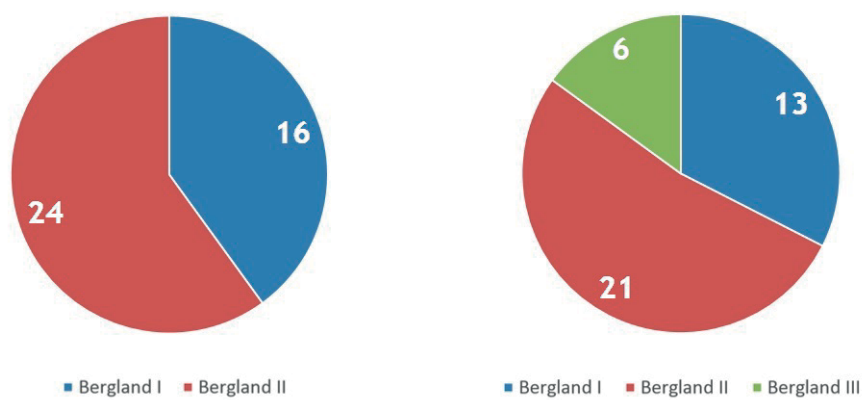
Figure 30. Alveolar bone height according to the Bergland index at the 10-year (left panel) and 20-year (right panel) follow-ups after SABG. The total number of patients is 40. The Bergland index was significantly lower at the 20-year follow-up ($p = 0.045$).

Table 8. Alveolar bone height according to the Bergland index at the 10-year follow-up. The total number of patients is 40.

Bergland Index at the 10- year follow-up		
Grade	Frequency	Percent
I	16	40
II	24	60

Table 9. Alveolar bone height according to the Bergland index at the 20-year follow-up. The total number of patients is 40.

Bergland Index at the 20-year follow-up		
Grade	Frequency	Percent
I	13	32.50
II	21	52.50
III	6	15.00

Table 10. Changes in alveolar bone height according to the Bergland index between the 10-year and 20-year follow-ups. The total number of patients is 40. The Bergland index was significantly lower at the 20-year follow-up ($p = 0.045$). BI = Bergland index.

"Bergland index, 10-year versus 20-year follow-up"				
Thus: "BI, 10-year"	"BI, 20-year"			
Grade	I	II	III	Total
I	11	3	2	16
II	2	18	4	24
Total	13	21	6	40

Table 11. Changes in alveolar bone height according to the Bergland index between the 10-year and 20-year follow-ups in patients with dental reconstruction. The total number of patients is 12. The Bergland index was significantly lower at the 20-year follow-up (p =0.078). BI = Bergland index.

"Bergland index, 10-year versus 20-year follow-up" Dental rehabilitation				
"BI, 10 years"	"BI, 20 years"			
Grade	I	II	III	Total
I	0	2	2	4
II	0	4	4	8
Total	0	6	6	12

Discussion

The three constituent studies of this thesis investigate the long-term results after SABG and identify predictors of outcomes. Study III is a comparative investigation of infant primary periosteoplasty versus SABG as means to reconstruct the alveolar cleft. The investigations presented here are based on series of consecutive patients with unilateral clefts, treated in one institution, i.e., the Cleft Lip and Palate Team of Uppsala University Hospital. Syndromic patients, non-Caucasian patients, and patients lacking records or dental casts were excluded. Studies I, II, and IV deal with complete UCLP, while study III concerns unilateral CLA. The material is also characterized by a limited number of surgeons involved in the treatment.

The success of alveolar reconstruction is captured by the alveolar bone height in the cleft area. Multiple scales are used to assess alveolar bone height. The Berglund and Kindelan indices are the scales most commonly used for this purpose.[99, 133] The BI has traditionally been used at our institution and was therefore chosen for use here.

Measurements were made longitudinally at a 10-year (study I) and 20-year (studies I and IV) follow-up. Factors affecting oral and dental health and status were identified as outcome predicators. In study III, the alveolar bone height and facial growth were compared in two groups of patients born with CLA, treated with either infant periosteoplasty or SABG. SABG was found to be a superior method for reconstructing the cleft alveolus. These findings have important implications for the treatment of patients with clefts involving the alveolus.

Alveolar bone height 10 years after SABG and predictors of outcome

Study I

This study demonstrates that in about half of the patients there is a reduction in alveolar bone height with time. This reduction is correlated with the degree of dental anomalies, dental malpositioning, and oral hygiene. This phenomenon has not previously been described.

The surgical method for SABG was introduced at our unit in 1984 after a visit by Frank Åbyholm from Oslo. Since then, the surgical procedure has

followed the same basic principles. The surgical procedure is performed with wide exposure through both palatal and vestibular accesses. Ample amounts of bone are grafted to fill the entire cleft space to the incisive foramen and alveolus up to the piriform aperture. The rationale is that a thorough approach, with meticulous closure of the nasal layer throughout the cleft, is necessary for reliable graft take and the expected achievement of all treatment goals: tooth support, fistula closure, and maxillary stability. We find support for this approach in the excellent one-year results presented here, with 97% of patients having mBI Grade I. It has previously been demonstrated that surgeon experience is positively correlated with outcomes after cleft surgery. The fact that one senior plastic surgeon (Valdemar Skoog) performed all SABGs in this study population is probably another important factor underlying the successful results.

The importance of the orthodontist in planning, preparation, and follow-up in conjunction with SABG is widely recognized. However, the negative impact of various dental anomalies and poor oral hygiene has, to our knowledge, not previously been investigated.

Dental anomalies occur with higher frequency in patients born with UCLP and their significance for treatment outcomes after SABG warrants close investigation.[33, 119] In this study, the preoperative degree of oral hygiene and enamel hypoplasia, as well as the degree of canine inclination, incisor inclination, and incisor rotation, were found to be related to reduced alveolar bone height after 10 years. The most common enamel alteration in patients with complete CLP is enamel hypoplasia due to deficient enamel formation and absence of the enamel surface.[62] These defects mainly affect the teeth close to the cleft. Enamel hypoplasia increases the susceptibility to plaque accumulation and increases the risk of tooth decay and gingivitis. The correction of central incisor rotation and inclination prior to SABG facilitates oral hygiene and prevents plaque formation. We believe that implementation of regular maintenance therapy is important and beneficial for these patients, and that bone grafting should not be performed until the gingiva is healthy.[134]

Impacted permanent maxillary canines occur in just 1–3% of the general population,[135] though it is seen more often in CLP patients due to canine inclination.[136] Impacted permanent maxillary canines occurred in 24% of the study group. High degrees of canine inclination indicate a risk of altered eruption and impaction, so canine inclination should be anticipated in patients with CLP before SABG and during the follow-up.

The most important benefit of SABG is that the newly grafted bone allows for spontaneous eruption of the adjacent canine and for orthodontic movement of teeth into the grafted bone.[111] It is crucial for the outcome to provide adequate assessment of dental status and appropriate interceptive management in order to achieve optimal dental rehabilitation prior to SABG.

Initial cleft size, dental status and the alveolar bone height

Study II

In the second study, we did not find any correlation between initial cleft size and SABG outcome. However, we did observe a correlation between initial cleft width and certain dental anomalies.

Initial cleft width varies in infancy.[120] Cleft size has been found to affect early outcome with respect to dental arch dimensions and crossbite occlusion, with crossbite developing more frequently at five years in UCLP children with smaller initial clefts.[122] The size of the nasal airway and its function on the cleft side in adulthood were reduced compared with the non-cleft side, but no correlation was found between size of the initial cleft in infancy and size and function of the nasal airway in adulthood.[137] It has previously been reported that the size of the alveolar cleft at the time of bone grafting does not influence bone-graft survival.[138] Similarly, after measuring cleft size on dental casts, we could not find any correlation between initial cleft size and SABG outcomes.

Wide clefts, reflecting a more severe initial deformity, are known to complicate primary surgery of the lip and palate. During surgery, they generally require more extensive dissection, which is associated with an increased risk of healing problems and soft tissue scarring. Furthermore, palatal exposure of the alveolar cleft, and obtaining a watertight seal of the nasal layer, is more challenging in patients with scarred, narrow, and high arched palates. Based on this, we hypothesized that initially wide clefts would be associated with inferior outcomes after the SABG procedure. The absence of such a correlation implies that other factors are more important for the long-term degradation of the grafted bone. In this study, we demonstrate several links between initial cleft dimensions and the degree of dental anomalies. The relative anterior cleft width correlated with the degree of enamel hypoplasia, i.e., a wider cleft at the level of the canine points in infancy, seemed to be associated with more enamel hypoplasia of the central incisor. All measurements capturing anterior cleft width correlated positively with the degree of central incisor rotation, wider initial clefts being associated with more rotated central incisors. However, we did not find any correlation between initial cleft width and the position of the permanent canine at the time of bone grafting. Anteriorly wide clefts in infancy could therefore signal a need for future more extensive orthodontic treatment in connection with the SABG procedure. Therefore, early identification of patients at increased risk would permit the establishment of an appropriate interceptive treatment plan, entailing early identification of enamel defects and other related dental abnormalities.

Long-term effects on alveolar bone height and maxillary growth

Study III

The long-term outcomes of PPP and SABG in terms of bone formation and facial growth in patients with CLA were studied. None of the patients treated with only PPP displayed adequate bone formation at long-term follow-up. Moreover, patients treated with both PPP and later SABG also displayed significantly less bone formation. This inferior outcome was probably due to late-performed bone grafting in some patients. Another contributing factor could be that scar tissue formed by PPP negatively affected the bone graft.

In terms of growth, patients treated with PPP experienced a relative restriction of anteroposterior maxillary growth at the ages of 5–10 years. However, at the conclusion of facial growth, there was a difference in the ANB only, with less maxillary retrusion in the PPP group. This was probably due to the observed mandibular growth differences between groups. Although the two groups displayed similar long-term maxillary growth comparable to that of the normal population, PPP was largely ineffective in reconstructing the alveolar cleft.

Studying patients with CLA obviated the need to consider complex effects of palatal surgery on growth outcomes. Another notable aspect is that the same surgeon performed all procedures of each type, Tord Skoog for PPP and Valdemar Skoog for SABG. The primary periosteoplasty technique was abandoned in Uppsala in 1977. However, variants of this procedure are still practiced today and comparative studies are therefore warranted. One important finding is that PPP seems to obstruct properly timed bone grafting in patients with inadequate bone in the cleft. The present results support the argument for using SABG in the reconstruction of alveolar clefts.

Oral status and alveolar bone height at 20-year follow-up

Study IV

In the last study we observed an additional reduction in the alveolar bone height in the cleft area between the 10- and 20-year follow-up. This reduction was positively correlated with gingival inflammation and the presence of dental restorations.

The follow-up of patients after SABG usually consists of clinical examinations and conventional radiographs including panoramic, periapical, and occlusal films to assess the alveolar bone height. The BI is considered the gold standard and is easy to apply in clinical routine. However, this method

only allows evaluation of the extent of the grafted bone in two dimensions.[139] Several authors have started to use CT scanning to evaluate bone stock after SABG.

In this study, we wanted to compare the data from CBCT with historical and concomitant bone analysis results according to the BI from occlusal radiographs. For this purpose, we used measurements from CBCT images to calculate an index of alveolar bone height according to BI principles. We found complete accordance between the data generated from CBCT analysis and the conventional BI assessment from occlusal radiographs. This implies that occlusal radiographs are adequate to assess bone height after SABG in clinical routine. There are also clear limits to the routine use of CBCT related to radiation exposure and accessibility of the technique. Nevertheless, we do believe that CBCT is of value as an adjunct in difficult clinical cases in which supplementary information in addition to conventional radiographic imaging would be beneficial for enhanced treatment planning.

It has been demonstrated that cleft patients have an increased risk of gingival inflammation and periodontal disease. This seems to be associated with anatomic deviations, eruption patterns, long-term orthodontic treatment, and the presence of dental restorations of teeth adjacent to the clefts.[140][83] Accordingly, we found that local bone loss in the cleft space was positively correlated with the general gingival inflammatory status. We also demonstrated that patients with dental restorations had lower bone height. Indeed, dental implants, crowns, and restorations may interfere with the maintenance of good oral hygiene and increase the constant inflammatory load on the periodontal tissues. This study reinforces the proposed specific link between a chronic inflammatory mechanism and long-term degradation of bone in alveolar cleft sites. It also points to the importance of the quality of restorations for periodontal health in cleft patients.

Clinical implications

Maintaining the alveolar bone height in the cleft area after receiving SABG is important in order to prevent long-term complications such as gingival retractions and periodontal disease. Moreover, maintenance of the grafted bone is vital for the long-term dental survival, especially in patients requiring dental restorations. Therefore, it is crucial to assess dental status such as enamel defects and other related dental abnormalities in order to achieve optimal dental rehabilitation prior to SABG.

Initial cleft width varies considerably in UCLP patients, the degree of enamel hypoplasia and central incisor rotation are positively correlated with relative anterior cleft width and with the cleft width anteriorly. This may imply that a more individualized approach based on cleft morphology rather than a pre-established treatment protocol would be advantageous. Such an approach would permit early identification of enamel defects and other dental abnormalities, facilitating the establishment of an appropriate interceptive treatment plan.

SABG should remain the standard treatment for reconstructing alveolar processes in cleft patients, as its success rate is approximately 90 percent. Primary periosteoplasty and the recently popularized GPP result in less, more poorly located bone than in SABG. Furthermore, a failed PPP or GPP is detrimental to subsequent bone grafting.

Cleft patients do not have a higher risk of developing periodontal disease, although they may have more gingivitis. However, implementing specially designed maintenance therapy can be expected to promote the preservation of dentition, especially after complex dental restorations in the cleft area.

Conclusion

Dental status factors have an impact on the long-term survival of alveolar bone height in the alveolar cleft.

Variation in initial cleft size has an impact on certain dental status factors.

Poor dental status, such as enamel hypoplasia followed by canine inclination, is correlated with lower bone height at the 10-year follow-up. Evaluating and improving these factors is important prior to SABG.

The initial cleft width is positively correlated with the degree of central incisor rotation and enamel hypoplasia. It should therefore be used as an early indicator of future need for treatment in conjunction with SABG.

In adults with UCLP, the alveolar bone height in the cleft was closely related to the presence of gingival inflammations and restorations at the 20-year follow-up.

The final outcome after SABG is inferior in patients with signs of gingivitis and dental restorations. The periodontal health status was more correlated with the presence of dental restorations and with gingivitis.

In adults treated for UCLP and rehabilitated with dental restoration, stringent supportive periodontal therapy should be implemented.

Primary periosteoplasty results in less bone in the cleft area than does SABG. The differences between groups in terms of maxillary growth were of minor importance.

When evaluating alveolar bone height in the cleft area, results from occlusal radiographs correspond well to those from CBCT according to the BI.

Populärvetenskap sammanfattning

Avhandlingen handlar om barn födda med Läpp-käk-och/ eller gomspalt (LK/G). Klinisk behandlar jag dessa barn med tandreglering och käkortopedi i Uppsalas Kraniofaciala Team.

Spalter i läpp, käke och gom hör till de vanligaste medfödda missbildningar i ansiktet som utan behandling ger betydande funktionella och psykologiska problem hos den drabbade individen. Behandlingen är multidisciplinär och involverar plastikkirurger, ortodontister, foniater, logopeder och käkkirurger. Målsättningen med behandlingen är att till största möjliga sluta spalten för att normalisera utseendet och de fysiologiska funktioner som tal, tuggning, sväljning och andning.

Spaltens ursprungliga storlek och anatomi varierar. Vid en käkspalt är överkäkens alveolarutskott (tandbärande käkben) delat i två delar och vid framtandsområdet föreligger en öppen förbindelse mellan mun och näshåla. Angränsade tänder är ofta felplacerade, d.v.s. roterade och tippade. De kan även ha atypisk form samt sämre kvalitet på emaljen. Innan bentransplantation till käkspalt genomförs sker förberedande behandling där tänder som står fel och defekter i emaljen korrigeras. Den icke frambrutna hörntanden befinner sig i käkbenet vid käkspalten. Dess rotutveckling bestämmer tidpunkten för bentransplantation till käkspalten. Syftet med bentransplantation är att låta angränsande tänder växa ner i den transplanerade benvävnaden, alternativt att med hjälp av tandreglering aktivt framflytta tänder in i området och säkra benstödet för tänderna. Vidare sluts den öppna förbindelsen mellan käkhålan och näshålan. Transplantation ger också den avflackande näsvingen ett förbättrat benstöd. Det är ett stort behov av bättre vetenskaplig underbyggnad för att studera faktorer som påverkar behandlingsresultatet.

Målet med avhandlingen är dels att studera faktorer som långsiktigt kan påverka resultatet av bentransplantation i käkspalten hos barn födda med enkel sidigt läpp-käk-gomspalt, samt att jämföra två kirurgisk protokoll for rekonstruktion av käkspalten. I detta fall sekundär bentransplantation och primär periosteoplastik hos barn födda med enkel sidigt läpp-käkspalt.

I delarbete I, II och IV ingår individer födda mellan 1987-1997. De är födda med enkelsidig LKG.

I del arbete III ingår individer födda mellan 1960-1998 och behandlade för enkelsidig LK.

Delarbete I. Läget för hörntanden och framtanden samt förekomst av emalj defekter vid käkspalten registrerades. Ben nivån i käkspalten graderades enligt fyrgradigt skala efter 1 år samt10 år.

Delarbete II. Den ursprungliga spalt storleken har mätts med ett digitalt skjutmått på gipsmodeller av överkäken tagna i samband med läppoperation-en.

Delarbete IV. Bennivån i käkspalten 20 år efter bentransplantation studera-des på röntgen bilder, slät röntgen och data tomografi (CBCT) tagna vid samma undersöknings tillfälle.

Delarbete III. Bennivån i käkspalten vid 16 års ålder studerades och jämför-des hos individer som behandlats med periosteoplastik i samband med pri-mär läppoperation eller med bentransplantation vid 8 till 10 års ålder.

Resultaten av delarbete I-IV:

Det finns ett negativet samband mellan graden av hörntanden och framtan-dens lutning och förekomst av emaljhypoplasier, på bennivån 10 år efter bentransplantationen.(Delarbete I)

Det finns positiv samband mellan spaltens bredd och förekomst av tänder med emaljhypoplasier och uttalade rotationer invid spalten. (Delarbete II)

Bennivån är sämre hos individer behandlad med primär periosteoplastik jämfört med dem behandlats med sekundär ben transplantation i käkspalten. Däremot, är det inga skillnader i den skeletala tillväxten av käkarna. (Delar-bete III)

Vuxna LKG patienter med lagningar, kronor och implantat i ben transplante-rade området hade sämre bennivå vid 20-års uppföljning jämfört med ben-nivå vid 10-års uppföljning efter bentransplantation i käkspalten. (Delarbete IV)

Sammanfattning av resultaten visar att tandstatus påverkar den långsiktiga överlevnaden av ben nivån i käksplaten. Dålig tandstatus såsom emaljhy-poplasi följt av tand lutning och rotationer är korrelerade med ett lägre ben nivå på 10 års uppföljning. Att utvärdera och korrigera dessa faktorer är viktigt före SABG.

Hos vuxna med UCLP, var bennivån i käksplaten mer relaterade till före-komsten av inflammation i tandköttet och restaurationer vid 20-års uppfölj-ning.

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