OUTCOMES OF SECONDARY ALVEOLAR BONE GRAFTS IN CLEFT PATIENTS

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DECLARATION

I, Matlaba Machaka, declare that this research report is my own. It is submitted for the Degree of Master of Dentistry in the branch of Maxillofacial and Oral Surgery at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.

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Signature of candidate

___31__ day of __May__2018

DEDICATION

I would like to dedicate this work to my beloved family:

My wife; your support and love was the source of my strength throughout this project. Thank you very much.

My parents; your undying support and love throughout my life has made this academic journey a pleasant one. Thank you very much.

My children; my prince Moloko and my princess Khothatso:

THIS IS FOR YOU.

ABSTRACT

Aim

The aim of this retrospective study was to determine the outcomes of secondary alveolar bone grafts (SABG) in cleft patients treated at the Wits Dental Hospital at the Charlotte Maxeke Johannesburg Academic Hospital.

Objectives

To record the demographic data of patients who had secondary alveolar bone grafts, and to assess the outcomes of SABG by evaluating clinical variables and the quantity of bone post SABG.

Methods

Records of 19 patients with a total of 23 clefts were examined to evaluate the amount of bone at the cleft site following secondary alveolar bone graft. Socio-demographic information was collected as well as the clinical variables of the type of graft used, canine eruption, keratinised tissue around teeth close to the cleft, and closure or persistence of any oronasal fistula. The amount of bone at the graft site was measured on CBCT images using the Chelsea scale. Comparisons of Chelsea scale scores and CBCT findings were carried out. SPSS ® 24 was used to analyse the data. All statistical tests were conducted at 5% significance level.

Results

Most (52%) patients were male, with 57% having left unilateral cleft. The majority of them received autogenous bone grafts from the chin. Most (65.2%) of the patients showed good clinical outcomes, whilst showing evidence of bone resorption in and around the graft site on CBCT images. Fifteen of the patients were considered to have partial alveolar graft resorption.

Conclusion

In the majority of patients, 3D CBCT images revealed bone resorption in areas that 2D images gave an impression of presence of bone. However, the majority of patients indicated good clinical outcomes despite the poor radiological findings.

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ABBREVIATIONS

BMPs	- Bone Morphogenic Proteins
CL	- Cleft Lip
CL/P	- Cleft Lip and Palate
CP	- Cleft Palate
CT	- Computed Tomography
CBCT	- Cone Beam Computed Tomography
GPP	- Gingivoperiosteoplasty
NAM	- Naso Alveolar Moulding
OFC	- Orofacial Clefts
ONC	- Oronasal communication
RCTs	- Randomised Controlled Trials
SABG	- Secondary Alveolar Bone Graft
SOHS	- School of Oral Health Sciences
SPSS	- Statistical Package for the Social Sciences
3D	- Three Dimensional
2D	- Two Dimensional

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CHAPTER 1: INTRODUCTION

1.1 OVERVIEW OF OROFACIAL CLEFTS

Orofacial clefts (OFC) comprise a multitude of anomalies some of which are typical, such as cleft lip (CL), cleft palate (CP) or a combination of both cleft lip and palate (CL/P), and others are atypical such as transverse, median, oblique and many other Tessier types of orofacial clefts.[1,2,3] These abnormalities can occur either as an isolated condition or as part of a syndrome.[2,4] Amongst all orofacial clefts, the most common is CL/P.[1]

The prevalence of OFC is reported to be between 9.9 - 20.0 per 10,000 live births; the incidence differs depending on geographical area and population group.[1] Clefts of the palate are embryological abnormalities which are caused by failure of fusion of the palatal shelves or failure of fusion between the primary and secondary palate and or both, depending on the extent of the cleft.[2,5] Hereditary and environmental factors are believed to be the main contributing factors in the development of CL/P. Metabolic imbalances such as folic acid deficiency, are also associated with OFC.[1]

CL/P may either be unilateral or bilateral.[2] The clefts may have soft or hard tissue bridges therefore making them incomplete, or may result in complete discontinuity of the tissues with resultant soft and hard tissue defects visible clinically.[2,6,7] CL/P results in a multitude of problems that can negatively affect the growth and development of the infant.[7] These will mostly affect feeding, appearance, speech, hearing and the dentition. The treatment of these abnormalities requires a multidisciplinary approach consisting of surgeons, orthodontists, dieticians, and speech and language therapists.[2,7]

1.2 OVERVIEW OF SECONDARY ALVEOLAR BONE GRAFT

The secondary alveolar bone graft (SABG) is a surgical procedure carried out in patients with CL/P after the age of two years, whereby different types of bone materials are grafted into the cleft alveolus.[7,8] It was first described by Boyne and Sands in 1972.[9] Different protocols have been developed over the years, as the alveolar cleft can either be treated with primary repair or SABG.[10] SABG is performed at early, intermediate or late stages depending on the age of the patient.[7]

Different bone graft materials that can be used for SABG, have been reported by Deatherage (2010), [11] who reported that an ideal bone graft material should be osteogenic, osteoconductive and osteoinductive. The different graft materials available are: autogenous, allogenic, xenogenic and alloplastic, as well as bone morphogenic proteins (BMPs).[11] However, the use of SABG is controversial, with few studies having been reported evaluating its success.[8,10,12,13]

The success of alveolar bone grafting has been attributed to many factors. These include: the position of the permanent canine; the eruption stage of the canine upon grafting; the role of orthodontic therapy; the surgical protocol used; the type of bone graft used; and the time of commencement of orthodontics post-surgery.[8,14,11] It is clear that further studies are required that would evaluate the outcomes of these types of grafts in order to develop consensus for treatment protocols.[15,16]

Several radiographic studies have been used to assist with the assessment of the long term outcomes of SABG.[14,15,16,17] Bergland et al. (1986)[14] suggested a scale that uses inter-alveolar septal height to grade bone height without considering the amount of bone fill at the root level. Kindelan et al. (1997)[17] introduced a four point scale using pre- and post-operative radiographs to assess bone fill at the graft site. Witherow et al. (2002)[15] introduced the Chelsea scale which used an eight point matrix to assess the amount of bone at the graft site while considering the amount of bone at all levels of the roots of the teeth on either side of the cleft.

These radiographic evaluation scales differed in their evaluation methods but they all used two dimensional (2D) radiographs to evaluate the amount of grafted bone in the cleft alveolus. Two dimensional radiographs are known to overestimate the results.[12] The development of cone beam computed tomography (CBCT) has revolutionised the evaluation of the amount of bone as CBCT images do not overestimate the results.[12] These scans are able to measure the length, width and height of alveolar bone grafts as well as the volume of the defects and therefore are now used in the pre-surgical planning of SABG and to assess the volumetric outcome of the procedure in CL/P patients.[18,19]

Even though SABG is accepted as a treatment modality for patients with CL/P, there are existing controversies relating to surgical technique, timing of surgery, the donor site, and the type of materials that may be used.[20,21] SABG is often incorporated in a multitude of treatment modalities; it therefore must be carried out in a technically effective way and at the right stage of development, to minimise morbidity and ensure favourable outcomes. Because SABG is carried out on patients who need a multidisciplinary team approach, it is therefore important to coordinate the planning of treatment for these patients especially between surgeons and orthodontists.[22] The use of protocols has been emphasised in the literature and their importance is unquestionable.[7,10,22]

CHAPTER 2: LITERATURE REVIEW

2.1 THE EMBRYOLOGY OF CL/P

In the early stages of the formation of the head, the embryo comprises three different layers of tissues; the ectoderm, mesoderm and endoderm.[23] Neural crest cell migration results in the formation and reinforcement of the mesenchyme that is important in the formation of the face, and also contributes to the development of the first pharyngeal arch.[5]

The development of the human face begins at the 4th week, and is completed by the 6th week of prenatal development. The face develops from two paired maxillary and mandibular prominences and the unpaired frontonasal prominence. Condensation of ectoderm within the frontonasal prominence results in the formation of paired nasal prominences. A central pit forms within the nasal prominences to become the nasal pit. Nasal prominences become divided into lateral and medial prominences which fuse and become the median nasal process. This gives rise to the dorsum of the nose, the philtrum, the columella and the primary maxilla from which incisors erupt. A failure of fusion between the medial nasal prominences results in midline clefts.[2,24]

The maxillary process fuses with the median nasal process to complete the formation of the upper lip. Failure of fusion will lead to a cleft between the philtrum and the upper lip. The maxillary process also fuses with the lateral nasal process, and failure of this fusion results in a cleft face.[2] The maxillary process also fuses with the mandibular process to form the lateral aspect of the cheek: failure of this fusion leads to a facial cleft.[2]

The palatal shelves fuse to form the secondary palate, and failure of this fusion results in an isolated cleft palate. The secondary palate also fuses with the primary palate anteriorly: failure will lead to a cleft alveolus. Failure of fusion of the palatal shelves and between the primary and secondary palate will lead to a complete cleft palate.[24]

The lower jaw and lower lip are derived from the mandibular prominences. Though rare, failure of fusion of these prominences may lead to clefts of the lower jaw and lower lip. When present, these clefts may lead to hypoplasia of the mandible when severe. Minor defects such as a notch in the vermillion border may also be seen. Clefts affecting the mandibular prominences can also affect the tongue and structures in the neck and sternum.[25]

2.2 DEVELOPMENT OF THE MAXILLA AFTER BIRTH

Multiple theories of craniofacial development have been widely reported in the literature as described by Carlson in 2005.[26]

2.2.1 The theory of bone as the primary determinant of growth

Brash et al. (1934)[27] reported on the remodelling theory of the cranial base. This postulated that all craniofacial skeletal growth occurs exclusively by bone remodelling, which involves selective addition and resorption of bone at its surfaces. They therefore concluded that bone is the primary determinant of its own growth. However, cleft patients present with parts of the craniofacial skeleton missing; even though the actual process of bone deposition and remodelling may not be affected, this will not result in normal growth as there will be no continuity of the bony segments.

2.2.2 The sutural theory

According to this theory, "*the connective tissue and cartilaginous joints of the craniofacial skeleton, much like the epiphyses of long bones, are the principal areas at which intrinsic, genetically regulated, primary growth of bone takes place*".[28] This theory supports the statement that transverse growth of the maxilla occurs mostly at the mid-palatal sutures. However, the same may not be true for patients with complete palatal clefts, because there will be discontinuity at the area at which the mid-palatal suture would have been under normal circumstances. Therefore, transverse growth in this area will be affected.[28]

2.2.3 The nasal septal/cartilage theory

This theory suggested that genetic control is expressed in the cartilage, while bone responds passively to being displaced.[26] This epigenetic control theory states that sutures play little or no role in the development of the craniofacial skeleton. The conclusion was that, "*the nasal septum is most active and important for craniofacial skeletal development in late prenatal and early postnatal age, during which time the antero-inferior growth of the nasal septal cartilage pushes the midface downward and forwards*".[26] This was thought to result in growth of the nasomaxillary complex in a downward and forward direction from the cranial base, with the cartilages of the cranial base synchondrosis playing a major role in craniofacial growth. In complete bilateral CL/P, if this theory is true, there would be asymmetric midfacial growth as the nasal septum will only be attached to the primary palate and not the rest of the secondary palate. This may result in protrusion of the primary palate labially, hence the need for nasoalveolar moulding in these patients.

2.2.4 The functional matrix theory

The Functional Matrix Theory was introduced in 1962, and was recently modified by Moss in 1997.[29] This theory postulates that, "*the soft tissues in which the skeleton is embedded are the primary determinant of growth, whilst cartilage and bone respond secondarily to it*". [29] Moss theorised that growth of the maxilla and mandible is determined by the enlargement of the nasal and oral cavities in response to increased functional needs with age. Vertical growth is influenced by the development of the alveolar bone containing the teeth. Transverse growth occurs mostly at the midpalatal sutures. The buccal eruption of permanent teeth with deposition of bone in that area also contributes to the transverse growth of the maxilla and mandible.[29]

Failure of the normal lengthening of the cranial base and growth of the maxilla in conditions like achondroplasia,[30] and some congenital syndromes like Apert syndrome, may result in midfacial deficiencies.[31] In CL/P patients, the anatomical abnormalities may render this theory redundant as normal function is hindered by such congenital abnormalities.

2.3 INCIDENCE OF CLEFT LIP AND PALATE

CL/P is the most common craniofacial abnormality.[1,2,6,32] In South Africa the incidence has been reported to be 0.1 - 0.4 per 1000 live births. In North America the incidence is approximately 1 in 940 live births each year, with the highest incidence seen among First Nation North Americans, followed in decreasing order by Asians, Caucasians, and African-Americans. CL/P has been reported to be higher in males, whereas females were mainly affected by CP.[33,34,35,36]

In the UK, the incidence of CL/P in the Trent region between 1973 and 1982 was reported to vary each year from 1.47 per 1000 live births in 1974 to 0.91 per 1000 live births in 1982.[37] The incidence in a Danish population from 1976-1981, was reported to be 1.89 per 1000 live births (isolated sub mucous clefts were excluded). The distribution of clefts in both of these studies was in accord with other reports in the literature.[36,38]

A higher incidence of CL/P has been reported in Caucasians and Hispanics and a lower incidence in Asian and Caribbean groups.[39] In a South African study in one Province of the country, “Caucasians” were reported to have a low frequency of CL/P with a predominance of

CP, whilst CL was not found. In "Coloureds" the frequency of CL was 25%, CP was 42% and CL/P was 33%. Only three "African" patients were evaluated and they presented with CL, making this study invalid in terms of any conclusions drawn.[35]

These reported variations in incidence, are an indication that there may be different aetiological factors that influence the pathogenesis of OFC. However, variations within the same regions could be attributed not only to environmental factors, but also to hereditary factors.[1]

2.4 THE AETIOLOGY OF ORO-FACIAL CLEFTS

There is still a lack of understanding of the aetiology and pathogenesis of OFC. This could be a reflection of the diverse processes involved at the molecular level during embryogenesis.[5]

The role of inheritance in the aetiology of OFC has been well reported. The sibling risk for CL/P is estimated at 30 times higher than the normal prevalence worldwide. The rate in monozygotic twins was estimated at 25-45% compared with 3-6% in dizygotic twins.[39,40] Single gene mutations varying in the level of expressivity and penetrance are responsible for syndromic disorders. There is a broad range of variations in structure and number of gene mutations that can cause altered gene function due to gene malformation. Deletions and duplications also play an important role in the aetiology of OFC.[39]

Environmental factors are also reported to play a major role. These may include prescription drugs, maternal smoking, consumption of large amounts of alcohol during pregnancy, pre-pregnancy diabetes mellitus, maternal obesity and maternal stress.[1,5] The high rate of dissimilarities among monozygotic twins is an indication that environmental factors play a critical role in many cases of CL/P.[39] Drugs such as phenytoin, and the positive or negative effects that dietary vitamins may play in CL/P have also been reported to be causative factors.[5,41]

Metabolic imbalances such as Vitamin A and folic acid deficiency have also been associated with OFC.[1] Alcohol consumption during pregnancy can lead to excess or deficiency in nutrition, which may lead to congenital defects of the neural tube, orofacial clefts, and other conditions such as congenital heart diseases and neurological abnormalities.[42] Maternal stress has been implicated in creating increased levels of corticosteroids which act as a teratogen and result in elevated corticotrophin hormones.[43] An increase in life stressful events has been shown to be directly proportional to the incidence of birth defects especially CL/P.[44]

Coupland et al. (1988)[45] observed a seasonal variation in CL/P with CP having the greatest variation in the month of August and the lowest in April. In patients with CL/P, the greatest occurrence was in December and the lowest in May. A seasonal variability has also been reported in neural tube defects.[37] High maternal and paternal age have also been implicated in the increased incidence of CL/P.[45]

2.5 CLASSIFICATION

CL/P morphology or embryologic principles have been used to classify OFC.[46]

Davis and Ritchie. (1922) introduced a classification system that categorised clefts into three groups according to the position of cleft in relation to the alveolar process.[47] They grouped the clefts into:

Group I: Pre alveolar clefts (unilateral cleft lip, bilateral cleft lip or median cleft lip).

Group II: Post alveolar clefts (cleft hard palate alone, cleft soft palate alone, cleft soft and hard palate and sub mucous cleft).

Group III: Alveolar clefts (unilateral, bilateral or median clefts).

Veau proposed the following classification (cited in Shah et al, 2011):[46]

Group 1: defects of the soft palate only.

Group II: defects involving the hard and soft palate extending not further than the incisive foramen, thus involving the secondary palate alone.

Group III: complete unilateral cleft, extending from soft palate to the alveolus, usually involving the lip.

Group IV: complete bilateral clefts, similar to group III but bilateral.

Kernahan et al. (1958) (cited in Shah et al, 2011 and Allori et al 2016)[46,48] proposed a system that categorised clefts according to the embryology. In this system the incisive foramen was designated as the dividing structure.

Group I: clefts of the primary palate up to the incisive foramen.

Group II: clefts of the soft and hard palate up to the incisive foramen sub grouped into unilateral or bilateral.

Group III: clefts of the soft or hard palate but not up to the incisive foramen; can be complete or incomplete as well as unilateral or bilateral.

In 1976, Tessier[2] proposed a classification system for facial clefts where 14 different clefts were described according to their location in relation to the eye and orbit. Clefts of the lip, alveolus and palate were classified under categories 1, 2 and 3, with class 3 also involving the buccal and orbital areas.

Kreins (cited in Shah et al, 2011 and Allori et al, 2016)[46,48] proposed the LAHSHAL classification system for CL/P, which has since been modified on the recommendation of the Royal College of Surgeons of Britain in 2005 by omitting one “H” from the acronym

“LAHSHAL”. Fig. 1 shows a diagrammatic classification of CL/P used in this system which divides the mouth into six parts:

Right Lip,

Right Alveolus,

Hard palate,

Soft palate,

Left Alveolus

Left Lip.

The LAHSAL system indicates complete cleft with capital letters and an incomplete cleft with small letters. No other characters are used to indicate clefts.

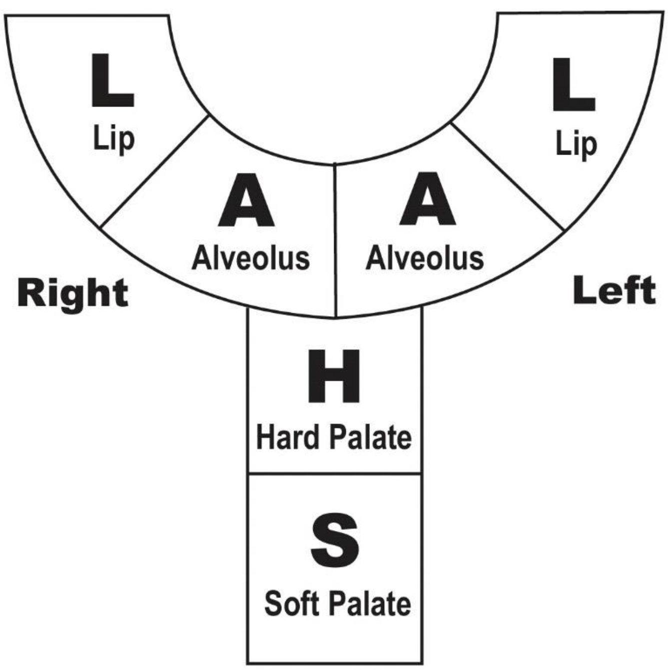

Figure 1. The LAHSAL code[46,48]

Allori et al. (2016),[48] proposed a new classification scheme that sought to simplify the previous systems and yet give the relevant details needed for a proper diagnosis of CL/P.

Millard in 1976,[49] published an historical review of the classification schemes at that time and concluded that because of the differences in languages across the world, there were inaccuracies, a lack of simplicity and omissions that led to none of the classification schemes being universally accepted. The situation is much the same today.

2.6 THE IMPACT OF ORO-FACIAL CLEFTS

Children with CL/P have a multitude of challenges to face as soon as they are born, the most immediate being the aesthetic compromise and feeding problems. Later complications include speech, hearing, malocclusion, oronasal fistula, and missing teeth.[2,7,50]

2.6.1. Family

For many families, having a child with CL/P can be a devastating event. After the birth, families can be subjected to many myths that can increase the stress already felt. Religious and cultural beliefs together with socio-economic circumstances all impact on people's reaction and their attitudes towards the child with a cleft. These are compounded by any lack of knowledge regarding CL/P on the part of both parents and family, which can add to the emotional stress that comes with caring for these children.[51,52,53]

2.6.2. Feeding

Studies have reported that feeding problems vary with the patients' anatomic lesion.[54,55] Children with CL/P as their sole problem are able to swallow normally but have an abnormal suckling action. A CL/P will prevent negative pressure generation unless the deficit can be sealed. The inability to create a good seal during suckling results in aerophagia, which may lead to malnutrition if not attended to.

Various feeding methods have been developed to help optimise feeding in these children, but some are dependent on the surgery performed.[56,57]

2.6.3. Respiratory Problems

Children with CL/P have varying respiratory problems due to the anatomic variations of their clefts. In CL/P children with Pierre Robin sequence, there is a retrognathic mandible together with glossoptosis, which will result in difficulty breathing due to blockage of the airway by the low set tongue and the retrognathic mandible. Children who present with U-shaped palatal clefts, may have the tongue dislodging into the cleft with displacement into the nasal cavity resulting in airway obstruction. A reduced severity of airway compromise has been reported in children who present with concurrent ankyloglosia and mid-facial hyperplasia.[57,58]

The incidence of airway related problems is reported to be higher during paediatric anaesthesia, and CL/P has also been included in this problem.[59] A prospective cohort study in Nigeria[59] reported that adverse perioperative airway events in CL/P surgery are common and most likely associated with combined CL/P. The patients had a higher occurrence of difficult intubation, compared with those with isolated lip or palatal defects.[59] These complications have been reported to occur immediately following extubation or in the early postoperative period.[59,60,61]

A retrospective study of 215 infants with Fairbairn-Robin triad, which is a syndrome associated with CL/P, reported that interventions to prevent airways obstruction could be non-invasive. During CL/P surgery the children were treated with suction and drinking plates together with other feeding aids.[57]

2.6.4. Hearing and middle ear infection

Cleft palate patients have a greater incidence of hearing loss compared with the general population. The main cause is Eustachian tube dysfunction, caused by abnormal insertion of the tensor veli palatini muscles into the posterior margin of the hard palate, and associated muscular hypoplasia.[62,63] A study of 66 patients with repaired and unrepaired cleft palates reported that in both groups there was a high rate of middle ear infection and low complaints of hearing loss or any associated symptoms. They concluded that cleft repair did not influence the frequency of middle ear infection.[62]

2.6.5. Speech

In patients with complete clefts of the soft and hard palate, air escapes through the nasal cavity due to the inadequate seal as a result of the soft and hard tissue defects. This results in velopharyngeal incompetence. This is one of the most common problems encountered in children with CL/P, which can contribute to the hyper nasality of speech often observed in these children. It is also a major aetiological factor that influences the speech production capabilities of a child with cleft palate.[62,64]

Speech development was reported to improve in CL/P patients with early repair, and those children with delayed repair failed to develop acceptable speech spontaneously.[65] This was attributed to the presence of anterior and posterior air escape which should be repaired with a pharyngeal flap.

2.7 MANAGEMENT OF CLEFT PATIENTS

The multitude of problems that these patients present with requires a multidisciplinary team approach. The following has been suggested by the American Cleft Palate-Craniofacial Association:[50]

Maxillofacial and Oral Surgeons, Plastic surgeons, Otolaryngologists, Orthodontists, Paediatric Dentists, Speech pathologists, dieticians, Paediatricians, Geneticists, Genetic councillors, Social workers, Psychologists and Nurses.

Management should start at birth, continue to adulthood, and be instituted in different stages of development. Treatment protocols have been proposed, which assist in the coordination of events amongst the multidisciplinary team members in their efforts to treat these children.[50]

2.7.1 Pre-Surgical Orthopaedics and Orthodontics

There is a variety of methodologies and devices available, the long term outcomes of which are inconsistent.[65] The main aim of pre-surgical orthopaedics is to reduce the size of the alveolar gap and the distance between the mediolateral alar cartilages, as well as to increase the projection of the nasal tip. This is to achieve approximation and alignment of the alveolar segments and to a certain degree, correct the nasal soft tissue and cartilage deformity. Although there is consensus on the advantages and disadvantages of the different methods, there is no consensus in the literature on the best protocol for the treatment of CL/P in infants.[66,67]

A study on the revision rate of SABG in 101 unilateral CL/P patients divided into two groups according to pre-surgical orthopaedic/orthodontic treatment, reported low revision rates in orthopaedic/orthodontic prepared patients and high revision rates in those who did not receive orthodontics and orthopaedics prior to SABG.[68]

Two types of appliances are broadly used in pre-surgical orthopaedics, passive and active. The Hotz plate is a passive appliance reported to have a positive impact on the maxillary growth of cleft patients.[68,69] An active appliance uses a screw which is activated to assist in the alignment of the cleft defect.[65,71] The nasoalveolar moulding (NAM) appliance has been recommended for alignment of the cleft segments and it has been reported to reduce the requirement of SABG when used in conjunction with gingivoperiosteoplasty (GPP).[72,73,74]

Orthodontists and paediatric dentists play important roles in the treatment of CL/P patients undergoing lip and palate repair. Cleft lip is usually repaired at the age of 3-6 months, to facilitate good aesthetics, feeding and speech development as well as proper facial growth.[69] The palate is repaired to provide normal speech, hearing, and swallowing, to facilitate normal dental occlusion and to separate the nasal and oral cavities.[81-83] The paediatric dentist provides information on oral health, nutrition, and dental treatment.[70] Orthodontists provide treatment of the primary dentition, assist with the alignment of the dentition and the dentofacial skeleton, provide treatment in the mixed dentition to facilitate the SABG procedure, as well as providing permanent dentition treatment including orthognathic surgery.[84]

2.8 REPAIR OF ALVEOLAR CLEFTS

The main objective of cleft repair is the optimisation of aesthetics and functional outcomes while taking care to reduce complications with the least amount of surgical intervention.[71] Alveolar defects need repair to stabilise the bony segments especially in bilateral clefts, to close any ONC present, to provide bone for eruption of teeth, and to provide a suitable environment for a healthy periodontium which is essential for survival of the teeth closest to the cleft area. Repair of alveolar clefts can be done at the same time as lip repair, at which stage this is referred to as primary alveolar bone graft or Gingivoperiosteoplasty (GPP). It can also be done at early, intermediate or late stages depending on the age of the patient, when it is referred to as SABG.

2.8.1 Gingivoperiosteoplasty

This is a surgical procedure that is used to cover alveolar bone defects with periosteal flaps without the grafting of bone into the defects. This is done with the hope of inducing bone formation without grafting. It was, however, discovered that for large bony defects surgeons are forced to expose a significant amount of bone in an effort to cover the defect. This has been attributed to the disturbance in maxillary growth usually seen after this procedure.[72] Millard et al. (1999),[73] introduced pre-surgical orthopaedics in an effort to reduce the gap between the maxillary bony segments at the cleft area. This procedure is used to facilitate stabilisation of the maxilla in patients with bilateral clefts, and also aids the preservation of the lateral incisor and improves arch form.[7,10] This type of bone graft was routinely used before the 1970s, until the negative impact on the developing maxilla was reported.[12] It was shown to result in a high incidence of malocclusion and insufficient bone formation which necessitated further bone grafting at a later stage.[7,10] GPP has been less successful clinically compared with SABG.[10,14,74] However; some studies reported that when preoperative nasoalveolar moulding was used in conjunction with GPP, the need for SABG was reduced by 60% in unilateral cleft lip and palate patients.[75]

2.8.2 Secondary Alveolar Bone Graft

First described by Boyne and Sands in 1972,[9] SABG is a surgical procedure carried out in patients with CL/P after the age of two years, whereby different types of bone materials are grafted into the cleft alveolus.[7, 8] SABG assists in the closure of the oronasal fistula; provides bone for eruption of teeth or for teeth to be moved with orthodontic treatment; establishes continuity of the maxilla and stabilisation of the maxillary arch especially in bilateral clefts;

provides support of the base of the nose; and allows for the placement of implants and therefore reduces the necessity for other prostheses.[8,14,15,74]

SABG is classified according to the age at which it is performed. The early stage is performed from 2 to 5 years, during which the child has a primary dentition, to stimulate the formation of high quality bone which will allow the eruption of the central or lateral incisor closest to the cleft.[7] The intermediate stage can be further divided into an early intermediate stage, in which patients only have primary teeth or mixed intermediates in patients having a mixed dentition. Five-year old patients could be placed into either of these categories. The late intermediate stage is performed between the ages of 6 to 9 years, when the child is in the mixed dentition stage, and has been reported as the most appropriate time for bony support of the permanent lateral incisor and canine, without restriction of maxillary growth.[12] However, some reports suggest that the optimal period of grafting is between 9-11 years.[14] The late stage is performed beyond the age of 12 years which is disadvantageous because it may result in lack of bone support and in root resorption due to direct contact of the bone graft and the roots of teeth adjacent to the cleft.[7]

2.8.3 Types of Grafts

The first recorded bone grafting procedure was in 1668.[73] The characteristics of various bone graft materials that can be used for SABG have been reported to be osteogenic, osteoconductive and osteoinductive. The different graft materials are: autogenous, allogenic, xenogenic and alloplastic bone graft materials, and BMPs.[11]

Cancellous autogenous bone such as from the iliac crest, has been found to integrate with host bone rapidly because of its quick revascularisation; it remodels quickly and responds favourably to spontaneous migration or orthodontic movement of teeth into the site.[14] Cortical bone survival on the other hand, is compromised by the lack of revascularisation due to the thick cortex.[7]

Mandibular symphysis block grafts involve the same operative field and have an embryonic origin comparable to that of the maxilla. The advantages have been reported as the absence of a visible scar; reduction of postoperative discomfort; reduced stay in hospital; faster vascularisation; and an improved preservation of the graft volume.[7]

It is important for the surgeon to be aware not only of the type of bone to be harvested, but also of the complications arising from the different anatomy and function that varies from site to site.[14] The different donor sites that can be used for CLP are:[76]

- Intra oral sites:
    - Mandibular symphysis
    - Mandibular angle
    - Mandibular ramus
    - Maxillary tuberosity
- Extra oral sites:
    - Skull
    - Scapular
    - Rib
    - Anterior/posterior iliac crest
    - Tibia
    - Fibular

The most commonly used autogenous bone grafts in CL/P are the mandibular symphysis and the anterior iliac crest. The anterior iliac crest has both cortical and cancellous bone, however the cancellous bone is the one often harvested for SABG.

A donor site retrospective review of 100 consecutive cases grafted with iliac crest reported that 92% of patients were discharged the day after surgery, with all receiving paracetamol for pain management.[77] Complications at the donor site included superficial donor site abscess, postoperative pyrexia, and seroma. The authors concluded that the iliac crest graft was suitable for SAGB because it had low complication rates and provided enough cancellous bone. A comparative study of patients treated with either endochondral bone (iliac or rib) or intramembranous bone (mandibular symphysis), assessed 30 patients through postoperative and follow-up radiographs to measure the bone height and compare the incidence of complication according to type of bone used. They reported no significant differences in bone height changes and the success rate between the different types of bone used. However, they indicated that if appropriate to the size of the recipient site, the chin bone was a useful graft material in alveolar clefts, as was the iliac bone.[78]

Allogenic grafts eliminate the shortcomings of a donor site, but are associated with the possibilities of viral and bacterial infections; they also do not have the osteogenic potential of autografts, and there is a possibility of graft rejection from an antigenic reaction from the host.[11]

Xenogenic grafts are bovine or porcine. They also lack osteogenic potential, but may be osteoinductive and osteoconductive.

Alloplastic grafts are synthetic bone substitutes made from materials such as calcium phosphates, glass ionomer and collagen. They have no osteogenic or osteoinductive potential, but are osteoconductive.[11]

BMPs are osteoinductive and osteoconductive. Their advantage is that they can be synthesised through the process of recombination and made available as an off-the-shelf material for bone grafting.[79]

2.9 FACTORS INFLUENCING THE OUTCOMES OF SABG

2.9.1 Age at Grafting

There are differences of opinion around the world regarding the ideal age for grafting, with some authorities preferring to graft early and others late.[7,12,14]

Calvo et al. (2014),[80] conducted a prospective study aimed at evaluating the surgical outcomes of alveolar bone grafting in subjects with bilateral CL/P. Twenty five patients were enrolled for the study, resulting in 50 clefts. They divided the subjects into a mixed dentition and a permanent dentition group, and used CBCT to assess the volumetric outcome of SABG. They reported that in the mixed dentition group, 96% of the grafts were classified as successful. In the permanent dentition group the success rate was 65%. They concluded that "*the timing of SABG is an important factor in determining the outcomes of SABG in patients with bilateral CL/P, with increasing age being associated with the worst outcomes*".[80]

2.9.2 Tooth Eruption

The subsequent eruption of teeth into the cleft site after SABG is regarded by many as an indicator of success of the graft.[15,16] The teeth that are mostly affected in a patient with CL/P are the canines, hence there are many reports on the eruption of canines into grafted bone post SABG.[81]

Deeb et al. (1982),[81] reported on 46 patients with alveolar cleft who had already undergone SABG. After a post-operative observation period of two to eight years, they reported spontaneous eruption of canines in 27% of their patients; 17% required surgical exposure, and 56% required both surgical exposure and orthodontically assisted eruption. In their conclusion, they indicated that "*the prognosis for canine eruption through grafted bone was most favourable if the graft is performed at ¼ - ½ canine root formation and when the patient is aged 9-12 years*".[81]

Jia et al. (1998)[82] reported 55 cases of bilateral alveolar bone grafting carried out before canine eruption. Of the 110 clefts, the canine erupted at 101 sites. They concluded that bone grafting before canine eruption had a higher success rate than treatment carried out after canine eruption. However, this has to be interpreted with caution as there was no reported control group.

Eruption of the lateral incisor into the grafted bone has also been reported in the literature. Ozawa et al. (2007)[83] examined the effect that migration of the germ of the lateral incisor into the grafted bone had on eruption factors and bone bridge resorption. They enrolled 25 patients who underwent SABG. They measured the volume of bone immediately post SABG, bone bridge formation six months post SABG and teeth migration into the bone bridge using a computed tomography image analyser. They reported that in patients with CL/P with a tooth germ of the lateral incisor, it was beneficial to do SABG at the age of 5-7 years, preceding eruption of the canine, in order to form a good bone bridge that will facilitate eruption of the lateral incisor and subsequent normal occlusion.

2.9.3 Postsurgical Orthodontics

After SABG, stability of the dental arches and of the occlusion is crucial.[84] Orthodontic treatment in these patients is dependent on the clinical presentation of the dental arch. If there are missing teeth in the cleft area, orthodontists can decide to close or maintain the space for future rehabilitation with implants or a fixed prosthesis. In patients who have moderate to severe maxillary sagittal deficiency who need orthognathic surgery for maxillary advancement, orthodontic treatment should be postponed to age 16-17 years.[85] In patients whose canines take longer to erupt, orthodontically moving them into the grafted bone can help speed up the eruption process and reduce treatment duration.[83]

2.9.4 Types of Graft materials

In CL/P patients, it is widely reported that most centres use autogenous bone grafts with a significant amount of success. Among the types of autogenous bone, the anterior iliac crest graft and the mandibular chin grafts are the most widely used with almost similar results in terms of their success rates and complication rates, although some authors have reported better results with anterior iliac crest graft.[77,78,86]

2.10 EVALUATING THE SUCCESS OF SABG

Due to the controversies surrounding SABG, studies have been conducted regarding its success.[8,10,12,13] It was generally agreed that there was a higher success rate of bone grafts when children underwent operation at a younger age (approximately 5years).[12] This is the time when the central incisors have not erupted and it was believed it will provide better bone support for the dentition.[8] Other studies advocated for the early application of surgical-orthodontic protocols for treatment of patients with CL/P in an effort to prevent postoperative bone resorption, and facilitate correct positioning of the teeth.[13,14] However, in the United

States some investigators recommended SABG at the 9 to 11 year age range or before eruption of the permanent canine.[8]

The success of SABG has been attributed to many factors including: the permanent canine position; the eruption stage of the canine when grafting; the role of orthodontic therapy; the surgical protocol used; and the type of bone graft used.[8,11,14] More studies that evaluate the outcomes of these types of grafts are required to help determine a consensus for treatment protocols.[15,16] The long term success evaluation criteria of SABG are reported to be: restoration of the width and height of the maxillary ridge; the overall periodontal health; eruption of the incisor and canine on the side of the cleft; and sufficient healthy masticatory mucosa on the cleft side.[13]

Several radiographic studies have been conducted to assist with the assessment of long term outcomes.[13-17] The grafted bone usually undergoes remodelling while angiogenesis and maturation of bone is taking place. The bone eventually transforms into normal trabecula bone by three months after grafting. It is therefore logical to assess bone fill at least three months post SABG.[14]

Bergland et al. (1986)[14] introduced a scale that used inter-alveolar septal height as a landmark for grading without assessing bone at the root level. This was used as the "gold standard" for evaluation of the success of SABG. Kindelan et al. (1997)[17] also introduced a four-point scale comparing the amount of bone fill at the site of the graft using pre- and post-operative occlusal radiographs while testing intra- and inter-observer reliability.

Witherow et al. (2002) [15] discovered a flaw in the Bergland scale whereby a defect in the bone at the root level could be detected but yet the interdental bone height was normal, resulting in the graft being considered a success. As a result of those flaws in the Bergland scale, they introduced the Chelsea scale which made use of the teeth on either side of the cleft present before or after the eruption of the canine. Intra-oral radiographs were used to measure the amount of residual bone after bone grafting. Therefore, unlike the Bergland scale, the Chelsea scale assesses the bone level along the full length of the root surface. The cleft is bisected vertically into two equal halves, whereas the teeth beside the cleft alveolus are divided into 4 quarters along the root length, resulting in an 8-point matrix. Measurement of the bone is then carried out using the midline of the cleft measured from the two teeth.[15,16]

Even though these radiographic scales differed, the common denominator was the fact that they all used 2D radiographs which overestimate the results, because they measure the height but not the volumetric infill within the defect of the cleft.[12] However, the Chelsea scale has improved on the previous scale and was found acceptable to use in studies such as this.

The emergence of CBCT scans has revolutionised the evaluation of the amount of bone post-SABG. CBCT offers 3D images that do not overestimate the results and are able to measure the length, width and height of alveolar bone grafts.[18] Their versatility also allows reproducible measurements of the volume of alveolar cleft defects and therefore can be used in pre-surgical planning and to assess the volumetric outcome.[18,19,87]. It is for these reasons that CBCT in conjunction with the Chelsea scale method was used in this study.

CHAPTER 3. AIMS AND OBJECTIVES

3.1 RATIONALE

As SABG for CL/P patients requires a multidisciplinary team approach, it is important to coordinate the planning of treatment, especially between maxillofacial and oral surgeons and orthodontists.[7] Our institution only recently started offering SABG to CL/P patients, and the outcomes have not yet been studied; indeed this has not been studied in South Africa.

3.2 AIM

The aim of this retrospective study was to determine the outcomes of secondary alveolar bone grafts in cleft patients treated at the Wits Dental Hospital situated at the Charlotte Maxeke Johannesburg Academic Hospital.

3.3 OBJECTIVES

1. To record the demographic data of patients who had secondary alveolar bone grafts.
2. To assess the outcomes of SABG by evaluating the clinical variables of: canine eruption; keratinised tissue around teeth close to the cleft; and closure or persistence of oronasal fistula.
3. To assess the outcomes of SABG by evaluating the quantity of bone post SABG on 2D CBCT images using the Chelsea scale and the 3D images produced by the CBCT scans.
4. To calculate the success or failure of SABG.

CHAPTER 4. METHODOLOGY

4.1 STUDY SAMPLE

All records of CL/P patients treated with SABG were enrolled for the study, and only those who were at least three months post SABG were included for the study.

Those excluded were patients with other orofacial cleft deformities without cleft alveolus, those with missing records, and those who were lost to follow up. Majority of patients in this study were still being followed up when the study was completed.

4.2 DATA COLLECTION

A structured, pre-tested record review form, (Appendix 1) was used to obtain demographic, clinical and treatment information on each CL/P patient from their hospital records.

The following information was collected from the records: age; gender; 'race'; type of cleft; type of graft; date of surgery; eruption of teeth, missing teeth, complications; details of pre- and post-operative orthodontic treatment and postoperative CBCT. The classification 'race' was recorded according to the 'population groups' as defined pre-1994 before the democratic elections, and does not imply that any genetic differences contribute to the outcomes. Rather, any differences observed are most likely to be due to environmental and hereditary factors, so the 'population groups' may merely be proxies for these differences.

The Chelsea scale[15] was used to measure the amount of bone at the graft site on 2D CBCT images, which is important in determining whether there is enough bone present before orthodontic teeth movement and whether the graft is successful or not. Although the Chelsea scale makes use of the teeth on either side of the cleft present before the eruption of the canine tooth, in this study it was used even in patients who already had erupted canines and in those that had the cleft space closed by teeth that were orthodontically moved into the grafted bone.

Traditionally, with the Chelsea scale, intra-oral and panoramic radiographs are used to measure the amount of residual bone after SABG. However, for this study 2D CBCT images were used instead of conventional 2D radiographs.

To compute the Chelsea scale measurements, the cleft site was bisected vertically into two equal halves, and the teeth on either side of the grafted area were divided into four quarters along the root length. Each root quarter was allocated a score depending on the amount of bone in that area. The measurements were recorded as follows: A score of 0 was given if no bone was detected from the root surface to the midline of the cleft; 0.5 if bone was present but did not reach the midline; and 1 if bone from the root surface reaches the midline. This resulted in an 8-point score as shown in Fig. 2.

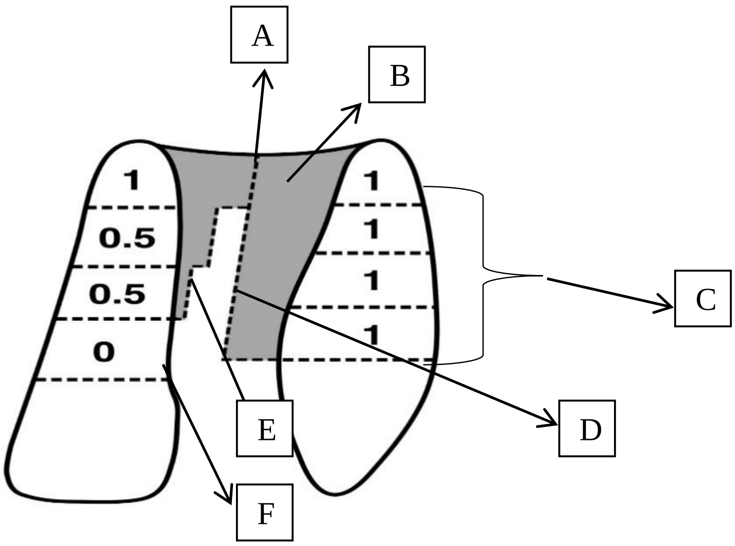

Figure 2. Chelsea scale measurements: A: vertical line dividing the grafted cleft area; B: bone following SABG; C: tooth divided into four quarters; D: bone level reaching the midline; E: bone level not reaching midline; F: no bone.

In addition to the Chelsea scale measurements; axial, coronal and sagittal CBCT 3D images were also used in cleft areas where the spaces were still maintained, to measure the residual bone at the graft site as depicted in Fig. 3.

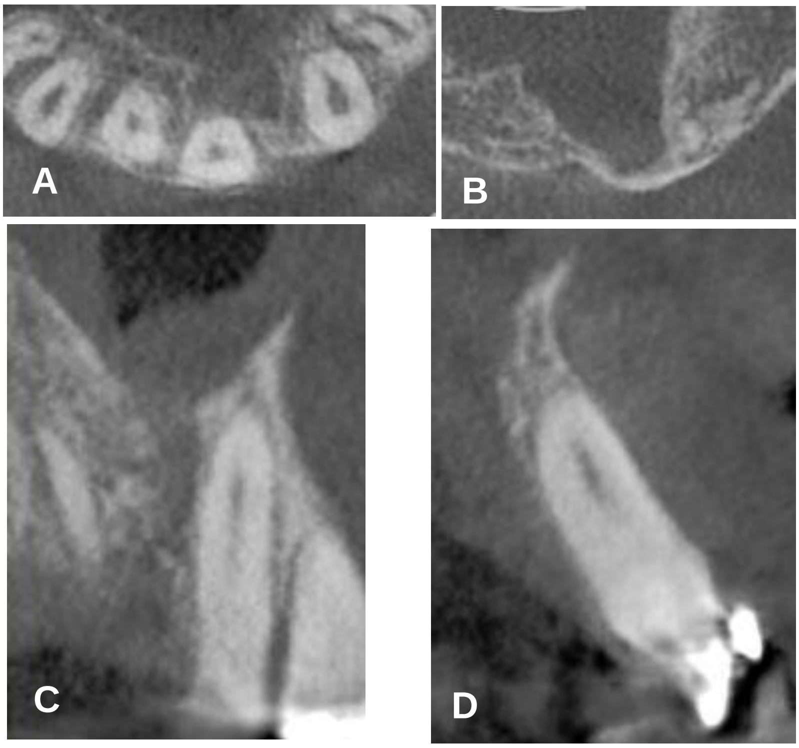

Figure 3. 3D CBCT views. A and B: Axial; C: Coronal; D: Sagittal

In cases were teeth had already erupted into the graft and the cleft space closed by the teeth, the examiner modified the Chelsea scale in an effort to measure the bone around the teeth at the former cleft site. The interdental spaces on the mesial and distal aspects of the tooth that erupted into the former cleft site were vertically bisected and the roots divided into quarters, with bone measurement also carried out as it is for the Chelsea scale, as demonstrated in Fig. 2 above, and Fig. 4 below. This was done in an effort to emulate the Chelsea technique, to facilitate measurement of bone around the erupted teeth.

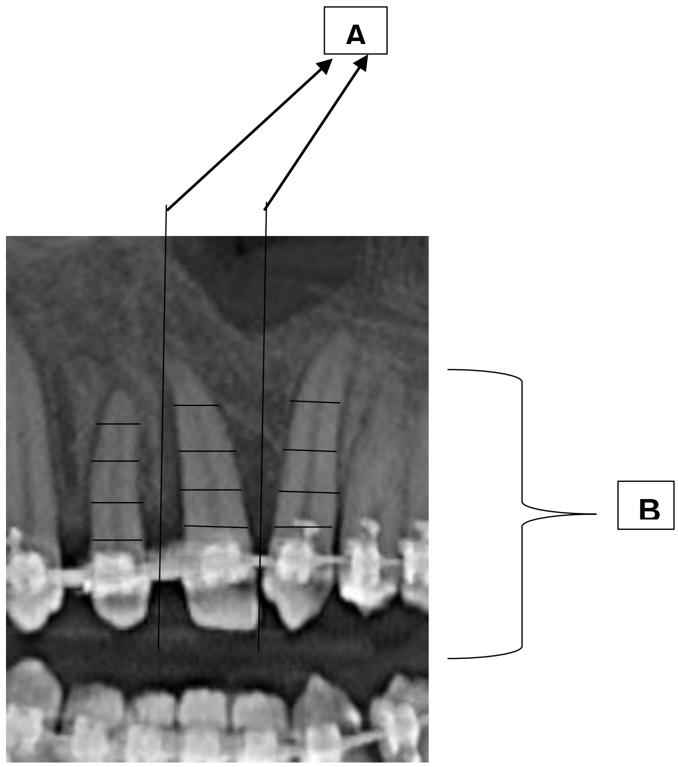

Figure 4. A modification of the Chelsea scale measurements in cases where teeth were moved into the graft site. A: vertical lines bisecting the interdental bone; B: horizontal lines dividing the teeth into quarters.

3D CBCT images of axial, coronal and sagittal views were used to measure the amount of bone from the palatal and buccal aspects of the teeth found in the graft area (Fig. 3, D). This was done in an effort to measure bone in those surfaces because the Chelsea scale does not have a provision for measuring these surfaces. The information obtained was correlated with that obtained from the Chelsea scale measurements.

Success of SABG was defined based on the number of outcome variables regarded as clinically successful. In this study we had 5 main outcome variables: teeth eruption into cleft site, keratinised tissue around teeth closest to the cleft, closure of ONC, functional stability and amount of alveolar bone around teeth that erupted into the cleft site. Each variable was weighed at 20%; therefore the total of the five variables combined makes 100%. Any outcome variables regarded clinically successful or failed, would add or deduct 20% to the final calculation of overall success or failure of SABG respectively. Any patient who scores 60% and below would be regarded as having a failed SABG treatment, and any patient who scores more than 61%, would be regarded as having had successful SABG treatment.

4.3 DATA MANAGEMENT AND ANALYSIS

- Data were entered into a Statistical Package for the Social Sciences (SPSS) data file, cleaned and coded to allow analysis using SPSS software (version 24).
- Chi-squared tests and logistic regression were used to determine if there were statistically significant associations between categorical variables such as canine eruption, type of clefts and type of grafts.
- Frequency tables and custom tables were used to assess frequency counts and respective percentages.

4.4 ETHICAL CONSIDERATIONS

Ethical clearance (M170619) was granted by the Human Research Ethics Committee of the University of the Witwatersrand (Appendix 2). Permission to access patient records was granted by the Head of the Department of Maxillofacial and Oral Surgery (Appendix 3), and the Chief Executive Officer of the Wits Dental Hospital (Appendix 4). Unique patient identifiers were allocated to each patient’s records to ensure anonymity.

CHAPTER 5: RESULTS

5.1 SAMPLE CHARACTERISTICS, FREQUENCIES AND PERCENTAGES

Nineteen patients who only had SABG done at WOHC were enrolled for the study. The majority were African males and most had their grafts before the age of 10 years. The majority of patients presented with left unilateral clefts, which were recorded to be cleft of the lip, alveolus and palate. One bilateral cleft patient presented with a premaxilla that had resorption of most of the underlying alveolar bone together with missing incisors, with no records of any tooth extractions found in the patient's file. The sample characteristics are shown in Table 1.

Table 1. Characteristics of the SABG sample

Characteristics	Frequencies and (percentages)
Sex/Gender	19 (100%)
Female	9 (47.4%)
Male	10 (52.6%)
Age	
Interquartile range	8
Median	12
Race	N=19
African	7 (36.8%)
"Coloured"	5 (26.3%)
Indian	3 (15.8%)
White	4 (21.1%)
Distribution of cleft	
Left	11 (57.8%)
Right	4 (21.1%)
Bilateral	4 (21.1%)
Description of cleft	
Lip and alveolus	2 (10.5%)
Lip, alveolus and palate	17 (89.5%)

The sample age was not normally distributed. The age range was 09 years to 27 years. The majority of patients were grafted before the age of 15 years. The median of the sample was 12 (Fig. 5).

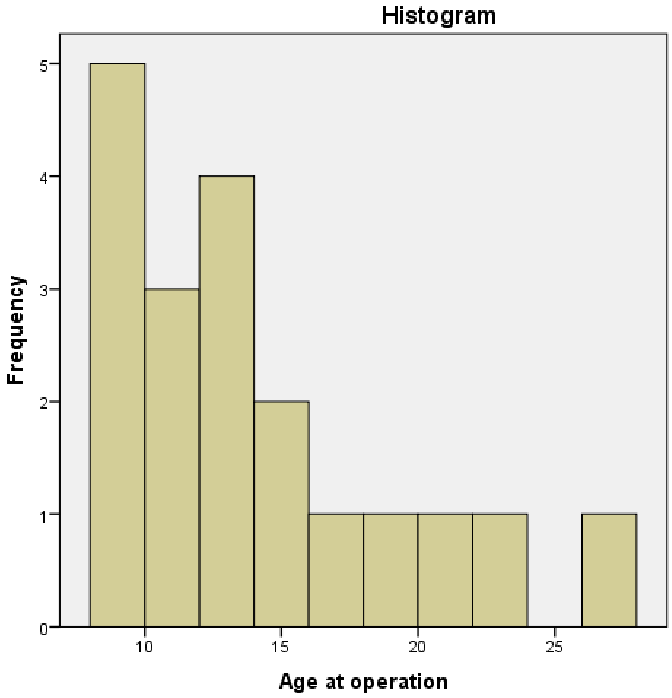

Figure 5. Histogram of age in years, and frequency at the time of SABG

Table 2 shows the characteristics of the type of grafts and the complications recorded from the sample. All patients received autogenous bone grafts and the majority were chin grafts. One patient who received a chin graft was later re-grafted with an allogenic graft due to resorption of the chin graft. The same patient had multiple supernumerary teeth extracted at the time of SABG. The oronasal fistula that this patient also presented with was persistent after both SABG procedures. Seventeen patients were reported to have presented with oronasal fistulae. Fifteen patients were found to have partial alveolar bone resorption at the graft site; they were therefore categorised as having “partial current graft resorption”.

Table 2. Characteristics of types of grafts and complications

Characteristics	**Frequencies and (percentages)**
Total grafts	23 (100%)
Autogenous	22 (95.6%)
Iliac	7 (30.4%)
Chin	15 (65.2%)
Allogenic	1 (4.4%)
Alloplastic	0
Xenogenic	0
BMPs	0
Complications	-
Previous graft failure (complete resorption)	1 (4.4%)
Current Graft resorption (partial)	15 (65.2%)
Infection	1 (4.4%)
Oronasal fistula after SABG	4 (17.4%)

Eighteen patients were recorded to have keratinised mucosa around the erupted canines. Some of the canines erupted before and others post SABG. Some canines erupted into the grafted bone, whilst others (8) were orthodontically moved into the grafted bone and aligned into occlusion (Table 3).

Table 3. Frequency of canine eruption before and after SABG

Characteristics	**Frequency and (percentages)**
Total number of erupted canines	22 (100%)
Congenitally missing canine	1
Erupted before SABG	9 (40.9%)
After SABG	13 (59.1%)
Orthodontically assisted eruption	0

Table 4 indicates that all patients who did not receive orthodontic treatment (seven patients) had alveolar bone resorption. Two of the five patients who had orthodontics before and after SABG had alveolar bone resorption. Six of the seven patients who had orthodontics only after SABG had alveolar bone resorption. Five patients had supernumerary teeth extracted in the perioperative period, the majority of which were removed at the time of SABG. None of the patients who had perioperative extractions had post-operative infections. Of the five patients who had the extractions during SABG, only one had an additional extraction post SABG. Only one patient had a combination of persistent ONC and alveolar graft resorption post-SABG.

Table 4. Orthodontic treatment, teeth extractions and complications

Case no	Ever had orthodontic treatment	Before SABG	After SABG	Alveolar bone resorption	Teeth extracted	ONC post SABG
1	Yes	Yes	Yes	Yes		YES
2	Yes	Yes	Yes	Yes		
3	No	No	No	Yes	YES	
4	Yes	Yes	Yes	No	YES	
5	Yes	No	Yes	Yes		
6	Yes	No	Yes	No		
7	Yes	No	Yes	Yes		
8	No	No	No	Yes		
9	Yes	Yes	Yes	No		
10	No	No	No	Yes		
11	Yes	No	Yes	Yes		
12	Yes	Yes	Yes	No	YES	
13	No	No	No	Yes	YES	YES
14	No	No	No	Yes		
15	No	No	No	Yes		
16	No	No	No	Yes		
17	Yes	No	Yes	Yes		
18	Yes	No	Yes	Yes		
19	Yes	No	Yes	Yes	YES	

Results of the Chelsea score measurements are shown in Table 5. Patients with bilateral clefts and those that had cleft spaces closed by teeth had two Chelsea scores for the left and right sides and mesial and distal sites respectively. The highest Chelsea score recorded was 8 and the lowest score was 1.

Table 5. Chelsea score results

Case no	Chelsea scores
1	R= 6.5 and L= 7
2	4
3	4
4	R= 7 and L= 8
5	2
6	R= 6 and L= 7
7	5
8	R=2 and L=5.5
9	R= 7 and L= 8
10	5
11	R=3 and L=3
12	L= 7.5 and R= 8
13	3.5
14	6
15	R= 1 and L= 1
16	L= 3.5 and R= 7
17	R= 4.5 and L= 8
18	L= 8 and R= 8
19	R= 8 and L= 7

Table 6 shows the results of the 3D CBCT findings of different types of grafts as seen on axial, coronal and sagittal views. They show that the majority of patients had residual clefts in the piriformis and nasal floor, but most importantly fifteen patients had partial alveolar bone resorption in the alveolar graft site. Only 4 patients did not have alveolar graft resorption. The only outstanding difference was the fact that none of the iliac graft patients presented with distal missing bone. Only one patient presented with buccal bone resorption in the chin graft category.

Table 6. 3D CBCT findings with comparison of chin and iliac grafts

Case no	**Chin grafts**	**Iliac grafts**
	Areas of bone defects post SABG	
1		Palatal, mesial, piriform and nasal floor and alveolar cleft
2	Palatal, piriform and nasal floor and alveolar cleft	
3	Palatal, piriform and nasal floor and alveolar cleft	
4	Palatal, distal, and piriform	
5	Mesial, piriform and nasal floor and alveolar cleft	
6	Palatal, piriform and nasal floor	
7	Palatal, piriform and nasal floor and alveolar cleft	
8		Mesial, left piriform and bilateral nasal floor and alveolar clefts
9	Palatal and mesial	
10		Palatal, piriform, nasal floor and alveolar cleft
11	piriform, nasal floor and alveolar cleft	
12	Buccal	
13	piriform, nasal floor and alveolar cleft	
14	Distal, piriform and alveolar clefts	
15		Mesial, piriform, nasal floor and alveolar cleft
16	Palatal, piriform, nasal floor and alveolar cleft	
17	Alveolar cleft	
18		Palatal, piriform, nasal floor and alveolar cleft
19	Palatal, piriform and alveolar clefts	

5.2 STATISTICAL TESTS

The logistic regression test indicated no statistically significant relationship between SABG complications and other independent variables including canine eruption, orthodontic treatment, supernumerary teeth, cleft location and age. The Fisher's Exact Test and Pearson Chi Squared tests were used to test for associations between: canine eruption and orthodontic treatment; residual clefts and the availability of keratinised mucosa; type of graft and graft complications; and residual bone defects and oronasal fistula. No significant associations were found.

However, when the relationship between location of cleft and missing teeth was tested using the Chi Squared test, it showed a statistically significant relationship between the location of the cleft and the missing right and left maxillary lateral incisors as shown in table 7. The rest of the variables were found not to have any significant relationship.

Table 7. P-values for relationship between side of cleft and missing teeth

Tooth number	P Value
Tooth 12	.002
Tooth 22	.003
Tooth 11	.500
Tooth 13	.138
Tooth 21	.015

5.3 OVERALL RESULTS

Although the sample size in this study was small, it is clear that a clinically successful outcome was achieved. As indicated under methodology, success was defined based on the number of outcome variables regarded as clinically successful. In this study only four patients were regarded as having failed SABG treatment. Three of the four patients were reported to have alveolar bone defects and persistent ONC. One of the four patients presented with non-keratinised mucosa around teeth close to the cleft site, alveolar bone defects and persistent ONC. Fifteen patients presented with 80% clinical success, and according to our success criteria, were regarded as having successful SABG treatment.

CHAPTER 6: DISCUSSION

6.1 CHARACTERISTICS AND DEMOGRAPHICS OF THE SAMPLE

The majority of the patients enrolled for this study were males with unilateral left CL/P; this was consistent with data from previous studies.[33,34,35,36] For example, in a study of 123 CL/P patients, 54% had unilateral CL/P, and 61% were male. The majority of their patients (58%) had left unilateral clefts, 90% of which were CL/P, with cleft lip and alveolus at 11%.[88]

In the present study, the distribution of clefts amongst the different population groups was 36.8% in Blacks, 26.3% in “Coloureds”, 21.1% in Whites and 15.8% in Indians. This was not consistent with the literature,[89] which is not surprising as these are not genetically distinct groupings.

The majority of patients who received SABG were under the age of 15 years, with very few beyond that age group. A retrospective review of patients with SABG which grouped patients into two groups aged 6-8 years and 9 years and older found no statistical significance between the two groups.[8] However a report of 46 patients divided into two groups found that patients who had mixed dentitions and received SABG at ages 10-13 years had better outcomes than the second group of patients aged 15-23 years.[80] These patients had permanent dentitions and received tertiary alveolar bone grafts. Ninety-six percent of the patients in the SABG group had no reported failure, but there was a 27% failure rate in the second group. Therefore the recommendation was that grafting should be done before eruption of the central and lateral incisors to provide bone support for the erupting teeth and to reduce donor site and recipient site morbidity.

6.2 CHARACTERISTICS OF THE TYPE OF GRAFT AND COMPLICATIONS

All patients in this study were grafted with autogenous grafts: the chin was used in 65% of the patients and the iliac crest in 31%. Only one patient had an alloplastic graft which was resorbed. Autogenous grafts have been highly recommended as the grafts of choice, so the surgical team's choice to use them in these patients was consistent with what is recommended in the literature. A retrospective study of 29 patients who had alveolar cleft defects repaired with autogenous mandibular block grafts[90] reported low infection rates, and loss of grafts due to infection in only two patients. Mandibular block grafts are advocated because of their similar embryonic origin to the alveolus, and the fact that they vascularise rapidly compared with endochondral bone grafts.

However, autogenous grafts are known to present with donor site morbidities that may be undesirable to the patient. Donor site morbidity of the iliac crest in children with CL/P was assessed by the patient's complaints and perceptions.[91] Two-thirds of the 50 patients reported no complaints regarding their donor sites, one patient reported pain four years post SABG, and one reported hip discomfort which resolved after physiotherapy. In the current study none of the patients reported adverse donor site morbidity apart from the expected immediate post-operative discomfort, which is consistent with other literature reports.[77]

Seventeen of the 19 patients in the current study presented with an oronasal communication before surgery. Thirteen of those patients had their ONC closed post SABG, but four reported to have persistent ONC post SABG. The two patients who did not have ONC pre-operatively did not develop it post-operatively.

Fifteen patients from the study were found to have partial alveolar graft defects in various areas within and around the graft site, detected on the 3D CBCT images (Fig. 3). Because 3D

CBCT images were not used pre-operatively to assess the full spectrum of the cleft defects, it is not known if the alveolar graft defects are due to resorption or inadequate grafting. The amount of mature bone post grafting (phase two bone) is dependent on the amount of bone that was initially grafted (phase 1 bone), as described by Axhausen et al. (1952).[93] It is possible that the bony defects seen on 3D CBCT images are not as a result of bone resorption but due to insufficient grafting. Multiple causative factors have been attributed to alveolar bone resorption post SABG, resulting in an overall survival rate of 88% and clinical success rate of 60% as reported by Wang et al. (2005).[94]

SABG done after tooth eruption has been reported to cause graft and root resorption in teeth that are closest to the cleft.[7] This has been reported to be due to the direct contact of the grafted bone to the roots of the teeth in the area and the fact that, due to the surgical procedure, the teeth may sustain damage to their periodontal ligaments and cementum leading to root resorption. Because the teeth would have already erupted, the stimulating effect that erupting teeth have on alveolar bone growth will also be lost, leading to increased resorption of bone in the area with resultant poorer outcomes.[7] Deeb et al. (1982), reported that "*the prognosis for canine eruption through a graft site is most favourable if the graft is performed at ¼ to ½ canine root formation and when the patient is aged 9 years to 12*".[81]

Only one patient developed postoperative infection, and oral antibiotics were prescribed and the infection resolved. The cause was probably minor wound dehiscence post SABG. In 2007 Diah et al.[92] reported that inadequate soft tissue closure post SABG can result in soft tissue dehiscence and exposure of the graft to the nasal and oral cavities which can increase the incidence of infections. However, postoperative infection rates seem to vary, as exemplified by a study which reported one donor site infection, and two recipient infections which resulted in complete removal of the graft four weeks post-operatively.[90]

6.3 ORTHODONTIC AND ORTHOPAEDIC TREATMENT

All patients were referred from the department of orthodontics. Most (12) of these patients were reported to have received pre-surgical orthopaedics. It is reported in the literature that SABG done without pre-surgical orthopaedics often results in the surgical procedure being repeated due to the associated complications.[96] However, its indiscriminate use may result in dehiscence of teeth through already compromised bone in terms of quality and quantity. Pre-surgical maxillary expansion can assist with better access to the nasal floor and can allow adequate bone graft material placement.[7,82]

The seven patients who had not received postsurgical orthodontic treatment in this study were all found to have partial alveolar bone resorption. This finding is suggestive of the positive role that post-surgical orthodontics can play in the prevention of graft resorption. Post-surgical orthodontics helps with the stabilisation of the dental arches and the occlusion. Furthermore, the cleft spaces can be closed by orthodontically moving teeth into the grafted bone, which has been reported to help stimulate new bone formation which in turn reduces the resorption rate of the grafted bone.[96] This may be the reason why all the patients who did not have postsurgical orthodontics had partial alveolar bone resorption as seen on the 3D CBCT scans, compared with bone resorption in 67% of those who received post SABG orthodontics (8 out of 12 patients). It has been reported that postsurgical orthodontics could assist with moving teeth that take a long time to erupt into occlusion. This can reduce the treatment duration, but more importantly, moving teeth into the graft could help stimulate osteogenesis and therefore minimise the rate of bone resorption.[7,83]

6.4 PERIOPERATIVE EXTRACTIONS AND COMPLICATIONS

Five of the patients in this study presented with supernumerary teeth. All of them had these removed at the time for SABG and one patient also had a tooth removed after SABG. Gomez et al., 2015, The prevalence of supernumerary teeth has been reported to be about 15%, and most are reported to be found on the cleft side.[97] Extraction of supernumerary teeth at the time of SABG has been discouraged, as it will cause soft tissue defects that may result in exposure of the grafted bone and possible failure.[86] This was the case in one of the patients who received an autogenous graft with simultaneous extraction of multiple supernumerary teeth. The graft was eventually resorbed and was replaced with an allogenic graft which also resorbed. At the time of writing, the patient has yet to be grafted. Even though only one patient who had extraction of teeth during SABG developed ONC, it could suggest that simultaneous extraction of teeth at the time of SABG should be discouraged in order to avoid associated complications as reported in the literature.[86] Extraction of teeth a few weeks before SABG may be beneficial, as it would allow healing and maturation of soft tissues that would lead to less incidence of tissue dehiscence post SABG.

The presence of non-inflamed keratinised tissue around cleft teeth has also been reported to be one of the outcome measures in SABG. In this study, 18 patients had keratinised mucosa around teeth closest to the cleft. A study on periodontal disease in patients with CL/P reported that these patients had a critical periodontal status compared with the normal population. A healthy periodontium around cleft teeth is vital for their survival and special attention should be given to these patients as they present with supernumerary teeth and crowding, all of which can hinder good oral hygiene measures. The presence of keratinised mucosa in the majority of the patients is one of the indications of the success of the surgical procedures. Trauma to the soft tissues during surgery could result in poor soft tissue healing which can compromise the quantity and quality of keratinised tissue post SABG.[98]

6.5 3D CBCT FINDINGS

CBCT scans are an important form of special investigation that offer a 3D image of the area of interest using low radiation doses with the benefit of high resolution images.[12,22] In this study all patients were found to have a certain degree of residual cleft and or resorption around cleft teeth when evaluated using 3D CBCT images. Craven et al. (2007) have argued that failure to appreciate the size and shape of the cleft defect prior to SABG is most likely to result in inadequate reconstruction of the cleft defect.[22]

Traditionally, 2D radiographic images were used to assess postoperative bone fill in cleft patients. These radiographs were found to overestimate the results and it was impossible to appreciate all the dimensions of the bone graft without CBCT.[16] Radiographic scales used to evaluate these grafts are often unreliable as they overestimate the results and only offer a 2D picture of a 3D image.[15,16] With CBCT, operators are able to quantitatively assess the graft.[10,99]

In this study, residual alveolar, piriform, and nasal floor bony defects were discovered in most of the patients from the 3D images. Using these images, bucco-lingual defects were also found. The information obtained from these images was more representative of the actual bone defects compared with those obtained from 2D CBCT images, confirming the superiority of 3D CBCT imaging. Furthermore, assessor agreement has been reported when evaluating outcomes using CBCT.[100]

6.6 LIMITATIONS OF THE STUDY

This was a retrospective study, and the sample size according to the inclusion criteria was small. However, this is the first analysis of its kind carried out in this hospital and will form an important baseline for future follow-up studies.

The majority of patients in this study were found to have residual cleft defects in a number of areas in and around the cleft site post SABG. It is not known if these defects were due to bone resorption post SABG or due to inadequate bone grafting.

CHAPTER 7: CONCLUSION AND RECOMMENDATIONS

7.1 CONCLUSION

Within the limitations of a small sample size, some of the sample characteristics were similar to those reported in a number of studies, although the age distribution was different. The clinical outcomes of this study were found to be good in relation to tooth eruption, keratinised tissue around the teeth closest to the graft site, functional stability, and closure of ONC. A few of the patients had already finished their treatment without any further complaints. Even though most of the patients showed graft defects on 3D CBCT images, the majority of them did not need to be re-grafted because of the good clinical outcomes recorded. 3D CBCT images revealed more details in relation to graft defects, which confirmed their superiority over 2D CBCT images. It is possible that the utilisation of pre-operative 3D CBCT views could have resulted in even more favourable outcomes.

7.2 RECOMMENDATIONS

There is a lack of sufficient data on the use of 3D CBCT imaging in the preoperative planning of SABG and this should be investigated, as it may result in improved surgical protocols and concomitant improved outcomes. For example, information from 3D CBCT images could obviate the need for piriform and nasal floor exploration in some patients, reducing the possibility of mid-facial hypoplasia.

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APPENDIX 1: ETHICAL CLEARANCE

R14/49 Dr Matlaba Machaka

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M170619

NAME: (Principal Investigator)	Dr Matlaba Machaka
DEPARTMENT:	Maxillofacial and Oral Surgery Wits Dental Hospital - Wits Oral Health Centre
PROJECT TITLE:	Outcomes of Secondary Alveolar Bone Grafts in Cleft Patients
DATE CONSIDERED:	30/06/2017
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr M. Mabongo and Prof P. Hlongwa
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	03/07/2017

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in June and will therefore be due in the month of June each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 6-9-2017

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX 2: APPROVAL LETTER BY HOD

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31 May 2018

Ms Modie Maumela
Postgraduate Office
Faculty of Health Sciences

Dear Modie

This serves to confirm that I have seen and approve the corrections made by Dr Machaka for the final submission of his research report "**Outcomes of secondary alveolar bone grafts in cleft patients**"

Yours sincerely

DR E RIKHOTSO
Head of Department
Maxillofacial and Oral Surgery