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Lucky Yadav
Senior Resident, Department of Dental and Maxillofacial Surgery, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India

Renuka Bamal
Senior Lecturer, Department of Orthodontics and Dentofacial Orthopaedics, NIMS Dental College and Hospital, Jaipur, Rajasthan, India

Akanksha Jaswal
Senior Lecturer, Department of Orthodontics and Dentofacial Orthopaedics, Mhatma Gandhi Dental College and Hospital, Jaipur, Rajasthan, India.

Pankaj Pareek
Senior Lecturer, Department of Orthodontics and Dentofacial Orthopaedics, Rajasthan Dental College and Hospital, Jaipur, Rajasthan, India

Ashish Kumar
Senior Lecturer, Department of Orthodontics and Dentofacial Orthopaedics, Rajasthan Dental College and Hospital, Jaipur, Rajasthan, India

Corresponding Author:
Lucky Yadav
Senior Resident, Department of Dental and Maxillofacial Surgery, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India

Secondary alveolar bone moulding in cleft lip and cleft palate: A review

Lucky Yadav, Renuka Bamal, Akanksha Jaswal, Pankaj Pareek and Ashish Kumar

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Abstract
Cleft involving the lip and palate are the most commonly seen congenital deformities that occurs at the time of birth. They are not life threatening unless associated with some syndromes having some systemic complications. Alveolar bone grafting is a common modalities of treatment for improving life of patients with CLCP with multidisciplinary approach. This article discusses secondary alveolar bone graft in detail with future prospects.

Keywords: CLCP, ABG, orthodontics, cleft surgery, cleft lip, cleft palate, alveolar graft, bone moulding

Introduction
Dentofacial clefts have intrigued the medical field for very long time. It is the second most common congenital deformity following clubfoot. It is a group of conditions that includes the lip, alveolar process and hard and soft palates which may be occurred alone or together in combination. World-wide, the rate of incidence is in between 1 and 2.2 per 1000, based on the geological variations [1]. Males with cleft lip and palate and females with isolated cleft lip are usually found [2].
Orofacial clefts may be seen in the both syndromic or non -syndromic form in childrens, the most common syndrome usually related with the lip is van der Woude. Orofacial clefts usually are presented as the cleft lip with or without palatal involvement. The cleft lip may be unilateral or bilateral and associated with an homolateral cleft of the alveolus. The alveolar involvement affects 75% of the patients with cleft lip [3] and area between lateral incisor and the canine is the most commonly affected. Primary cleft palate consists of cleft lip, alveolar process and palate (part of hard palate), while secondary cleft palate composed of CP (rest of hard and soft palate, from the incisive foramen) [4].
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History of Secondary Alveolar Bone Moulding in Cleft Lip and Palate
There is no hiding the blemish of the unrepaired cleft lip. It is likely, for this reason, that the first cleft lip surgical repair goes back to the times of Hippocrates in 400 BC and Galen 150 AD [5]. Constant upgradation in technique and outcomes have continued throughout these years. There are also early reports of surgical correction for cleft palate for similar reasons. In 1764, Le Monnier, a French dentist, repaired a cleft velum as the documented case [6].
The very first documented report of bone grafting to the alveolus were reported in 1901 by Von Eiselsberg. It is documented that he used a pedicled osteocutaneous flap to reconstruct a palatal defect [7]. Drachter in 1914 did the first successful bone graft to an alveolar defect, he utilized a tibial bone graft, including periosteum [8]. Veau attempted a unsuccessful in attempt to graft the alveolar cleft with tibial chips in 1931. Millard wrote that there was a relative lack of enthusiasm for alveolar grafting until the 1950s. During the 1950s and 1960s, many surgeons started employing primary bone grafting of the alveolus during the early months of life. Following is the three-stage operation for primary bone grafting described by Johanson and Ake Ohlsson in 1961 [9].

A relatively early article by Brauer, Cronin, and Reaves in 1962 gave valuable insight into what one group of surgeons and orthodontists were trying to accomplish with "early" alveolar bone grafting. The authors stated that in the unilateral cleft, the "absence of bone and soft tissue" on the cleft side, as well as the pull of the repaired lip on the noncleft side, causes flattening and retrusion of the central face [10]. they belived that early repair of the unilateral alveolar cleft provided a bridge between the retruded cleft side and the maxillary growth center of the cartilaginous septum that was attached to the noncleft side. This early bridging via bone grafting would allow the retruded cleft-sided maxilla to experience more normal growth and result in less maxillary hypoplasia. With regard to the bilateral deformity, the authors felt that the premaxillary segment being bridged to the adjacent maxillary components helped to stabilize and create more predictable/manageable premaxillary/maxillary relationships [10] This same thought process was echoed by Skoog in 1965 when he stated that the alveolar cleft will require "special measures" to prevent or correct collapse of the maxilla; he included bone grafting as one of these "special measures." [11] This technique of early primary bone grafting continued throughout the 1970s in many parts of the developed world.

However, longe-term follow-up and close examination by some called into question the practice of primary alveolar bone grafting. As stated by Millard in Cleft Craft [6], Kenneth L. Pickrell followed 25 patients that received primary alveolar bone grafting and reported the following findings:

1. "Primary rib grafts in the maxilla do not increase in size concomitant with facial growth and development.
2. Teeth do not migrate and erupt spontaneously through a rib bone graft.
3. Rib bone grafts do not form a true alveolar process; a permanent alveolar notch remains.
4. The orthopedic effect of the bone graft decreases as its incorporation increases." [6]

These exact observations were not documented by all of the opponents in regard to primary bone grafting, but definitely there were some other negative observations regarding primary alveolar bone grafting which were documented by other authors.

Epidemiology of cleft lip and cleft palate

The cleft lip and palate anomaly constitutes nearly one-third of all congenital deformations, thus making the most conservative incidence of this anomaly as 1.6 per 1000 live births excluding those associated with syndromes. Robert, Kallen and Harris (1996) [14] pooled the data from five birth registries from California, Sweden and France to document the prevalence of CLP malformations. From their pooled data, they calculated the incidence of CLP as 1.57/1000. The incidence of this anomaly is reported to be highest in Afghans [15] as 4.9 and least in Negroid population, 0.4 per 1000 live births [16]. According to rough estimates, about 30,000 children afflicted with CLP anomaly are born every year in India [17]. Although organised epidemiological surveys to evaluate the incidence of CLP in India are yet to be carried out, more than two dozen studies have been done on newborns in the past three decades for evaluating the incidence/prevalence of congenital malformations in them (including cleft lip and palate). From these reports, the pooled incidence for cleft lip and palate is estimated to be 1.2 per 1000 births and 0.46 per 1000 for cleft palate alone [18]. A recent study conducted in south India reported the incidence of cleft lip and palate as 1.15 and that of the isolated cleft palate as 0.08 per 1000.[19] The incidence of CL ± P anomaly in AIIMS New Delhi Hospital births has been calculated as 1.4 per 1000 live births for CL ± P and 0.3 per 1000 live births for isolated CP [20].

Etiology [21]

- Genetic origin is believed to be cause of less than 40% of the clefts of the lip and palate.
- Mutations in specific collagen genes in Stickler syndrome, homeodomain-containing protein PAX3 in Waarden burg's syndrome, and sonic hedgehog in midline craniofacial defects are examples of direct genetic correlation with cleft lip and palate.
- Environmental factors play key role in gene expression, which affects the phenotype of the individaul. For example, Hwang *et al*. report the direct link between maternal smoking and clefting in newborns. Similarly Antiepileptic drugs also have been linked to clefting. Maternal alcohol consumption is also under extensive debate as an etiologic factor for CLP. Infections (rubella and toxoplasmosis) and growth factor deficiency are among other environmental factors influencing the same [22].

Orofacial clefts are etiologically different in syndromic and non-syndromic form. Non-syndromic form of orofacial clefts occurs in 70% of documented cases, while 30% with orofacial clefts associate with additional congenital anomalies are known to be part of syndrome [23, 24]. Aetiology of orofacial clefts is multifactorial and relate with gene factors, environmental factors, and teratogens etc [25, 26]. Genetic susceptibility is the major contributer of orofacial clefts. Monozygotic twin studies state that genetics account for 40–60% of orofacial cleft [27]. The most widely investigated gene variants are TGF and MTHFR genes. Phenotypes significantly associated with particular partial aneuploidies have identified through the survey of chromosomal deletions and duplications and found 1q25, 3p21, 4p15, 4q32 and 10p15 regions significantly associated with orofacial clefts. Moreover, the identification of candidate genes is made complex by some factors like genetic heterogeneity, departure from Mendelian inheritance patterns, limited availability and the high cost of genomic tools used, and the necessity for very large datasets and there analysis [23, 26, 28, 29].

Orofacial clefts can be influenced by environmental factors. Folate supplementation in early months of pregnancy has reduced the risk from 25 [30] up to 75% [31], although not all studies have reported statistical significant results for the same [32]. Deficiency of zinc causes orofacial clefts in animals [33] and may increase risk in humans too [34]. Maternal diabetes might show non-cardiac defects including orofacial clefts [35]. In case of increased maternal age, the chance of orofacial clefts is more in above 40 years old comparison with 20-29 years old [36]. Maternal smoking enhances the risk of orofacial clefts up to 30% [37] while indirect smoke exposure does not seem to affect its occurrence [38]. It is bit controversial for the maternal alcohol consumption, but excessive drinking increases the possibility [39]. Maternal exposures to effective teratogens like phenytoin, valproic acid and retinoic acid [40] may cause the cleft. Other pobable causative agents such as maternal obesity or infection and hormonal drugs, chemical or radiation exposures, stress etc, [23, 41].

Management of Alveolar Cleft [42]

Management of orofacial clefts is confounding in nature. A well coordinated multidisciplinary collaboration team with

experts like maxillofacial surgeon, orthodontist, speech therapist, paediatrician, phoniatric specialist, otolaryngologist, and dentist is necessary for treating the patient at different stages of growth until maturity [43, 44].

Surgery is the choice of treatment to repair the deformities usually started from early months of life and most of the cases also need additional surgical interventions later in life for better outcomes. Improvement of aesthetics, feeding, speech, breathing and hearing problems, can be achieved by surgical treatment. Along with that patients also need orthodontic help, speech therapy as well as social and psychological services. Treatment plan of orofacial clefts consists of wide verities of treatment in a sequential manner from birth may up to adulthood stages [45, 46].

The alveolar osteoplasty is a surgical procedure to fill up the cleft gap with alveolar bone grafts with aim to remove the oronasal fistula, establishes maxillary arch continuity, limits growth disturbance and helps eruption of permanent dentition into the graft bone, enhance nasal symmetry, orthodontic movement and insertion of dental implants, speech improvement, oral hygiene maintenance and improves of periodontal health [47].

On the basis of growth of palate, alveolar osteoplasty can be classified into:

1. Primary alveolar osteoplasty is done after lip repair but before repair of the palate and should be done <2 years of age. Preferred choice of graft are rib graft and calvarial bone graft are usually used for primary alveolar osteoplasty [48].
2. Secondary alveolar osteoplasty is performed after repair of the palate. It can be categorized into early secondary (2-5 years), early (6-8 years) or late (9- 12 years) mixed dentition, and late secondary grafting (after 13 years age) [49, 50].

Complete palatal cleft and exactly aligned (end to end) alveolar segment are prerequisites for the primary alveolar osteoplasty attempt, because of available space between the maxillary segments will be exerted tension on flap over the graft bone and enhance the possibility post-operative wound dehiscence, disclosure of graft and subsequent collapse of graft [51]. Secondary alveolar osteoplasty helps to form the stable united alveolar arch as well as provide mature bone for supporting the tooth eruption [52, 53]. Secondary alveolar osteoplasty is the most widely used and popular for treating alveolar cleft and commonly chose for the patient with age of 6-13 years, usually before the permanent canine eruption. The alveolar bone graft may be done along with the Le Fort 1 osteotomy procedure which is called tertiary alveolar bone graft (TABG) [60].

Primary Bone Grafting

Primary and early secondary bone grafting were used mainly in the 1950s and 1960s by a whole generation of cleft surgeons [54]. The indication for primary bone grafting was-elimination of bone deficiency, stabilization of the pre-maxilla, providing bone for eruption of teeth in the cleft area and augmentation of the alar base. There were also thoughts of normalization or even stimulation of maxillary growth [55]

Since 1964 many literature have been suggesting that grafting at this early stage causes serious growth disturbances of the middle third of the facial skeletoal region [56, 57]. The surgical procedure that involves the vomero-premaxillary suture was found to cause inhibition of maxillary growth [58]. Though some CLP centres still perform the early bone grafting technique while it is abandoned in most cleft lip and palate centres worldwide.

Secondary Alveolar Bone Grafting

Secondary alveolar bone grafting in the mixed dentition, became an established procedure after abandoning primary bone grafting worldwide. The pre-requisites are precise timing, operating technique, and sufficiently vascularized soft tissue. The advantages of primary bone grafting allowing tooth eruption through the grafted bone could also be maintained. Furthermore, secondary bone grafting can stabilize the dental maxillary arch, improving the conditions for prosthodontic rehabilitation such as crowns, bridges and implants. It will also help in eruption of teeth increasing the amount of bony tissue on the alveolar crest allowing orthodontic treatment possible.

Bony support to teeth in region of the cleft is a pre-requisite for orthodontic closure of the teeth in the cleft region. Hence it helps in favourable hygienic conditions reducing caries and periodontal inflammation. Speech problems caused by irregular positioning of articulators, or escape of air through the oronasal communication may also be improved. Secondary alveolar bone grafting can also be used to augment the alar base of the nose to achieve symmetry with the non-cleft side, thereby improving facial appearance of the patient [59].

Boyne and Sands introduced secondary alveolar bone grafting (SABG) technique in 1972, and it has greatly influenced the cleft lip and palate treatment approach around the world. This technique is aimed to bridge the cleft segment with grafted cancellous bone, harvested from the iliac crest. Norwegians were the first to adopt, practise and report findings of SABG. After an average period of 3 months Grafted cancellous bone fills in the residual alveolar cleft and is anatomically joined to the adjacent bone, becoming indistinguishable in radiographic images. These changes were observed histologically in young Rhesus monkeys. It seems to occur more rapidly in younger patients operated with secondary alveolar moulding.

Merits of secondary alveolar bone graft

Prior to the era of secondary alveolar bone graft, the teeth in the area of the bony cleft used to be sacrificed due to non-availability of the bony support. The orthodontic closure of the space was not possible, and hence the prosthodontic rehabilitation was the only option. The secondary alveolar bone graft has now minimised the need for prosthodontic rehabilitation. It has several other benefits:

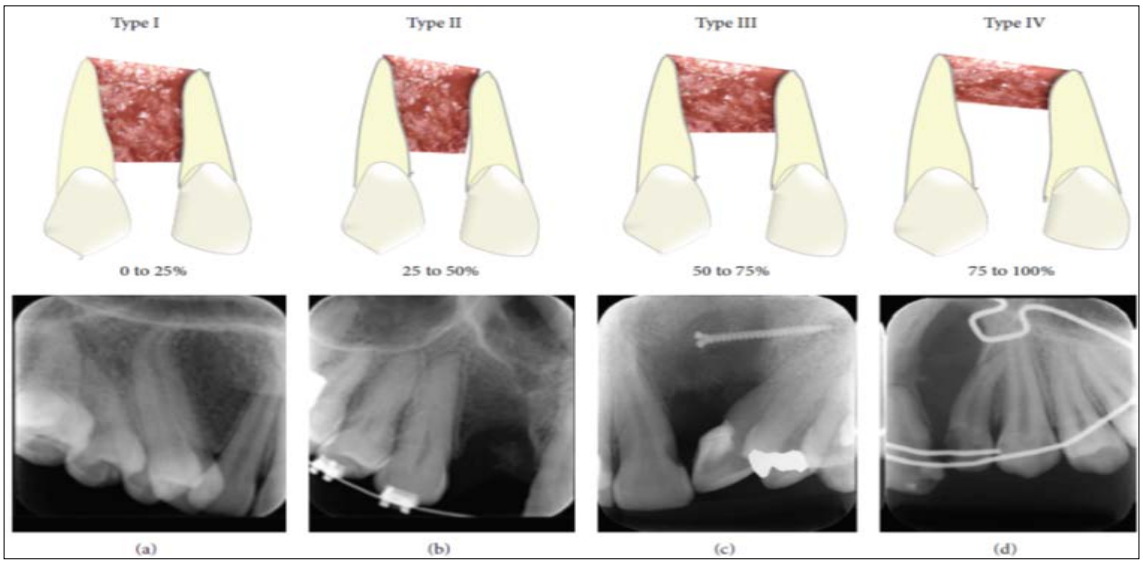
- Elimination of bony clefts and thereby encouraging a normal eruption of lateral incisor and canine through cancellous bone. The most important benefit of secondary bone grafting is that the newly grafted bone acts as the alveolar bone, allowing for spontaneous migration of the erupting canine towards the alveolar ridge and for the creation of a functional periodontium around the tooth.
- Orthodontic treatment of cleft space becomes possible thus minimising the need for prosthodontic rehabilitation of the missing teeth in the cleft area.
- In case lateral incisor is missing, and a decision is made to maintain the space, the grafted bone provides an excellent site for the prosthetic implant placement.
- SABG helps in the closure of oronasal fistulas in patients.
- The stabilisation of maxillary segments, which is helpful during the orthognathic surgery.
- Provides structural support to the alar base and improvement in aesthetics.

Late Secondary Bone Grafting

When performed after canine eruption success of bone grafting has a lower success rate compared to before the eruption. Similarly it is found that the possibility for orthodontic closure of the cleft in the dental arch is smaller than in patients grafted before the eruption of canine. In adults oral hygiene is of major concern. During the surgical procedure it should include drilling of multiple small openings through cortical layer into the cancellous layer helping in growth of blood vessels into the graft [59].

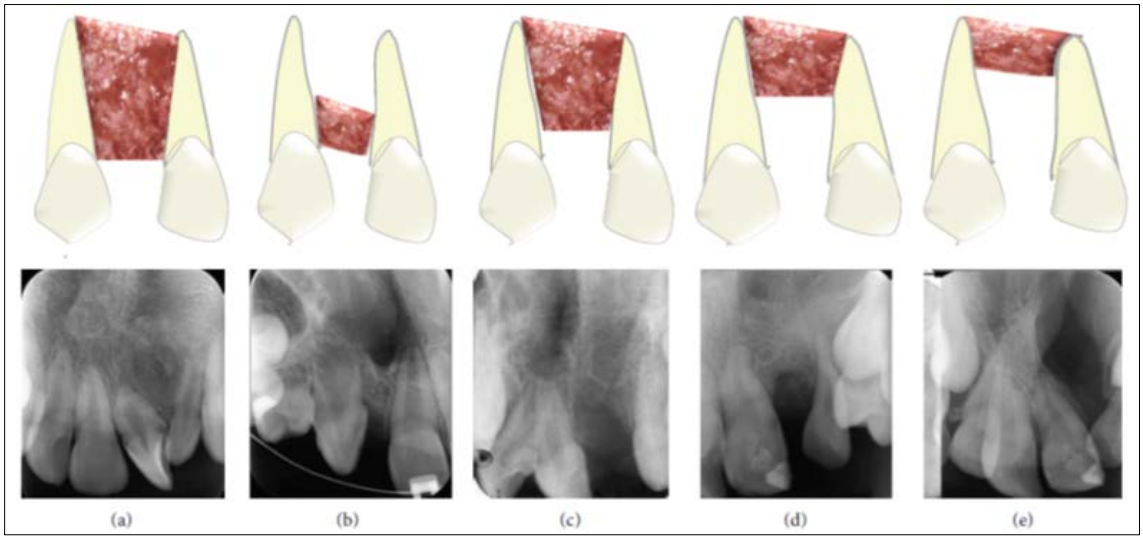
Assessment for secondary alveolar bone graft SABG requires careful clinical and radiological assessment-

The clinical and radiological methods are used for assessment of success for the bone graft. Eruption of cleft teeth, periodontal status, alveolar height and alar base support are used for clinical evaluation of the graft [60]. Radiologically, the outcome will be assessed on the basis of appearance of the bone [61] by using the Bergland scale and Chelsae scale [62] which are evaluated at least six months postoperatively. Radiographic assessment is more reliable and superior to clinical methods. CT scan should be used to overcome the draw-backs of conventional radiographs in evaluating the alveolar cleft. CT scan and specialized software are necessary to assess the defect, for determining the amount to be required for grafting as well as evaluation for postoperative bone formation to access the success of the graft [63, 64].



- Type I: 0 to 25% of bone resorption.
- Type II: 25 to 50% of bone resorption.
- Type III: 50 to 75% of bone resorption.
- Type IV: 75 to 100% of bone resorption with no continuous bony bridge through the cleft.

Fig 1: Bergland classification. (Periapical radiographic images of autogenous bone grafts)



- Type A - the presence of bone tissue at the cementoenamel junction of the teeth adjacent to the cleft and at least 75% of both roots covered by bone.
- Type B - the presence of bone tissue at the cementoenamel junction of the teeth adjacent to the cleft and at least 25% of both roots covered by bone.
- Type C - the presence of bone tissue surrounding at least 75% of the roots in the cleft area with an apical direction.
- Type D - the presence of bone tissue surrounding at least 50% of both roots in the cleft area, with an apical to coronal direction.
- Type E - the presence of 25% or less of bone tissue in both roots in the apical direction

Fig 2: Chelsea classification (Periapical radiographic images of autogenous bone grafts).

Choice of Bone Grafting Material for Alveolus

Important aspect in bone grafting is survival of the donor tissue. The osteogenic cells should survive the surgical procedure in optimum conditions. In histological and micro-radiographical clinical and experimental studies Johanson and Röckert (1961) proved, that cancellous autogenous bone grafts, harvested from either tibia or iliac crest, were transformed to the same structure as the surrounding palate. Micro-radiographically or morphologically after six months it was not possible, to distinguish a biopsy sample between the graft region and normal palate at the same age and the architecture of the graft appears to adapt to the functional needs [59].

Cancellous bone

Surface of the pre-existing trabeculae helps in formation of new bone. Cancellous bone is more vascular, has more space, contains more bone regeneration and has better in growth of new bone from the adjacent bone segments and found to help in tooth eruption. Cancellous grafts consist of actual cells and the incorporation process is much faster due to osteoinduction and osteoconduction. In principle, cancellous autografts heal primarily by osteogenesis, followed considerably later by resorption of the bone trabeculae in the transferred donor tissue [65].

Cortical bone

Early establishment of nutrition to cortical bone cells requires restoration of flow through existing vessels or canaliculi and ingrowth of capillaries. Cortical bone takes a longer time to incorporate because it relies on vascular in growth via a process called creeping substitution. A cortical graft will usually die and be replaced by invasion of bone cells originating from the recipient site [65]. The metabolic turnover and remodeling/transformation of cortical bone are much slower than in cancellous bone, making re-establishment of the tooth-bearing function of the alveolar process in the cortical graft unfeasible.

Soft Tissue Coverage

Importance of flap design with the gingival mucoperiosteal flaps in secondary bone grafting to maxillary clefts was first stressed by Boyne and Sands 1972, and Åbyholm *et al*. 1981. Histological composition of gingival/masticatory mucosa consists of a layer of keratinized stratified squamous epithelium and dense and firm lamina propria with immovable attachments to underlying teeth and bone. Hence the gingiva, is a suitable surface to support the masticatory load and protect against chemical and bacterial damage. The gingival muco-periosteal flaps have a broad base and excellent vascularity and provide adequate mobilization and a tension-free closure [66].

Techniques

A review of the literature regarding techniques for alveolar bone grafting over the years and practice reveals that there is no unison on the correct method to reconstruct the alveolus. In addition, there are still some practioners who feel that there are advantage for primary bone grafting. In many studies and documented literature, the emphasis is not necessarily on what is done during the surgery, but often on what is not to be done. Some advocates of primary alveolar bone grafting have argued that because of a lack of standardized techniques, it was the overly aggressive technique and not the timing that led to the failure of some primary alveolar bone grafting to prevent midface growth restriction.

Historical documented uses of primary alveolar bone grafting have run the spectrum from wedging rib graft into the cleft to transplanting resected segments of vomer into the alveolar cleft all the way to wide dissection along the alveolus, vomer, and hard palate for tibial graft placement. [67, 68, 69, 13] Technique for primary alveolar bone grafting that requires minimal dissection so as not to disrupt the vomeromaxillary suture and thus helps to avoid midface hypoplasia was described by van Aalst *et al*. [13] in 2005. This method requires that patients with complete unilateral and bilateral cleft lip and palate be fitted with a palatal obturator soon after the birth of child, which results in alignment and approximation of the greater and lesser maxillary segments. The cleft lip repair that is undertaken at 10 weeks also acts to help align the maxillary segments. Not all patients are candidates for primary alveolar bone grafting; after the obturator, primary alveolar bone grafting is thought to be of less benefit. if the maxillary segments are not approximated or up to 1 mm apart. In patients that meet the right criteria, rib graft is placed into the cleft at between 7 and 9 months of age. Unilateral clefts require a approximately 2.5-cm segment of rib and bilateral clefts require a approx 3.5-cm segment of rib. A trapezoidal flap elevation is done of mucosa to create a pocket into which the graft is placed and here is no dissection extending on the palate or piriform aperture. It is interesting to note that in cases where the mucosa of the maxillary segments is close, a gingivoperiosteoplasty is sometimes performed without bone grafting. This suggests/reinforces that there may be limited utility of this technique and primary bone grafting for most alveolar clefts [13].

There are a lot of different techniques suggested for delayed alveolar bone grafting. A sophisiticated, straightforward approach was described by Craven *et al*. [71] which states the conceptualization of the defect in three dimensions is essential to adequately reconstruct the alveolar cleft with a bone graft according to this technique. The surgeon must take into account the need to reconstruct all of the surfaces of the anatomic subunits of the alveolar cleft, which includes the nasal floor, lateral cleft margin, anterior alveolus, medial cleft margin and the posterior alveolus (palate). If there are any concerns about soft tissue integrity (e.g., oronasal fistula), staged/delayed bone grafting should take place after the soft tissue defect has been reconstructed. The method requires that labial gingival periosteal flaps be elevated mesial and distal to the cleft region. The incision is near the teeth adjacent to the cleft and fans out over the more lateral and mesial teeth to leaving a 2- to 3-mm gingival cuff and the lateral flap extends to the mesial aspect of the first molar. Immediately beyond the contralateral incisor is the limit of the incision extending toward the midline. Gingival periosteal flaps are elevated to close the palatal defect, while the nasal floor is closed with mucoperiosteal flaps elevated off the pyriform aperture. These flaps are sutured for closure of the alveolar cleft. If this maneuver creates an apparently stable soft tissue envelope, then bone grafting can be done. If the soft tissue integrity does not appear to be adequate, then the soft tissue is completely closed and bone grafting is delayed for 3 to 4 months and attempted later.

Conclusion

Treatment of the alveolar cleft should not be delayed in the care of cleft lip and palate patients as it carries functional and aesthetic significance and reconstruction potentially carries a significant benefit to the patient. For the success of alveolar

graft timing of repair is an important consideration and successful reconstruction depends on several factors. The team approach to care depends on collaboration with other specialists (e.g., pediatric dentists, orthodontists, oral surgeons, and speech pathologists) and provides optimal care to the patient. The choice of graft source must take into account depending on the cost of donor site morbidity as well as the intrinsic characteristics of the type of bone selected for the graft. New methods, such as BMP, are being utilized in hopes of finding an alternative to autologous bone graft harvesting. The ideal substitute has not been discovered yet, but the investigative search still continues.

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