Assessment of Periosteal Free Grafts versus Platelet Rich Fibrin as an Adjunct to Alveolar Cleft Grafting

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List of abbreviations

ACG: Alveolar Cleft Grafting.
AIC: Anterior Iliac Crest
AICG: Anterior Iliac Crest Graft.
ALT: Alanine Transaminase.
AST: Aspartate AminoTransferase.
BCLP: Bilateral Cleft Lip and Palate.
BMPs: Bone Morphogenetic Proteins.
CBCT: Cone Beam Computed Tomography.
CCC: Cleft Care Center
CLAP: Cleft Lip, Alveolar and Palate.
CLP: Cleft Lip and Palate.
CT: Computerized tomography.
GPP: GingivoPeriosteoPlasty.
Lt-PRF: Left side – Platelet Rich Fibrin
ONF: Oro-Nasal Fistula
PDGF-AB: Platelet-derived Growth Factor.
PFG: Periosteal Free Graft.
PRF: Platelet Rich Fibrin.
PRP: Platelet Rich Plasma.
RAP: Regional Acceleratory Phenomenon.
Rt-PFG: Right side - Periosteal Free Graft
TGFβ-1: Tissue Growth Factor.
TSP-1: Thrombospondin-1.
UCLP: Unilateral Cleft Lip and Palate.
VEGF: Vascular Endothelial Growth Factor.

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Clefts of lip and/or palate (CLP) are the most common congenital malformations in the cranio-facial region. Despite many improvements over the years, the treatment of children with clefts remains a challenge. The ultimate objective of all cleft surgeries is to minimize the visible stigmata of the cleft related deformity. From birth until early adulthood, growth, aesthetics, function, and psychosocial development must be balanced during treatment. In addition, many problems remain to be solved. Standardized treatment programs are common, but still treatment outcome varies.[1]

The primary palate is formed during weeks' four to seven of gestation by the median palatine process derived from the fronto-nasal prominence. The lip and hard palate anterior to the incisive foramen are formed during this developmental process. Variations from normal development during this period may result in cleft of the primary palate, manifesting either as incomplete or complete and unilateral or bilateral cleft extending into the lip. It is important to state that the alveolus lies within the primary palate; thus, an alveolar cleft is a result of divergence from normal development during fronto-nasal prominence growth, contact, and fusion. Therefore, alveolar clefts are associated with cleft lip but not with isolated cleft palate deformities. The cleft in the alveolus is typically located between the lateral incisor and the canine, although it can also occur between the central and lateral incisors. [2]

Classification schemes for cleft palate are usually anatomically based. This may include complete or incomplete, unilateral or

bilateral, a sub-mucous cleft, and bifid uvula. The primary goal of cleft palate repair is to restore the function of the palate and aid the development of normal speech. Maxillary alveolar clefts can prevent normal eruption of the permanent dentition and can therefore inhibit facial growth and symmetry. Alveolar bone grafting in the mixed dentition phase allows the canine teeth to migrate and erupt through the cancellous bone.[3]

From birth to adulthood, management of patients with CLP depends on multidisciplinary approach (this includes surgeons, orthodontists, speech therapists and dentists) which defines the general, anatomical and functional framework until the final stages of treatment.[4]

Alveolar cleft grafting (ACG) is part of the general management of patients with CLP. It is considered an essential procedure to further improve the functional and esthetic rehabilitation of patient with unilateral or bilateral (CLP). It is recommended during the mixed dentition period. [5,6]

ACG achieves the following objectives: obtains maxillary arch continuity, improves bone support for the dentition, stabilizes the maxillary segments following orthodontic treatment, supports nasal alar cartilage, establishes ideal alveolar morphology, and it also provides available bone with attached soft tissue for future endosteal implant placement whenever there is a residual dental space.[7]

One of the most important objectives of ACG is the closure of oro-nasal fistula (ONF). During speech, ONF allow air leakage to the anterior nasal cavity. They also affect oral hygiene and periodontal health, which are unpleasant to the patient as they allow regurgitations during eating and drinking. In addition, ONF are associated with nasal sill and alar base deficiency and premaxillary instability in bilateral clefts. Hence, addressing ONF may benefit both hygiene and speech by improving nasal emission and nasality. [8,9]

The literature is inconclusive regarding the most favorable time for alveolar bone grafting. There are two possible approaches regarding the time of alveolar bone reconstruction: (1) primary bone grafting surgery during infancy and (2) secondary bone grafting during the mixed dentition stage.[10] The staging of alveolar bone reconstruction is based chronologically on the patient's age classified as follows: (1) Primary stage: patients younger than 2 years old, (2) Early secondary stage-:patients from 2 to 5 years of age, (3) Late secondary: patients older than 5 years of age.[11]

The standard of care in patients who have a complete cleft is to perform secondary bone grafting of the absent bone in the alveolus and anterior maxilla with autogenous cancellous bone. Although other treatment protocols have been suggested, no protocol has proved to be equal, and certainly not superior, to this protocol.[12]

Great controversy still exists regarding the type of bone graft used either autogenous, allogenic or alloplastic.[13] There is a consensus that autogenous bone grafting is the gold standard for ACG as it supplies osteogenic cells into the cleft area. However, controversy exists as regards the source of autogenous bone. The anterior iliac crest graft (AICG) has for long been considered as the standard donor site for ACG.[14] Alternative sources of autogenous bone have been employed such as: the calvarium, the mandibular symphyseal region as well as the tibia.[15]

Several variables may interfere with the outcomes of bone grafting of the alveolar cleft and affect the stability of bone graft. Patient factors (such as age, status of tooth eruption on the cleft side, cleft width, ratio of cleft to nasal cavity and the patient's general health). Moreover, there are surgical wound conditions (overall oral health, quality and amount of soft and hard tissue adjacent to the cleft, blood supply, donor site, and scar tissue from previous operations). Finally, there are technical characteristics (graft material, and the surgeon's experience) which may, with the previously mentioned factors, play a part in the surgical outcomes.[16–19]

In a previous study, the volume of the grafted alveoli at one year was significantly decreased compared with that at three months [20] . In other studies, approximately 30% of the volume of bone transplanted from the iliac crest had resorbed in the first year, and the total volume loss was approximately 43.1% at one year after secondary alveolar cleft repair from the iliac crest.[21],[22]

Whenever a postoperative complication develops, the surgical outcome may be compromised and reoperation might be necessary. The need for reoperation increases the overall cost of treatment, exposes the patient once more to risks related to the operation and general anesthesia, and might even be a reason for the patient or family to refuse further treatment. Reoperation will also result in formation of more scar tissue and further compromise the local blood supply and healing of hard and soft tissue.[23,24]

In many studies, PRF has direct or indirect effects on bone regeneration in bone grafting or bone defect healing. In the literature, authors have reported many advantages of PRF for bone regeneration.[25,26]

The periosteal bone-forming capacity has been well known since the eighteenth century, and was first described by Duhmal de Monceau.[27] It is generally accepted that the free periosteal graft has good growth potential and osteogenic activity in children.[28]

This study was designed to provide a comparison between these two grafting adjuncts in the field of ACG.

Cleft lip and palate is a congenital defect with the overall prevalence of 7.94 per 10,000 live births and wide variability of clinical expression and severity, from orbicularis oris muscle defect to cleft lip, alveolar cleft and cleft palate alone. [29]

Alveolar cleft is a result of an improper fusion of the maxillary prominences around the 5th–6th week of gestation, that is caused by both environmental and genetic factors.[30] It comprises a heterogeneous group of defects with large differences in volume and shape. Affected children suffer from speech and hearing disorders, their academic achievements might be affected as well.[31]

The osseous closure of the alveolar cleft, which is required for the formation of a stable maxillary dental arch, occupies a special position within the whole concept of cleft lip and palate therapy.[32]

Clefts of the alveolus and anterior palate have been recognized by many surgeons as one of the most difficult steps in the treatment of patients with cleft lip and palate. This procedure is not only complicated by the sensitivity of the surgical technique applied but also the ambiguity surrounding many of the surgical principles of the grafting procedure shed further difficulty upon this crucial step.[13]

Rationale for alveolar cleft grafting

The restoration of jaw function and morphology in CLP patients is critically important and requires reconstruction of the maxillary alveolar clefts depending on the principles of bone regeneration in osseous defects.[33]

The primary goal of maxillary alveolar cleft reconstruction in CLP patients is to build bone in the cleft area which in turn: eliminates the ONF, reestablishes maxillary arch continuity, limits growth disturbance and allows the movement of permanent dentition into the grafted bone. Furthermore, ACG enhances nasal symmetry, facilitates orthodontic movement and subsequent insertion of dental implants. It is important to emphasize that speech improvement, oral hygiene maintenance, and maintenance of periodontal health are also facilitated by the ACG.[34,35]

Adequate surgical preparation of the alveolar cleft site is paramount to facilitate introduction of a sufficient quantity of autogenous bone. Healthy mucogingival coverage over this recipient site establishes enhanced functional and anatomical unity of the pre-operatively cleft maxilla. Deferring this procedure until the secondary mixed dentition stage when maxillary transverse growth is almost complete will limit the hazards of growth disturbances. [36–38]

The ONF(s) in CLP patients vary in size and consequently, offer several challenges for surgical management. ONF allow air leakage to the anterior nasal cavity during speech, affect oral hygiene and periodontal health, and are unpleasant to the patient especially during eating and drinking. They are also associated with nasal sill and alar base deficiency and pre-maxillary instability in bilateral clefts. Hence, addressing ONF may provide an added benefit for both hygiene and speech by improving nasal emission and nasality.[34,36]

An ONF can adversely affect speech due to air leakage through the fistula. The ONF is most likely to adversely affect speech when it is 4.5 mm^2 or larger. However, grafting the alveolar cleft and closing the ONF have been associated with apparent improvement in tone and the reduction of hyper-nasality.[39] Nasal deformity associated with unilateral CLP is associated with social stigma and can be a psychological burden to the patient. Bone support to the alar base is one of the most important goals of alveolar cleft reconstruction.[40]

Absent or malformed lateral incisors are generally considered an issue for a permanent prosthetic or occlusal problem even when the alveolar cleft reconstruction is successful. This problem has been successfully overcome recently by inserting an endosseous implant.[38] In addition, placing a dental implant in the grafted cleft area maintains