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REVIEW ARTICLE

# Is alveolar cleft reconstruction still controversial? (Review of literature)



Sameh A. Seifeldin \*

Maxillofacial Department, College of Dentistry, King Saud University, Saudi Arabia  
Maxillofacial Department, Faculty of Oral and Dental Medicine, Cairo University, Egypt

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**Abstract** Cleft lip and palate (CL/P) is a frequent congenital malformation that manifests in several varieties including unilateral or bilateral and complete or incomplete. Alveolar cleft reconstruction remains controversial with regard to timing, graft materials, surgical techniques, and methods of evaluation. Many studies have been conducted addressing these points to develop an acceptable universal protocol for managing CL/P. The primary goal of alveolar cleft reconstruction in CL/P patients is to provide a bony bridge at the cleft site that allows maxillary arch continuity, oronasal fistula repair, eruption of the permanent dentition into the newly formed bone, enhances nasal symmetry through providing alar base support, orthodontic movement and placement of osseointegrated implants when indicated. Other goals include improving speech, improvement of periodontal conditions, establishing better oral hygiene, and limiting growth disturbances. In order to rehabilitate oral function in CL/P patients alveolar bone grafting is necessary. Secondary bone grafting is the most widely accepted method for treating alveolar clefts. Autogenous bone graft is the primary source for reconstructing alveolar cleft defects and is currently the preferred grafting material.

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\* Corresponding author at: 11545, Riyadh- B.O. 60169, Riyadh, Saudi Arabia. Tel.: +966 506944359; fax: +966 14678548.

E-mail address: [samehseif@doctor.com](mailto:samehseif@doctor.com).

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## Contents

1. Introduction . . . . .	4
2. Pathogenesis . . . . .	4
3. Etiology . . . . .	4
4. Classification . . . . .	5
5. Rationale for alveolar bone grafting . . . . .	5
5.1. Pre- versus post-surgical orthodontics . . . . .	6
5.2. Timing of the graft . . . . .	6
5.2.1. Primary grafting . . . . .	6
5.2.2. Secondary bone grafting . . . . .	7
5.3. Types of bone grafting . . . . .	7
5.4. New grafting materials . . . . .	8
5.5. Evaluation of alveolar cleft bone grafting . . . . .	9
6. Summary . . . . .	10
Disclosure of funding . . . . .	10
Conflict of interest . . . . .	10
References . . . . .	10

## 1. Introduction

Fifty years ago, the procedures for grafting bone were inconvenient, sporadically used, and lacked clear objectives. Alveolar cleft reconstruction has been one of the most controversial surgical procedures since it was the first at the beginning of the 20th century. There were multiple philosophies and preferred treatment modalities regarding each step in alveolar cleft management including grafting, the most appropriate age, the ideal material, and whether adjunctive procedures such as orthodontic expansion should be used before or after grafting (Horswell and Henderson, 2003).

Cleft lip and/or palate (CL/P) is considered the most prevalent of the common human congenital craniofacial birth defects. The approximate incidence ratio of CL/P has been reported as 1:700 live births. In addition, CL/P is the second most common congenital malformation following clubfoot (Peter and Larsen, 2004).

## 2. Pathogenesis

Cleft palate deformities occur when fusion of palatal shelves fails to occur. These deformities are classified according to the extent of the palatal involvement. Failure of the primary and secondary palate to fuse leads to complete cleft palate, in which the palatal shelves also fail to fuse. Complete palatal clefts are typically associated with uni- or bilateral cleft lip (Sadove et al., 2004). When the facial processes or palatine shelves do not fuse, incomplete palatal clefts might occur which could either affect the primary or secondary palate. Consequently, the incomplete cleft palate can involve only the posterior part of the soft palate, it may extend through the hard palate to the incisive foramen, or it could be confined to the primary palate resulting in alveolar cleft (Jennifer et al., 2007).

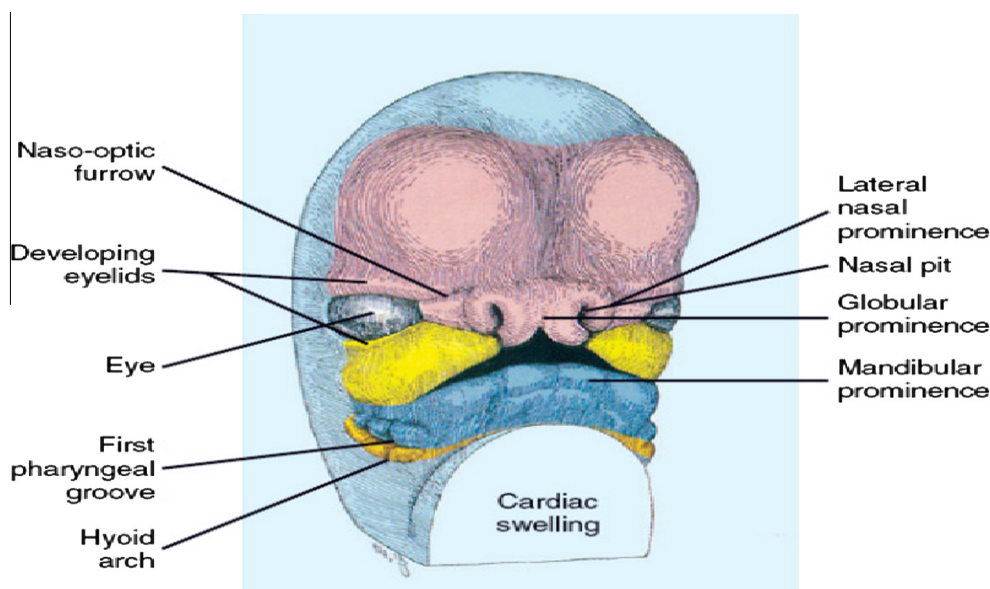
CL/P are more often unilateral than bilateral and more common in males than in females. Unilateral defects on the left side occur more often than on the right side. Cleft palate is more common in females and most often associated with other

developmental anomalies. Depending on the existence of associated developmental anomalies, CL/P may be classified as syndromic or isolated anomalies (Hagberg et al., 1998). Isolated CL/P is a complex trait that usually results from a combination of hereditary and environmental etiological factors. Previous research to identify the etiological genes and loci responsible for CL/P has suggested that there may be anywhere from 3 to 14 genes involved (Cobourne, 2004). For isolated CL/P, candidate genes and loci have been identified on chromosomes 1, 2, 4, 6, 11, 14, 17 and 19 (Blanton et al., 2004).

## 3. Etiology

Environmental factors that contribute to the etiology of facial clefting disorders can be divided into four groups: drugs, chemicals, maternal metabolic imbalances (as folic acid deficiency), and maternal infections. Maternal exposure to alcohol and teratogenic medications such as retinoids, corticosteroids, and anti-convulsants (phenytoin and valproic acid), and folic acid deficiency during the periconceptional period can cause clefting disorders. Consanguineous marriages, maternal diabetes, and obesity have also been linked to an increased risk of orofacial clefts (Eppley et al., 2005).

The embryo undergoes rapid changes in shape and growth between 4 and 8 weeks as the brain expands and the six branchial arches are formed. The first two branchial arches are primarily responsible for the development of the face and the cranium. The development of the face begins from the ectomesenchyme of the neural crest, which forms five prominences: the frontonasal process and two maxillary and mandibular processes (one of each on a side) surrounding a central depression. During the 5th and 6th weeks, the bilateral maxillary processes derived from first branchial arch fuse with the medial nasal process to form the upper lip, alveolus, and primary palate. The lateral nasal process forms the alar structures of the nose. The mandibular processes form the lower lip and jaw. During the 8th week, the bilateral maxillary palatal shelves ascend to an appropriate level above the tongue and then fuse to each other and the primary palate to form the secondary palate (Fig. 1; Sperber et al., 2001).



**Figure 1** Embryonic development of the face, 6th week [Avery and Chiego \(2006\)](#).

The process of forming facial structures is the result of cell proliferation, differentiation, adhesion, and apoptosis. The processes of the neural crest cells are directed by molecular signals that are controlled by a group of genes that include the transforming growth factor beta (TGF- $\beta$ ) super family, sonic hedgehog (SHH), fibroblast growth factors (FGFs), and bone morphogenic proteins (BMPs). Failures or errors in any of these intracellular mechanisms can disrupt the normal fusion of the medial and lateral nasal processes and maxillary process to cause orofacial clefts ([Marazita and Mooney, 2004](#)).

Every child born with a cleft lip or palate should be thoroughly assessed and evaluated by assessing their breathing and looking for signs of airway obstruction; ability to feed; nutritional intake; weight gain and growth; concomitant anomalies (cardiac/renal/pulmonary/musculoskeletal); syndromic associations that require genetic testing; and craniofacial examination including head shape and circumference, ears, eyes, nose, jaws, and oral cavity. Moreover, it is important to evaluate the severity and type of cleft defect, the width of the cleft, position of alveolar segments and premaxilla, nasal deformity, the need for presurgical orthopedics and type of appliance necessary, and to prepare the child and parents for surgical repair of cleft lip ([Bagheri et al., 2012](#)).

#### 4. Classification

Classification schemes for cleft palate are usually anatomically based. This may include complete or incomplete, unilateral or bilateral, a submucous 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. Success rates with bone grafting are generally reported at 90–95% ([Bagheri et al., 2012](#)).

#### 5. Rationale for alveolar bone grafting

The restoration of jaw function and morphology in CL/P patients is critically important and requires reconstruction of the maxillary alveolar clefts depending on osteogenic potential and bone regeneration in osseous defects ([Kawata et al., 2004](#)).

The primary goal of maxillary alveolar cleft reconstruction in CL/P patients is to build bone in the cleft area which in turn allows: removes the oronasal fistula, establishes maxillary arch continuity, limits growth disturbance and movement of the permanent dentition into the grafted bone, enhances nasal symmetry, orthodontic movement and insertion of dental implants, speech improvement, oral hygiene maintenance, and improves periodontal health ([Peter and Larsen, 2004](#)).

Adequate preparation at the site of the alveolar cleft defect enables it to receive an appropriate quantity of autogenous bone graft, which followed by healthy mucogingival flaps adequately covering the graft, results in a functional and anatomically united maxilla. Deferring this procedure until the secondary mixed dentition stage when maxillary transverse growth is almost complete will limit the hazards of growth disturbances ([Horswell and Henderson, 2003](#); [Trindade et al., 2005](#); [Le and Woo, 2009](#)). Moreover, bone grafting achieves a stable dental arch that will minimize inward collapse of the alveolar segments and provide subsequent improvement in orthodontic stability ([Peter and Larsen, 2004](#)). Alveolar cleft reconstruction provides a bone matrix to support permanent dentition movement once orthodontics are completed. Providing space for lateral incisor and/or permanent canine eruption into stabilized alveolar bone maintains bony support of the teeth adjacent to the alveolar cleft ([Hynes and Earley, 2003](#); [Peter and Larsen, 2004](#)).

Oronasal fistulas in CL/P patients vary in size and consequently, offer several challenges for surgical management. Oronasal fistulas 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 premaxillary instability in bilateral clefts. Hence, addressing oronasal fistula may benefit both hygiene and speech by improving nasal emission and nasality (Horswell and Henderson, 2003; Peter and Larsen, 2004).

Nasal deformity associated with unilateral CL/P 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 (Honma et al., 1999). Alveolar bone reconstruction in conjunction with nasal correction can be performed later in childhood. To improve nasal projection, the alveolar cleft defect can be reconstructed with autogenous bone and a small stent fitted at the anterior nasal spine simultaneously (Horswell and Henderson, 2003).

Absent or malformed lateral incisors are generally considered to be 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 (Le and Woo, 2009; Ronchi et al., 1995). In addition, placing a dental implant in the grafted cleft area maintains the grafted bone in patients who underwent secondary bone grafting for alveolar cleft repair. This is attributed to bone remodeling in response to implant loading (Takahashi et al., 2008).

An oronasal fistula can adversely affect speech due to air leakage through the fistula. The oronasal fistula is most likely to adversely affect speech when it is 4.5 mm<sup>2</sup> or larger. However, grafting the alveolar cleft and closing the oronasal fistula have been associated with apparent improvement in tone and the reduction of hypernasality (Bureau et al., 2001).

Alveolar cleft grafting also improves oral hygiene and preserves dentition, as CL/P patients have some periodontal struggles due to oronasal fistula, inadequate oral hygiene, and long-term orthodontic therapy (Brägger et al., 1985; Peter and Larsen, 2004).

### 5.1. Pre- versus post-surgical orthodontics

Most authors prefer presurgical expansion, citing easier expansion due to less resistance, improved access to the cleft for closing the nasal floor, better postoperative hygiene, and less chance of reopening the oronasal fistula (Ochs, 1996; Peter and Larsen, 2004). Unilateral or bilateral CL/P patients may require orthodontic treatment to minimize the deformity of the anterior maxillary projection using orthopedic devices during infancy. Orthodontics, with or without orthopedic treatment, might also be required during the deciduous dentition stage. In addition, during both the mixed and permanent dentition phases, orthodontic treatment is frequently required either alone or in association with orthognathic surgery (Machos, 1996).

Orthodontic treatment should be started at least 6 months before bone graft placement using fixed appliances in the maxillary dental arch. Developing a favorable arch form by expanding the anterior and/or posterior maxillary dental arch is considered the main treatment goal at this stage. While partially or completely eliminating the misalignment of the incisors and cross bites are the corner stone of orthodontic treatment, improvement of dental function and esthetics should also be the required objectives. Orthodontists should

avoid moving teeth roots into the cleft defect. However, the incisor root could be moved distally into a cleft, if pre-angulated brackets are used, but the subsequent prognosis is poor. Keeping the incisor roots invested in bone at the presurgical stage is preferable; the correct tooth angulation can be achieved after successful bone grafting (Machos, 1996).

Advocates of expansion following grafting cite the advantages that bone consolidation is improved when the graft is placed under a dynamic load during healing, a smaller soft tissue defect to close, less difficulty procuring an adequate volume of bone, and a narrower defect, which will regenerate bone more quickly (Peter and Larsen, 2004; da Silva et al., 2009). Both approaches have been used in conjunction with autogenous grafting in the mixed dentition stage with success. Not only is it controversial whether expansion should be undertaken pre- versus post-surgery, there are also two schools of thought regarding orthodontic movement of the erupted permanent teeth adjacent to the cleft site. Previous reports have directly correlated the success of grafting with the presence of adequate bone on the distal surface of the central incisor preoperatively (Enemark et al., 2001; Peter and Larsen, 2004).

### 5.2. Timing of the graft

Review of the literature is inconclusive regarding the most favorable time for alveolar bone grafting (Freihofer et al., 1993). 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 (Eichhorn et al., 2009). 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) Mixed secondary stage- patients from 5 to 16 years of age, and (4) Late secondary- patients older than 16 years of age (Eppley, 1996).

#### 5.2.1. Primary grafting

Primary bone grafting involves alveolar cleft reconstruction in association with soft tissue repair to the lip during infancy. Early alveolar repair was described in the 1950s by (Nordin and Johansen) who presented concomitant autogenous bone grafting of the alveolar bone performed with soft tissue repair to the lip and palate. This concept gained popularity because it simultaneously addressed both soft tissue and bony deficit repair and created the possibility for harmonious facial growth and development (Ochs, 1996). Bone grafting at an early age stabilizes the arch and allows the deciduous teeth to erupt into the newly formed bone (Eichhorn et al., 2009). The primary goal of alveolar cleft repair performed before palatal closure is to prevent the limiting effects of surgical palate closure on early midfacial development, which decreases the need for subsequent arch expansion during orthodontic treatment (Rosenstein, 2003).

Although performing an iliac crest bone graft before canine eruption is generally considered the gold standard for alveolar cleft reconstruction, previous studies have concluded that tooth eruption has never occurred in synthetic bone substitutes. Lazarou et al. (1997) demonstrated for the first time that teeth can erupt through calcium-based bone substitutes that turn into a normal functioning bone in the alveolar ridge.

Calcium substitutes provide substantial advantages over other biomaterials and autologous bone grafts for primary alveolar cleft grafting.

Not all patients are suitable for primary grafting, those that should meet the following criteria: (1) complete palatal cleft (patients with intact part of hard palate are not candidates for primary grafting) and (2) the alveolar segments should be properly aligned (end-to-end) orthodontically before grafting, because the presence of a gap between the maxillary segments will create tension on the flap over the grafted bone and increase the risk of postoperative wound dehiscence, graft exposure, and subsequent failure of the graft (Eppley, 1996). Bone grafts used for primary grafting include the onlay rib graft and calvarial bone graft (Eichhorn et al., 2009).

### 5.2.2. Secondary bone grafting

Secondary alveolar bone grafting is the most appealing and popular method to treat alveolar clefts. It is usually suggested when half of the canine root is almost complete. At this stage of root development, the tooth shows accelerated and active eruption. Moreover, most of the mid-facial growth and development is completed. This corresponds to a chronological age of 9–12 years (Hynes and Earley, 2003; Ochs, 1996). The primary goals of secondary alveolar bone reconstruction are to provide a mature bony matrix that supports canine movement and the formation of a stable united dental arch. The orthodontic movement of teeth facilitates complete dental rehabilitation and prosthodontic reconstruction, oronasal fistula repair, and provides bony support for the lip and nose (Baqain et al., 2009; Hynes and Earley, 2003).

### 5.3. Types of bone grafting

The ideal bone graft material for alveolar cleft reconstruction remains as controversial as the timing issue for osseous repair in CL/P management. Various sources of bone graft material have been suggested in the literature including autogenic, allogenic, xenogenic, and alloplastic grafts. The outcomes achieved with different graft sources have been extensively compared in the literature (Horswell and Henderson, 2003; Ochs, 1996). Identifying the optimal donor site for alveolar cleft reconstruction has been a dilemma for many years. Several factors influence the choice of donor site for harvesting the bone graft for cleft reconstruction including the expertise and preference of the surgeon, the available bone volume, and the morbidity associated with harvesting from a particular site (Rawashdeh and Telfah, 2008).

Bone grafts harvested from autogenous donor sites are used extensively in oral and maxillofacial surgery to rebuild small and large bony defects. Multiple donor sites have been suggested in the literature including the anterior and posterior ilium, proximal tibia, rib, mandibular symphysis, and calvarial bone. However, every site has potential complications; therefore, the optimal donor site remains open to debate (Baqain et al., 2009; Eichhorn et al., 2009). Previous research concluded that the corticocancellous blocks used for grafting facial bony defects in an onlay fashion can maintain their volume when a membranous bone source is used rather than an endochondral bone (Rawashdeh and Telfah, 2008).

In contrast, other scholars (Ozaki and Buchman, 1998; Ozaki et al., 1999) have compared the ability of inlay bone

grafts from membranous bones (mandibles) to maintain their volumes in the craniofacial skeleton to the endochondral cortical and cancellous bone harvested from iliac crests of rabbits. The results indicated that in contrast to the data for onlay bone grafts that resorbed over time, inlay bone grafts were maintained and increased in volume over time. Furthermore, cancellous bone of endochondral origin had the greatest volume. They concluded that the dynamics of cancellous inlay bone grafts were different from onlay cortical bone grafts.

The alveolar process defect in CL/P patients is considered to be a marginal defect in the continuity of the pyriform aperture and the alveolus. Thus, alveolar cleft reconstruction is assumed to be inlay grafting between the osseous segments, rather than an onlay graft on the maxilla (Rawashdeh and Telfah, 2008).

An autogenous bone graft harvested from the anterior or the posterior iliac crest is considered the optimal source of autogenous bone for alveolar cleft reconstruction and hence it is termed the “gold standard bone graft.” Moreover, there is a consensus that iliac bone is the standardized graft to which different types of alveolar bone grafts should be compared. The anterior iliac crest has the advantage of providing a large quantity of cancellous bone and easy surgical access. Furthermore, it has great osteogenic potential especially in the early phase following grafting due to abundant pluripotent osteogenic precursor cells. Cancellous bone is considered superior to corticocancellous bone, because it is relatively easy to harvest, reduces the operative time, and contains a greater number of osteogenic precursor cells. In addition, cancellous bone from the ilium placed in the alveolar cleft has a predictable outcome and a high success rate. However, reflection of musculo-periosteal flaps during surgical exposure of the iliac crest can result in significant post-operative morbidities including hematoma, pain, discomfort, delayed ambulation, and prolonged hospitalization (Baqain et al., 2009; Rawashdeh and Telfah, 2008; Swan and Goodacre, 2006).

Previous reports have suggested that the calvarial bone graft has the advantage of being superior in the esthetic outcome due to inconspicuous scar formation. In addition, lack of functional deformity, a convenient surgical field, and the volume of bone that can be harvested make the calvarial bone graft a good choice for postoperative morbidity (Keese and Schmelzle, 1995; Strong and Moulthrop, 2000). However, calvarial bone harvesting carries the risks of wound infection, minimal cancellous bone, intracranial complications, and thin bone (Strong and Moulthrop, 2000; Vahtsevanos et al., 2007). Harvesting from the calvarial donor site might also reduce the strength of the skull. Consequently, different donor sites are recommended for those who have a high probability of multiple head injuries such as some athletes (Rawashdeh and Telfah, 2008).

Tibial bone graft has been advocated widely in orthopedic surgery. Consequently, it has gained popularity as autogenous grafting material for jaw reconstruction, orthognathic surgery, cleft repair, and preprosthetic surgery (Amin Kalaaji et al., 2001; Rawashdeh and Telfah, 2008). The tibia is preferred because it is easy to harvest, has minimal bleeding, allows rapid ambulation, and has a rich cancellous bone marrow depository (Horswell and Henderson, 2003; Hughes and Revington, 2002). However, the proximal tibia has the disadvantage in children of growing epiphyseal cartilage and being limited in size. Consequently, the surgical operating field

should be limited and placed at a lower on the tibia to avoid possible injury to the growth center. Some long-term follow-up studies have concluded that potential injury to proximal tibial growth center has not been reported in CL/P patients (Besly and Booth, 1999; Rawashdeh and Telfah, 2008).

Mandibular symphysis bone graft was first introduced by Bosker and van Dijk (1980) for secondary alveolar cleft reconstruction with good results. The symphyseal bone graft harvested from the mandible has advantages in that both the surgical fields for the donor and recipient sites are confined to the oral cavity, reduced operative time, minimal postoperative complications and morbidity, and no extra oral scars. Moreover, the symphyseal bone is thought to show superior integration into the cleft defect since both the donor bone and recipient bed have the same intramembranous origin. Nevertheless, the main disadvantage of symphyseal bone graft is the limited quantity available thus, it is considered less suitable for large unilateral or bilateral cleft reconstruction (Bähr and Coulon, 1996; Enemark et al., 2001; Rawashdeh and Telfah, 2008).

The rib is the second most frequently used autogenous graft for alveolar cleft defect repair. Together with the calvarial bone, the ribs are thought to be a practical donor site for autogenous bone for primary alveolar grafting (Eichhorn et al., 2009; Eppley, 1996; Horswell and Henderson, 2003). Incomplete graft integration into the alveolar bone, a lack of bone reservoir, and teeth being unable to erupt are the primary disadvantages reported in the literature for rib grafts. In addition, inadequate alar base support, the possibility of a pneumothorax, and persistent postoperative pain are frequently reported disadvantages. Ribs do not have significant advantages over bone harvested from the ilium for alveolar cleft reconstruction that would warrant a preference for using rib grafts in the mixed-dentition stage (Eppley, 1996; Horswell and Henderson, 2003).

(Allografts) allogeneic bone has been suggested for alveolar cleft reconstruction because it overcomes the disadvantages of autogenous bone grafts. It has the advantages of limiting surgery time, providing an abundant quantity of bone, and eliminates donor site morbidity. Allografts offer both osteoinduction and osteo-conduction properties. Bone morphogenetic proteins (BMPs) provide osteoinduction, and are released in response to osteoclastic activity to stimulate bioincorporation of the graft. The calcified collagen structure presents osteo-conduction properties forming a scaffold that facilitates bone deposition (Filho et al., 2013).

It is not recommended to use bone substitutes (alloplastic grafts), such as hydroxylapatite, for alveolar cleft reconstruction in growing children with unerupted teeth near the cleft defect. Alloplastic grafts should be offered for alveolar ridge augmentation in adult patients who do not plan on future insertion of endosteal implants. Research data and clinical experience regarding the use of xenografts and bioceramics in alveolar cleft reconstruction are highly controversial and there is insufficient evidence in the literature. Therefore, their use in alveolar cleft reconstruction is not recommended (Ochs, 1996).

Recently, the use of alloplastic grafts and xenografts has gained much popularity in sinus grafting and alveolar grafting for dental implants due to their availability, although they are expensive; but there is not enough data about their use alone without autogenous bone for alveolar cleft reconstruction (Kasabah et al., 2002; Tadjoedin et al., 2003).

Another possible type of bone graft utilized a 1:1 mix of decalcified freeze-dried bone and a granular bioactive glass graft material to rebuild the alveolar cleft defect. The results of the case report showed proper cleft repair as well as better periodontal conditions of the teeth around the cleft area. Teeth were successfully moved into the reconstructed bone composed of demineralized freeze-dried bone and bioactive glass (Yilmaz et al., 2000).

Skoog (1965) first introduced the term “boneless grafting,” which was later modified by others to primary gingivoperiosteoplasty. He hypothesized that closure of the healthy mucoperiosteum over the alveolar cleft site in conjunction with primary lip repair would create a favorable environment for potential osteogenic effects that would in turn allow bony bridging to cross the alveolar cleft defect. (Brusati and Mannucci, 1992; Horswell and Henderson, 2003; Rawashdeh and Telfah, 2008).

In 1980 Ralph Millard pioneered the use of a small gingivoperiosteal flap for alveolar cleft repair at the age of 5 months. The flap was elevated from both the alveolar cleft margins and then rotated over in the form of a tunnel to close the alveolar defect. This technique had the advantage of maintaining good periosteal vascularity. However, the disadvantage of the procedure is that it can be applied to limited defects only. In cases of wide alveolar clefts, Millard suggested the use of active orthopedic devices at 3 months of age pre-surgically. The orthopedic device was known as the ‘Latham device’ (Henkel and Gundlach, 1997).

Previous studies have reported that alveolar clefts treated with primary cleft repair that filled with adequate bone supported erupting teeth. Bone formation after primary cleft reconstruction using gingivoperiosteoplasty has been reported to occur in 50–100% of cases (Brusati and Mannucci, 1992; Horswell and Henderson, 2003; Rawashdeh and Telfah, 2008). While bone grafting is not a common pediatric procedure in some medical centers, other medical centers, for example the Oslo group, take the position that almost all alveolar clefts even if treated with gingivoperiosteoplasty, will eventually require bone grafting due to deficient bone quantity. Medical centers that perform primary gingivoperiosteoplasty question whether infants who have undergone primary bone grafting may have received unnecessary grafts. (Horswell and Henderson, 2003).

#### 5.4. New grafting materials

The TGF- $\beta$  family includes multifunctional bone morphogenetic proteins (BMPs) that are the only molecules that signal to induce new bone formation at either orthotopical or heterotopical sites. In addition, their osteoinduction power suggests that they may have clinical benefits as novel alternatives to traditional bone grafts (Kirker-Head, 2000).

Tissue engineering has been used to provide new alternatives for bone reconstruction. Tissue engineering uses three dimensional bone-like scaffolds that are loaded with bone cells that are planted in the bony defect for bone reconstruction. The scaffolds used can be of natural or synthetic origin. Tissue engineering has clinical applications that have progressed from the laboratory to the bedside. The clinical applications for tissue engineering include augmenting alveolar ridge defects and filling limited sized defects in the jaw bone (Pradel et al., 2008; Schmelzeisen et al., 2003).

A combination of autologous mesenchymal stem cells and platelets rich in plasma was first introduced by [Hibi et al. \(2006\)](#) for alveolar cleft reconstruction, which provided adequate bone bridging at the cleft site. Furthermore, the permanent lateral incisor and canine teeth had moved into the newly formed bone. [Behnia et al. \(2009\)](#) utilized mesenchymal stem cells carried on a scaffold that combined demineralized bone and calcium sulfate for alveolar cleft reconstruction. The results suggested that the amount of bone formation was inadequate and indicated that the conventional bone substitute was a suitable scaffold for mesenchymal stem cells for alveolar bone regeneration.

Guided bone regeneration (GBR) is a surgical technique that has broad appeal to improve both the quality and the quantity of the newly formed osseous structures in localized areas of alveolar ridge discontinuity defects. It also enhances the osteoinduction power of different grafting materials that are extensively used for bone reconstruction ([Sanchez et al., 2003](#)).

Autologous platelet concentrates contain storage pools of growth factors, which are assumed to promote tissue repair. The growth factors retained in the platelet concentrates include platelet derived growth factor (PDGF), tumor growth factor beta (TGF-beta), vascular endothelial growth factor (VEGF), and other cytokines. For these reasons, treatment with autologous platelet concentrates in clinical situations that require rapid healing and augmented tissue regeneration have gained popularity and shown some positive outcomes. Their application in the form of fibrin meshwork that gives rise to support and adhesion will result in confinement of growth factors secretion to a limited area ([Anitua et al., 2004](#)).

Platelet-rich plasma (PRP) is the first generation of platelet concentrates that has been utilized widely to accelerate both soft and hard tissue healing. Isolation of PRP is the first step in preparing PRP, then calcium chloride and bovine thrombin were added to accelerate gel formation. [Sanchez et al. \(2003\)](#) studied the potential hazards that accompany the use of PRP. They concluded that the generation of antibodies to factors V, XI, and thrombin might be attributable to the use of bovine thrombin, and life-threatening coagulopathies could occur ([Sunitha and Munirathnam, 2008](#)).

Platelet-rich fibrin (PRF) was initially introduced by [Choukroun et al. \(2006\)](#). PRF was considered as the second-generation platelet concentrate. It has been shown to be superior to the first generation traditionally prepared PRP. These advantages include the absence of biochemical handling of the blood and simplified preparation ([Sunitha and Munirathnam, 2008](#)). Furthermore, it demonstrated that bovine thrombin added during preparation of PRP may have toxic effect on body cells. On the other hand, PRF preparation is a mechanical and non-biochemical procedure that does not add thrombin. In contrast to PRP, which rapidly releases growth factors just before cell outgrowth from the surrounding tissue, the fibrin meshwork formed within PRF minimizes proteolysis and the rapid destruction of growth factors. Therefore, the activity of the growth factors can be retained for a longer time due to controllable, long-term growth factor release. Levels of released TGF- $\beta$ 1 and PDGF-AB are markedly increased and peak at day 14, then decrease slightly ([Ling et al., 2009](#)).

Prepared PRF comes as a gel like material that can be used in conjunction with bone substitutes. The combination offers

several advantages including enhanced wound repair, improved bone maturation and growth, stable grafting, adequate wound sealing and hemostasis, and improved handling of the graft materials. Moreover, PRF can be pressed into a membrane and used for guided bone regeneration. Clinical studies have emphasized that combining growth factor rich PRF and bone grafts could enhance bone quality and quantity ([Sunitha and Munirathnam, 2008](#)).

### 5.5. Evaluation of alveolar cleft bone grafting

Numerous studies have been done to compare the complex methods used for analyzing bone grafts. The analytical techniques attempted to trace the position height and width of bone close to the roots of the teeth is at the cleft site. Inter- and intra-examiner variability affects the reliability of these analytical methods for use in clinical management ([Hynes and Earley, 2003](#)). In the past standard periapical radiographs were obtained in order to evaluate the reconstructed alveolar cleft, and evaluated using the Bergland scale and Chelsae scale ([Trindade et al., 2005](#)).

For many years, bone graft success and measurement relied on what was considered the gold standard method. In Bergland grading system, a four point scale was used to classify and evaluate each graft depending on the coronal level of the interdental bone graft compared to the normal bone ([Hynes and Earley, 2003](#); [Kindelan and Roberts-Harry, 1999](#); [Nightingale et al., 2003](#); [Trindade et al., 2005](#)). One drawback of the Bergland scale was that the graft was compared only at the interdental level using the normal bone level as a reference. To overcome this disadvantage, the Chelsea scale was developed to assess the level of the bone within the cleft compared to the full length of the root surfaces of the teeth next to the cleft and cleft midline at eight sites. Another four point scale developed by Kindelan compared the percentage of bony infill at the cleft site to the pre surgical occlusal radiographs and post-operative records ([Nightingale et al., 2003](#)).

Conventional periapical, occlusal, and orthopantomogram radiographs that are used for alveolar cleft assessment are not reliable due to distortion of the images at the cleft area. In addition, the two dimensional evaluation does not provide a reliable anatomical index, which creates subsequent difficulties for accurate three dimensional evaluation of the cleft area. Therefore, CT scan should be used to overcome these drawbacks in evaluating the alveolar cleft ([Nightingale et al., 2003](#)). Recently, studies have assessed reconstruction of the alveolar defects using CT scan and specialized software to measure the volume of the defect and determine the amount needed for grafting. Moreover, CT scans can also be used to evaluate the amount of newly formed bone in the defect and provides accurate results based on 3D analysis ([Honma et al., 1999](#); [Tai et al., 2000](#)).

Between 1998 and 1999 cone-beam (CB) systems were introduced for oral & maxillofacial imaging, and numerous CB devices are commercially available. Currently, CB systems have been extensively indicated for several maxillofacial surgery imaging ([Robert et al., 2007](#)). CB scanners offer several advantages over conventional CT scanners including a limited radiation dose that is approximately 15-times less than conventional CT scanners, minimal scanning time (10–70 s), and high quality, high resolution diagnostic imaging ([Scarfe et al.,](#)

2006). The available CB machines are capable of matching the geometric range of the conventional CT scanners in terms of accuracy. It has also been demonstrated that accurate volumetric measurements can be achieved with the data acquired from CBCT devices. Halation artifacts of the image intensifier produce potential impairment of the segmentation quality in objects located at the periphery of the imaging field should be taken into consideration (Robert et al., 2007).

## 6. Summary

In terms of promoting growth and restoration of function, secondary bone grafts of the alveolar cleft are the most widely accepted timing for surgical reconstruction. Autogenous bone grafts are still considered the gold standard for alveolar cleft reconstruction with most reliable, predictable, and best outcomes despite the emergence of novel composite grafting materials with powerful osteoinductive capabilities.

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## Conflict of interest

The author declares that he has no conflict of interest associated with the material used in the current article and no financial interest as well.

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