A COMPARATIVE NASAL ANTHROPOMETRIC MEASUREMENT IN UNILATERAL CLEFT LIP AND PALATE PATIENTS AFTER RHINOPLASTY AND NORMAL POPULATION

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SPSS    Statistical Package for Social Sciences
UCLP    Unilateral Cleft Lip and Palate
UCL     Unilateral Cleft Lip

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The nasal deformity in cleft has been viewed as the most challenging reconstructive problems in cleft surgery. Nose anthropometric measurement in post cleft repair patient is to determine the goal of surgical repair in producing nose in most “normal” outcome. Nose anthropometric measurement in these patients is to determine that this goal is achieved by comparing measurements in post rhinoplasty with cleft nasal deformity with normal population. A retrospective study was carried out in Department of Plastic and Reconstructive Surgery, Hospital Kuala Lumpur. Direct anthropometric measurements were performed on post rhinoplasty patient with cleft nasal deformity and results were compared with normal population. A total of 72 patients were participated in this study. All open rhinoplasty were performed with augmentation with rib cartilage graft. Eight anthropometric measurements selected included nasal height (n-sn), nasal width (al-al), nasal tip protrusion (sn-prn), columella length (sn-c’), width of columella (sn’-sn’), width between the facial insertion (ac-ac) and width of nostril floor of right and left (sbal-sn). The post rhinoplasty patients had an increase in nasal height, nasal tip protrusion and columella height. The nasal index in both group are within mesorrhine nose type, the UCLP group had higher nasal index compared with control group. Open rhinoplasty with rib cartilage graft had improving esthetic appearance of nose in cleft nose deformity. Further additional other surgical techniques may enhance further the appearance by addressing other issues in secondary cleft nose deformities.
INTRODUCTION
CHAPTER 1

INTRODUCTION

Cleft lip and/or palate is the most common congenital craniofacial abnormality; occurring approximately 1:1000 live births (Dixon et al., 2011). They may be affected by combination of facial difference, swallowing and speech disorders. Birth prevalence and incidence of oral facial clefting showing ethnic variation.

It is generally thought that populations of Asian descent have the highest prevalence about 2 per 1000 births with Caucasian population having intermediate prevalence with 1 per 1000 and Africans populations having lowest prevalence (Cooper et al., 2006).

As a central and prominent landmark of the face, the nose is the focal point of the attention during social interaction and affecting overall facial appearance. Physical attractiveness plays an important role in the social life and interactions of children, particularly during adolescence. Repair of unilateral cleft lip and palate (UCLP) rarely produces ideal facial esthetics. After closure of UCLP, patients invariably demonstrate some degree of deformation of the nose and upper lip, such as nasal asymmetry, scarring of the philtral area and uneven mucocutaneous junction. These craniofacial impairments can result in negative psychosocial consequences ranging from low self-esteem to the risk of social rejection. (Tobiasen, 1987; Semb et al., 2005).
Cleft lip nose deformity (CLND) is composed of multiple features, including thin and philtral dimple of the upper lip, retracted columella, deformed nasal cartilaginous framework, a hanging nasal tip and a convex nasal profile (Stal and Hollier, 2002; Guyuron, 2008).

Secondary cleft nasal reconstruction should not be performed without first evaluating and correcting any significant problems with the skeletal base under the nose. This may involve alveolar bone grafting and orthognathic surgery (Posnick and Tompson, 1992). All of these maneuvers increase the projection of the lower maxilla without changing projection of the nasal dorsum. The “tripod” of the lower lateral tip cartilage composite is elevated anteriorly by these procedures, thereby increasing tip projection. (Cutting, 2000). The most challenging aspect of cleft lip surgery is correction of nasal deformity, therefore secondary surgery to improve nasal contour and symmetry is commonly required. The aim of rhinoplasty is to create a nose that esthetically pleasing to the patients without compromising nasal function.

Nowadays an attractive nose in Asian countries is a nose where the nasal dorsum and tip is slightly accentuated instead of the natural looking nose. The use of the rib cartilages in cases needing major augmentation of the dorsum, had robust strength and ample volume. However, the use of the rib cartilage for dorsal augmentation has been continuously criticized for its tendency to warp and donor site morbidity. With continuous efforts and increasing experience with rib cartilage harvesting techniques, these disadvantages have been overcome in many aspects. (Gunter et al., 1997)
Accurate preoperative and postoperative analysis with evaluation of the anatomy and appearance of the nose are essential for assessing the efficacy of surgical techniques as well as for modifying surgical procedures based on their long term outcome. Anthropometric measurements, photographs and cephalometric radiographs are the primary means by which the nose following rhinoplasty has been assessed. (Farkas et al., 1993; Liou et al., 2007). A standardized method of assessment for the cleft deformity and the treatment outcomes is important. However, much controversy remains systemic, valid and reliable methods for evaluating the outcomes after rhinoplasty. (Kosowski et al., 2009)

Anthropometry is the measurement of living objects. It has been shown to be useful in orthodontic research, where the soft tissue morphology of the face can be studied more reliably than comparisons from radiographs. (Farkas et al., 2000). Several studies used anthropometry, which provides a means of quantitative analysis of the extent of abnormal morphology and degree of disproportion associated with the repaired cleft lip and palate through direct linear and proportional measurement. (Farkas et al., 1993).
The purpose of this thesis to evaluate whether rhinoplasty with rib cartilage graft is feasible in cleft lip nose deformity to create near normal nose after repair. By using direct anthropometric measurements, we can compare the outcome after open rhinoplasty with control group. Thus, with these we can enhance and improve our surgical technique to achieve near normal nose appearance cleft patients. Direct anthropometric measurement is reliable, easily accessible and cheap.
LITERATURE REVIEW
CHAPTER 2

LITERATURE REVIEW

2.1 Epidemiology of oral clefts

Cleft lip, cleft palate or both are among the most common congenital malformations. Cleft lip and palate and cleft palate can be syndromic but majority are isolated defects, often termed as non-syndromic. (Dixon et al., 2011). The incidence varies with ethnicity, geography and nature of the cleft itself. The incidence reported in many parts of the world varies from 0.8 to 2.69 per 1000 live birth. There were higher occurrence of cleft lip and/or palate in Asians compared with Caucasians. The incidence of isolated cleft palate is racially homogenous at approximately 0.5 per 1000 live birth. (Vanderas, 1987)

Unilateral clefts are nine times as common as bilateral cleft, and occur twice as frequently in the left than the right. The ratio of left: right : bilateral clefts is 6 : 3 : 1. Males are predominantly affected by cleft lip and palate (male: female 2:1) whereas females are more commonly affected by isolated cleft palate. (Lieff et al., 1999; Chung et al., 2000). In Malaysia, a study conducted in Kuala Lumpur Maternity Hospital reported the incidence was 1.24 per 1000 live birth. The Chinese had the highest incidence of 1.9 per 1000 live birth, while the Malay had the lowest incidence of 0.98 per 1000 live birth and the most common type was reported to be unilateral cleft of hard and soft palate. (Boo and Arshad, 1990).
2.2 Embryology of clefts

The face is formed from fusion of five different prominences (paired maxillary and mandibular and single frontonasal prominences). The development of face begin during the fourth to ninth week of pregnancy. Facial clefts have been considered as a result of failure of this normal fusion. The obliteration is achieved by mesodermal migration and merging. The failure of obliteration leads to an abnormal persistence of groove which produces a cleft (STARK and KAPLAN, 1973). The cleft can be unilateral, complete or bilateral. (Millard, 1980).

The nose arise from nasal placodes during the fourth week of pregnancy. The nasal placodes develop as bilateral thickening on the surface ectoderm of the lateral surface of the frontonasal prominence. Hypertrophy of the tissue surrounding the nasal placodes creates the nasal pits that divide medial and lateral nasal prominences. The medial nasal prominences form the philtrum, septum and the premaxilla of the nose, whereas the lateral nasal prominences form the nasal alae. The septum continues to grow posteriorly, reaching the palatine structure. Through the fusion, the nasal and oral cavities as well as the right and left nasal chambers are formed. (Thorne, 2013)
The upper lip is derived from medial nasal and maxillary prominences. Failure of fusion between these prominences results in cleft lip. The cleft may affect only the upper lip or it may extend more deeply into the primary palate and thus the floor of the nose. Cleft of the primary palate always include cleft lip and cleft of the alveolus. Development of the secondary palate is by fusion of secondary palatal prominences beginning during eight week’s gestation until twelve week’s gestation. Failure of this fusion, the cleft lip is combined with cleft palate, forming the cleft lip and palate formation. (Millard, 1980).

In Carsten neuromeric model of developmental fields, the face could be conceptualized as a series of independent fields with separate blood supply and embryonic behavior. Cleft lip and palate repairs should be sequentially performed to respect the vascular territories that supply osteogenicmucoperiosteum of the alveolus. A model of midline fusion or paired A fields that includes the columella and philtrum as soft tissue components sharing a common blood supply with the premaxilla, septum, vomer and ethmoid permits relocation of the Cupid’s bow in repair of cleft lip repair. The architecture of the A fields is defined the perfusion pattern of the internal carotid artery via the ophthalmic artery. (Carstens, 2002).
The B fields are derived from paraxial mesoderm. As the forebrain elevates, the maxilla (B field) grows forward to merge with the medial and lateral nasal prominences (A fields) that surround the invaginating nasal placodes. Lip closure is completed as the lateral lip element fuses with A field nasal elements and pulls prolabial element downward. Increased vertical height of the lateral wall comes primarily from the B field for as the maxilla grows it contributes proportionally more to lateral wall surface. Failure of bridge results in complete cleft lip.

B field shelf elevation occurs such that primary contact with the A field midline is timed occur immediately upon completion of alveolar fusion. If no deviation of the A fields from the midline, primary contact of palatal shelves (B fields) with the septo-vomerine-ethmoid complex (A field) will occur at the incisive foramen, the “zipper” will engage and full palatal closure. Such primary contact failure results in a complete palatal cleft. (Carstens, 2002)
2.3 Aetiology of Cleft Lip and Palate

Cleft lip and palate is etiologically heterogenous and this has critical implications for understanding the biology of facial development, how environmental risks interact with genetic factors. Since 20% of patients in different populations have a positive family history, genetic factors thought to play an important role in the etiology of this birth defect. Families of patients affected by the cleft lip and palate have different genetic background in comparisons to families with isolated cleft lip. (Goto et al., 2013).

There is no single etiologic model would be appropriate for oral clefts. Oral clefts divides into three groups which are represented by syndromic which includes monogenic (single-gene disorders), chromosomal and environmental etiologies. The next group is familial which includes those with two or more affected individuals in first, second or third degree relatives. Familial accounts for 25% of UCLP and 12% of isolated cleft palates. Last group of oral clefts are isolated or non-familial. This group accounts for 75% of UCLP and 80% of isolated cleft palate cases. (Bixler, 1981). Predominance of left sided clefting and the male excess of cleft lip with or without cleft palate also suggests the importance of genetic susceptibility. (Mossey and Little, 2002).
One of the most important factors affecting safety is the stage of pregnancy during which an exposure occurs. Organogenesis (18-60 days post conception in humans) is the time during which the embryo is most sensitive to many teratogenic exposure and when most structural anomalies are produced. (Polifka and Friedman, 2002).

Maternal smoking and alcohol consumption has been associated with increased risk of cleft lip and palate. The risk of maternal smoking (1-10 cigarettes per day) in the first trimester is more critical than that before pregnancy. So it is more likely to have a child with orofacial clefts if smoking happens in the first trimester. Combination of maternal smoking and paternal preconception smoking in general was associated with significantly increased risk of having newborn with oral facial clefts. (Lieff et al., 1999).

Vitamin B6 (pyridoxine and related compounds) is also a cofactor in homocysteine metabolism and reduces the occurrence of these clefts in animals (Schubert et al., 2002). B vitamins are essential in various stages of metabolism and growth mainly as coenzymes. Therefore, supplementation of B vitamins in pregnancy for prevention of CLP may be useful. The teratogenic factors was most pronounced in B1 and total B group deprivation experiments through 1-18 days of gestation but absent in B12 and folic acid restriction. In contrast, there was no substantial effects on prenatal development of total food deprivation in the critical period of palatogenesis on gestational days 12 and 13.
Maternal alcohol is a well-known cause of fetal alcohol syndrome with positive association reported in orofacial clefts. The incidence of CLP was significantly elevated when mothers consumed ≥ 4 drinks / month (Romitti et al., 1999).

Zinc is important in fetal development and its deficiency causes isolated cleft palate and other malformations in animals. It may important to add that in the etiology of cleft lip and palate, zinc deficiency status alone may not be a strong risk factor (Munger et al., 2009). Other nutrients that could play a part in development of orofacial clefts include riboflavin and vitamin A. Fetal exposure to retinoid drugs can result in severe craniofacial anomalies but the relevance of this finding to dietary exposure to vitamin A is uncertain. The increased frequency of defects was concentrated among the babies born to women who had consumed high levels of Vitamin A before the seventh week of gestation. The ratio of prevalence among the babies born to women who consumed more than 15,000 IU per day to the prevalence among the babies born to women who consumed 5000 IU or less per day was 3.5 (Rothman et al., 1995).

Anticonvulsant drugs notably diazepam, phenytoin and phenobarbital increase risk of these anomalies. It has been suggested that genetic differences in folate metabolism may account for the increased of congenital anomalies in the children of women with epilepsy treated with anticonvulsant drugs. The most susceptible period at 18-60 days post conception. Positive associations with maternal corticosteroid use in pregnancy have been reported (Polifka and Friedman, 2002).
2.4 Anatomy of cleft lip and nose

Unilateral cleft lip and palate (UCLP) has a typical appearance which involves structural framework of the nose as well as the soft tissue envelope. The platform for the nose in the maxilla is cleft wide alar base at affected side and skewed nose. The anterior portion of the septum deviated with its base dislocated out of the vomerine groove and with the anterior nasal spine on the floor. The dislocation is responsible for a deviation of nasal tip. There is loss of nasal tip definition and tendency to bifidity (Byrd et al., 2007).

The asymmetric nasal tip results from the irregularly formed lower lateral cartilage on the cleft side. On the cleft side, the medial crus is shorter than the lateral crus longer, with a less defined and wider dome. This further results in a poorly defined nasal tip with less projection (Li et al., 2002).

The columella is shortened on cleft side with deviated columella base towards the non-cleft side. The lower lateral alar cartilage is deviated with the medial crus lowered on the columella and the lateral crus displaced laterally resulting in downward rotation of the nasal tip and alar cartilage, causing thickening of the ala and hooding of the nostril rim. Since there is no skin bridge connecting the alar base to the footplates of the lower lateral cartilages of the nose, the unopposed pull of orbicularis oris muscle results in a more severe nasal deformity (de Sá Nóbrega, 2005).
The alaes of the nose are flattened, causing in horizontal orientation of the nostril. It extends laterally with displaced alar base. The nostrils are asymmetrical and retropositioned because of deficiency in the underlying frame. There is hypoplasia of maxilla on the cleft side with displaced premaxilla and maxillary segments (Stal and Hollier, 2002; Guyuron, 2008; Kaufman et al., 2012).
2.5 The nose – a central problem

The nose is the central feature of the face, and its dimension and proportions, whose imperfections rhinoplasty aims to correct, play an important role in the overall perception of facial symmetry. A major goal of the repair of cleft patients is to improve the esthetics and function that enhance social perceptibility. Balance, symmetry and proportion are the components of the esthetic appearance.

This complexity results from combination of altered anatomy, surgical scarring from previous reconstructive attempts and the effects of nasal growth (Wang and Madorsky, 1999). Distortions of the nose can vary from almost invisible to catastrophic, mostly dependent on the severity and type of cleft (Van Beek et al., 2004). To correct the nasal deformity in cleft lip and palate patient is a challenge.

Despite careful treatment during childhood and adolescence, adults with cleft lip and palate are left with residual deformities—primary related to the malformations or secondary to earlier treatment. In the long term, the treatment of cleft lip and palate patients should provide good esthetic and functional (speech and occlusion) results (Jeffery and Boorman, 2001; Marcusson et al., 2002).
Definitive nasal correction is planned after completion of the nasal growth, typically after the age of 14-15 years old (Matukas and Louis, 1993). The cleft lip nasal deformity is often retained during primary lip repair due to interference with nose growth, ineffective repair and resulting scars that make secondary correction difficult (Broadbent and Woolf, 1984; Byrd et al., 2007).

Information about nasal dimensions is essential in esthetic and functional reconstruction of the nose. Many studies about anthropometric measurements of the nose have been performed, and there are various reports on the racial and ethnic morphometric differences on the nasal complex in the literature (Porter and Olson, 2003; Farkas et al., 2005; Dong et al., 2010). However, report of anthropometric measurements of the Malaysian noses (including Malay, Chinese and Indian) are limited. There are anthropometric studies in Malay and Malaysian Indian was done on the parameters of the face and head regions, but not extensive enough (Ngeow and Aljunid, 2009b; Ngeow and Aljunid, 2009a).

The measurements of the “ideal” nose found in the literature are not necessarily accepted in all cultures and patient’s satisfaction is not guaranteed by following these measures. There exists in major differences in esthetic perception among plastic surgeons and the general public depending on their gender, age, country of origin and ethnic background (Broer et al., 2012).
2.6 Psychosocial Factors

Cleft lip and palate frequently had stigma experience by peers due to less attractive facial appearance, speech difficulty and hearing impairment. Cleft lip and palate patients were perceived to have lower esteem, difficulty in the learning process and a tendency to be more depressed and anxious (Ramstad et al., 1995; Noor and Musa, 2007). Most of them were not satisfied with their facial appearance and desire further treatment (Hunt et al., 2005).

Albeit completely treated in cleft patient, they had delay in education and marriage. They also received lower income, had a lower chance of employment and became more dependent on their families compared with non-cleft individuals (Oosterkamp et al., 2007). Facial appearance is an important factor in treatment outcome in cleft lip and palate patient (Kuijpers-Jagtman et al., 2009). This visible defects seems of greater concern to patients than functional problems. Dissatisfaction with the appearance of the lip and nose may be due to poor surgical outcome.

In general, patient’s subjective assessment and satisfaction is essential in determining success in esthetic surgery. Previous studies indicated that cleft patients were less satisfied with the outcomes, whilst medical professionals usually judged the outcomes more optimistically (Marcusson et al., 2002; Sinko et al., 2005).
In some studies, many adult patients with repaired cleft lip and palate are satisfied with their facial appearance and dental function (Noar, 1991; Ramstad et al., 1995). Noar reported that 85.7% of patients were satisfied with their appearance after the completion of treatment, although 54% of patients were unhappy with some features of their faces. In cleft patients and their family, they considered teeth and nose as the most important organs (Noor and Musa, 2007). The findings on cleft patients dissatisfaction with their nasal appearance and still needed further surgical correction, including rhinoplasty (Ramstad et al., 1995)(Marcusson et al., 2002).

Parents of unilateral cleft patient were most concerned about the asymmetrical position of the nose within the face and the nasal tip. Hence, a depressed tip or a double tip deformity requires surgical attention, optimized tip definition is important (Mommaerts and Nagy, 2008).

Surgery being the immediate option of dealing with certain issues related to disfigurement, is beneficial in dealing with both physical and psychological issues. Surgery usually results in increased self-esteem, self-confidence and satisfaction with appearance (Sousa et al., 2009). Finally regardless of intervention, patient expectations must be considered before and after surgery. No amount of surgery will achieve the perfect anatomy and symmetry in most of these patients.
2.7 Surgical treatment of cleft nose

A major goal of cleft lip and palate treatment is to improve the facial esthetic appearance and enhance the social acceptability in society. The most common features to be the focus of teasing are appearance of the nose and the lip when compared with teasing about speech, appearance of teeth and facial appearance (Semb et al., 2005).

Although nasoalveolar molding and initial lip surgery in early infancy minimize the cleft lip and nose deformity, many patients require secondary rhinoplasty to correct alar-columellar disproportion in their teenage years once growth is complete (Stal and Hollier, 2002).

Cleft lip and nasal deformity is three dimensional structures because it involves skin envelope, nasal bone and cartilage, nasal vestibular lining and skeletal platform. Each of these components requires particular attention during planning the surgery. Secondary cleft rhinoplasty usually attempts to improve the nasal tip, dorsum, alar position and symmetry of the nostrils (Sandor and Ylikontiola, 2006).
In patients with no nasal repair or failed primary repair, the presence of dorsal deficiency or inadequate tip projection in association with a deformed ala is the driving force in rib cartilage graft reconstruction. The great majority of these patients are approached with an open rhinoplasty (Byrd et al., 2007).

Average Asians have bulbous and inadequate nasal tip definition (Mao et al., 2008). In patients with cleft lip nasal deformity, the collapse of the medial and intermediate crura of the lower lateral cartilage seemed more common and severe, which leads to poor tip definition.

The cleft nasal deformities in the adult are related to what is found during the primary repair, but will be altered by any previous surgery e.g. primary rhinoplasty that has been performed. The nasal root is wide and deviated away from the cleft. There is distortion of cleft side lower lateral cartilage with significant nasal tip symmetry. The cartilage is hypoplastic with depressed nasal dome and flattened nasal ala on the cleft side. The cleft side nares can have smaller circumference that its counterpart. Nasal tip support will be weak because of the hypoplastic cleft side lower lateral cartilage (Kaufman et al., 2012).
Many approaches can be used to correct the nasal deformities due to different pathology anatomy. An inherent problem in the treatment of the unilateral cleft nasal deformity is asymmetry at the level of the alar base. One of the most important aspects of cleft lip rhinoplasty is the creation of a symmetric and ideally positioned maxilla, without which the outcome of rhinoplasty, will not be optimal. Therefore, the first step of the surgical procedure is to correct the recessed alar base, which results from hypoplasia of the pyriform aperture such as alveolar bone grafting, distraction osteogenesis and orthognathic surgery (Guyuron, 2008).

Alar base support is essential for attaining definitive repair and relies on the skeletal foundation of the face. Alignment of the maxillary segments and augmentation of the depressed and hypoplastic bony platform with bone grafts assist in better positioning of the base of the nose before the final procedure. Closure of coexisting oronasal and possibly other palatal fistulas results in re-establishment if the normal barrier between the oral and nasal cavities, preventing regurgitation of food and saliva in nasal cavity and eliminating chronic irritation to the nasal lining (Cohen et al., 2003). Alveolar bone grafting should be performed prior to eruption of the canine teeth, between the ages of 9 to 11 years old (Fisher and Sommerlad, 2011). This serves to support and reposition the alar base.
Rhinoplasty aims to improve facial esthetics by improving the dimensions and symmetry of the nose, and objective measurement of facial dimensions could, in time form part of an evidence based approach to evaluating patients who are undergoing rhinoplasty. (Nouraei et al., 2009). Rhinoplasty is a challenging surgical procedure, and alteration of the three dimensional aspects of the nose created by congenital changes will challenge the surgeon’s skill and judgment. The three main factors contributing to this cleft lip nasal deformity are congenital anatomic deficiency, surgical scarring from previous reconstructive attempts and changes related to growth (Wang, 2010).

Timing of cleft lip nasal surgery can be divided into primary and secondary repairs. Primary nasal repair at the time of primary lip repair can improve significantly the cleft lip nasal deformity by achieving greater symmetry and improved overall long-term appearance of the nose. Multiple studies have disproved the idea that early manipulation of the nasal cartilage interferes with growth (McComb, 1985). It is important to note that any surgery done at an early age will subsequently result in scar tissue and consequently affect future surgeries.
Secondary rhinoplasty is a procedure to correct the nasal deformity in cleft lip patients which is performed not in conjunction with the labioplasty procedure. It needs to be performed after facial growth is completed. The definitive rhinoplasty is performed when maxillary and nasal growth has been completed, between 16 and 18 years of age, when more aggressive septoplasty, osteotomies, and cartilage grafting can be done. Each patient requires an individualized approach to timing of secondary rhinoplasty based on the severity of soft tissue and skeletal deformities. (Matukas and Louis, 1993). Surgical techniques rely on well-accepted rhinoplasty principles and are applied for unilateral or bilateral cleft nasal deformities. Reconstruction of the osteocartilaginous framework is the foundation for obtaining consistent esthetic and functional result in secondary rhinopasty.

Rhinoplasty can be performed through and endonasal / close or and open technique. However, because of common asymmetry in the nasal frame, the majority of the cleft lip related nasal deformities are more successfully corrected through an open technique (Guyuron, 2008). The open rhinoplasty approach is preferred for better exposure and visualization of the nasal elements especially nasal cartilage in cleft lip patients. Releasing the latero-superior cartilage attached to the nasal bone and skin, which caused webbing inside the nostrils, addition of strut in columella as a pillar to adjust the dropping of the nose to the upright position, addition of cartilage plate whenever needed in the cleft side, the nostril narrowing on the cleft side could be reduced by enlarging the nostril diameter, the new nostril shape is maintained using a device for several weeks until the healing process is achieved (Gunter et al., 2006).