# PALATAL CLEFT DIMENSION IN PATIENTS WITH UNILATERAL CLEFT LIP AND PALATE AMONG ETHNIC MALAYS: AN IMPLICATION ON SURGICAL OUTCOMES

**BY**

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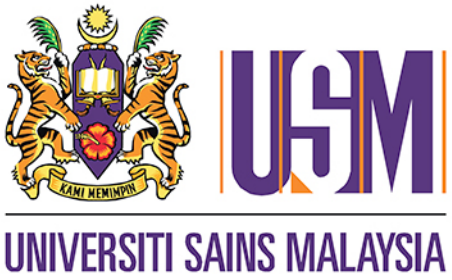



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## IV. LIST OF ABBREVIATIONS

| | |
|---|---|
| **SPSS** | **Statistical Package for Social Sciences** |
| **CL/P** | **Cleft Lip and/or Palate** |
| **CLP** | **Cleft Lip and Palate** |
| **CPO** | **Isolated cleft palate** |
| **UCLP** | **Unilateral Cleft Lip and Palate** |
| **VPI** | **Velopharyngeal Insufficiency** |
| **LL'** | **Alveolar gap width** |
| **CC'** | **Anterior arch width** |
| **TT'** | **Posterior arch width** |
| **AA'** | **Anterior cleft width** |
| **PP'** | **Posterior cleft width** |
| **L-TT'** | **Palatal length** |
| **UvP** | **Uvula-pharyngeal wall distance** |

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## IX. ABSTRAK

Kajian perbandingan tentang pesakit sumbing/rekah bibir dan lelangit antara negara adalah sukar disebabkan variasi kes, protokol merawat yang berbeza, dan juga variasi bangsa dan kaum etnik yang ada pada komuniti yang dikaji. Di negeri Kelantan, di mana majoriti penduduk terdiri dari bangsa Melayu, mempunyai jumlah pesakit sumbing/rekah bibir dan lelangit yang lebih tinggi berbanding purata insiden negara. Ini memberi peluang yang unik kepada pusat kami untuk mengkaji ciri-ciri kumpulan penduduk ini dan melihat keterukan sumbing/rekahan bibir dan lelangit. Satu kajian retrospektif dibentuk untuk mengkaji faktor demografik yang menyumbang kepada insiden dan keterukan sumbing/rekahan bibir dan lelangit berdasarkan ukurun antropometrik. Data antropometrik dianalisa untuk menilai hasil rawatan pesakit sumbing/rekah bibir dan lelangit. Sejumlah 100 pesakit yang menjalani pembedahan sumbing/rekah lelangit ('*palatoplasty*') dari tahun 2000 hingga 2012 dikenalpasti dan rekod mereka dikaji semula. Data kami menunjukkan umur, berat, jantina, bahagian sumbing/rekahan yang terlibat dan salasilah keluarga tidak mempengaruhi keterukan sumbing/rekahan yang dialami. Mengguna nilai antropometri sumbing/rekahan kami mendapati kadar insiden fistula selepas pembedahan dipengaruhi oleh jarak '*posterior palatal arch*' (>35mm) manakala kehadiran '*velopharyngeal insufficiency*' dipengaruhi oleh '*posterior cleft width*' (≥12mm) dan '*relative width of palatal shelves*'. Kami mendapati keterukan sumbing/rekah adalah satu entiti mutifacet dan keterukan ini bergantung kepada pilihan rawatan yang telah dijalankan. Oleh itu, klasifikasi sumbing oleh Veau untuk keterukan sumbing/rekahan bibir dan lelangit yang diterima ramai harus dikembangkan untuk mengambil ukuran antropometry bagi mendapat nilai keterukan yang lebih jitu. Data yang diterima dari kajian ini memberi

nilai tambahan yang bermakna untuk memperbaiki memajukan pemahaman pasukan kepakaran yang merawat pesakit sumbing/rekah bibir dan lelangit.

## IX. ABSTRACT

Comparative studies in cleft lip and palate patients between different countries have been difficult due to regional variations of cases, different management protocols, and racial and ethnic variation that is intrinsic to the population. In the state of Kelantan, which is largely populated by ethnic Malay, it has higher than average national incidence of patients with cleft lip and palate. This presented our centre a unique opportunity to characterize this population patient group, and investigate their cleft severity based on palatal fistula incidence and velopharyngeal insufficiency. A retrospective study was designed to assess and evaluate the demographic factors that may contribute to their clefts' incidence and severity using cleft anthropometric measurements. The cleft anthropometric data was analysed to assess its effect on cleft treatment outcomes. A total of 100 patients who had palatoplasty between 2000 and 2012 were recruited and their record was reviewed. Our results revealed that age and weight at palatoplasty, gender, cleft sidedness and family history did not significantly influence the cleft severity in our population. Using cleft anthropometry, we found that the rate of palatal fistula incidence was significantly affected by posterior palatal arch width (>35mm) whereas the presence of velopharyngeal insufficiency was significantly affected by posterior cleft width (≥12mm) and the relative width of palatal shelves. Therefore, cleft anthropometric measurement is essential to accurately determine cleft severity and thus, their treatment outcomes. The data obtained from this study forms invaluable information to improve the local cleft team's understanding, and advances their management of cleft patients in this region.

# INTRODUCTION

# CHAPTER 1

## 1.0 Introduction

Cleft lip and/or palate (CL/P) is the fourth most common birth defect and the most frequently encountered congenital craniofacial anomaly (Normastura *et al*., 2008). The incidence of clefts varies between countries and racial or ethnic groups (Schutte and Murray, 1999). While 1 of 800 children in the United States is born with a cleft lip or palate, developing countries demonstrate a higher rate estimating 1 in every 500 to 600 births (Bender, 2000). In Malaysia, the incidence of cleft lip and palate ranged from one in 1006 to one in 941 live birth with the Northeastern state of Malaysia, Kelantan, recorded higher than the average incidence of one in 700 patients (Halim and Singh, 2000).

There has been a large volume of studies conducted to review the management of cleft lip and palate patients. However, comparative studies in cleft lip and palate patients between different countries have been difficult due to regional variations of cases, different management protocols in each centres, and racial and ethnic variations that are intrinsic to the population (Zreaqat *et al*., 2009). With a wide variety of incidence, features and treatment outcomes of cleft lip and palate in the world, the Northeastern state of Malaysia, Kelantan, present a unique opportunity to study the epidemiology of the local Malay population that has a higher than average incidence of cleft lip and palate in Malaysia.

The goals of a successful cleft palate repair (palatoplasty) consist of complete palatal closure, normal speech development, and maintenance of undisturbed maxillary growth (Losken *et al*., 2011). Although there are many methods to evaluate the outcome of cleft palate repair, one of the most important outcome measures in cleft palate surgery is its complication rate such as palatal fistula formation, and the adequacy of velopharyngeal closure (Lam *et al*., 2012). Occurrence of palatal fistula may give rise to complaints of hypernasal speech, articulation problems, and food and liquid nasal regurgitation (Landheer *et al*., 2010). Inadequacy of velopharyngeal closure after cleft palate surgery results in velopharyngeal insufficiency (VPI), which can also manifest as hypernasal speech and nasal air escape during speech production (Lam *et al*., 2012).

Although numerous techniques have been described in closure of cleft palate, it remains a challenging endeavor with incidence of palatal fistula remained high in many series, ranging from 3.4-45% (Muzaffar *et al*., 2001, Wilhelmi *et al*., 2001). Velopharyngeal insufficiency after cleft palate repair is typically reported in 2% to 30% of patients with cleft palates (Lam *et al*., 2012). Over the years, many factors attributed to outcomes of cleft palate repair had been identified (Lam *et al*., 2012, Becker and Hansson, 2013). One of the most important factors identified is the initial cleft width or severity (Cohen *et al*., 1991, Muzaffar *et al*., 2001). The classification of cleft severity generally is based on bilateral or unilateral, and complete or incomplete (Slade *et al*., 1995). However, cleft severity also can be determined on the basis of cleft or palate size within the general classifications of clefts (Chiu and Liao, 2012). It seems intuitively clear that patients with more severe clefting, which is technically more challenging to repair, are more likely to have poor outcomes.

The size or width of the cleft in newborn children with unilateral cleft lip and palate showed a wide variation (Chiu and Liao, 2012). The degree of separation of the maxillary segments and the amount of tissue deficiency determine the size of the cleft in infancy (Chiu and Liao, 2012). Although there had been numerous studies on the effect of cleft width on palatal fistula, most of these studies involved examining correlation between the cleft width and the rate of postoperative fistula formation through severity classification or direct cleft width measurement (Landheer *et al*., 2010, Lam *et al*., 2012). There have been very few authors who have attempted to specifically quantify cleft to palatal arch width ratio as a risk factor for poor postoperative outcomes (Landheer *et al*., 2010).

The quantitative measurement of cleft width directly as a measure of cleft severity are not accurate and proportionate enough to reflect the actual cleft severity that is also influenced by the size of the palatal arch width (Suzuki *et al*., 1993). The mere quantitative measurement of the cleft width would not have provided the correct picture of the degree of severity of the cleft. Therefore, the present study aimed at finding an association between the actual cleft width in relation to its corresponding palatal arch width, and attempt to establish the association between their width ratio to the incidence of postoperative complications such as palatal fistula and velopharyngeal insufficiency.

## 1.1 Rationale

There are numerous treatment protocols available in different centres for cleft lip and palate patients all over the world but none is universally accepted (Precious, 2001). The presence of palatal fistula compromises the treatment quality and is a great challenge in the rehabilitation of individuals with cleft lip and palate. Having recorded higher incidence of cleft lip and palate than the average Malaysian across all the states, Kelantanese population in this Northeastern state provided us with a unique opportunity to study this population consisting of majority ethnic Malay (Normastura *et al*., 2008).

To date, there have been numerous studies conducted among this group of subjects with cleft lip and palate such as dental arch relationships, psychological status, facial morphology and their genetic inheritance (Salahshourifar *et al*., 2011, Zreaqat *et al*., 2012). However, to optimize the treatment of this selective group of patients, there is a fundamental need for data on their cleft severity, and the preoperative and postoperative outcomes. This is imperative if local surgeons are to have a sound basis on which they can tailor their treatment and improves the outcome of these patients. It is therefore of great interest that the outcome of cleft palate repair is evaluated against cleft severity in this region, and it should provide the region with a level of information that is presently unavailable.

# LITERATURE REVIEW

# CHAPTER 2

## 2.0 Literature Review

### 2.1 Classifications of Facial Clefts

Craniofacial anomalies are relatively uncommon. This is marked by the lack of concensus in their classification and terminology over the years. Some authors focused their analysis to restricted areas of the face while others tried to classify based on anatomical malformations (Karfik, 1966, Tessier, 1976, van der Meulen *et al*., 1983, van der Meulen and Vaandrager, 1989, Gunther *et al*., 1998). Only a handful of authors employed morphogenesis basis in their consideration (DeMyer, 1967, Mazzola, 1976). The above approaches showed the dual conceptualization between morphological (anatomico-clinical) and morphogenetical classification.

The first classification of rare craniofacial clefts was by Morian in 1887, who described three types of clefts (Whitaker *et al*., 1981). The American Cleft Palate Association classification devised a more pathogenetic classification and focused particularly on cleft lip and palate (Harkins *et al*., 1962). This was later modified by Boo-Chai in 1970, who subdivided oro-ocular clefts into Type I (coursing from lateral to cupids bow to medial canthus) and Type II (from lateral to cupids bow to mid-lower lid or lateral canthus) (Boo-Chai, 1970). In 1966, Karfik *et al*. also proposed a detailed classification of rare clefts based on their embryologic and morphologic

knowledge (Karfik, 1966). Tessier formulated an anatomical classification system based upon the orbit as the frame of reference, and the clefts are based around this axis (Tessier, 1976). This system is still widely adopted today for its ease of use and description.

In 1981, the Committee on Nomenclature and Classification of Craniofacial Anomalies of the American Cleft Palate Association grouped craniofacial disorders according to their etiology, anatomy, and current treatment principles (Whitaker *et al*., 1981). The committee proposed five categories of deformity identified as I, facial clefts/encephaloceles and dysostosis; II, atrophy/hypoplasia; III, neoplasia/hyperplasia; IV, craniosynostosis; and V, unclassified. With better understanding of the development of facial skeleton, van der Meulen *et al*. proposed a comprehensive system of classification based on embryogenesis, in which they described anomalies originated from an S-shaped craniofacial developmental helix (van der Meulen *et al*., 1983). Under their classification system, cleft lip and palate is classified as premaxillo-maxillary and intermaxillo-palatine dysplasia. Further understanding of faults in embryogenesis can be attributed to Carstens *et al*. in 2002 (Carstens, 2002). Using Carstens's neuromeric theory, Tessier's observational cleft classification system was redefined using neuroanatomic embryology and provided a more rational rearrangement of cleft zones, particularly near the midline. His theory allowed understanding of common craniofacial problems such that cleft palate, encephaloceles, craniosynostosis and cranial base defects can be analyzed in the same way.

Of all facial deformities, classification of cleft lip and palate has received the most attention. Over the years, there has been numerous classification systems described by various authors based on their embryological and anatomical understandings. Berlin and Millard in the 1970's had provided comprehensive reviews of these classification systems (Whitaker *et al*., 1981). While the earlier classification systems of Davis and Ritchie (1922), Veau (1931) and Fogh-Andersen (1942) were based upon anatomic findings, recent advances in understanding the embryology of cleft lip and palate laid the foundations of a more complete classification (Whitaker *et al*., 1981).

Despite its lack of completeness, the Veau classification described in 1931 is still commonly used in the literature in studies related to cleft lip and palate repair (Parwaz *et al*., 2009). Veau's classification includes: Class I, cleft of soft palate; Class II, cleft of hard and soft palate; Class III, unilateral complete cleft lip and palate; and Class IV, bilateral complete cleft lip and palate (Singh *et al*., 2015).

The most important cleft lip and palate embryological classification described in this era comes from Kernahan and Stark, in which incisive foramen was used as a landmark in their classification (Kernahan and Stark, 1958). Under these authors, clefts were classified as clefts of the primary or secondary palate. Further description as to left, right, complete, and incomplete were added subsequently. A similar classification system was later also adopted by American Cleft Palate Association in 1962 (Harkins *et al*., 1962). Pictorial descriptive version of Kernahan and Stark classification was later supplemented as Kernahan's 'Striped-Y' in 1971 to improve accuracy and ease of use in research (Kernahan, 1971). This classification was

further modified by Elsahy (1973), Millard (1976) and Smith (1998) (Elsahy, 1973, Millard, 1976, Smith *et al*., 1998). Kriens from Germany in 1989 depicted another diagrammatic system of classification of cleft lip and palate as 'LAHSHAL' (Kriens, 1989).

## 2.2 Epidemiology of Unilateral Cleft Lip and Palate

Orofacial clefts, particularly cleft lip with or without cleft palate (CL/P) and isolated cleft palate (CPO), are major public health problems, affecting 1 in every 500 to 1000 births worldwide (Bender, 2000). Cleft lip and/or palate was the fourth most common birth defect and the most frequently encountered congenital craniofacial anomaly (Luiza *et al*., 2013). It occurred twice as common in males than in females to a ratio of 2:1 (Coleman and Sykes, 2001). Males predominate in isolated cleft lip without cleft palate in about 60% of cases and cleft lip with cleft palate in 67% of the cases. In contrast, complete clefts of the secondary palate are twice as common in females as in males. Such difference in gender distribution can be attributed to the difference in timing in embryological development between the sexes (Burdi and Silvey, 1969). Cleft lip and/or palate also affected left side more with left-sided clefts twice as frequent as right-sided clefts and 6 times more frequent than bilateral clefts (6:3:1 ratio) (Watkins *et al*., 2014). It is unilateral in 80% of patients and bilateral in 20%. Approximately 10% of the cleft lips are incomplete and 70% of unilateral cleft lips are accompanied by cleft palate (Coleman and Sykes, 2001, Watkins *et al*., 2014). Isolated cleft lip without cleft palate is typically unilateral by approximately 80% and on the left side in 70% of the cases.

The incidence of clefts also varies between countries and racial or ethnic groups (Lithovius *et al*., 2014). Its incidence is highest among Asians, followed by Caucasians, and lowest in people of African descent (Tanaka *et al*., 2012). It is likely that environmental factors play a role in the incidence and distribution of cleft types among different populations with varying susceptibilities.

## 2.3 Embryology of Unilateral Cleft Lip and Palate

The first 12 weeks of gestation represent the crucial period of organogenesis, and it is during this period that the majority of congenital craniofacial anomalies are established (Hunt and Hobar, 2003) The earliest signs of the future face appear at approximately day 23 or 24 of embryonic life. By the end of the eighth week, the face assumes most of the characteristics that make it recognizable as human. The face is derived from five facial prominences that surround the future mouth, namely, the single frontonasal process and the paired maxillary and mandibular processes. The grooves between these facial prominences usually disappear by day 46 or 47 of gestation, as the processes meet their equivalents from the contralateral side and fuse in the midline.

The understanding of normal embryological development of the human face and cranium are important (van der Meulen *et al*., 1983). Following the formation of zygote and blastocyst, neural crest cells of neuroectoderm has taken centre stage on the development of craniofacial structures. The uninterrupted orderly migration and

differentiation of these cells enforced the classic theory of fusion of processes by Dursey and His, and mesodermal migration by Pohlmann, Veau, and Stark (Hunt and Hobar, 2003). More recent discovery by Carstens incorporated complex arrangement of developmental fields in facial prominences that is guided by a specific genetic component, as a fundamental developmental functional matrix (Carstens, 2002, Carstens, 2004). Many of the genes within a specific zone share an identical base pair sequence called a homeobox (hox).

In the theory put forward by Dursey (1869) and His (1874), facial embryogenesis occurred through the formation, migration, and fusion of five facial processes namely the frontonasal, the bilateral maxillary and the bilateral mandibular processes (Hunt and Hobar, 2003). The primary palate was formed by a fusion of the medial and nasal prominences of the frontonasal process with the maxillary prominences during weeks 4 to 7 of gestation. The secondary palate was formed when the two lateral palatal processes of the maxillary prominences fused during gestational weeks 5 to 12. This model of facial development involves the assembly of formed structures also known as processes based on a simplified description of external morphology.

In Carstens's neuromeric model of developmental fields, the face is conceptualized as a series of genetically defined developmental fields on the embryo called neuromere (Carstens, 2002). Each neuromere has a specific cellular content and a recognizable functional matrix. Their unique patterns of gene expression determine the anatomic boundaries of each zone within the neural tube of the embryo. In this theory, facial development involves the formation, migration, coalescence, and interaction of separate genetically based developmental fields. Any disruption of the neuromeric

zone will result in abnormalities in the developmental field originating from that zone and disrupt normal interactions with adjacent fields, resulting in field mismatch. With the necessary hox gene, the growth factors, their concentration gradients and diffusion, a regulated intercellular communication can occur that governs normal facial development. Any event that disrupts this gene-controlled, growth-factor mediated cell differentiation, migration, and fusion may result in congenital malformations (Marazita and Mooney, 2004).

## 2.4 Aetiology of Unilateral Cleft Lip and Palate

The etiology of cleft lip and palate is multifactorial (Jones, 1993, Marazita and Mooney, 2004). Many factors are known to contribute to its incidence but not all of them have direct causal effect relationship. They consist of the patient's gender, parental age, and ethnicity, as well as genetic disorders and environmental factors.

Gender factor affects the distribution of cleft incidence between the sexes. Isolated cleft lip, and cleft lip and palate occurred to a males to females ratio of approximately 2:1 (Coleman and Sykes, 2001). Isolated cleft palate occurred more commonly in females with a ratio of 2:1 females to males (Fraser, 1970).

Age factor such as increased parental age has been associated with a slightly increased incidence of congenital cleft. Paternal rather than maternal age appears to be more important in this regard (Fraser and Calnan, 1961).

Ethnicity or race appears to play a significant role in the incidence of cleft lip and palate (CLP) but not in isolated cleft palate (Chung and Myrianthopoulos, 1968). Studies in the past had shown the highest incidence among native Americans, followed by Orientals, whites, and lastly blacks (Vanderas, 1987). Some researchers had put forward theory that embryonic face shape may be a predisposing factor in orofacial cleft in their effort to explain ethnic differences in cleft incidence (Suzuki *et al*., 1999, Yoon *et al*., 2004). In their studies, they found that the parents of CLP children showed a distinct craniofacial morphology consisting of increased interorbital and intercoronoid process distance, and wider nasal cavity. The increased transverse facial dimension may be a risk factor for palatal clefts due to the longer distance between palatal shelves that must be overcome for fusion. Therefore, they postulated that Asians, who typically have wider faces may contribute to the more frequent failure of palatal shelves fusion in this ethnic group.

Parental transverse craniofacial form and dimension have also been investigated as etiologic factors associated with the development of orofacial clefts. Suzuki and others compared the dento-craniofacial morphology of parents of children with CL/P with that of parents of children without clefts (Suzuki *et al*., 1999).

Studies by Fogh-Anderson in the 1940s indicated that CL/P is distinct from CPO but both tend to cluster in families (Fraser, 1970). The incidence of CPO is not increased in relatives of patients with either isolated cleft lip or combined cleft lip and palate. Conversely, patients with CPO also fail to have an increased incidence of isolated cleft lip or combined cleft lip and palate in their relatives. Overall, approximately 33% to 36% of cases of CL/P have a positive family history (Jones, 1993).

Classic Mendelian inheritance of congenital clefts is rare (Marazita and Mooney, 2004). Approximately 30% of oral clefts are associated with a syndrome and 70% are nonsyndromic (Jones, 1988). Almost half of these syndromes are due to Mendelian inheritance of alleles at a single genetic locus (Marazita and Mooney, 2004). A study done in Malay population in Kelantan showed a contribution of MSX1 genes in aetiology of CLP (Salahshourifar *et al*., 2011). Occasionally CLP is seen in syndromes that demonstrated both autosomal dominant and recessive inheritance (Prescott *et al*., 2001). In addition, CLP is also occasionally associated with chromosomal abnormalities, such as trisomy D (Perrotin *et al*., 2001). The fact that clefts can occur in families over several generations without concrete pattern of inheritance demonstrated the multifactorial nature of its inheritance. Only 20% of patients in different populations have positive family history or familial (Lithovius *et al*., 2014). The predominance of left-sided clefting and male preponderance of CL/P also suggested the importance of genetic susceptibility (Mossey and Modell, 2012).

In addition to its multifactorial inheritance pattern, environmental factors have also been shown to play a significant role in phenotypic clefts. Environmental factors associated with CLP include maternal smoking, alcohol, teratogenic drugs such as anti-epileptics and corticoids, and low levels of folic acid (Abrishamchian *et al*., 1994, Chung *et al*., 2000, Romitti *et al*., 2007, Carmichael *et al*., 2007, Johnson and Little, 2008). Exposure to organic solvents and agricultural chemicals and viral infections can also increase the risk of orofacial clefts (Shaw *et al*., 2003, Acs *et al*., 2005).

## 2.5 Anatomy of Unilateral Cleft Lip and Palate

The facial skeleton is frequently deformed in patients with a cleft of the lip and palate (Huffman and Lierle, 1949, Millard, 1964, Spira *et al*., 1970, De Mey *et al*., 1989). The severity of this deformity is often related directly to the severity and degree (unilateral or bilateral) of the cleft. In the normal lip, the orbicularis oris muscle forms a complete sphincter around the oral cavity. In patients with incomplete unilateral cleft lip that does not involve more than two thirds of the height of the lip, have intact upper orbicularis fibers that pass over the top of the cleft and connect the medial and lateral lip segments. This creates a partial oral sphincter thereby, reduced the severity of the deformity. The lower orbicularis fibers are directed upward and usually attach to the subcutaneous tissue of the cleft margins or to the underlying bone. In a complete unilateral cleft lip, the muscle fibers are directed upward, parallel to the margins of the cleft, and terminate beneath the ala nasi laterally and the base of the columella medially. This causes the full fledge deformity that is well known among patients with cleft lip and palate.

The normal palate separates the oropharynx and nasopharynx (Maue-Dickson and Dickson, 1980, Nguyen and Sullivan, 1993, Huang *et al*., 1998). It consists of an anterior bony and posterior soft tissue component. The mobility in the soft palate component is essential for normal speech and swallowing function. There are six muscles that normally insert onto the soft palate, and play indispensible role in its mobility. These muscles work in synchronism to maximize each other's efficiency. The muscles that have the greatest impact on velopharyngeal competence are levator veli palatini, musculus uvulus, and superior pharyngeal constrictor. The levator veli

palatini pulls the soft palate, or velum, superiorly and posteriorly, allowing it to appose the posterior pharyngeal wall. The musculus uvulus increases the bulk of the velum during its contraction, aiding in closure of the oropharyngeal-nasopharyngeal communication. The superior constrictor is responsible for the sphincter function of the pharynx, moving the pharyngeal walls medially during phonation and swallowing. The palatopharyngeus also play a role in medialization of the pharyngeal wall and causes downward displacement of the palate. The palatoglossus is also a palatal depressor that is believed to be responsible for the production of nasal phonemes by allowing controlled passage of air to the nasal chamber. Both the palatopharyngeus and palatoglossus play important roles in swallowing. The tensor veli palatini tenses its aponeurosis for the other muscles and also moderates patency of the Eustachian tube.

In patients with cleft palate, the cleft extends from alveolus into the palatal part of the maxilla and separate the palatal bone at the level of the nasal septum (Maue-Dickson and Dickson, 1980, Nguyen and Sullivan, 1993, Huang *et al*., 1998). As a result, the alveolar arch and palate are separated into a large and a small segment. The muscle insertions to the bony structures are also different from normal in which the aponeurosis of the tensor veli palatini inserts onto the bony edges of the cleft, rather than onto its normal insertion on the posterior edge of the hard palate. The levator veli palatini muscles normally interdigitate at the midline behind the palatal aponeurosis to form a sling. This levator sling is also interrupted by insertion of this muscle onto the posterior edge of the hard palate in cleft palate patients. The velopharyngeal sphincter function is compromised, leading to VPI and problems with speech development. The function of the tensor is also compromised because of its

abnormal insertion, leading to inadequate ventilation of the middle ear space. The lost of muscle control of the Eutachian tube often leads to chronic otitis media and risk permanent hearing loss (van Aalst *et al*., 2008). Because the aponeurotic attachment is more anterior in the cleft palate, the cleft palate is also shorter than the normal palate.

## 2.6 Facial growth in Unilateral Cleft Lip and Palate

Patients with clefts have a deviant facial morphology, compared to non-cleft individuals (Dahl, 1970, Semb, 1991, Holst *et al*., 2009). An intrinsic tissue deficiency, medial displacement of the segments, especially the minor segment, and mode of breathing and resting posture of the oral cavity had been shown to influence maxillary arch dimensions in unilateral cleft lip and palate (UCLP) (da Silva Filho *et al*., 1992, Kozelj, 2000, Lo *et al*., 2003). Therefore, the maxillary arch constriction in UCLP should not solely be interpreted as a consequence of primary surgery. Surgery, functional factors and intrinsic effects of the cleft in themselves are considered responsible for the different facial morphologies and facial growth in these patients. However, the precise extent of each factors' contribution to the normal facial growth is unknown.

Cleft severity and maxillary morphology can influence facial growth. Studies have shown large clefts and small maxillae to be generally associated with worse maxillary growth (Suzuki *et al*., 1993, Peltomaki *et al*., 2001, Honda *et al*., 2002, Liao *et al*., 2010, Chiu *et al*., 2011). Others nonetheless reported that the majority of clefts are

capable of developing an essentially normal facial skeleton except in the area of the cleft defect (Ortiz-Monasterio *et al*., 1966, Bishara *et al*., 1976, Bishara *et al*., 1978). Thus, the surgical procedures performed to correct the deformity may play a greater role than the actual cleft deformity in the abnormal facial growth frequently observed in patients with cleft lip and palate. It has been shown that repaired clefts of the lip and palate patients may demonstrate impaired maxillary growth with collapse of the maxillary arches, producing midface retrusion (Williams *et al*., 2001).

Inter-center studies evaluating treatment outcome in UCLP, show craniofacial morphology also vary in relation to the surgical treatment protocol used (Brattstrom *et al*., 1991, Friede *et al*., 1991, Molsted *et al*., 1992, Daskalogiannakis *et al*., 2011). In general, facial growth appears to be adversely influenced by the age at the palate repair, the type of repair used, and the tension of the repaired palate.

The interrelationship of all these variables from intrinsic to extrinsic factors preclude any definitive statement regarding the precise effect of each on facial growth, but their total combined effect does frequently appear to cause a clinically significant inhibition of facial growth.

Today, there is still controversy about the type and timing of palatal surgery and its effect on facial growth (Liao and Mars, 2006a, Yang and Liao, 2010). The timing of palatoplasty repair at age 9 to 12 months optimizes speech development; however, it is recognized that palatal repairs that denude bone heal with scar contracture resulting in midfacial growth distortion. Delaying surgery of the hard palate can reduce impairment of facial growth, but negatively affect speech instead (Rohrich *et al*.,

2000, Liao and Mars, 2006b). According to Berkowitz *et al*., the timing of palatal closure should be based on the ratio of the area of the cleft to the palatal segments, and the best time to close the palatal cleft is when the cleft size is 10 percent or less of the total palatal surface area (Berkowitz *et al*., 2005). In addition, both primary and secondary bone grafting in UCLP can have an inhibitory effect on maxillary development (Ross, 1987, Brattstrom *et al*., 1991).

## 2.7 Cleft size

The size of the cleft at birth varies considerably, and the extent of the tissue defect in infancy depends on the degree of separation of the segments and the degree of tissue deficiency (Aduss and Pruzansky, 1968, Hellquist and Skoog, 1976, Johnson *et al*., 2000, Peltomaki *et al*., 2001). The width of the cleft in infancy influences the difficulty of surgical repair and, indirectly, the treatment outcome. Many retrospective studies have correlated the severity of the palatal cleft using Veau classification, which is rather generic, to their outcomes studies (Parwaz *et al*., 2009).

There is no established method for measuring cleft severity. In children with UCLP, the method of measuring the cleft differs, some investigators only measure the separation between the two segments anteriorly, whereas, others measure the cleft width on several palatal levels or measure the cleft area in relation to the total palatal area. Some also taken into account the maxillary arch dimensions such as arch widths and arch depths (Kramer *et al*., 1996, Heidbuchel *et al*., 1998). Both clinical measurements and measurements on dental casts are reported.

Cleft size and its relation to various treatment outcome variables in cleft patients have been evaluated earlier. These studies indicated that cleft size is related to arch dimensions and crossbite occlusion, maxillary growth, certain speech variables, alveolar bone graft success and fistula formation (Hellquist *et al*., 1978, Suzuki *et al*., 1993, Heliovaara *et al*., 1994, Long *et al*., 1995, Lohmander-Agerskov *et al*., 1997, Peltomaki *et al*., 2001, Persson *et al*., 2002, Kawakami *et al*., 2002, Parwaz *et al*., 2009, Liao *et al*., 2010, Chiu *et al*., 2011).

The primary surgical repairs affect maxillary arch dimensions in children with clefts. Lip repair in UCLP has a moulding effect on the forward and outward rotated segments, which creates a more normal alveolar arch shape and the surgical closure of the palate in both UCLP and cleft palate children affects the growth of the maxillary arch in both the transverse and the antero-posterior dimensions (Kramer *et al*., 1994, Honda *et al*., 1995, Kramer *et al*., 1996, Huang *et al*., 2002). In patients with clefts, maxillary arch dimensions, such as arch widths and arch depths, are generally larger at birth, but smaller in the primary dentition than in normal children (Kramer *et al*., 1996, Heidbuchel *et al*., 1998). Mazaheri *et al*. evaluated early changes of maxillary alveolar arches in operated UCLP from 1 months to 4 years of age, and found the percentage of children with contact between the segments and overlap of the segments anteriorly steadily increases after lip and palatal surgery (Mazaheri *et al*., 1993).

Lohmander-Agerskov *et al*. measured the area, length, and maximal width of the residual cleft in the hard palate and correlated these with speech variables

(Lohmander-Agerskov *et al*., 1997). They perceived oral pressure and resonance appeared related to the size of the residual cleft, whereas audible nasal escape and articulatory compensations were not.

Parwaz *et al*. studied cleft width on dental models in UCLP and cleft palate patients before palatoplasty, and evaluated fistula formation after a mean follow-up period of 12.6 weeks (Parwaz *et al*., 2009). The width of the cleft affected the occurrence of postoperative palatal fistula formation. A width of 15 mm or more had a statistically significant risk of fistula formation. The strongest association was found for the ratio of the cleft width to the sum of the palatal shelf width. If this ratio was 0.48 or more, the risk of fistula formation increased with statistical significance. Despite substantial work in this field, many questions are still unanswered, because methodology, cleft types and outcome measures varies greatly between studies.

## 2.8 Timing of Palatoplasty

The timing of cleft surgery is controversial due to the act of balancing between achieving optimal speech outcome and minimizing facial growth disturbance. It is generally accepted that early cleft repair results in a more normal speech pattern whereas delayed surgery achieved a more normal facial growth (Rohrich and Byrd, 1990). Because midfacial growth occurs by bone deposition by the hard palate periosteal osteocytes with concomitant osteoclastic bone resorption along the nasal floor and in the maxillary sinuses, subperiosteal scarring impairs midfacial growth. Mucoperiosteal repair of the hard palate cleft is known to result in subperiosteal

scarring.

The modern trend is for early complete closure of the lip and palate to achieve the best speech outcome with minimal growth disturbance. If hard palate closure is delayed until full facial growth has been attained, it will nearly eliminate facial distortion but at the expense of abnormal speech (Vig and Turvey, 1985, Nguyen and Sullivan, 1993, Rohrich *et al*., 2000, Liao and Mars, 2006b). Abnormal speech patterns are more difficult to correct later than facial growth deficiencies, which can be treated surgically. Therefore, most craniofacial surgeons advocate complete repair of palatal clefts between age 9 and 12 months to prevent the detrimental effects of delayed repair on speech and language development (Nguyen and Sullivan, 1993, Kirschner and LaRossa, 2000, Salyer, 2001, Van Lierde *et al*., 2004). Advocates of two-stage palatal repair performed repair of the soft palate between 3 and 8 months of age while delaying hard palate repair until 15 months to 15 years of age.

## 2.9 Type of Palatoplasty

The primary palatoplasty aims to reconstruct the anatomical structures that separate the nasal and oral cavities. The goals of a successful cleft palate surgery consist of complete palatal closure and normal speech development without disruption of maxillary growth (Losken *et al*., 2011). There are various palatoplasty techniques and their modifications that have been described over the years (LaRossa *et al*., 2004, Losken *et al*., 2011). Some of the more commonly used techniques are as illustrated in Appendix II.

The choice of repair technique is surgeon-dependent. The surgical technique selected for cleft palate repair depends on the extent of the cleft, and whether or not the cleft is unilateral or bilateral. The natural variety of the cleft defect may require the use of different techniques that are individually suited to the specific deformity in order to optimize outcome. Musgrave and Bremner compared different types of clefts and found a fistula incidence of 4.6% in incomplete cleft palate, 7.7% in complete unilateral cleft palate and 12.5% in complete bilateral cleft palate (Musgrave and Bremner, 1960). These findings might be explained by the technical difficulty in closing wider clefts and the greater tension at the site of closure.

The management of the cleft palate has evolved in accordance to the understanding of its anatomy and function. Such evolution of knowledge has led to the transition of its management from obturation in the 1700s to simple repairs of the cleft soft palate in the early 1800s to two-flap complete palatal repairs, such as von Langenbeck's palatoplasty in the late 1800s. Subsequent understanding of the functional deficits of cleft palate gave rise to techniques of repair that aim to lengthen the palate, such as the Veau-Wardill-Kilner V-to-Y advancement technique in the 1930s to repairs that not only close the palatal cleft and lengthen the palate but also correctly align the palatal musculature (Nguyen and Sullivan, 1993). Recreation of the levator sling during cleft palate repair has been associated with a higher probability of successful speech development (Gage-White, 1993, Kirschner and LaRossa, 2000).