CHAPTER II
LITERATURE REVIEW

1. Classification of Clefts

According to Kernahan and Stark[27], clefts can be classified into three main categories based on development of the embryonic primary and secondary palates as follows:

1.1 Clefts of the primary palate, involving the upper lip, anterior nares, and anterior dento-alveolar process, extending as far as the incisive papilla region of the anterior alveolar process, briefly described as cleft lip with or without cleft alveolus (CL/A).

1.2 Clefts of the secondary palate, involving all of the soft palate and some of the hard palate up to the incisive foramen, simply called cleft palate (CP).

1.3 Clefts involving both primary and secondary palates (CLP)

Other description with unilateral (U) and bilateral (B) types can also be included, and may identify complete or incomplete forms as well.

In addition, there have been several suggested refinements of the original Kernahan and Stark classification to further cover other specific features of oral clefts conditions.[28, 29]

2. Factors Relating to the Craniofacial Morphology in Cleft Patients

There are many factors that may involve postnatal growth of the oral cleft patients, including the aberrant growth patterns due to individual intrinsic growth potential[30, 31], the controversial effect from the use of presurgical orthopedics[32-34], and the surgical intervention.[11-13, 30, 35, 36]

Van Limborgh[31] studied cleft skulls of different ages and types and concluded that in individuals with oral clefting, the growth process was slower than in normal individuals, whereas the growth potential was essentially the same, except in the region of the cleft. Although it is not known whether the growth retardation is a temporary or permanent effect, and whether it will be compensated by later growth or not, it should be realized that some patients have potential for attaining favorable facial appearance, whereas some do not have this potential.[30, 37] A study of changes in maxillary arch dimensions in various cleft types from infancy to 4 years of age by Honda et al.[32] also confirmed that there was a variety of growth patterns observed among different patients. Furthermore, generalized mid-face retrusion usually found in isolated palatal clefts[38], and cleft neonates[39] indicates that there may be some degree of intrinsic maxillary growth variation among the cleft patients. Nevertheless, further embryological studies of fetal development, in particular, of cleft lip and palate fetuses, are necessary.

Considering the effect on maxillary growth from presurgical orthopedics, it was first introduced by McNeil[40] and had been modified later by Burston.[41] The purpose of the treatment was to correct segmental displacement to facilitate primary surgery by reducing the size of the cleft[40, 42, 43] and also allow for spontaneous growth by modifications of the plate.[44] Extraoral strapping may be an essential component for the treatment in bilateral CLP cases with excessive protrusion of the primary palate.[43] Nonetheless, Ross[13] suggested that collapsing forces such as those from extraoral strapping might produce detrimental effects on the arch dimension, as it might prevent the expected increase in arch width permanently.[45] The contemporary use of preoperative orthopedics, especially in the unilateral cleft lip and palate, has been a controversial issue. There have been many studies supporting the benefits of using presurgical orthopedics[34, 36, 42, 43, 46-51], while many other studies reported that the lip surgery alone had the same effect and the presurgical orthopedic plate was only an expensive appliance used to comfort the parents by starting the treatment at the earliest moment possible.[13, 25, 33, 36, 52, 53] Some reports claimed that orthopedic treatment could even impair facial growth[13, 49, 51, 54] and offered no significant advantages over nasolabial repair alone in aligning the alveolar segments.[33, 55]

Early surgical intervention during the rapid growth period of infancy may have a detrimental effect on future midfacial growth, especially in cases where scar tissue is excessive and placed in areas more sensitive to abnormal soft tissue influence. This is because surgery in a smaller individual leads to a possibility of greater tissue trauma, more extensive scarring, or both.[13] Friede and Pruzansky[56] suggested that it was the palatoplasty, not the lip repair, that most affected midfacial development. Similarly, Ross[13] claimed that repair of the hard and soft palate provided the greatest potential for inhibiting the maxilla growth in length, forward translation, and posterior height. By contrast, recent studies demonstrated that the major disturbance in maxillary growth was attributable to lip and not the palatal surgery.[57, 58] Generally, repairing lip and palate by surgical procedures that minimally involved bone growth potential, instead of restricting the maxillary growth, guides and facilitates maxillofacial development.[13, 59] Moreover, appropriate timing for repairing of the alveolus, hard palate, and soft palate is essential. It has been demonstrated that early closure of the alveolar cleft at the nasal side by means of nasal mucosa or vomer flaps could adversely affect the palatal growth.[60] Early alveolar bone grafting may limit the subsequent sutural remodeling between the zygomas and the maxilla, and in the midline. This result may relate to the extent of the operative procedure and the mobilization of soft tissues to cover the graft which subsequently causes scarring, rather than the restrictive effect of the bone graft itself.[59] To date, several studies have suggested that the surgical interventions might be responsible for some of these facial deviations in operated children, adolescents, and adults with CLP.[11, 61-63] Nevertheless, it is still obscure as to which of the observed deviations are caused by the surgical interventions and to what degree different surgical protocols lead to differences in development of the craniofacial complex in subjects with CLP.[64]

To date, the reasons why these aforementioned factors may produce aberrant growth are still controversial. Wada and coworkers[65] claimed that the secondary displacement of the alveolar segments following surgery was one of the major factors that caused the underdevelopment of the maxilla.

3. Malocclusion in the Cleft Patients

Smahel[66] summarized the basic patterns found in both UCLP and BCLP were retroclination of the dentoalveolar component of the upper jaw, the retroposition of the mandible and of the maxilla *per se*, the posterior growth rotation of the face, the reduction of the upper lip thickness and retrocheilia. There was also an identical impairment of vertical growth within the lateral parts of the upper face as well.

In Thailand, Tekunatorn[67], studied the lateral cephalometric radiographs of 72 complete UCLP and 43 complete BCLP from 8 to 18 years of age, concluded that both UCLP and BCLP had small anterior cranial bases, short maxilla and mandible. The gonial angle was obtuse with steep mandibular plane and more upright lower incisors compared with noncleft. The differences among these cleft types were that in individuals with UCLP, although the upper incisors were less retroclined, the maxilla was more retruded, producing more concave profile compared with BCLP.

Generally, it is suspected that no significant differences exist between patients with and those without cleft deformities in the distribution of vertical or anteroposterior skeletal jaw relationships, except that posterior crossbites may be more common in patients with a cleft deformity.[68] Nevertheless, significant disturbances of growth of the jaws, particular the maxilla, usually occur in patients with cleft lip and palate as a result of surgical repairs and other factors. The scarring that results from these procedures has been shown to affect the maxillary growth, creating the Skeletal Class III problems due to maxillary deficiency among these patients.[13, 58] A study in Korea in 2002 demonstrated that in Korean cleft patients, the incidence of Class III malocclusion was common, especially in patients with clefts that involved the secondary palate (CP and CLP), and when the degree of cleft involvement in the palate increased.[69] Along the same lines, Pisek[70] reported that 72 Thai patients with UCLP, analyzed from the lateral cephalometric radiographs, had Class III malocclusions and Skeletal Class III patterns and observed a higher frequency than among Caucasian cleft groups. This finding was attributed to the effects racial differences as well as to primary surgery.

For noncleft Asians, the incidence of Class III malocclusion was observed with a high incidence of 14 % among Chinese, Japanese and Korean populations.[71] This frequency of Class III malocclusions in Asians was high due to a large percentage of patients with maxillary deficiency.[72] However, in a study in Korean patients, Baik and colleagues[73] reported that the combination of a normal maxilla and overdeveloped mandible were the majority of the Class III group with 47.7% occurrence, while patients having an underdeveloped maxilla and overdeveloped mandible comprised 13.5% of their sample. In Thai noncleft patients, it has been reported that they were comprised of Skeletal Class III types with large and protrusive mandible in the male group, whereas in the female group the maxilla was found in retrognathic position with the mandible in prognathic position.[74] With a tendency of mandibular prognathism among the Asians, it may accentuate the severity of Class III malocclusion in cleft patients in this region.

Interestingly, although the length of the maxilla in cleft patients, as described previously, tends to be somewhat shorter than normal, the retrusive mandible reported among subjects in some studies[75-77] can maintain a positive dental overjet and decreased sagittal growth disturbance in these patients. These features seem to explain the normal skeletal relationships that may be found in particular types of cleft such as isolated CP and CL. They also imply differences in treatment required among the clefts since the degree of deformation, in other words, the extent of the correction required, largely depends upon the severity of the cleft.

4. Orthodontic Management of Late Adolescent Cleft Patients

Similar to Skeletal Class III noncleft patients, a final treatment planning for the clefts is usually performed during late adolescence or adulthood when most of the growth is stabilized. Treatment can be either by orthodontic camouflage treatment or combined orthodontic and surgical treatment, depending on the pattern of malocclusion and its severity. In addition, other factors can also affect the decision for treatment in each patient, i.e., perception of their problems, psychosocial factors (fear, stress, motivation), financial support, timing, etc.[78]

4.1 Orthodontic Treatment

In patients who have mild skeletal discrepancy, near completion of facial growth and acceptable facial esthetics, camouflage treatment with orthodontic tooth movement alone is usually sufficient. Individuals with Class III malocclusions are commonly found with dentoalveolar compensations with maxillary incisors proclined and mandibular incisors retroclined. These compensations also help to maintain function and mask the underlying skeletal discrepancy. The concept in camouflage treatment of Class III malocclusion is to compensate for skeletal discrepancy or moderately increase already-existing dental compensations by proclination of the maxillary incisors and retroclination of the mandibular incisors. Selective tooth extraction (lower premolars, lower incisors, or lower second molars) and/or the use of mini-implants may be anticipated.[79, 80] The multiple edgewise archwire (MEAW) technique, introduced by Kim[81], is also claimed to correct the Class III discrepancy by increasing cant of the occlusal plane when there is associated anterior open bite. After camouflage treatment, dental occlusion will be improved but the underlying skeletal problem or facial profile may not be corrected.

Generally, it is recommended that patients who have only mild to moderate skeletal Class III discrepancy with hypodivergent skeletal pattern are indicated for camouflage treatment. Good candidates for camouflage treatment should present with little residual growth potential, and mild to moderate crowding in order to be able to use the space of mandibular teeth extractions for achievement of orthodontic camouflage and improving dento-skeletal relationship.[82] On the contrary, patients with severe skeletal discrepancy, or who will likely have continuing growth of the mandible, are not candidates for camouflage treatment.[80] This is because the residual growth may provoke a worsening of the deformity after treatment. An effort to improve the overjet in cases with severe skeletal discrepancy may also adversely result in an unaesthetic outcome as the chin may appear even more protrusive. Besides, overcompensation, especially as the lower incisors are retroclined, will likely be unstable and may cause gingival recession and dehiscence of the alveolar bone especially when there is thin or inadequate attached gingiva.[83, 84]

4.2 Orthodontic Treatment Combined with Orthognathic Surgery

In contrast to mild skeletal discrepancy, in cases where severe skeletal discrepancy is involved, additional surgery is usually required to achieve satisfactory results. The main objectives of surgical orthodontic treatment are to normalize the facial profile, occlusion and function. It is generally performed after 16 years for females and 17 - 18 years for males when most of the facial growth is completed.[68] Performing the surgical correction during these ages reduces the recurrence of facial deformity from subsequent surgical effect on maxillary growth and continued growth of the mandible in cleft patients. The surgical prerequisites are largely similar in both cleft and noncleft patients as the orthodontic presurgical treatment is usually required before surgical correction. The basic presurgical orthodontic principles are to align and level teeth over the basal bones of the maxilla and mandible, decompensate the Class III malocclusion by retroclining the proclined maxillary incisors and proclining the retroclined mandibular incisors to more normal axial inclinations.[85] The result is increasing severity of the Class III dental malocclusion often producing a more unesthetic facial profile before surgery. Surgical corrections that are usually performed in cleft patients are maxillary advancement, mandibular set-back, or both, with an aim to yield satisfying functional and esthetic results. It was reported that the magnitude and type of surgical correction could be dictated by the amount of presurgical orthodontic decompensation.[85] This also indicated treatment success since lack of optimal dental decompensation compromised the quality and quantity of the orthognathic surgical correction. The pretreatment SNA and SNB angles also reflected the choice of orthognathic surgery as suggested by Johnston and coworkers.[86] They found that bimaxillary surgical cases had larger ANB angle discrepancies, while single jaw mandibular surgery was used with more normal pretreatment SNA angle values.

Considering the need for othognathic surgery in cleft patients, Gaggl and coworkers[87] demonstrated that patients with CLP mostly required additional orthognathic surgery of the maxilla because of their sagittal deficit whereas patients with isolated CP could be treated satisfactorily by orthodontics alone. Gedrange and colleagues[88] suggested that good occlusion could be obtained in most individuals with unilateral clefts of lip, alveolus and palate using only conventional orthodontic appliances. On the other hand, individuals with bilateral cleft lip and palate usually encounter more severe occlusal and aesthetic problems which often require additional orthognathic surgery to obtain optimal result. It was estimated that orthognathic surgery would be necessary in approximately 25% of a sample of males with UCLP to establish adequate functional jaw relations, harmonious facial esthetics, or both.[13] Several studies also supported this finding.[33, 89] However, Posnick[90] reported that the need for orthognathic surgery could be varied between 25% and 75% of a cleft population, depending on the criteria applied. A recent Canadian study by Daskalogiannakis and Mehta[91] also demonstrated that 65% of patients with complete BCLP and 48% of patients with complete UCLP would benefit from orthognathic surgery. These elevated percentages were attributed to an attempt to improve the profile esthetics, and closure of previously ungrafted alveolar clefts and associated fistulae, and increasing government financial support for treatment. Additionally, it was suggested that the use of surgical methods should not be regarded as a failure of orthodontic therapy. Rather, optimal management could be ensured by a combination of orthodontic and maxillofacial therapy.[88] It is possible that the frequency of orthognathic surgery among cleft patients may increase in the future as the stability and esthetics of treatment results become of more concern with further improved surgical techniques. This may relate to a suggestion from Rosenstein[92] that reports on the orthognathic surgery need were helpful in determining just how important varying methods of treatment could influence this need. Instead, one should realize that the need for surgery is subjectively perceived. Allowance must be made since there are other variables besides the skeletal relationship and profile esthetics that can influence the decision to opt for orthognathic surgery, such as periodontal condition, missing of teeth, patient's demand and cost.[80, 83]

5. Prediction of Orthodontic Treatment Plan in Cleft Patients

According to differences in the direction of tooth movement, orthodontic mechanics, and extraction plan, the decision whether to perform orthodontics alone or combined orthognathic surgery should be made as early as possible.[80] However, the criteria for recommending orthognathic surgery in cleft patients can be quite variable, ranging from the need to correct major jaw size discrepancy to more minor corrections of maxillary occlusal plane cant, maxillary midline discrepancies, and segmental crossbite relations.[33]

Efforts had been made to identify the cleft patients who would require orthognathic surgery, for instance, the GOSLON Yardstick.[23] It is intended to assess the inter-center treatment outcomes by evaluating the teeth positions and dental occlusion in UCLP children during late mixed or early permanent dentition. Moreover, it also signifies type of treatment required for each individual as GOSLON categories 4 and 5 can be considered as likely surgical cases. This system is based mostly on the anteroposterior discrepancy (overjet) which makes it simple to use. Nonetheless, the subjectivity in judgment of the clinician during scoring, as noted before, is inevitable and considering only overjet may not appropriately distinguish the type of treatment needed. It has been demonstrated that overjet is not a good predictor of sagittal relationship in both cleft and noncleft Class III subjects.[85, 93-95]

This is because skeletal malocclusions can be hidden due to dental compensation or inclinations of the upper and the lower incisors, and/or the functional shift of the mandible with acute mandibular plane angle. These characters allow some cleft patients with large negative overjet to tolerate dental compensation by orthodontic treatment alone. Therefore, for accurate determination of jaw relationship, it is recommended to use cephalometric analysis.[95]

Attempts to classify the candidates for orthognathic surgery more objectivity using cephalometric measurements have been of more interest lately. Several studies indicated significant differences of some pretreatment cephalometric measurements among the surgery and the camouflage groups in both cleft and noncleft subjects. Troy and coworkers[85] observed in noncleft Class III patients at the pretreatment stage that L1-GoGn, L1-NB, SNB, ANB, and Wits appraisal were significantly different comparing surgery and camouflage groups. This surgical group usually has more retroclined mandibular incisors, more protrusive mandible, and more severe Class III skeletal discrepancy which limit tooth movement with orthodontics alone. Correspondingly, Linton[93] compared the cephalometric measurements in adolescent non-surgery and surgery UCLP groups. His finding showed that the ANB, Wits appraisal, and ABGoGn angle were significantly different. These parameters were claimed beneficial for delineating the diagnostic measures in borderline surgical cases of UCLP. Some studies tried to establish a model with multiple regression analysis, using cephalometric values at early ages (8 - 9 years of age), to provide individual growth prediction in cleft subjects.[19, 21] These equations would aid in early decision making whether orthognathic surgery should be included in the treatment plan of UCLP subjects. However, it is important to realize variations among cleft types, treatment protocols and populations. Additionally, limited sample size and range of cephalometric measurements employed must be taken into account in developing any prediction models. Scheuer and coworkers[19] recommended that when using regression equations for prediction of facial growth, it was better to predict facial growth by analyzing parameters within an individual treatment center to avoid the problems of population variables.

To predict the treatment need in adult Class III noncleft patients, Kerr and colleagues[96] used univariate statistical methods to analyze cephalometric values with an aim to allocate the treatment need more objectively. In their study, ANB angle, maxillo-mandibular (M/M) ratio, mandibular incisor inclination, and Holdaway's angle were the most different factors, comparing surgery and non-surgery groups. However, univariate statistical technique seems to be insufficient for the differentiated diagnosis and treatment planning of Class III malocclusion patients; instead, it is recommended that a multivariate approach is more appropriate.[97] In later study, Stellzig-Eisenhauer and coworkers[97] used discriminant analysis, a multivariate procedure, to distinguish between adult Class III patients who could be properly treated by orthodontics alone and those who required orthognathic surgery. Wits measurement, maxillary/mandibular length ratio, gonial angle, and sella-nasion distance were considered to be the most efficient identifiers between surgery and non-surgery groups. These parameters were incorporated into a scoring equation, providing another objective tool to be used as a part of decision making process during treatment planning in adult Class III patients. Along the same line, a recent study from Singhawannakul[22] introduced the Formula for Orthodontics and Surgery Prediction (FOSP) to predict treatment need in cleft patients. This prediction equation was developed from a discriminant analysis as well. The ANB angle, U1-APog (mm) and L lip-Nperp. (mm) were found to be the most significant factors to discriminate between orthodontic treatment alone and the surgery group. The FOSP approach included soft tissue profile assessment which was not part of previous prediction methods. It was also claimed benefit for treatment planning in both adult and young subjects with all types of cleft deformity.

Even though using the multivariate technique is better than using single factors, its limitations should be recognized. Most multivariate models, based on cephalometric analysis, may be hindered by difficulties in landmark identification. Additionally, the selected parameters may not include all the variables required to precisely separate the groups.[98, 99] In developing and testing any prediction system that can be applied to patients, a relatively large sample is necessary.[98]

6. Development of the Formula for Orthodontics and Surgery Prediction (FOSP)

With an intention to identify cleft patients for whom orthognathic surgery was required, Singhawannakul[22] established the Formula for Orthodontics and Surgery

Prediction (FOSP). This study was performed on 119 patients with all types of cleft lip and/or palate who received treatment at the Orthodontic Department, Khon Kaen University. Study subjects were collected with an age range between 8 and 24 years, irrespective of gender. Each subject was firstly classified into an orthodontic treatment alone or additional orthognathic surgery group according to an expert clinician's assessment with consideration mainly on dental occlusion and soft tissue profile. The dental occlusion aspects comprised labio-lingual occlusion of central incisor(s) and lateral crossbite(s) and/or open bite(s) while soft tissue aspects consisted of total facial profile (an indirect skeletal A-P indicator), and lips profile (another indirect skeletal A-P indicator). General features of the expert clinician's clinical assessment were summarized as follows:

Score 1: Straightforward fixed orthodontic appliance treatment (with or without pre-bone graft), alignment, and space closure

Score 2: Straightforward fixed appliance treatment, 2-phase camouflage, with pre-bone graft, alignment, and space closure

Score 3: Complex fixed appliance treatment, 2-phase camouflage with pre-bone graft, likely face mask, alignment, space closure

Score 4: Complex orthodontic treatment, 2-phase camouflage with pre-bone graft, face-mask, likely distraction osteogenesis (DO), and/or pre-and post-orthognathic surgery

Score 5: Complex orthodontic treatment, with 3-phase, including pre-bone graft, and early permanent dentition alignment. Expected for distraction osteogenesis (DO), and/or pre-and post-orthognathic surgery.

Scores 1, 2 and 3 were indications for camouflage orthodontics only, while Scores 4 and 5 indicated most likely need for surgery.

In the establishment of the Formula for Orthodontics and Surgery Prediction (FOSP), the variables that could possibly influence on decision making during treatment planning process were analyzed. Multivariate F-test was used to identify parameters that were significantly different and maximized the separation between camouflage and surgery group. These variables were not only considered from the cephalometric measurements but also from other clinical records such as study models and panoramic films. After examining the assumptions for discriminant analysis by evaluation of the multivariate normal distribution with univariate ANOVAs, and testing of variance and covariance matrices equity by Box's M test. 38 variables were accepted to be included in the discriminant analysis (Table 1).

Table 1 Thirty-eight variables included in discriminant analysis

Skeletal measurements	**Dental measurements**	**Soft tissue measurements**	**Model and radiograph analysis**
NSAr (deg)	U1-APog (deg)	Facial angle (deg)	Overjet
SNA (deg)	U1-APog (mm)	Li-SnV (mm)	Overbite
FH-NA (deg)	L1-MP (IMPA) (deg)	Li-Ls to SnV differential (mm)	
A-Nperp. (mm)	L1-FH (FMIA) (deg)	Pog' to SnV (mm)	
Co-A (mm)	L1-NB (deg)	Sn to H line (mm)	
SNB (deg)	L1-APog (deg)	ILS to H line (mm)	
FH-Npog (deg)	L1-APog (mm)	U lip length (mm)	
Pog-Nperp. (mm)	Interincisal angle	U lip - E line (mm)	
SN-MP (Go-Gn) (deg)		L lip-N perp. (mm)	
ANB (deg)		L lip-U lip to N perp. differential (mm)	
Wits Appraisal (mm)		Mid U lip to Mid upper incisor (upper lip thickness)	
Mx-Md length differential (mm)		L lip-U lip thickness differential (mm)	
PP-MP (Go-Gn) (deg)			
LAFH (mm)			
Y-axis to FH (deg)			
Facial axis angle (deg)			

After evaluation of these variables with the discriminant analysis, ANB (deg), U1-APog (mm) and L lip-Nperp. (mm) were found to be the most significant factors in decision making for orthognathic surgery in cleft patients. Two equations were used to classify candidates for each group of treatment by evaluation of the discriminant score (D) as follows;

6.1 For Orthodontic Treatment Alone Group

D = -5.504 + 0.187 ANB (deg) + 4.141E-02 U1-APog (mm) + 0.573 L lip-Nperp. (mm)

6.2 For Additional Orthognathic Surgery Group

D = -7.365 - 0.191 ANB (deg) - 0.204 U1-APog (mm) + 0.702 L lip-Nperp. (mm)

6.3 When Combining the First and Second Equations, the Formula for Orthodontics and Surgery Prediction (FOSP) is:

D = -1.861 - 0.378 ANB (deg) - 0.245 U1-APog (mm) + 0.129 L lip-Nperp. (mm)

A prediction of treatment allocation was evaluated through the discriminant score in classifying whether an orthodontics alone or additional orthognathic surgery was required. The predicted treatment plan derived from the Formula for Orthodontics and Surgery Prediction (FOSP), by analyzing of the discriminant score, was compared with the treatment plan from an expert clinician's judgment to evaluate the success rate of prediction and classification. In this analysis, it was observed that 83.2% of all subjects were correctly classified.

There were several advantages of the FOSP as it was developed from various possible influencing factors not only from 60 variables from cephalometric measurements but also four variables from the model analyses and one variable from the panoramic film. It was also expected to be applicable to all cleft types with no account of age or gender, providing an opportunity to give more objective judgment during treatment planning. Moreover, since it was developed in Thai population, it might be possible to be applicable among other Thai cleft lip and palate centers.

Nevertheless, for confirmation of the predictive value, it was recommended that further study should be done with a large numbers of cleft samples with followed-up through the final phase of treatment for patients. This was because approximately 73.1% of the original subjects in her study were aged less than 15 years. Their further growth might finally alter the type of recommended treatment need in the future. Moreover, since the critical D score used to discriminate the type of treatment required was unclearly defined in Singhawannakul's study, there would be a need to select proper critical or cutoff D score before clinical application.