CHAPTER III

RESEARCH METHODOLOGY

1. **Overview of the Study:** Overview of this study is shown in Figure 1.

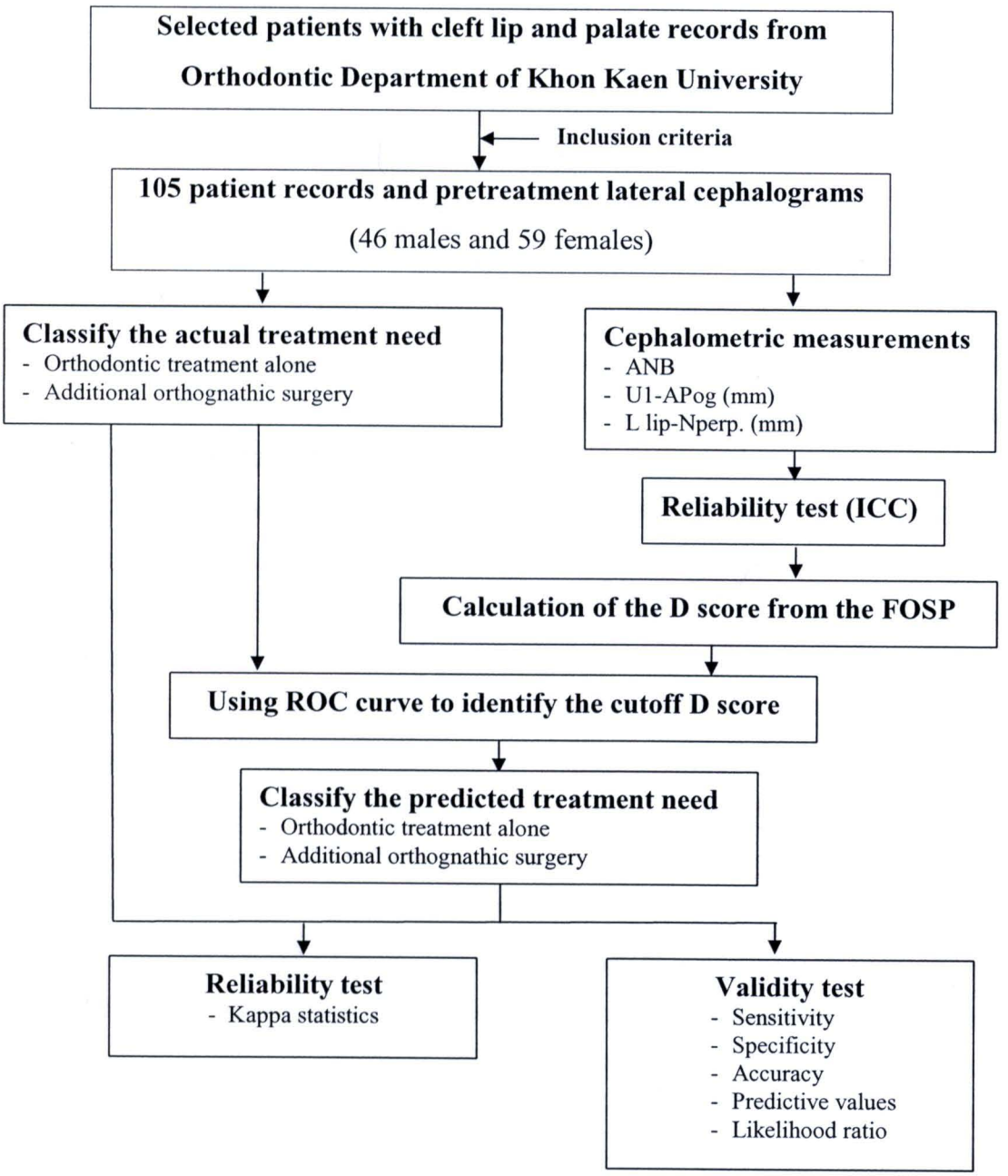

Figure 1 A diagram showing an overview of the study

2. Study Design

This study is an observational cross-sectional descriptive design.

3. Study Sample and Selection Criteria

3.1 Target Population

The target population consists of patients with cleft lip and/ or palate.

3.2 Study Population

Inclusion criteria and exclusion criteria were established for subject selection for the study.

Inclusion criteria are described as follows:

a. Patients with non-syndromic cleft lip and/or palate who were accepted to receive final correction of their Class III malocclusion in the Orthodontic Department, Faculty of Dentistry, Khon Kaen University.

b. The patients noted in (a) who had already completed or were in the process of completion of their final treatment with orthodontic treatment alone or with orthodontics combined with orthognathic surgery.

c. There was availability of records which consist of pre-treatment lateral cephalometric films and study models. The radiographs should have good quality of sharpness, brightness, and contrast.

The exclusion criteria are as follows:

a. Cleft patients who had history of trauma affecting craniofacial growth and development.

b. Patients whose upper anterior teeth in the lateral cephalometric film are missing.

3.3 Sample Size Determination

The amount of samples for this study could be estimated by using sample size calculation for Cohen's kappa[100], evaluating the agreement and disagreement proportion of predicted and actual type of treatment, as demonstrated here;

$$n = \frac{Z_{\alpha/2}^2 \, Po \, (1\text{-}Po)}{\delta^2 \, (1 - Pe)^2}$$

n = sample size

Z = the critical value

α = 0.05

$Z_{\alpha/2}$ = 1.96

δ = confidence interval was set at 0.2

Po = from the previous study[22], observed level of agreement is 0.83.

Pe = from the previous study[22], expected probability of chance agreement is 0.5.

After calculating, there are 55 samples that required for testing of agreement and disagreement proportion.

Additionally, the amount of samples to evaluate for the validity of the FOSP also calculated as follows[100];

$$n = \frac{Z_{\alpha/2}^2 \, P \, (1\text{-}P)}{d^2}$$

n = sample size

Z = the critical value

α = 0.05

$Z_{\alpha/2}$ = 1.96

P = from the previous study, the sensitivity of the FOSP for prediction of orthognathic surgery is 0.83.[22]

d = acceptable error at 0.08% (calculate from 10% of the p-value)

Substituting the respective values in the above described formula, the sample size for this study to cover both agreement/disagreement proportion analysis and FOSP validity test, should be at least 79 subjects. The total subjects of this study were 105, thus, the sample size was sufficient for statistical analyses.

4. Study Tools

4.1 Data collection record which consists of;

a. Random numbers to represent for each sample identity

b. Sex

c. Age

d. Type of cleft deformity

e. Received treatment plan (camouflage or additional orthognathic surgery)

f. Cephalometric values: ANB (degree), U1-APog (mm), and L lip-Nperp. (mm)

4.2 Cephalometric protractor (Ormcocepha, Ormco-Sybron)

4.3 The Formula for Orthodontics and Surgery Prediction (FOSP)

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

5. Data Collection

5.1 Outcome Measurement

In this study, cephalometric values of pre-orthodontic treatment which consisted of the skeletal type (ANB angle in degrees), upper incisors position (U1-APog in millimeters), and lower lip profile relationship (L lip-Nperp. in millimeters) were measured. Definitions of the landmarks and cephalometric measurements were illustrated in Appendix A. These values were placed into the Formula for Orthodontics and Surgery Prediction (FOSP), taking account of positive or negative values, to calculate for the discriminant scores (D). The D score calculated from the FOSP was described as follows:

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

Using the receiver operating characteristic (ROC) curve, the critical D score that represented an appropriate cutoff point in distinguishing which treatment need was selected. All subjects were separated into two groups, orthodontics alone and additional orthognathic surgery via this critical D score. Then a paired comparison of predicted treatment and actual treatment for each subject would be performed to evaluate for agreement and disagreement which was the main outcome of this study.

Additionally, validity of the concluded treatment plan derived from the FOSP compared to the actual received treatment was evaluated through sensitivity, specificity positive and negative predictive values, and positive and negative diagnostic likelihood ratios, using the actual treatments as a reference.

5.2 Additional Patient Data Collected

General patient information such as gender, age, and cleft type were also recorded to explore whether they affected the agreement/disagreement proportions in the cleft subjects.

5.3 Examiner

Each lateral cephalometric radiograph, patient's name and hospital number were covered and coded with the random number by a non-examiner to blind the examiner from knowing the received treatment of each patient. Cephalometric measurements of ANB angle (degree), U1-APog (mm), and L lip-Nperp (mm) were made manually, using the cephalometric protractor (Ormcocepha, Ormco-Sybron). Cephalometric tracing and measurements were done twice by an experienced examiner with two weeks separation. After that, the intra-reliability was tested to evaluate reliability of the measurements.

All patients' information, including their actual received treatment plans were recorded into the computer by non-examiner twice, at a different time, with confidential password entry. Patients' names were recorded separately and the random numbers were assigned to represent for identity instead during recording of other patients' information.

6. Data Analyses

6.1 Descriptive Statistics

Descriptive statistics were used for describing the general characteristics of subjects such as age, gender, cleft type.

6.2 Reliability Test for Cephalometric Measurements

Reliability of the three cephalometric measurements from the examiner was assessed using the intraclass correlation coefficient (ICC) Model 3 with SPSS® Version 13.0 (Statistical Package for Social Sciences for Windows) to evaluate intra-observer reliability.

Considering interpretation of the ICC values, Landis and Koch[101] have proposed the following as standards for strength of agreement for the ICC value: ≤ 0 = poor, 0.01 – 0.20 = slight, 0.21 – 0.40 = fair, 0.41 - 0.60 = moderate, 0.61 – 0.80 = substantial, and 0.81 – 1.00 = almost perfect.

In addition, the ICC values in this study should not be less than 0.61 in all three cephalometric measurements to represent a good repeatability. If not, new measurements must be performed until achieving of the desired ICC values.

6.3 Reliability Test for the FOSP

The agreement-versus-disagreement comparison between the conclusion from using the FOSP and the actual treatment of each subject was determined, using the Cohen's Kappa statistics for testing the significance of numerical agreement/ disagreement of predicted treatments and actual treatments. Furthermore, incorporation of variables such as gender, age, and cleft type would be considered as well.

The kappa value was interpreted similar to the ICC as described above.[101]

6.4 Validity Test for the FOSP

Statistical analysis for validity of the concluded treatment plan derived from the FOSP compared to the actual received treatment was evaluated through sensitivity, specificity, accuracy, positive and negative predictive values, or positive and negative diagnostic likelihood ratios, using the actual treatments as a reference.

Considering reliability and validity of the treatment plan derived from the FOSP would reflect the possibility to apply the FOSP as a tool in treatment planning among the cleft patients. In this study, the FOSP would be considered as a valuable clinical tool if it provided the kappa values of more than 0.61 with the percentage of accuracy not less than 75%.

7. Ethical Considerations

This research project was approved from the Ethical Committee of Khon Kaen University for permission of the human research (HE 532081). This study was ensured the confidentiality of the data obtained by using the confidential computer password entry to protect patients' data such as name, address, telephone number, and treatment records.