CHAPTER III

METHODS

1. Participants

Twelve patients who were diagnosed with advanced stage of lung cancer whether NSCLC or SCLC from Maharaj Nakorn Chiang Mai Hospital, Chiangmai province were recruited by a purposive sampling method (see. Sample size calculated in Appendix A). All participants were given an informed consent form prior to entry into the study and ethical clearance was obtained from the Research Ethics Committee, Faculty of Medicine, Chiang Mai University.

Inclusion criteria

1. Had been diagnosed as advanced NSCLC and SCLC within one month after diagnosis.
2. Male or female aged greater than 18 years old.
3. Had the Eastern Co-operative Oncology Group performance status of 0-1.
4. Patients can read (the assistance can be offered if necessary), write and understand the informed consent form, questionnaires form, and had good communication skills in Thai language.

Exclusion criteria

Participants were excluded from the study if they demonstrated any of the following criteria;

1. Existing contraindications for exercise testing. (Appendix B)
2. Had history of heart or lung surgery.

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

3. Had history of prior radiotherapy and chemotherapy.
4. Had any cardiopulmonary signs and symptoms i.e., symptomatic cardiac disease, any neurological deficit (i.e., dementia and poor mental status) and orthopedic problems that limit ability to ambulation or walking.
5. Documented brain or bone metastasis.

Drop out criteria

During the period of study, participants were excluded from the study if they had at least one of the following;

1. Participants had other treatments such as radiotherapy, targeted therapy and surgery.
2. Participants did not complete the fourth course of chemotherapy.
3. Participants were not willing to join afterward and could not be contacted.

2. Study design

This study was a prospective case series study design. Participants were newly diagnosed in advanced NSCLC or SCLC and before receiving chemotherapy. Patients were selected if they met the inclusion and exclusion criteria. The outcomes were changes in cardiorespiratory fitness and QoL after patients receive the second courses and the fourth courses of chemotherapy. These outcomes were evaluated three times, at baseline (before receive 1st course of chemotherapy), after 2nd course and 4th course of chemotherapy. The protocols were approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University.

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

3. Instruments

1. Pulmonary function test machine (SensorMedics®, Yoba, Linda, CA, USA) with mouth piece.

2. Equipment for the 6MWT: oxygen pulse oximeter, sphygmomanometer, stethoscope, stopwatch, chair, orange traffic cone, meter-cassette, thermometer, Borg's scale, and supplemental portable oxygen.

3. Quality of life questionnaire (The European Organization for Research and Treatment of Cancer Quality-of-life Questionnaire, EORTC QLQ-C30 and QLQ-LC13, Thai version) (Appendix C)

4. Outcome measures

1. Cardiorespiratory fitness was composed of pulmonary function and exercise capacity (6MWD)

2. Quality of life (EORTC QLQ-C30, LC-13)

Cardiorespiratiory fitness;

Includes 1) Pulmonary Function Tests (PFTs) and 2) exercise capacity. Tests were administered at three difference times at baseline (prior to receive 1st course of chemotherapy), after the 2nd courses, and the 4th courses of chemotherapy, respectively. The PFTs that were conducted in this study was the method of spirometry test, measured in several values of %predicted FEV_1, %predicted FVC, FEV_1/FVC ratio, %predicted$FEF_{25-75\%}$ and %predictedPEFR. It was done by using the SensorMedics®, Yoba, Linda, CA, USA, and administered by the physical therapist at the pulmonary laboratory test, Department of Physical Therapy (4th floor of 12 Floor Building, Faculty of Associated Medical Science).

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

Before testing, all patients did not perform any physical exercise for at least 30 minutes, they wore comfortable garments, avoided a big meal, caffeine, alcohol and tea for at least 2 hours, stopped bronchodilator drugs and stop smoking for at least two hours. After body weight and height was measured, they were recommended to rest at least 15 minutes before basic vital signs were examined before testing. Next, the physiotherapist explained the purpose and procedure for the test to the patients. Then, patients were instructed to sit with a straight back and look forward. A clip was placed on the nose, a mouthpiece placed in position and patients had to close lips around the mouthpiece. After that, patients were instructed to deeply and forcefully inhale and forcefully and rapidly exhale at least six seconds until no more air could be expelled while maintaining an upright posture and then, patients were commanded to deep inhale again for the finish of the test. The measurement was performed following the American Thoracic Society guideline (77). The best values chosen from three acceptable trials were used for data analysis. The maximum of eight attempts were allowed for each participant.

The 6MWT also was tested at three difference times similar to the pulmonary function tests. It was a commonly used measurement for exercise capacity, by measures the distance in meters that patients can quickly walk to cover as much distance as possible on a flat and hard surface within six minutes. The test would be done one time with the physical therapist at the pulmonary laboratory test, Department of Physical Therapy (4^{th} floor of 12 Floor Building, Faculty of Associated Medical Science). Before the test, the subjects were informed of the purpose, method and procedure in all these experiments. First, patients were instructed to walk in a 25 meters corridor at their own pace and were advised they could slow down and can

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

stop if they feel uncomfortable and after feel better commence walking as soon as possible. At the end of 6MWT, the distance was measured by the physiotherapist also the dyspnea and fatigue levels were measured by using the Rating Perceiving Borg scale (RPE). In addition, the oxygen saturation, heart rate and blood pressure were recorded both before and immediately after finishing the test. All above procedures were administered following the American Thoracic Society guidelines (81). All of cardiorespiratory fitness tests were documented in the data recording sheet. (Appendix D)

Quality of life questionnaires

EORTC QLQ C-30 and supplementary module was LC-13 translated in Thai (88). QLQ C-30 was an instrument that has an integrated system for evaluating the health-related quality of life specificity in cancer patients. It has been extensively used in cancer clinical trials composed of 30 items of questions and was divided into three major groups composed of two items of global health status, five subgroups of functional scale (five items of physical functioning, two items of role functioning, four items of emotional function two items of cognitive functioning, two items of social functioning), and eight symptom scales (three items of fatigue, two items of nausea and vomiting, two of pain and one of dyspnea, insomnia, appetite loss, constipation and diarrhea) and one of financial difficulties. The two items of the global QoL scale uses a modified seven point numerical analogue scale whereas all others items were scored on a four point categorical scale. It took about 11 minutes to complete the questionnaire (83). All scales and single items were linearly transformed to a 0-100 scale. A high score of functional scale and global QoL represents a high level of QoL and a high score of symptoms scale/ items represents a

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

high level of symptomatology. It was recommended that patients should answer all questions by themselves, however, assistance could be provided if necessary. The patients were required to do the questionnaire three times similar to the cardiorespiratory fitness test. LC-13 was used parallel with the core QLQ C-30. It is designed for use whilst patients received chemotherapy or radiotherapy; it is composed of 13 questions**.** The questions are included to determine lung cancer related-symptoms, treatment-related side effects and pain medication. All scales and single items were linearly transformed to a 0-100 scale. A high score of symptoms scale/ items represents a high level of symptomatology.

5. Procedures

This part describes all the procedure in the study, starting with the patients selection into the study until finishing the 4th course of chemotherapy and all of the outcomes were reassessed again, the details are described as follows:

1. After patients were diagnosed in advanced NSCLC and SCLC, they were also screened and evaluated first time by an oncologist based on inclusion and exclusion criteria such as:
    a. The medical history, complete physical examination including chest X-ray, CT scan of the thorax / upper abdomen and bone scan
    b. Complete blood count and blood chemistry (BUN, creatinine, electrolytes and liver function test)
    c. Performance status examined by using the ECOG

    Following on, the physician determined on day that the patients should come back to received the first course of chemotherapy and made an

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

appointment with the patients. Whereas, the second screening such as the indication and contraindication for exercise test and PFTs were also screened by the physiotherapist on day before received chemotherapy.

2. Willing patients signed the consent form. After that patients were assessed baseline start with PFTs followed by 6MWT, and concluded with the quality of life questionnaires were asked by EORTC QLQ- C30 and LC-13.
3. After patients completed the 2nd course of chemotherapy, they had appointments prior to receiving the 3rd course of chemotherapy for the 2nd assessment.
4. Three to four weeks after patients completed the 4th course of chemotherapy, they had an appointment for the final assessments. And all of the procedures of the study were finished at this point. The total time frame from the 1st step until end was at least three months. By which, all of the procedures were demonstrated as the flowchart as follows (Figure 2).

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

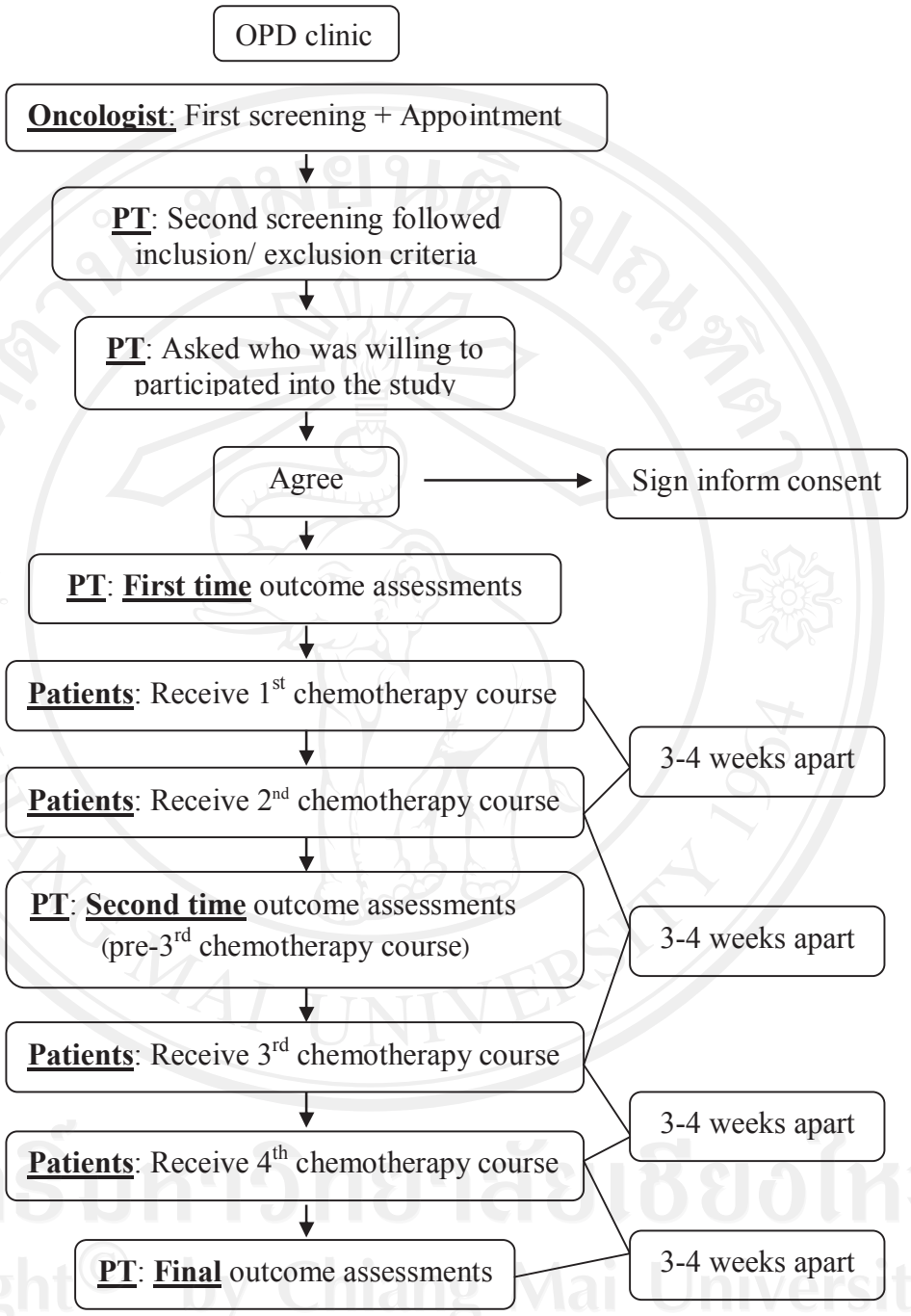

Figure 2 Flowchart all of the procedure of participants through study.

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

6. Statistical analysis

All data were summarized by mean and standard deviation, except Qol items were summarized by median. The normal distribution of each variables were determined by using 1 sample Komogorov-Sminov test. The comparisons of 6MWD and PFTs scores between pre receiving 1st course, after 2nd course and 4th course of chemotherapy were done using one-way repeated measure ANOVA. If there were any differences for each time points, the post-hoc test was done by using the Bonferroni method. For QoL items were analyzed by using the Friedman test and the Wilcoxon Signed Ranks test was applied as the post hoc test. All the statistical tests were one tailed, the data analyses were undertaken using the Statistical Package for the Social Sciences (SPSS version 16.0 for Windows). Significance level was set at 5 %.

7. Reliability of measurements

All measurements used in this study were determined for reliability by the test-retest method. The PFTs and 6MWT were done in ten healthy subjects with one day apart. Intra-tester reliability was determined using Intraclass Correlation Coefficient (ICCs). Whereas, the quality of life questionnaires (EORTC QLQ-C30 and LC-13) that were used in this present study was based on the latest validity and reliability that were done by Silpakit et al (88), the results was found to be a reliable and valid quality of life measure for Thai patients with various types of cancer.

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

8. Location

The study was conducted at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai.

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved