EFFECT OF RESPIRATORY MUSCLE TRAINING ON FUCTIONAL CAPACITY AND QUALITY OF LIFE IN COPD PATIENTS

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Thesis

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EFFECT OF RESPIRATORY MUSCLE TRAINING ON FUNCTIONAL CAPACITY AND QUALITY OF LIFE IN COPD PATIENTS.

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ABSTRACT

Patients with chronic obstructive pulmonary disease may have respiratory muscle weakness that can lead to a decrease in functional exercise capacity and poor quality of life. Previous studies on the effects of respiratory muscle training on exercise capacity of these patients have been controversial and there have been few studies on its effects on quality of life. This study is aimed to investigate the effect of respiratory muscle training on functional capacity and health-related quality of life in patients with chronic obstructive pulmonary disease. Eighteen patients from the outpatient clinic of Suratthani hospital were randomly assigned to control and exercise groups.

Subjects in the exercise group were supervised and trained three times a week for six weeks using a modified apparatus, a u-shaped water manometer, to provide 30% (progressing 5% per week up to 55%) of maximum inspiratory and expiratory pressure as training loads. Respiratory muscle strength was measured on a weekly basis. Quality of life score and functional exercise capacity (six minutes walking distance) were obtained before and after the six weeks of training.

After the six weeks of training, the exercise group exhibited a 24% increase in maximum inspiratory pressure and a 29% increase in maximum expiratory pressure, while there was no change in the control group. The quality of life score increased by 26% in the exercise group and the six minutes walking distance increased by 13%, while no change occurred in the control group. Respiratory muscle training using the modified u-shaped water manometer can increase inspiratory and expiratory muscle strength, capacity to walk, and quality of life in chronic obstructive pulmonary disease patients.

KEY WORDS: RESPIRATORY MUSCLE TRAINING / MAXIMUM INSPIRATORY PRESSURE / MAXIMUM EXPIRATORY PRESSURE / QUALITY OF LIFE.

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ผลการฝึกกล้ามเนื้อหายใจต่อความสามารถในการออกกำลังและคุณภาพชีวิต ในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง (EFFECT OF RESPIRATORY MUSCLE TRAINING ON FUNCTIONAL CAPACITY AND QUALITY OF LIFE IN COPD PATIENTS)

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บทคัดย่อ

ผู้ป่วยโรคปอดอุดกั้นเรื้อรังอาจมีการอ่อนแรงของกล้ามเนื้อหายใจ ซึ่งทำให้ความสามารถในการออกกำลังลดลง คุณภาพชีวิตต่ำลง การศึกษาที่ผ่านมาเกี่ยวกับผลการฝึกกล้ามเนื้อหายใจต่อความสามารถในการออกกำลังยังไม่มีข้อสรุปที่ชัดเจน นอกจากนี้ยังมีการศึกษาค่อนข้างน้อยเกี่ยวกับผลของการฝึกต่อคุณภาพชีวิตในผู้ป่วยกลุ่มดังกล่าว การศึกษาครั้งนี้จึงมีจุดประสงค์เพื่อพิจารณาผลของการฝึกกล้ามเนื้อหายใจต่อความสามารถในการออกกำลังและคุณภาพชีวิตในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง จำนวน 18 คนจากแผนกผู้ป่วยนอก โรงพยาบาลสุราษฎร์ธานี โดยแบ่งออกเป็น 2 กลุ่ม คือ กลุ่มควบคุมและกลุ่มฝึก

ผู้ป่วยในกลุ่มฝึกจะได้รับการฝึกโดยใช้ water manometer เป็นอุปกรณ์ในการฝึกกล้ามเนื้อหายใจ โดยมีระดับความหนักของการฝึกเริ่มต้นที่ 30% ของค่า maximum inspiratory pressure (MIP) และ maximum expiratory pressure (MEP) และเพิ่มขึ้น 5% ทุกสัปดาห์ จนเท่ากับ 55% ในสัปดาห์ที่ 6 จำนวนครั้งในการฝึก 3 ครั้งต่อสัปดาห์ ตัวแปรที่ทำการศึกษา คือ ความแข็งแรงของกล้ามเนื้อหายใจ ได้แก่ MIP, MEP ความสามารถในการออกกำลัง ได้แก่ six minute walking distance (6MWD) และคุณภาพชีวิต ได้แก่ quality of life scores โดยทำการวัด ค่าความแข็งแรงของกล้ามเนื้อหายใจทุกสัปดาห์ ความสามารถในการออกกำลังและคุณภาพชีวิตจะทำการประเมินก่อนและหลังการฝึก

ผลการศึกษาพบว่ากลุ่มฝึกมีการเพิ่มขึ้นของค่า MIP และ MEP = 24%, 29% ตามลำดับ ส่วนค่า 6MWD และ quality of life scores เพิ่มขึ้น 13% และ 26% ตามลำดับหลังจากการฝึกเป็นเวลา 6 สัปดาห์ จากการศึกษาแสดงให้เห็นว่าการฝึกกล้ามเนื้อหายใจด้วย water manometer สามารถทำให้ความแข็งแรงของกล้ามเนื้อหายใจ ความสามารถในการเดินและคุณภาพชีวิตเพิ่มขึ้นหลังจากได้รับการฝึกเป็นเวลา 6 สัปดาห์

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CONTENTS

CONTENTS (Continued)

CONTENTS (Continued)

LIST OF TABLES

LIST OF TABLES (Continued)

LIST OF FIGURES

LIST OF ABBREVIATIONS

bpm	beat per minute
BTPS	body temperature and pressure, saturated
cm	centimeter
cmH_20	centimeter water
COPD	chronic obstructive pulmonary disease
CRQ	chronic respiratory questionnaire
$FEV_{1.0}$	forced expiratory volume in 1 second
$\%FEV_{1.0}$	percent forced expiratory volume in 1 second
FVC	force vital capacity
HR	heart rate
HRQL	health related quality of life
IMT	inspiratory muscle training
L	Liter
L/s	liter per second
mmHg	millimeter mercury
min	minute
MSVC	maximum sustainable ventilatory capacity
MVV	maximum voluntary ventilation
P_{dimax}	maximal trandiaphragmatic pressure
P_{esmax}	maximal esophagal pressure
RMS	respiratory muscle strength
RMT	respiratory muscle training
RPD	rate of perceived dyspnea
RR	respiratory rate
RV	residual volume
VC	vital capacity
VO_2max	maximum oxygen uptake
V_T	tidal volume
wk	week

CHAPTER 1
INTRODUCTION

Chronic obstructive pulmonary disease (COPD) ranks behind heart disease as a major cause of disability in older patients. This disease is characterized by a progressive airflow limitation, which is caused by inflammation of either airways of alveoli from chronic inhalation of particles (1). The mechanisms of airway obstruction include airway inflammations, mucous gland enlargement, hypersensitivity of airway smooth muscle and alveolar wall destruction. The remarkable of clinical manifestations of COPD patients are cough and dyspnea. As a result, airway obstruction leads to the increase in work of breathing, breathlessness and the decrease of exercise tolerance. Consequently, patients with COPD commonly experience dyspnea and impaired exercise performance. Medical and rehabilitation interventions are generally directed towards relief of symptoms and improvement of lung function and exercise tolerance. The key component of the rehabilitation program is physical exercise training. Physical training, which may be selected in rehabilitation program, includes upper extremity, lower extremity and inspiratory muscle training. It is expected that quality of life may be improved thereafter.

It has been proposed that nonrespiratory muscle training, including walking, cycling, upper and lower limb training, is associated with the benefit of the increase in exercise capacity, the decrease in dyspnea and tolerance of the limbs. It is generally accepted that increasing in ventilation during exercise is the result of increasing in metabolism from limbs. This type of training may or may not improve respiratory muscle function, particularly in patients with respiratory problem. Belman and Kendregan (2) suggested that exercise training in patients with COPD might desensitize to dyspnea-induced by the respiratory loading. They randomly assigned patients to undergo muscle either upper limb or lower limb training and measured ventilatory muscle endurance and exercise capacity. In spite of a significant increase in exercise endurance, no change occurred in ventilatory muscle endurance. In addition, Wanke et al. (3) and Weiner and coworkers (4) suggested that combination of general exercise reconditioning (GER) and inspiratory muscles training (IMT) led to the improvement of dyspnea and exercise performance more than GER alone. Controversial results obtained from previous literatures may be caused by different age of subjects, protocol and duration of exercise training. It is possible that IMT may benefit to COPD patients as it is added to an exercise program.

Since airflow obstruction increases the work of breathing, which lead to placing inspiratory muscles at a mechanical disadvantage, especially the diaphragms. For this reason, respiratory muscles in patients with COPD are vulnerable to fatigue and inspiratory muscle inefficiency may be recognized (5). Hence, a specific inspiratory muscle training play a crucial role technique in COPD patients to improve respiratory muscle function. Several previous studies have reported that inspiratory muscle training may enhance respiratory muscle function and reduce dyspnea in patients with COPD. Belman and coworkers (6) studied effect of ventilatory muscle endurance training on exercise capacity in COPD patients. They found that while ventilatory muscle training improved the maximum minute ventilation, submaximal exercise endurance increased the distance covered in the 12-minute walk. In addition, Lisboa and associated (7) found that IMT relieved dyspnea, increased walking capacity and reduced the metabolic cost of exercise. In contrast, in double blind study of Chen and coworkers (8) reported that inspiratory muscle training improved inspiratory muscle endurance in patients with COPD without changing exercise performance. In addition, the controlled trail of Guyatt and coworkers (9) found that IMT failed to show the improvement of respiratory muscle strength, endurance and exercise capacity. The efficacy of IMT on exercise performance among patients with COPD is, however, controversial. In addition, there are several reports showing that expiratory muscle strength (10,11) and endurance can be impaired in patients with COPD (12). The expiratory muscles have been specifically trained in several settings other than COPD. It has been shown that such training tended to enhance expiratory muscle strength and to improve cough efficacy in severely disabled patients with multiple sclerosis (13) and to reduce sensation of respiratory effort during exercise in healthy subjects (14). Thus, expiratory muscle should also be trained simultaneously with inspiratory muscle strength in patients with COPD.

As progressive physical disability, previous reports have suggested that there is a high prevalence of depression and anxiety among patients with COPD. Light et al in 1985 (15) found that the prevalence of depression in patients with moderate or severe COPD approaches 50 percent while the incidence of anxiety is much lower (2 percent). Several studies have shown that COPD may lead to an impaired quality of life. Therefore, improvement in quality of life should be one of the aims of treatment of COPD. However, little is known about whether improvement of respiratory muscle strength affects quality of life in COPD patients. Guyatt and coworkers in 1992 (10) used Chronic Respiratory Questionnaire (CRQ) in COPD patients, which showed no improvement of quality of life after inspiratory muscle training. In contrast, Riera et al in 2001 (16) found that IMT improves health related quality of life in COPD patients after training for 6 months.

Because the change in exercise capacity and quality of life were controversial with IMT. It is because of the diversity of indices specified in those literatures. This study aimed to investigate the effect of respiratory muscle training (RMT) on functional capacity and quality of life in patients suffering from COPD using the main respiratory indices, maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP).

Purpose of the study

General objective

The purpose of the study is to investigate the effect of 6 week respiratory muscle training (RMT) on respiratory muscle strength, functional capacity and quality of life in patients with COPD subjected to either RMT(exercise) or no training (control).

Specific objectives

1. To investigate inspiratory muscle strength in term of maximum inspiratory pressure (MIP) at Residual Volume (RV) between pre, post 3rd and 6th week of RMT in COPD.
2. To compare inspiratory muscle strength in term of maximum inspiratory pressures (MIP) at RV between control and exercise group.
3. To compare expiratory muscle strength in term of maximum expiratory pressures (MEP) at Total Lung Capacity (TLC) between pre, post 3rd and 6th week of RMT.
4. To compare expiratory muscle strength in term of maximum expiratory pressures (MEP) at TLC between control and exercise group.
5. To estimate the quality of life score between pre and post exercise 6 weeks
6. To compare quality of life score between control and exercise group.
7. To compare walking distance between pre and post RMT
8. To compare walking distances between control and exercise group.

Parameter of the study

1. Maximum inspiratory pressure (MIP) which represents inspiratory muscle strength (cmH_2O)
2. Maximum expiratory pressure (MEP) which represents expiratory muscle strength (cmH_2O)
3. Quality of life scores (point)
4. Functional capacity: walking distance within 6 min duration (meters)

Scope of the study

This study investigated COPD patients who attend at outpatient clinic at Suratthani Central hospital. Independent variable include respiratory muscle training protocol, which is particularly designed for this study. Dependent variables are maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), quality of life score and 6 minute walking distance.

Hypotheses of the study

1. There is significant difference in maximum inspiratory pressure (MIP) between pre and post RMT in control and exercise group
2. There is significant difference in maximum inspiratory pressure (MIP) between control and exercise group.
3. There is significant difference in maximum expiratory pressure (MEP) between pre and post RMT
4. There is significant difference in maximum expiratory pressure (MEP) between control and exercise group.
5. There is significant difference in quality of life scores between pre and post RMT
6. There is significant difference in quality of life scores between control and exercise group.
7. There is significant difference in walk distance between pre and post RMT
8. There is significant difference in walk distance between control and exercise group.

Advantages of the study

1. To be used as guideline to develope appropriate particular strength training protocol for respiratory muscle in COPD patients who have had respiratory muscle weakness.
2. To be used as guideline for prospective study in other condition of respiratory muscle weakness such as quadriplegia and neuromuscular disease.
3. To introduce a simple instrument (water manometer) which can be used in clinical setting.

CHAPTER 2
LITERATURE REVIEW

2.1 Respiratory system, respiratory muscle and mechanic of breathing

2.1.1 Function of respiratory system

The goal of respiratory system is to provide oxygen to the tissue and to remove carbon dioxide. This function is carried out by 4 major functional events: 1) pulmonary ventilation, which means the gas get into and out from alveoli; 2) diffusion of oxygen and carbon dioxide across blood gas interface; 3) transportation of oxygen in the blood and 4) exchange of CO_2 and O_2 between the blood and cell (17).

2.1.2 The muscle of respiration

The lung can be expanded and contracted in two modes: 1) by downward and upward movement of the diaphragm and 2) by elevation and depression of the ribs.

Inspiratory muscles include the primary muscle of inspiration, the diaphragm, the external intercostal and the accessory muscle of inspiration (18).

1.The diaphragm. Diaphragm is a dome-shaped muscle. Normal inspiration is mainly performed by contraction of the diaphragm to compress the abdominal content, which vertically lengthen the chest cavity.

2. The external intercostal muscles. The most inspiratory muscles that raise the rib cage is external intercostal muscles. During inspiratory effort, the muscles that help raising rib cage are 1) sternoclidomastoid, which lifts the sternum and increase antero-posterior diameter of the upper rib cage 2) scalene, which lifts the first two ribs.

Expiratory muscles

The abdominal muscles. Tidal expiration is usually passive and achieved by the recoiled of the lungs, chest wall and abdominal structure. During heavy breathing, however, active expiration is achieved by contraction of the abdominal muscles that push the abdominal contents upward. The contraction of this muscle decreases size of rib cage and lung volume. The muscles that help to pull the rib cage downward during expiration are 1) the rectus abdominis, which pull lower ribs downward and compress the abdominal contents upward and 2) the internal intercostal muscles.

2.1.3 Mechanic of Breathing

Compliance

Compliance of the total respiratory system consists of two components- lung compliance and chest wall compliance. The slope of the relaxation pressure-volume curve is known as static compliance. Compliance is defined as the volume change per unit pressure change. Lungs with high compliance have a steep slope on the pressure volume curve. That is, a small pressure change will cause a large change in volume. It is important to remember that compliance is the inverse of elasticity or elastic recoil of lung. Compliance refers to mechanical characteristics, which can be stretched or distorted, while elasticity refers to ability to return to its original configuration after the distortion. Various pathological states of the lung change compliance. The fibrosis lung makes the lung less compliant and increases alveolar elastic recoil. In patients with emphysema, the lung compliance is increased because of the destruction of alveolar septal tissue (17).

Elastic recoil of lung

Elastic recoil of the lung is the function of the elastic properties of the pulmonary parenchyma and the surface tension force. Special fluid, secreted by pneumocyte Type II, is responsible for surface tension. The surface tension force contributes to alveolar elastic recoil. Alveolar elastic recoil makes a physiologic stable of alveoli by providing air into most alveoli (17,19).

The work of breathing

The work of breathing can be defined, as the work is required to move the lung and chest wall. This work is required to overcome the elastic force and viscous resistance which are normally caused by inward recoil of alveoli, tissue_distortion and inertia of gas-tissue interface. Therefore, high airway resistance or inspiratory flow rate would increases work of breathing. In addition, the higher respiratory rate, the faster the flow rates increases viscous resistance. The work of breathing can be divided into 2 types (17).

Elastic work**.** This work is required to overcome the elastic recoil of the chest wall, the pulmonary parenchyma and the surface tension of the alveoli. In patients with fibrotic lung, their elastic work of breathing is increased because of the diminished of collagen which is the extensible tissue of alveoli (17).

Resistive work. This is the work that required to overcome dynamic changes the tissue resistance and airway resistance during respiratory cycle. In patient with chronic airway obstruction, elevated airway resistance is more commonly characterized (17).

Total work of breathing is the combination of both mentioned works. The total work of breathing can be calculated by measuring of O_2 cost of breathing. The O_2 cost of normal breathing is normally less than 5% of the total requiring O_2 consumption. This percentage increases to 30% during exercise. In patient with obstructive lung disease, the work of breathing may limit their exercise capacity (17,19).

2.2 Assessment of respiratory muscles strength

2.2.1 The indications of respiratory muscle testing

The most common clinical utility of measurement of maximum respiratory pressure is explained below:

In diagnosis

Maximum respiratory pressure assessment is particularly relevant to the patients who have unexplained dyspnea, reduction in vital capacity (VC) or maximum voluntary ventilation (MVV). Patients with hypercapnea respiratory failure or difficulty in weaning from ventilator, respiratory muscle weakness is usually severe. Measurement of maximum pressure is used for diagnosis (20).

Assessing the contribution of respiratory muscle weakness to symptoms in certify diseases.

As it is prevalent, respiratory muscle weakness contributes to the symptoms of patients with known respiratory and non-respiratory diseases. These, include patients with COPD, neuromuscular disease, endocrine collagen disease and patients with a long-term treatment with corticosteroid (20).

Assessment of severity

Measurement of maximum respiratory pressure is especially relevant to quantitate the degree of respiratory muscle weakness present in patients with neuromuscular disease and patients with hypercapnia respiratory failure (20).

Following progress and response to treatment.

MIP and MEP tests can be used as outcome variable for treatment such as pulmonary rehabilitation or steroid administration (20).

2.2.2 The measurement of the respiratory muscle strength

Simple test

1. Vital capacity (VC)

The ability of the respiratory muscles to maximally shorten against elastic forces of lung and chest wall is vital capacity. Because inspiratory muscle weakness reduces inspiratory capacity, and expiratory muscle weakness reduces expiratory capacity. Therefore, global respiratory muscle weakness reduces vital capacity. The important shortcoming of VC is non-specific maneuver. Furthermore, a fall in VC may be caused by reduction in lung compliance and chest wall (21,22).

2. Maximum voluntary ventilatory (MVV)

MVV is an indirect measure of respiratory muscle function, it measures the capacity of subjects to ventilate the lungs fastly and deeply as possible. It is a reflection of the respiratory musculature against resistant of lung and chest wall to expansion and contraction. A disadvantage of this test is the unreliable values when it is performed by inexperience personnel or by unmotivated patients (21,22).

3. Maximum mouth pressure

The most common maneuver to assess respiratory muscle strength is the measurement of maximum static inspiratory and expiratory pressure in centimeters of water. Maximum expiratory pressure (MEP) is recorded during a maximum expiratory effort at TLC, whereas MIP is measured during a maximum inspiratory effort against closed airway at either RV or FRC. These pressures measured at the mouth by a mouth pressure meter i.e., Bugle dynamometer, mouth pressure meter, mercury manometer, and pressure transducer. The disadvantage of this measurement is underperformance commonly occurred because of the difficulties of the maneuver. Furthermore, a normal range of MIP and MEP in healthy persons is very wide (21,22).

Sniff tests

1. Maximum sniff esophageal pressure (sniff P_{es})

Sniff P_{es} is the best maneuver for measurement of global inspiratory muscle strength. Sniff P_{es} is an invasive technique because of the placement of an esophageal balloon. The normal value of sniff esophageal pressure is narrow than that for MIP (22,23).

2. Sniff transdiaphragmatic pressure (sniff P_{di})

The sniff P_{di} is the measurement for the assessment of diaphragm muscle strength. This maneuver is an invasive test, which requires esophageal and gastric balloon to measure change in transdiaphragmatic pressure. This pressure expressed as the difference between esophageal (P_{es}) and gastric (P_{ga}). As a result, sniff P_{di} has a narrow normal range and more reproducible. Ideally, sniff P_{di} is the excellent choice for the assessment of diaphragm strength (22,23).

Non- volitional tests

1. Transcutaneous electrical stimulation

Transcutaneous electrical stimulation is used for evaluation of diaphragm muscle function by stimulating phrenic nerve. This technique has been little used clinically because of using surface electrode to stimulating nerve. A high twitch response of diaphragm muscle excluded diaphragm weakness (22).

2. Ultrasonography

Ultrasonography used for evaluating diaphragm thickness and for estimated diaphragm shortening by change in thickness. This technique is useful for evaluating condition such as disease atrophy or loss of muscle mass due to undernutrition (22).

2.2.3 Measurement of respiratory muscle endurance

Endurance time

The most common method is to assess endurance time, which is a measure of the time to task failure in response to and externally applied ventilatory or pressure load. Endurance time is probably a reflection of a combination of endurance and force production characteristics of the muscle (21).

Maximum sustainable ventilatory capacity (MSVC)

MSVC is the maximum ventilation that can be sustained for 15 min under normocapnic conditions. MSVC is measured by setting the flow rate at approximately 70% of the previously measured MVV and adjusting the flow rate during the first 2 min using the target spirometer as guide. The average ventilation that can be maintained over the eight minute is considered the MSVC (21).

2.2.4 Previous studies of respiratory muscles strength in normal subjects

Black and Hyatt in 1963 (24) studied respiratory muscle strength of normal adult. They reported mean MIP and MEP were 124/232, and 87/152 cmH_2O in women. In this study, they found no relationship between maximal inspiratory pressure and age in person younger than 55 years old. They suggested that MIP should be measured at RV and TLC for MEP measurement.

Leech et al in 1983 (25) studied the relationship of lung function to respiratory pressure in 924 young adults (both female and male 15 to 35 yr of age). MIP and MEP were measured using a Validyne transducer. Each measurement was made three times. This study concluded that respiratory pressure was the main determinants of lung functions such as force vital capacity (FVC), force expiratory volume in one second (FEV1), and peak flow.

Wilson et al in 1983 (26) measured maximal respiratory pressure at the mouth in 370 normal Caucasian children and adults. This study used the apparatus based on that used by Black and Hyatt but all pressures were measured without a noseclip. Most of subjects were hospital staff. Both MIP and MEP in women and girl were significantly lower than in men and boys.

Smyth et al in 1984 (27) used simple mercury manometer to measured MIP and MEP in 76 adolescents. The value was recorded as the level of mercury was sustained for two to three seconds. The highest value from 2 trials was recorded and expressed in centimeters of water. The value of MIP and MEP were 76±25 and 86±22 cmH_2O for female adolescents. The means of MIP and MEP for male adolescent were 107±26 and 114±35 cmH_2O, respectively. They believed that a careful instruction and observation of the subject during MIP testing was essential for preventing glottic closure and artifactually high inspiratory pressure.

Chen and Kuo in 1989 (28) measured respiratory muscle strength and endurance in 160 Chinese subjects who were 16-75 year of age and divided in four age groups. Maximum respiratory pressures (MRP) were measured in three trials, and the best value was recorded. Inspiratory muscle strength at RV was 104±27 cmH_2O for men and 74.2±21.4 cmH_2O for women. Expiratory muscle strength at TLC was 132.2±38.5 for men, and 88.5±24.6 cmH_2O for women. These measurements indicated that Chinese men had greater MRP than in women but inspiratory muscle endurance is not different.

Enright et al in 1994 (29) studied maximum respiratory pressure in a large elderly population. All of subjects were 65 year of age and older. The mean MIP/MEP of women was 57/116 cmH_2O and that of men was 83/174 cmH_2O. They found that MIP of current smoker was 15% lower than non and former smokers.

Jarungjitaree and Chaipiyaporn in 1997 (30) studied an average value of strength of inspiratory and expiratory muscle in young Thai adults (18-25 years). The strength of the two muscle groups was measured by Bugle dynamometer in two positions, sitting standing. The MIP values in sitting position for male were 125.31±12.04 cmH_2O and 69.83±8.95 cmH_2O for female. In male the value of MEP were 135.42±23.38 cmH_2O, and 71.76±9.76 cmH_2O in females. They concluded that MEP in males showed significant difference between two positions.

Table 2.1 Ranges of maximal respiratory pressure in health persons from previous literatures. Values are mean and SD.

Reference	Age	Men		Women	
		MIP (cmH_2O)	MEP (cmH_2O)	MIP (cmH_2O)	MEP (cmH_2O)
Black&Hyatt, 1963 (24)	20-54	124±22 (N= 60)	233±42 (N=60)	87±16 (N= 60)	152±27 (N=60)
Leech et al.,1983 (25)	15-35	114 (N=108)	160 (N=108)	67 (N=81)	94 (N=81)
Wilson et al.,1982 (26)	19-65	106±31 (N=48)	148±34 (N=48)	72.9±22 (N=87)	93±17 (N=87)
Smyth et al,1984 (27)	13-18	107±26 (N=29)	114±35 (N=29)	76±25 (N=37)	86±22 (N=37)
Chen&Kuo, 1989 (28)	16-75	104±27 (N=80)	132±39 (N=80)	74±21 (N=80)	117±33 (N=80)
Enright et al,1994 (29)	>65	82.8±26 (N=1269)	175±46 (N=1269)	74±21 (N=1602)	65±2 (N=1602)
Jarungitaree& Chaipiyaporn, 1997 (30)	18-25	125.3±12 (N=137)	135.4±23 (N=137)	69.8±8 (N=127)	71.7±9 (N=127)

2.2.5 Factors influence maximum respiratory pressure

1. Age

Studies suggested that respiratory muscle strength can be affected by age. Chen and Kuo (28) confirmed that respiratory muscle function and pulmonary function related with aging. This study showed that respiratory muscle strength and pulmonary function decreased with aging. They revealed that influence of aging on respiratory muscle strength started at 30-40 year of age. Black and Hyatt (24) show a significant relationship between age and respiratory muscle strength in subjects older than 55 year of age. Wilson et al in 1984 (26) observed that respiratory muscle pressure in male was related to age, while in women respiratory muscle strength was not related to age. In contrast, Mcelvaney et al in 1989 (31) determined correlation between age and maximum static respiratory pressure in normal subjects older than 55 yr. They concluded that there is no existing age-dependent on maximum static respiratory pressure.

2. Height

Wilson et al in 1984 (26) show that respiratory muscle pressure in women was related to height. In addition, Johan and coworker in 1997 (32) found a significant correlation between maximal respiratory pressure and height in men.

3. Weight

Enright et al in 1994 (29) concluded that weight was positively correlated with MEP, while waist circumference was negatively correlate with MIP. Wilson and associated in 1984 (24) found that maximum inspiratory pressure in children was correlated with weight. Furthermore, a significant correlation between respiratory muscle strength with weight was found in study of Leech and coworkers in 1983.

4. Smoking status

Enright et al in 1994 (29) reported a significant difference in respiratory pressure value between non and current smokers. They found a 15% lower of mean MIP and MEP in current smokers.

5. Physical activity

Fuso and coworkers in 1996 (33) reported a significant difference in respiratory muscle strength between soccer players and normal subjects with sedentary life-style. This study found that inspiratory muscle strength was higher in soccer players than in sedentary. In addition, the study of Inbar and coworkers in 2000 (34) indicated that elite endurance athletes have greater inspiratory muscle strength and endurance than untrained subjects.

2.2 Pathophysiological effect of respiratory muscle on the respiratory system

2.3.1 Conditions associated with respiratory muscle dysfunction

The factors contributed to respiratory muscle dysfunction can be broadly divided into 3 groups as follow (35):

1. Group that decrease the force of respiratory muscle

2. Group that increase work of breathing caused by change in lung or chest wall

3. Group that decrease respiratory muscle efficiency.

An acute condition contributed to inspiratory muscle weakness can include metabolic abnormalities, shock, sepsis, steroid administration, and disuse. There are also many chronic condition contributed to respiratory muscle weakness such as neuromuscular disease, connective tissue and endocrine disorders (35).

Chronic obstructive lung disease has respiratory muscle dysfunction because of increased work of breathing due to airway obstruction and inefficiency of inspiratory muscle caused by lung hyperinflation. Hyperinflation produces all of inspiratory muscles to work at length shorter than normal. This condition places inspiratory muscles at a disadvantage for tension generation (36,37)

In kyphoscoliosis, stiffness of chest wall leads to increased work of breathing. On the other hand, primary pathology in interstitial lung disease causes an increased stiffness of the lungs. Therefore, the work of breathing is increased because of the less compliant lungs. Furthermore, patients with this condition may develop respiratory muscle compensation when treated with high dose steroids to alleviate inflammation of the lung (38).

2.3.2 Problems associated with respiratory muscle dysfunction

Exercise intolerance

There are various conditions in which respiratory muscle dysfunction may contribute to exercise intolerance. The poor respiratory muscle function contributed to exercise intolerance has primarily been examined in patients who have COPD. Respiratory muscles may be weaken due to metabolic abnormalities or because of other factors such as prolong inactivity, steroid use, poor nutrition and hyperinflation. Exercise and other daily activities produce higher ventilatory levels and ventilatory rates. As ventilatory rate increase, expiratory and inspiratory times are shortened. Therefore, respiratory muscles may be further weakened owing to higher speed of shortening and shorter operating length of inspiratory muscle during high ventilatory level. Airway obstruction and loss of structural stability of small airways leads to greater dynamic compression of the airways than at rest and increased air trapping.

Because lung hyperinflation places all the inspiratory muscles in shorter position, the mechanical disadvantage of inspiratory muscle is increased. For this reason, exercise and increasing ventilatory loads in patients with COPD require greater inspiratory muscles work at higher lung volumes and faster speed in order to overcoming airflow obstruction (34).

Dyspnea

The most common symptom which limits exercise ability and activity of daily living in patients with COPD is dyspnea. The etiology of dyspnea, the relationship among respiratory muscles and exercise intolerance, is unclear. However, dyspnea on exertion seems to originate from the outflow of central nervous system out to respiratory muscle. Thus, respiratory muscle training may relieve dyspnea by decreasing muscle weakness or by improve efficiency of breathing (34).

Hypercapnic ventilatory failure

Respiratory failure is an inability of lungs to ventilate adequately which demonstrated by a decrease in the partial pressure of arterial oxyen (PaO_2) below 55 mmHg or arise in the partial pressure of carbon dioxide ($PaCO_2$) above 45 mmHg. There are two types of respiratory failure, hypoxic respiratory failure and hypercapnic respiratory failure. Hypercapnic can arise due to a failure of respiratory muscle pump and an alteration in breathing pattern. This type of respiratory failure is manifested by an increase in $PaCO_2$. Respiratory muscle dysfunction has been involved as the inducement of hypercapnic respiratory failure (34).

2.4 Respiratory muscle training

2.4.1 Types of respiratory muscle training.

Respiratory muscle training has been conceptually accomplished using two different strategies: strength and endurance training.

1. Strength training. The aim of strength is to improve force production of respiratory muscles. This training is accomplished by the application of a high intensity with low repetition

2. Endurance training. It is achieved by the application of low intensity, high repetition, and the following three techniques: resistive loading, threshold loading and

ventilatory isocapnic hypernea. The endurance training duration is usually at least 15 minutes and may consist of continuous or multiple interval training period.

2.4.2 Principles of Muscle training

Training of the respiratory muscles must follow the basic principle of training for any skeletal muscle with regard to the overload, the specificity of training, and reversibility of training (39).

1) Overload principle

Overload must be applied to a muscle for a load greater than normal capability in order to exhibits training effect. Overload may be applied by increasing the frequency of training, duration of training, the intensity of the loading or a combination of these factors.

2) Specificity of training

Specificity principle means that training should be specifically directed to the muscle function. Training must be similar of identical to the activity that the subject wishes to improve and must directly involve the muscles, which is being trained.

3) Reversibility principle

If the training or overload is ceased for a certain period of days or weeks, the training effects will be deteriorated. The functional characteristics will gradually return to baseline levels or detraining.

2.4.3 Methods of respiratory muscle training

1) Voluntary isocapnic hyperpnea

This technique requires subject to hyperventilate for 15-20 minutes. Because the person is hyperventilating, partial pressure of carbon dioxide level will be decrease. Special care is necessary to maintain arterial blood gas within a physiological range. The outcome of this type of training is generally measured by evaluating the change in MVV or in maximal sustainable voluntary capacity (MSCV) (39).

2) Target resistive training

Respiratory resistive trainer consists of a mouthpiece attached to a T-piece with a one-way valve on one side and inspiratory resistance attached to the other side. The subject must breath against the inspiratory resistance knob, which is a colored disk with a small hole in the center. As inspiratory resistance change, the flow rate is altered. Since the inspiratory resistance is nonlinear. Therefore, the breathing pattern and flow rate must be controlled throughout the training session for maintenance of a constant load (39).

3) Threshold inspiratory training

This technique use an apparatus that consists of a mouthpiece connected to a one or two-way valve, which in turn is attached to some sort of inspiratory threshold load. The subject breaths in against the threshold load (usually a weight plunger or spring load valve) and breaths out unimpeded. A valve is automatically opened when a critical pressure is reached. Therefore, threshold loading is probably the most practical approach to inspiratory muscle training to date (39).

2.4.4 Respiratory muscle training in normal subject

Leith and Bradley in 1976 (40) first demonstrated that it was possible to improve respiratory muscle function in normal subjects by specific training. Time course of training is five days a week for five weeks. Strength trainers performed repeated maximum static inspiratory and expiratory maneuvers against obstructed airways, and endurance trainers performed normocarbic hyperpnea to exhaustion at level of ventilation equivalent to 50% MVV. They have shown that, subjects trained for strength increase their strength by 55% whereas those who trained for endurance increase their maximum sustained ventilatory capacity from 81-96% of their MVV.

Merrick and Kenneth in 1981 (41) studied the effects of abdominal weight exercise program on inspiratory muscle function in a group of healthy young adults. All subjects performed 30 maximal voluntary diaphragmatic contractions in supine position with a moderately heavy weight (7-23 Kg), 3 times/week for 6 week. This protocol failed to improve inspiratory capacity, peak inspiratory flow rate and maximal pressure. Results indicate that isotonic exercise regimen does not increase the maximum shortening, velocity of shortening or strength of the diaphragm in healthy subjects.

Clanton and coworker in 1985 (42) showed the effectiveness of the threshold loading techique in volunteers who trained for half an hour each day over 10 weeks. The mean MIP increased by 50 cmH_2O and the endurance time for a load at 65% of the initial MIP increase by six minute.

Belman and Gaesser in 1988 (43) studied the effects of respiratory muscle training (RMT) on respiratory function and exercise performance in the elderly. Respiratory muscle training was performed by isocapnic hyperpnea for 30 min /day, 4 day a week for 8 weeks. They found a significant increase in maximum sustainable ventilatory capacity (MSVC) and maximum voluntary ventilatory (MVV) after RMT. Maximum exercise capacity and ratings of perceived exertion (RPE) during incremental and steady state exercise are not improved by respiratory muscle training.

Suzuki and colleagues in 1993 (44) studied the effect of inspiratory muscle training (IMT) on changed of respiratory sensation during exercise in 12 healthy women. The modified Borg scale was used to evaluate respiratory sensation. The IMT was performed by a pressure threshold loading device for 15 minutes, twice daily continued for 4 weeks. The inspiratory threshold was set to 30% of MIP. After IMT, both MIP and maximal transdiaphragmatic pressure increased by 30% in the trained group, but did not change in the control group. They showed no difference in the sensory score- exercise stage curves before and after IMT. Although, IMT increased diaphragmatic strength, it did not affect respiratory sensation during exercise in normal subjects.

Inbar and coworker in 2000 (34) studied the effects of specific inspiratory muscle training (SIMT) in twenty well-trained endurance athletes. Ten athletes comprise the training group who received SIMT, and ten athletes were assigned as control group and received sham treatment. Inspiratory training was performed using a threshold inspiratory muscle training device for half hour/day, six times a week for 10 weeks. The intensity for training started at a resistance equal to 30% of MIP for 1 wk. The resistance was then increased serially, 5% each session, to reach 80% of their MIP at the end of first 4 week. Intensity for training maintains at 80% of their MIP for the next 5 wk. The MIP was adjusted every week to the new MIP achieved. Inspiratoy muscle strength and endurance increased significantly in trained group after training.

Nualnim in 2002 (45) investigated the effect of RMT on respiratory muscle function, pulmonary function, maximum oxygen uptake and respiratory work in Thai female subjects. All subjects performed 5sets of 10 static maximal inspiratory or expiratory pressure, by suckling of blowing, to created level of water difference at the pre-determined of 80%MIP or MEP. Respiratory muscle training performed by water manometer 3 day a week for 6 week This studied demonstrated that RMT exerts significant improvement of MIP and MEP and maximal inspiratory and maximal expiratory pressure work in trained group. However, RMT exerts no alteration of pulmonary function (VC, FVC, FEV_1 and PEFR) and did not change maximum oxygen uptake.

2.4.5 Respiratory muscle training in COPD patients

Most published studies of RMT have focused on patients with COPD because the high prevalence and morbidity of this condition. Several studies have demonstrated that patients with COPD have inspiratory muscle weakness (47,48). Furthermore, weakness of the respiratory muscle may contribute to dyspnea as well as reduced exercise performance. Therefore, the rational for RMT in patient with COPD is that the increase in strength and / or endurance of the respiratory will reduce the severity of dyspnea and improve exercise capacity. The investigators have studies the efficacy of inspiratory resistance training in patient with COPD. Then, this review will focus on the randomized controlled trials of RMT (Table 2.2).

Table 2.2 Randomized trials of respiratory muscle training

Study	Patients	Training program	Outcomes
Harver et al.,1989(47)	10T 9C	T: 15 min twice a day With gradual ↑ in resistance C: same except sham training Duration: 8 wk	T: ↑MIP and TDI C: ↑minimal MIP and TDI
Guyatt et al.,1992(9)	43T 39C	T: 10 min five times a day With resistance↑ as tolerated. C: same except sham training with minimal resistance. Duration: 12 wk	No significant difference in MIP between T and C group No change in 6 MWD
Lisboa et al,1994(48)	10T 10C	T: 15 min twice a day at 30% MIP with load increased as tolerated C: same except sham training at 12%MIP Duration: 5 wk	T: ↑strength, IMPO, SIP, 6MWD,↓ Dyspnea C: no significant change
Preusser et al,1994(49)	12T 10C	T: 15 min/session at week 1 to 18 min/session at week 12, three times per week at 52% of MIP C: same except at 22% MIP Duration: 12 wk	T: ↑strength, ↑endurance, ↑12 MWD C: ↑endurance, ↑12 MWD
Lisboa et al.,1997(7)	10T 10C	T: 30 min/d at 30%MIP for 6 d/wk C: same except at 10% MIP Duration: 10 wk	T: ↑strength , ↑dyspnea ,and ↑6MWD C: ↑strength
Riera et al.,2001(16)	10T 10C	T: 30 min daily , 6 d/wk at 60-70%SIP C: same except sham training Duration: 6 month	T: ↑strength, ↑SWD, ↓dyspnea and ↑quality of life C: no significant change

T: training group, C: control group, TDI: Transition Dyspnea Index, 6MWD: 6 minute walking distance, 12MWD: 12 minute walking distance, IMPO: inspiratory muscle power output, SIP: sustainable inspiratory pressure, SWD: shuttle walking distance, MIP: maximum inspiratory pressure.

2.4.6 RMT combined with exercise training

Three studies of examined the efficacy of RMT combined with general exercise training (Table2.3). The studied of Weiner (4) and Wanke (3) showed significant improvements in MIP and exercise performance in RMT plus exercise training compared with the control group. However, neither dyspnea nor health status was measured in these studies. Berry et al (50) showed that RMT combined with lower extremity exercise resulted in greater improvement in walking distance compared with a control group, but not difference in MIP or exercise capacity were present compared with a group who only performed exercise training. In general, these results indicated that the addition of RMT to exercise training can enhance exercise ability.

Table 2.3 Randomized trials of respiratory muscle training and exercise training.

Study	Patients	Training program	Outcomes
Weiner et al.,1992(4)	12T 12C 12C	T: 15 min three times per week at 15%MIP for 1 wk, then 60% MIP C: cycle ergometer and sham RMT C: no RMT or exercise training Duration: 6 mo.	T: ↑MIP, ↑respiratory muscle endurance and ↑cycle endurance compared with exercise only and control groups
Wanke et al.,1994(3)	21T 21C	T: 12 maximal static inspiratory efforts and 10 min at 70%MIP daily C: cycle ergometer 4 d/wk Duration: 8 wk	T: ↑MIP, ↑ respiratory muscle endurance and ↑VO_2max compared with exercise group
Berry et al.,1996(50)	25T 9C 8C	T: 15 min twice a day at 15%(2wk),30%(2wk),60%(2wk) ,and 80%(2wk) of MIP daily C: walking and upper extremity resistance training and sham RMT(15%MIP) C: flexibility training and sham RMT(15%MIP) Duration: 12 wk	T: ↑12 MWD compared with control group, but no difference in VO_2 max, MIP, or treadmill time for the three group

T: training group, C: control group (exercise with or without sham respiratory muscle training (RMT) or other control conditions), 12MWD: 12 minute walking distance, MIP: maximal inspiratory pressure, VO_2 max: maximal oxygen consumption.

2.4.7 Outcomes of RMT

1. Respiratory muscle function

Of the six studies listed in Table 2.2, MIP was measured as an outcome variable in all. However, in the study of Guyatt et al (9), neither the training nor the control group exhibited and improvement in respiratory muscle strength; this result indicate that the training load was inadequate. In the remaining five investigations significant increases in MIP occurred with RMT in the training group (Table2.2). In further support of he benefits of RMT, Villafranca et al (51). reported that resistance training led to a significant increase in the maximal power output of the inspiratory muscles and that the resistive load was overcome with a shorter inspiratory time, with no change in tidal volume.

2. Dyspnea

Only Harver et al. (47) and Lisboa et al. (7) measured breathlessness as an outcome as part of the RMT trials. Patients in the training group had significant improvements in the Transition Dyspnea Index whereas minimal change occurred in the control group of these three studies. Furthermore, the changes in MIP were correlated significantly with the change in the Transition Dyspnea Index in the training group.

3. Exercise performance

The changes in exercise performance were variable with RMT. Although Riera et al. (16) demonstrated increases in the shuttle walk distance after RMT, Guyatt et al. (9) and Preusser et al (49) showed no difference in the timed walking distance between the training and the control groups. However, in the training groups with improved MIP walking distance also increased.

4. Health related quality of life (HRQL)

Only Riera et al. (16) measured quality of life score as outcome as part of RMT trial. Patients in the training group had significant improvement in the score of Chronic Respiratory Questionnaire (CRQ) whereas no changes in the control group. Not all the problem associated with development of COPD are described by physiological variable (FEV1 and arterial blood gas), especially quality of life. Therefore health related quality of life questionnaires, which provide an accurate estimation of a patient's quality of life in chronic disease, are the tools for evaluation this dimension of patients with COPD. These tools can be divided in two types; 1) disease-specific instrument, 2) generic instrument. The selection of the type of instrument depends on the question being asked. (52) There are four generic HRQL instruments and four disease- specific instruments that have been used extensively in patients with COPD. (51) Some important features of each of

Instrument	Domain and dimension examined	Number of items	Administration
Generic:			
Sickness impact profile (SIP)	Physical: ambulation, mobility , body care Social: general well being, work/social role performance, social support and participation, global social function, personal relationships and global emotional functioning	136 items	Self-administration
Medical outcomes study (MOS)	Functioning: physical, role, and social Well being: mental health, health perceptions and bodily pain	20 items	Self-administration
Quality of well being (QWB)	Mobility: access to modes of transportation Physical: limits to activity Social: limits to activity Symptoms: review of systems	50 items	Trained interviewer administration
Nottingham health profile (NHP)	Health: energy ,pain, emotional reactions, sleep, social isolation, physical mobility Life functioning: employment, relationships, personal life, sex, hobbies, vacations, housework	45 items	Self-administration
Specific:			
Chronic respiratory questionnaire(CRQ)	Dyspnea, fatigue, mastery over disease, emotional dysfunction	20 items	Trained interviewer administration
St George's respiratory questionnaire (SGRQ)	Symptom: cough, sputum, wheeze, breathlessness Activity: physical functioning, housework, hobbies Impact on daily life: social and emotional impact	76 items	Self-administration
Oxygen cost diagram(OLD)	Single vertical line to marked in location indicate degree of disability caused by dyspnea	1 item	Self-administration
Baseline dyspnea index(BDI)	Functional impairment, magnitude of task evoking dyspnea, magnitude of effort evoking dyspnea	3 indices with four grades	Trained interviewer administration

2.5 Definition, sign and symptom, and stage of COPD

2.5.1 Definition of COPD

Chronic obstructive pulmonary disease is characterized by slowly progressing, chiefly irreversible airflow obstruction and a decrease expiratory flow rate. COPD encompass chronic bronchitis and emphysema. Emphysema is defined as permanent extension of airspace, mostly the alveolar area. Chronic bronchitis defined as morning productive of sputum for as least 3 months a year for at least 2 consecutive year (55).

2.5.2 Sign and Symptom

Chronic bronchitis: usually, cough with productive of sputum begin during and acute respiratory infection and persist after subsidence of acute infection. The sputum may be mucoid or mucoperulent, but it becomes more purulent during exacerbation.

Emphysema: a symptomatic patient has a hyperresonant chest to percussion and a limited diaphragmatic excursion. Frequently, expiratory rate is elevated. During exacerbation, patients are usually dyspenic, often at rest and exercise thereby tachypnea and tachycardia will be occur (55).

2.5.3 Stage of COPD

At present, grade of the severity of COPD based on objective physiological measure of pulmonary function, usually FEV_1. ATS classify severity of COPD according to the degree of FEV_1 value (Table 2.4). This staging system provides a rough estimation of the patient's diagnosis. It also helps the clinician and health care provider recognize the possible level of care and complexity of the patients (56,57).

Table 2.4 Stages of COPD

	Stage I	Stage II	Stage III
FEV_1(%predicted)	≥50% - Most of the patient may be symptomatic - Small impact on health related quality of life - Usually managed by primary care physicians	36%- 49% - Minority of patients symptomatic - Moderate impact on health relate quality of life - May be hypoxemic - May be helps by evaluation by specialist	≤35% - Small minority of patients severe symptoms - Large impact on health related quality of life - Hypoxic, may show hyperpnea - Best managed by professionals familiar with COPD

2.6 Pathophysiology and Diagnosis of COPD

2.6.1 Pathophysiology of COPD

Several pathophysiologies mechanism can cause airflow limitation: (1) contraction of airway smooth muscle lead to airway narrowing and airflow obstruction, (2) inflammation, edema and peribronchiola fibrosis can cause airway narrowing, (3) destruction of alveolar walls and loss of elastic recoil result in reduction of driving and intraluminal pressure and (4) airway occlusion may caused by secretion. The mechanism may not affect to fixed airway obstruction, secretion generally has a substantial role in acute exacerbation of both asthma and chronic bronchitis (58).

2.6.2 Diagnosis of COPD

Most COPD patients are smokers. The main diagnosis components of COPD are emphysema, chronic bronchitis and asthmatic bronchitis. Sign and symptoms of three major diseases can overlap. A diagnosis of COPD is proposed by history and physical examination and confirmed by spirometry. Spirometry is the most common lung function test because it is simple and inexpensive test to perform. This instrument is an instrument that can include both quiet and forced vital capacity maneuvers. Forced spirometry used to quantify obstruction. Three spirometric measures in the forced test are force vital capacity (FVC), force vital capacity in one second (FEV_1) and ratio of FEV_1 and FVC (59).

CHAPTER 3
MATERIALS AND METHODS

3.1 Subjects

COPD patients were recruited from outpatient clinic of Suratthani hospital. The patients in this study were diagnosed to have COPD by a pulmonary medicine according to the following features: 1) ratio of forced expiratory volume in one second to force vital capacity (FEV_1/FVC) less than 70%, 2) having dyspnea during daily activity but in stable conditions.

3.1.1 Inclusion criteria

COPD patients were included in this study if they: -

- are free from symptoms of respiratory exacerbation for at least 1 weeks
- are on optimal bronchodilator therapy and clinically stable defined as no change in medical dosage or frequency of administration.
- have ability to self-ambulate.
- are_able to understand verbal instruction/ willingness to undergo testing and intervention procedure

3.1.2 Exclusion criteria

COPD patients were excluded from this study if they have: -

1. one of these diseases that would interfere exercise performance:
    - Unstable chronic obstructive pulmonary disease
    - Cardiac disease
    - Uncontrolled hypertension
    - Uncontrolled diabetic
    - Cor pulmonale
2. verbal, hearing or neurological system deficits
3. musculoskeletal problem, which limits walking ability.

3.2 Design of the study

This study was a randomized controlled clinical trial.

3.3 Instrumentation

3.3.1 Micro mouth pressure meter (Micro MPM)

The Micro Medical Mouth Pressure Meter (Micro Medical Limited, UK) is a handheld device for assessment of maximum respiratory pressure, which provide digital display of both maximum inspiratory and expiratory pressure strength in unit of cmH_2O. The strength of the inspiratory and expiratory is, therefore, isometric strength. The calibration of mouth pressure meter is factory set and remains stable indefinitely. The operation pressure is 0 ± 300 cmH_2O with ± 3% accuracy. The mouth pressure meter is supplied by 9 V PP3 battery.

Figure 3.1 Mouth pressure meters (Micro MPM)

3.3.2 Water manometer.

This apparatus was specially developed for respiratory muscle training. It is a U-shaped made of two 150-cm glass tubes, connected the lower ends with a rigid flexible plastic tube. The tube is filled inside with red colored water. One end of tube is connected to a mouthpiece with have a small hole. There is a scale to indicate water pressure (cmH_2O) beside the tube. This local made water manometer is routinely calibrated every week.

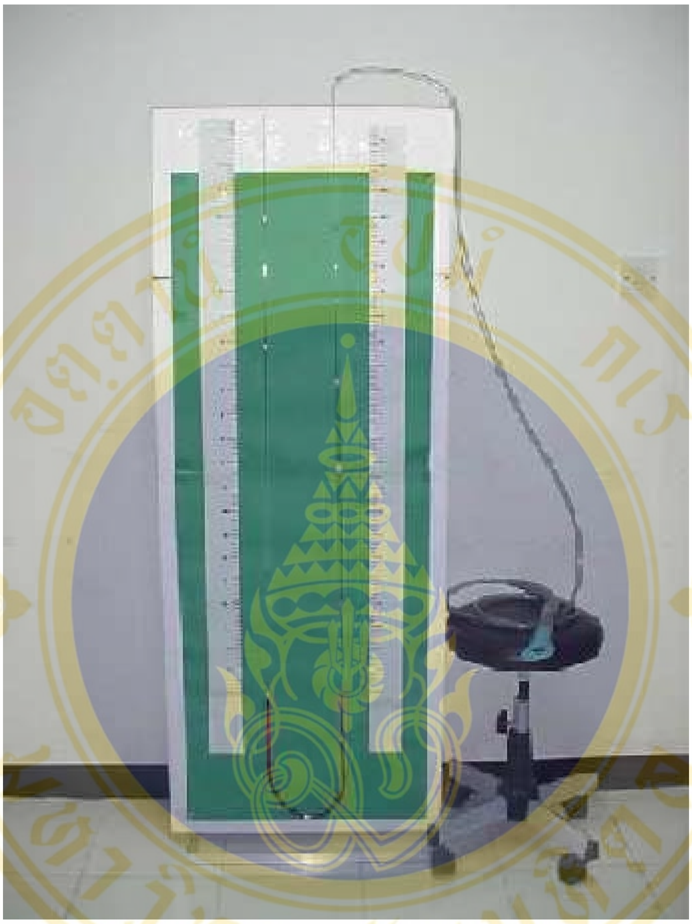

Figure 3.2 Water manometer for respiratory muscle training

3.3.3 Spirometer

In this study, force expiratory spirometry was performed. Force expiratory spirometry, including force vital capacity (FVC) and force expiratory volume in one second (FEV_1), were measured with Spirometer (Spirotouch^R Spirometry system)(Burdick, INC., USA) in order to confirm the diagnosis of COPD. The spirometer was calibrated with 3-liter syringe. All volumes was presented as different body temperature, ambient pressure and saturated air with water vapor (BTPS).

Figure 3.3 Spirometer

3.3.4 Stethoscope

3.3.5 Mercurial sphygmomanometer.

3.3.6 Standard stop watch.

3.3.7 Measurement tape.

3.3.8 Data collecting forms

Initial data collection form.

Initial data collection form was used for recording medical treatment, pulmonary function, risk factor, and patient history baseline data in COPD patients (Appendix A).

Chronic respiratory questionnaire (CRQ)

Chronic respiratory questionnaire (CRQ), a disease specific questionnaire consists of 20 items. This questionnaire examines physical and emotional function and was proved to be reproducible, responsive and valid. The CRQ is divided into 4 dimensions: dyspnea, fatigue, emotional, and mastery. Dyspnea assessment include asking patients to quantify their dyspnea on five activities, which are frequently performed and are important in their day to day lives. There are four items relating to fatigue and energy level. Questions regarding emotional function include frustration, depression, anxiety, and fear and panic with dyspnea. Each item has 7 response options, where 7 is the best possible function and 1 is the worst. Response options are printed on different color cards. These cards are composed of blue, yellow, green, and gray. The response option will be used as guideline for patient to answer question (Appendix B).

Six-minute walk test form

This form is used for recording the distance in which the patient can walk for 6 min (6MWD). Walking distance is present in unit of meters by calculate number of round which subject can walk. In addition, Heart rate (HR), Respiratory Rate (RR), and Rate of Perceived Dyspnea (RPD) are recorded at rest and immediately after walking cessation (Appendix A).

3.4 Procedure

Firstly, subjects were diagnosed by the physician and selected by the investigator from outpatient clinic according to their inclusion and exclusion criteria of this study. Then, patients who met the inclusion criteria were randomly assigned to respiratory muscle training group (exercise) and control group by the investigator prior to the study began.

Secondly, the investigator explained the purpose, principle and method of respiratory muscle training in the exercise group. Subjects in the control group were asked to participate in the study. After that, the patients signed an inform consent (Appendix C), complete initial evaluation form, and pulmonary function test were performed.

Thirdly, maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), distance walking in 6 min and patient's quality of life by CRQ questionnaire were separately evaluated.

Fourthly, exercise program for respiratory muscle training, education and breathing exercise were prescribed to the exercise group. On the contrary, the control group was received only education and breathing exercise.

Finally, reassessment of the MIP, MEP were performed on a weekly basis, the functional capacity by six minutes walk test and interviews patient's quality of life with CRQ questionnaire were performed post RMT

Evaluation of pulmonary function

Determinations of forced expiratory spirometry including force vital capacity (FVC) and force expiratory volume in one second (FEV_1) were achieved using a spirometer. According to standard procedures of American Thoracic Society (60), each spirometric parameters was performed 3 times and accepted when the variations between trials fall less than +/- 5%.

Evaluation of respiratory muscle strength.

MIP and MEP were evaluated separately by pressure dynamometer model Micro MPM every week for 6 weeks. The patients, with a nose clip, were instructed to place the mouthpiece of Micro MPM into the mouth. It was ensured that the mouthpiece was located over the gum, and the bite blocks were kept between the teeth. To generate maximum inspiratory pressure (MIP), the patient exhaled to residual volume (RV) and make the most powerful inspiratory effort via a mouthpiece. Similar procedure was repeated to obtain an expiratory pressure, except that the patient inhales maximally approaching total lung capacity (TLC) then exhales with his maximum effort. Both efforts should be sustained for 2-3 seconds. At least one-minute rest was permitted between maximum effort. Each test was performed 3 times and the best score was selected. In training group, measurement was performed once a week for adjustment of training load with increasing MIP and MEP. Patients in control group were evaluated every week.

Figure 3.4 Evaluation of respiratory muscle strength

Evaluation of 6 minute walk test.

Six-minute walk test was administered at pre and post training program. This test was performed along a 12 meter hospital hallway, where 2 chairs were placed at both end. Patients had to walk at their own pace in the period of 6 minutes. The patients were instructed to walk from end to end as far as they could in 6 minutes and allowed slowing down or stopping as necessary whenever they felt uncomfortable. In addition, they were suggested to avoid talk unless they had unusual symptom during the 6 min period. Heart rate (HR), respiratory rate (RR), and rate of perceived dyspnea (RPD) were recorded at rest and immediately after the walking test.

Evaluation of quality of life

All patients received the response color cards. The investigator read the definition of each scale of all cards. After that, the investigator gave interview to the patient according to each item of CRQ questionnaire, while the patients answered by response option scales. Finally, score for each of dimension were added together. Total time was about twenty minutes.

Intervention

Respiratory muscle training (RMT)

Patients in training group received RMT. Inspiratory and expiratory strength training were performed using a respiratory training device 3 times a week for 6 weeks. For strength training, patients performed static inspiratory effort for generating pressure equal to 30% of their MIP and MEP, 5 session a day for 1 wk. The target pressure was progressing adjusted, 5% each week, to reach 55% of their MIP and MEP at week six. Thus, the new MIP and MEP were achieved on weekly basis.

Intervention for control group included education and 10 times, 5 sessions/day breathing exercise. Breathing exercise included both diaphragmatic and pursed-lip breathing exercise. Time course of training was 3 days/week for 6 weeks.

Figure 3.5 Respiratory muscle training with water manometer.

Subject selection

↓

Subjects are randomly allocated to control or training group

Control group
Assessed MIP, MEP, functional capacity and quality of life pre-training

↓

Breathing exercise + education

↓

Assessed MIP and MEP 1time/wk

↓

Assessed MIP, MEP, 6MWD and quality of life after 6 wk of study period

↓

Data analysis

Exercise group
Assessed MIP, MEP, functional capacity and quality of life pre-training

↓

Training at 30 % MIP and MEP + Breathing exercise + education

↓

Assessed MIP and MEP 1 time/wk

↓

New resistance was adjusted every week and increased 5% /wk
Assessed MIP, MEP, 6MWD and quality of life after 6wk of training

↓

Data analysis

3.5 Statistical analysis

Results are reported in average and standard deviation. The level of statistical significant is set at 0.05 for all analyses. The statistical analyzed of the data will be performed by SPSS/PC Window release 9.0

1. Kolmogorov-Smirnov Goodness of Fit-test was performed to determine the normal distribution of the data.
2. Two- ways ANOVA mixed design was used to test the compare MIP and MEP values among pre and during 6 weeks of training within and between control and exercise group. Tukey's test with Bonferroni adjustment was used for post hoc analysis.
3. Unpaired t-test will be performed where necessary to determine the difference in the value of MIP, MEP and walking distance between control and exercise group.
4. Friedman test was used to investigate the statistical significance of quality of life scores within group.
5. Mann- Whitney U test was used to evaluate the significant difference of quality of life scores between the two groups

CHAPTER 4
RESULTS

The aim of this study was to investigate the effect of respiratory muscle training on respiratory muscle function, functional capacity and quality of life in patients with COPD. Eighteen Thai male COPD patients participated in this study in which ten of them were trained with a respiratory pressure device three times a week for six weeks. The rest was served as control. Respiratory muscle strength was measured on a weekly basis. Distance walk in 6 minutes and quality of life scores were obtained at pre- and after-six week training.

4.1 Characteristics of Subjects

Eighteen male subjects were recruited in order to avoid any differences caused by gender. Mean values and standard deviations of age, weight, height and physiological data of subject groups are presented in Table 4.1. Both groups were similar in age, weight, height and physiological data with no significant differences between groups (p>0.05). Thus, two groups were matched with all basic variables.

Table 4.1 Anthropometric and Physiologic data of control and exercise groups

Variables	Control group (n=8)	Exercise group (n=10)	*p*-value[a]
Age(year)	67.63±6.95	68.70±6.83	0.746
Weight (kg)	56.13±7.85	51.20±8.75	0.233
Height (cm)	160±5.86	163.4±7.21	0.297
FVC	2.49±0.51	2.89±0.54	0.128
$FEV_{1.0}$	1.07±0.38	1.21±0.33	0.425
$\%FEV_{1.0}$	43.87±17.14	41.60±7.69	0.711
$\%FEV_{1.0}/FVC$	50.22±11.27	54.5±8.70	0.377
MIP (cmH_2O)	81.50±17.75	79.3±14.08	0.773
MEP (cmH_2O)	97.88±42.19	71.10±15.92	0.081

a; *p*-value from unpaired t-test

4.2 Effect of Training on Respiratory Muscle Strength.

The initial values of maximal inspiratory pressure (MIP) in control and exercise group were 81.50±17.75 and 79.30±14.08cmH_2Orespectively, there was no significant difference between the two groups (Table 4.1). Whereas maximal expiratory pressure (MEP) of control and exercise group were 97.88±42.19 and 71.10±15.92 cmH_2O, which were not significantly different. After six-week training, the values of MIP and MEP in exercise group were statistically different from pre-training period.

4.2.1 Comparison of MIP at pre, 3rd week, and 6th week within group

There was no significant difference of MIP at pre, Wk3 and Wk6 in exercise group and control group comparing to their corresponding pre training values (p>0.05)(Table 4.2).

Table 4.2 Comparison of absolute values of MEP between control and exercise groups in pre-training and during 6 weeks training period.

Maximum inspiratory pressure (cmH_2O)				
Week	**Control group(n=8)**	**Exercise group(n=10)**	**F**	***p-value***[b]
PRE	81.50±17.75	79.30±14.08	0.086	0.773
Wk1	77.38±16.61	86.70±10.47	2.119	0.165
Wk2	81.50±19.23	88.20±15.57	0.669	0.425
Wk3	77.13±13.87	90.30±13.71	4.062	0.061
Wk4	79.88±14.27	95.60±11.21	6.881	0.018*
Wk5	82.37±14.73	94.00±11.68	3.500	0.080
Wk6	83.75±16.25	96.40±13.28	3.312	0.088
F	1.478	2.701		
p-value[b]	0.271	0.073		

b; Two way ANOVA mixed design *statistically different at $p<0.05$

4.2.2 Comparison of MIP between two Groups.

Comparison to the pre-training baseline values, the values of MIP during training week1 to week 6 were calculated as a percent differences (relative values). The present study found that the relative value of MIP of the exercise group was increased by 23.90% whereas the control group increased by 3.94%. There was a significant difference of MIP in exercise group when compared to the control group throughout the entire period of training except at week 2 (Table 4.3). At 3rd week of training, MIP in exercise group increased by 15 percent and at 6th week, it was elevated by 23.9 percent, from 79.30± 14.08 on pre training to, 90.03±13.71 and 96.40±13.60 cm H_2O, respectively.

Table 4.3 Comparison of relative value (% from initial) of MIP between control and exercise groups in pre-training and during 6 week training period.

Maximum inspiratory pressure (% from initial)				
Week	**Control group(n=8)**	**Exercise group(n=10)**	**F**	***p-value*** [b]
	X ±SD	**X ±SD**		
Pre	100	100		
Wk1	95.51±10.07	111.20±16.93	5.314	0.035*
Wk2	100.32±11.40	112.07±15.63	3.157	0.095
Wk3	95.69±7.98	115.84±21.69	6.168	0.024*
Wk4	99.52±14.03	122.47±16.93	9.464	0.007*
Wk5	102.17±10.38	120.65±19.52	5.800	0.028*
Wk6	103.94±11.91	123.90±22.31	5.174	0.037*
F	1.462	2.994		
p-value [b]	0.277	0.055		

b; Two way ANOVA mixed design *statistically different at $p<0.05$

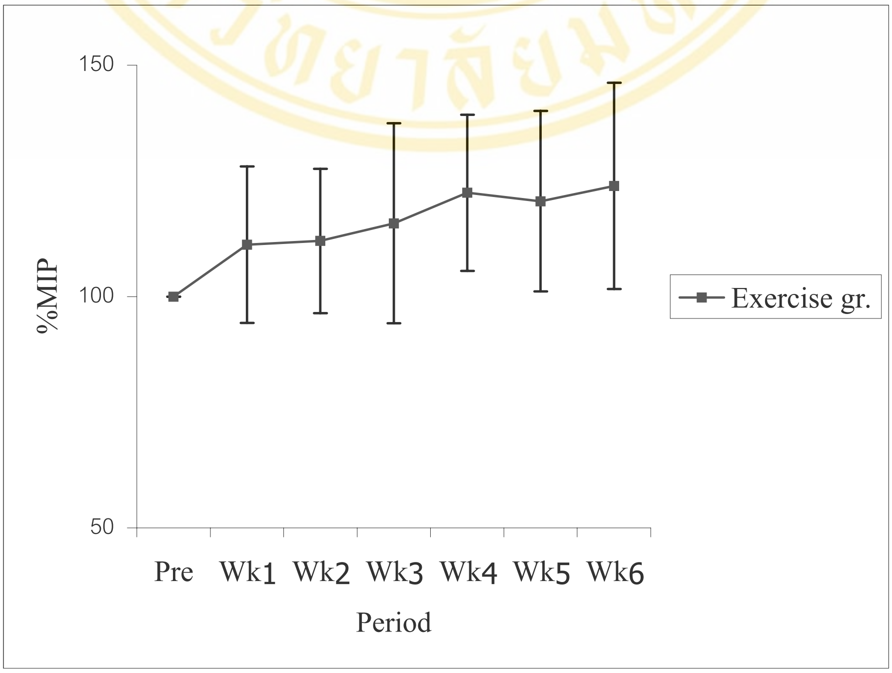

Figure 4.1 Percent of change of MIP in exercise group during 6week of training

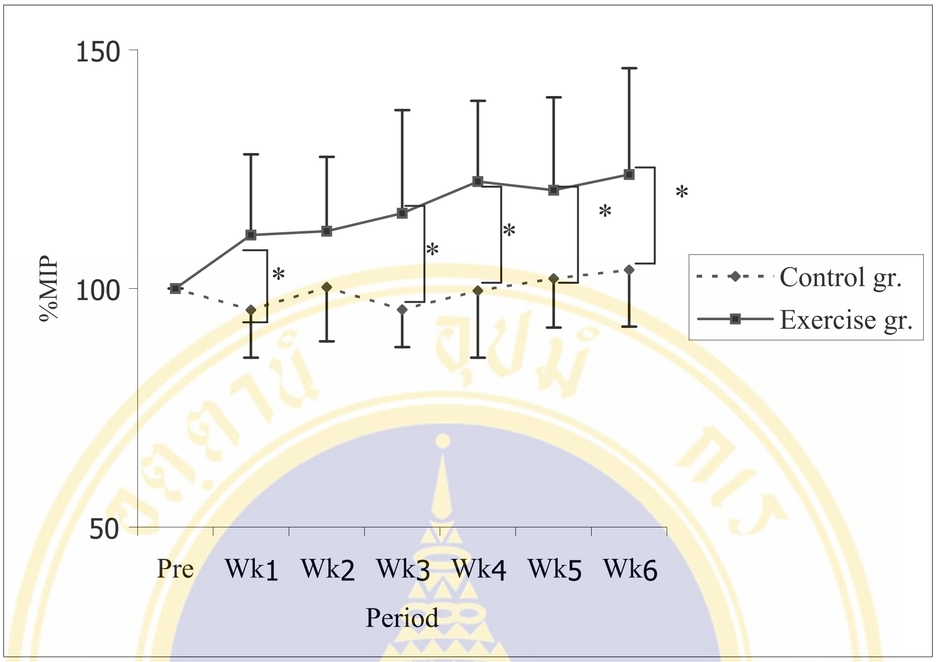

Figure 4.2 Comparison of % MIP between control and exercise group during 6 weeks of training

4.2.3 Comparison of MEP at pre, 3rd week and 6th week within group

Within the group comparison of MEP in exercise group, there was a significant difference between pre training, 3rd week and 6th week (p< 0.001)_whereas, maximal expiratory pressure of the control group was no significant difference between pre-training, 3rd week and 6th week (p>0.05).

Table 4.4 Comparison of absolute value of MEP between control and exercise groups in pre-training and during 6 week training period.

Maximum expiratory pressure (cmH_2O)				
Week	Control group(n=8)	Exercise group(n=10)	F	*p-value*
	X ±SD	X ±SD		
PRE	97.88±42.19	71.10±15.92	3.458	0.081
Wk1	90.63±41.51	89.90±30.27	0.002	0.966
Wk2	89.00±43.80	88.10±31.58	0.003	0.960
Wk3	94.38±53.66	87.80±29.41	0.113	0.741
Wk4	84.50±42.98	95.90±28.31	0.459	0.508
Wk5	94.13±42.83	99.10±34.12	0.075	0.787
Wk6	90.25±34.13	112.20±35.23	1.773	0.202
F	1.290	5.717		
p-value	0.338	0.006*		

Table4.5 Multiple comparison of absolute mean difference of MEP on pre training and post training week 1-6 within the exercise group

Periods	Pre	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6
Pre							
Wk1	0.001*						
Wk2	0.005*	0.618					
Wk3	0.012	0.663	0.906				
Wk4	<0.001*	0.316	0.161	0.185			
Wk5	0.001*	0.131	0.052	0.088	0.560		
Wk6	<0.001*	0.003*	<0.001*	0.004*	0.009	0.014	

* = Significant difference from Tukey's Post Hoc test with Bonferroni adjustment statistical significant level of 0.008

4.2.4 Comparison of MEP between Two Groups

Similar to MIP, the values of MEP during training week1 to week 6 were calculated as percent difference (relative values) and compared to the pre-training. The present study demonstrates a significant increase in MEP after 6 weeks of expiratory muscle training when mean MEP was 29.49% above the initial values in exercise group. In contrast, decrease in MEP was 5.32% below the initial value in the control group (Table 4.6).

Table 4.6 Comparison of relative value (% from initial) of MEP between control and exercise groups in pre-training and during 6 week training period.

Maximum expiratory pressure (% from initial)				
Week	**Control group(n=8)**	**Exercise group(n=10)**	**F**	***p-value*** [b]
	X ±SD	**X ±SD**		
Pre	100	100		
Wk1	92.45±6.70	110.14±25.2	11.370	0.004*
Wk2	89.97±8.33	107.37±28.09	7.686	0.014*
Wk3	93.25±13.83	109.25±25.59	7.901	0.013*
Wk4	85.95±18.38	112.60±31.61	24.215	<0.001*
Wk5	94.04±15.96	118.00±32.58	13.527	0.002*
Wk6	94.68±14.89	129.49±41.91	22.479	<0.001*
F	0.766	7.745		
p-value [b]	0.612	0.002*		

b; Two way ANOVA mixed design *statistically different at $p<0.05$

Table 4.7 Multiple comparison of the mean difference of relative MEP on pre training and post training week 1-6 within the group

Periods	Pre	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6
Pre							
Wk1	0.001*						
Wk2	0.012	0.530					
Wk3	0.005*	0.694	0.844				
Wk4	<0.001*	0.250	0.132	0.125			
Wk5	<0.001*	0.067	0.018	0.041	0.675		
Wk6	<0.001*	0.001*	<0.001*	0.001*	0.005*	0.003*	

* = Significant difference from Tukey's Post Hoc test with Bonferroni adjustment statistical significant level of 0.008

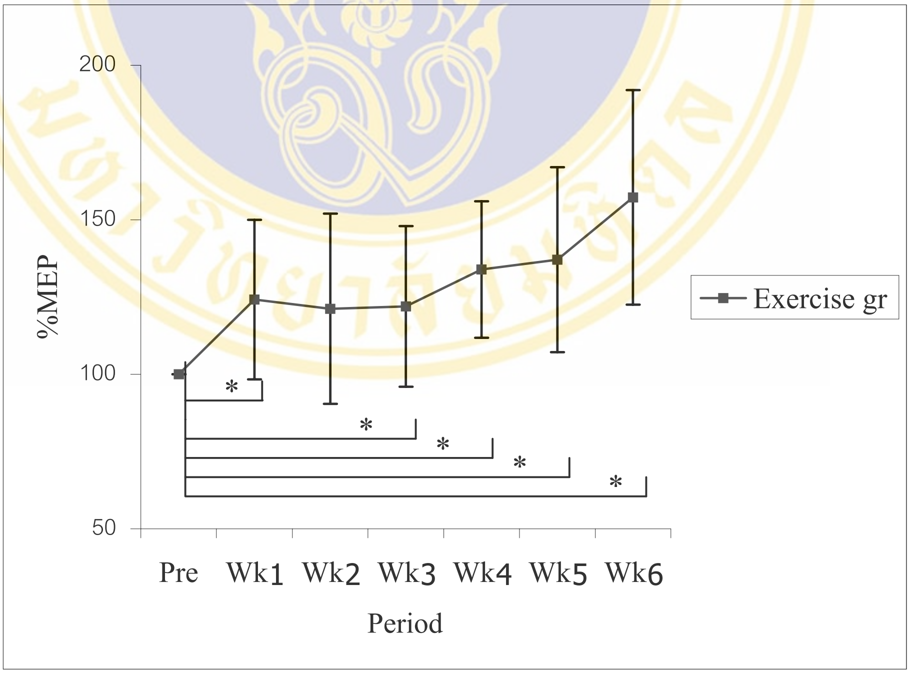

Figure 4.3 Percent of change of MEP in exercise group during 6 week of training

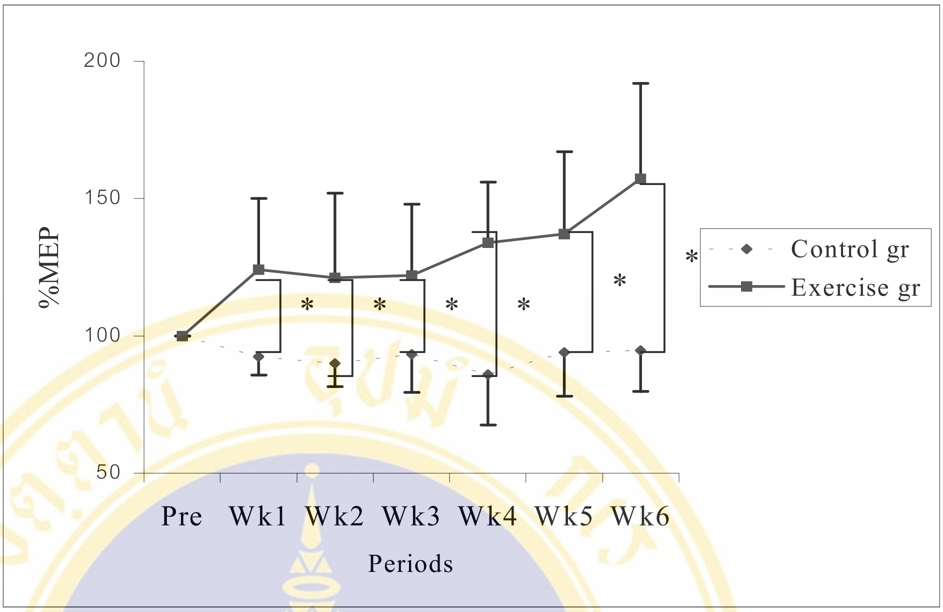

Figure 4.4 Comparison of % MEP between control and exercise group during 6 week of training

4.3 Effect of training on functional exercise capacity

4.3.1 Comparison of walking distance in 6 minute between pre and post training

The six minute walking distance of the exercise group increase significantly at 6 weeks of training compared with baseline value ($p<0.05$), while no changes were seen in the control group. Table 4.8 shows the mean distance walking in six minutes of both groups, at pre and at the end of week 6

Table 4.8 Comparison of 6 MWD within group.

Variable	Control group		*p-value*	Exercise group		*p-value*
	Pre	Week 6		Pre	Week 6	
6MWD (meter)	357.00±51.61	358.50±50.68	0.732	368.40±81.00	415.20±82.98	0.001*

* Significantly different by paired t- test ($P<0.05$)

4.3.2 The comparison of distance walked in 6 minute between control and exercise group.

The baseline 6 MWD was similar in both groups. In the exercise group, a significant increment in the 6 MWD was observed after 6 weeks of training (368.40±81.00 to 415.20±82.98 m)($p<0.05$), with no significant change in the control group.

Table 4.9 Comparison of 6MWD between control and exercise group

Variable	Pre		*p-value*[a]	Week6		*p-value*[a]
	Control	Exercise		Control	Exercise	
6MWD (meter)	357.00±51.61	368.40±81.00	0.735	358.50±50.68	415.20±82.98	0.110

a; p-value from unpaired t-test

The relative value of 6MWD of the exercise group was increased by 13% whereas the control group increased by 0.5%. There was a significant difference of 6MWD in exercise group when compared to the control group (Table 4.10).

Table 4.10 Comparison of relative value (% from initial) of 6 MWD between control and exercise group.

Variable	Control group	Exercise group	*p-value*
6 MWD	100.53±3.44	113.41±8.58	0.001*

* Significantly different by unpaired t- test ($P<0.05$)

4.4 Effect of training on quality of life

4.4.1 Comparison of the quality of life scores between pre and post training.

The baseline data showed no significant difference between the two groups in the scores of the category of dyspnea, emotion, fatigue and mastery (Table 4.11). Only exercise group had significantly higher score for dyspnea, fatigue and mastery. For each category, the treatment effect was greater in the category dyspnea, fatigue and emotional at post training compare with baseline values.

Table 4.11 Comparison of median and quartile (Q_1 and Q_3) of quality of life scores between pre and week 6 of training within group.

Dimension	Control group		*p-value*	Exercise group		*p-value*
	Pre	**Week 6**		**Pre**	**Week 6**	
Dyspnea	20 (16.5,21)	16.5 (16,21)	0.257	17 (13.7,18.7)	23.5 (17,31.2)	0.011*
Emotion	44 (32.2,45.7)	41.5 (38,46)	0.705	38 (33.7,45.7)	47 (36.7,49)	0.020*
Fatigue	19 (15.5,22)	20 (17.7,22.5)	0.157	16 (14.2,23)	25.5 (19.2,27)	0.034*
Mastery	19 (14.2,21.5)	18.5 (17.2,21)	0.480	18 (16,22)	22.5 (20.7,24.2)	0.096
Total	101 (85,107)	99.5 (96.2,103.7)	1.000	91.5 (83.5,105)	115 (100.7,131.2)	0.011*

* Significant different by Friedman ($p<0.05$)

4.4.2 The comparison of the quality of life scores between control and exercise group.

Both groups had similar baseline quality of life scores in each dimension. After 6 weeks of training, the quality of life scores was 115(100.7,131.2) points in exercise group and 99.5(96.2,103.7) points in control group. The differences in the quality of life sum scores between control and exercise were significant difference after 6 weeks of training ($p<0.05$). The median and quartile values of quality of life score in control and exercise group are shown in Table 4.12. For each dimension, the treatment effect was greater in dyspnea and mastery dimension in the exercise group than the control. The quality of life score at week 6 is shown in figure 4.5 in term of median values for both groups.

Table 4.12 Comparison of median and quartile (Q1 andQ3) of quality of life score between control and exercise group

Dimension	Pre		p-value	Week 6		p-value
	Control	Exercise		Control	Exercise	
Dyspnea	20 (16.5,21)	17 (13.7,18.7)	0.146	16.5 (16,21)	23.5 (17,31.2)	0.034*
Emotion	44 (32.2,45.7)	38 (33.7,45.7)	0.696	41.5 (38,46)	47 (36.7,49)	0.237
Fatigue	19 (15.5,22)	16 (14.2,23)	0.696	20 (17.7,22.5)	25.5 (19.2,27)	0.122
Mastery	19 (14.2,21.5)	18 (16,22)	0.829	18.5 (17.2,21)	22.5 (20.7,24.2)	0.027*
Total	101 (85,107)	91.5(83.5,105)	0.034*	99.5(96.2,103.7)	115(100.7,131.2)	0.033*

* Significantly different by Mann- Whitney U test (P<0.05)

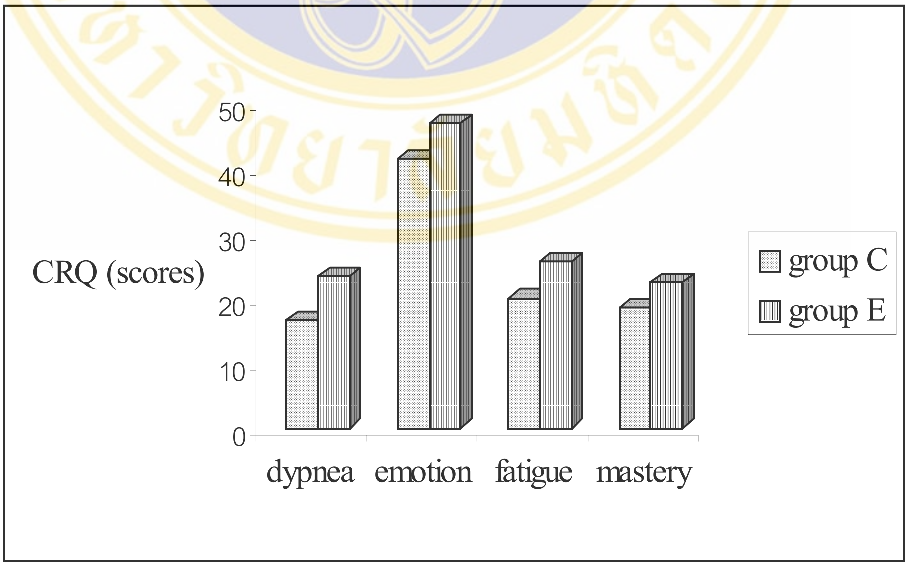

Figure 4.5 Comparison of median value of quality of life score at week 6 of between control and exercise group

CHAPTER 5
DISCUSSION

5.1 Characteristics of Subjects

The control and exercise groups of COPD patients showed the similarities in age, weight, height and lung function values. This is because the study was designed to match between the subjects in each group. In addition, all subjects were patients with COPD recruited from only one place; out- patients clinic of Suratthani Hospital. Even the numbers of subjects are small because of 1) lacking of subjects according to the strict criteria 2) two persons from control group were dropping out of the program from the long term study (6 weeks), the results are still valuable. As the fact that males are the majority of COPD in Thai population and there are effects of gender on COPD, this study recruited only male subjects (61).

The values of maximal inspiratory pressure (MIP) of control and exercise groups at the pre-training period are 81.50±17.75 and 79.30±14.08 cmH_2O, and maximal expiratory pressure (MEP) are 97.88±42.19 and 71.10±15.92 cmH_2O. These values are less than those of previously published data in normal subjects with the same age range. Mcelvaney et al (29) studied maximum respiratory pressure (MRP) in the population of persons older than 70 yr of age and reported mean MRP of 98/163 cmH_20 (MIP/MEP). Black and Hyatt (22) also reported mean values for healthy elderly men which were 83/175 cmH_2O. For the data from Asian subjects, Chen and Kuo(26) reported mean values of MRP in Chinese volunteers which were 83/117cmH_2O. These above results and the finding from the present study confirmed that COPD patients have lower both MIP and MEP than healthy subjects. In other words, COPD has effects on both inspiratory and expiratory muscle strengths. In addition, Rochester and coworkers (10) determined the value of MIP and MEP in 32 patients with COPD. This study showed that the MIP average was 56±25 cmH_2O whereas MEP average was 137±48 cmH_20. It can be seen that the MIP and MEP in patients with COPD are lower than normal subjects. As chronic airflow limitation in patients with COPD can result in impaired respiratory muscle function because of increased work of breathing due to change in the lungs, and inefficiency of the inspiratory muscle because of hyperinflation.

5.2 Effects of respiratory muscle training on respiratory muscle strength.

It is well established that respiratory muscles exhibit similar adaptation to training as other skeletal muscles, provided that the training follows the basic training principles for any striated muscle, with regard to intensity, duration of training and the specificity of the training (35). Specificity means that the response of the trained muscle is specific to some operating characteristics of the muscle. Inspiratory resistance training does not always increase in respiratory muscle strength. From previous studies (9,9,63), it was shown that most patients breathing against inspiratory resistance trainers failed to improve respiratory muscle performance after training. However, these studies used inspiratory resistive devices, which the resistance is nonlinear. The nonlinear resistance can lead to inconsistent intensity for training. Furthermore, the failure to show the improvement of respiratory muscle performance may be related to inadequate intensity and period of training.

Training protocol used in this present study is modified from previous investigations where a close relationship between training intensity and percent improvement of respiratory muscle strength is clearly demonstrated. The low load training (30% of MIP) in study by Suzuki and associated (44) and Lisboa and colleagues (10) resulted in 35 and 34% increase in MIP, respectively. In this present study, the training program consisted of exercise 3 times a week for 6 weeks. Subjects performed 10 static inspiratory and expiratory maneuvers with water manometer at resistance equal to 30% of MIP at initial and increase 5% every week until 55% of MIP at the 6th week. The percentage of the increment in the inspiratory muscle strength after training in this present study was close to the report by Larson and coworker (63) (25% vs 23.9% MIP from this study).

This present study demonstrated a simple technique or water manometer for improving the strength of the expiratory muscles The advantages of this water manometer technique are that it can be used for training both inspiratory and expiratory muscle strength. Strength as measured by MEP was increased by 30 percents in the exercise group. Most of previous studies have been emphasized on the effect of inspiratory muscle training on inspiratory muscle strength. There is a few evidence of effects of expiratory muscle training in COPD patients. The study by Weiner et al. (64) showed the 21% improvement of MEP after 3 months of specific expiratory muscle training in COPD patients. Compared to the study of Weiner and coworkers, this present study showed higher improvement in expiratory muscle strength (29.4%)

It was surprising that this study could not identify strong difference in absolute values of MIP and MEP at the 6th week in between groups. It is feasible that the duration of training, 15 min a day 3 days per weeks for 6 weeks, may not be insufficient to discriminate between exercise and control group. Conversely, it is possible that the inspiratory muscles require only a modest conditioning stimulus to receive a significant training effect. Alternatively, the lack of distinction between results of two groups may reflect inherent difference between groups. For example, (1) Subjects in exercise group tented to be more debilitated than the control group as evident by the fact that 20 percent of subjects in exercise group were steroid dependent compare with 12.5 percent in the control. (2) The incidence of infection differed between groups; two subjects in exercise group (20 percent) had two infections whereas five subjects in the control (62.5 percent) had at least one infection over the training period (total of 6 infectious episodes). This implies that the exercise group was weaker than the control group at the beginning of the study. As shown in the result (Table 4.2, 4.4), the absolute values of MIP and MEP of the exercise group were lower than the control group; however, these differences were not statistically significant. Even there are significant effects of training on MIP and MEP shown by percent increment (Table 4.3, 4.6) but the fact that the absolute values of MIP and MEP of the exercise group were lower at the beginning of the study influence the absolute values of MIP and MEP at the week 6. Therefore, no differences of absolute values of MIP and MEP were shown at the end of the study.

5.3 Effects of respiratory muscle training on functional exercise capacity.

It has been shown several times that IMT has a beneficial effect on exercise performance in COPD patients. Depending on which tests were used to evaluate performance, improvements could be demonstrated in maximal exercise ventilation and oxygen uptake measured by an incremental cycle ergometer (65,66), in the endurance time whilst cycling at a constant submaximal work load (65,66), and in the 6 or12 min walking distance (9,67).

The improvement in exercise tolerance following specific inspiratory muscle training (SIMT) is still controversial. Belman and Mittmen (66) were the first to use inspiratory muscle training as a therapeutic modality in adult patients with COPD. They noted patients with COPD were able to increase their respiratory muscle endurance and this increase was associated with improvement of both clinical and laboratory exercise tests. However, they did not have a control group. Chen et al. in 1985 (8) found that although inspiratory muscle endurance of patients with COPD were improved after IMT for 4 weeks, their exercise performances were unchanged. Flynn and colleagues in 1989(68) found that IMT improved inspiratory muscle performance, but these improvements did not translate into improvement in exercise performance.

The 6 minute walk test is a commonly used test of general functional ability. In present study, the exercise group showed significant increased in distance walking. Although, there was no statistically difference in the effects of IMT on the means difference in 6 MWD between the two groups. However, the increase of 13.4 percent in exercise group may be a clinically relevant distance. The results in present study are agreed with those reports by Lisboa et al in 1997(7). After 10 week of training, they observed a significant improvement in 6 minute walked distance (6MWD). In contrast, study by Guyatt et al.in1992 using inspiratory resistance device (PFLEX) to train for 10 minutes five time a day for 6 months, and found no significant improvement in respiratory muscle strength and 6MWD. It is possible that the successful in improving respiratory muscle strength would have led to the increase in exercise capacity (6MWD). Also, the present results are in agreement with those reported by Riera et al. in 2001(16), which employed a target flow IMT. After 6 months of training, they observed a significant improvement in inspiratory muscle performance and the distance walked in the shuttle-walking test (SWT). In other words, the effect of RMT in the present study on functional capacity (walking test) was significantly improved probably by the increase in respiratory muscle strength within 6 weeks

5.4 Effects of respiratory muscle training on quality of life.

This present study assessed quality of life by Chronic Respiratory Questionnaire (CRQ), which was shown to be valid and responsive. This questionnaire had previously demonstrated that the question related to the categories of fatigue, emotion and mastery are reproducible and valid for patients with severe COPD but the dyspnea category showed low and unreliable internal consistency (56). However, there are two studies have assessed the clinical consequences of IMT with a specific quality of life test for COPD patients. The first study (9) used a COPD specific measure quality of life (the CRQ) in the clinical assessment of IMT protocol but yield negative results because they did not found the improvement of the respiratory muscle strength. The other was a randomized study (16). They found that IMT lasted for 6 months, achieving clinically significant differences between the treatment and control group. Although this present study lasted shorter (6 week), it has shown statistical significance difference between the exercise and control group in regard to dyspnea and mastery.

This study shows that RMT using water manometer for 6 week, was sufficient to improved quality of life score. Exercise group showed improvement in their quality of life compared with the baseline. In addition, there was a significant greater quality of life score in exercise group compared with control group. Guyatt et al. (69) considered that an improvement of at least four points in the total quality of life score, consisting of four dimensions, is necessary to allow a patient subjective improvement in quality of life. Thus, in this study the mean overall increase at 6 weeks of twenty points from baseline in the quality of life scores, consisting of four dimensions, is clinically relevant. In contrast, control group did not show an increase of more than four points compared with baseline values. As a result, this present study showed that RMT under supervision lasted for 6 weeks improved quality of life, as assessed by a validated questionnaire.

Because respiratory muscle function limits exercise in COPD patients, it is conceivable that improved respiratory muscle training could improved overall exercise tolerance. The present results confirm this hypothesis. In exercise capacity, a 13.4% increase in the distance covered in the 6-min walk was seen. The improved function in these patients was a reflection of greater effort they could make as a result of the improved respiratory capacity. Wijkastra and coworker (70) have showed that maximal inspiratory pressure and Transfer factor for carbon monoxide (TLCO) are important variables in determining exercise capacity in patients with COPD with severe airways obstruction. The results suggest that the relation of six minute walking distance with of objective measurement – that is, TLCO and MIP.

Increase in respiratory sensation has been reported in respiratory muscle fatigue and weakness (44). In such studies, the relationship of the central motor command signal to respiratory muscle force may have been altered because the maximum strength of the inspiratory muscle was decreased, resulting in an increase in respiratory sensation. Thus this present study expected an improvement in inspiratory muscle strength to diminish respiratory sensation and infer that trained patients tolerated the walking exercise better since there were no change in dyspnea intensity for more substantial effort. There are two possibilities that could be responsible for this present results: 1) a decreased respiratory stimulus. Casaburi et al. (71) have recently demonstrated, in COPD patients, that exercise training diminishes lactic acid production during exercise, thus lowering the ventilatory drive. ; 2) an increase in the efficiency of the respiratory pump lead to the fall in $V'O_2$ during exercise after IMT. Couser et al. (72) have demonstrated in COPD patients that training the upper extremities reduces the metabolic cost and the ventilatory requirements of elevating the arms, a maneuver that also elicits dyspnea. The effects of IMT on exercise capacity found in the present study could be analogous to this situation. However, this present study did not measure lactic acid and $V'O_2$ during exercise test. Further investigations are needed in this issue.

Furthermore, Riera et al and Lisboa et al have shown that there was significant correlation between change in the MIP and the component of the transitional dyspnea index (TDI). This supports the concept that an increase in the strength of inspiratory muscle can ameliorate dyspnea. There is also the possibility that as dyspnea decreased as a result of IMT, the patients spontaneously increases his physical activity, leading to improved physical deconditioning. Consequently, patients were accustomed to inactivity, and when the sensation of dyspnea decreased they showed greater mobility, resuming activities that they abandoned and experiencing emotional improvement along with better control of their disease. The interaction between dyspnea and quality of life has been studied (73,74). A popular questionnaire, Chronic respiratory questionnaire, focuses on four dimensions of illness: dyspnea, fatigue, emontional and patient's feeling of control over the disease (mastery). The present study demonstrated improvement in quality of life measuring by this questionnaire. The results from present study can infer that improvement in respiratory muscle strength and dyspnea. These influence on the increase in physical and emotional status of patients.

In present study, respiratory muscle training performed by water manometer for 6 weeks. The water manometer is useful to control the depth of inspirations and to encourage the patient to perform them by means of visual feedback. Moreover, the water manometer is a simple material and is less expensive than a pressure threshold-training device.

5.5 Clinical implication and Further study

According to the recommendation of American Association for Cardiovascular and pulmonary rehabilitation committee (75), this present study included the following two basic outcome measures in evaluation of RMT in the COPD patient: functional capacity and quality of life. The results from present study indicate that RMT can be a useful part of pulmonary rehabilitation for COPD patients.

Further study is required to determine effects of respiratory muscle training with water manometer in the larger group of subjects with COPD and adapts this apparatus to train respiratory muscle endurance in COPD patients. In addition, the further study should adapt this technique for determining effect on respiratory muscle training on others parameter such as dyspnea scores and study in other kinds of patients for an example, neuromuscular patients.

CHAPTER 6
CONCLUSION

The present study demonstrated that respiratory muscle training exerts significant improvement of inspiratory and expiratory muscle strength simultaneously. After six week of training period, the values of maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) in exercise group were statistical different from pre training. The percent improvement was 23.9% and 29.4% in MIP and MEP, respectively. In addition, there was significantly different of weekly MEP in exercise group comparing to the previous week ($p<0.05$), which MEP in control group remain unchange.

In addition, six minute walking distance (6MWD) in exercise group exert significant improvement after week 6 of training, while 6MWD in control group was not statistically different from pre and post week 6 of training. The percent of improvement was 13.4% in 6MWD of exercise group. Moreover, the score of quality of life of exercise group was statistically different from pre training period, especially regard in dyspnea and mastery dimension.

Therefore, results from present study indicate that RMT can be a useful part of pulmonary rehabilitation for COPD patients. Because the results of present study show an improvement of respiratory muscle performance which lead to improve in functional exercise capacity and quality of life in patient with COPD. Furthermore, respiratory muscle training performed by water manometer in the present study is a simple material and is inexpensive and simple apparatus. Thus, this apparatus should be widely used for respiratory muscle training in pulmonary rehabilitation.

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APPENDIX

APPENDIX A

A.1 INITIAL EVALUATION FORM

Name……………………………………………HN………………………………

Age…………Sex…………Height……………...cm. Weight………………Kg.

Address…………………………………………….Tel…………………………..

Occupation……………………………………………………………………………..

1. General condition

   BP…………mmHg. HR………..b/min RR………b/min

2. Chest and pulmonary condition

   Chest wall □ Normal □ Deformity……………………………………..

   Breath sound

   Type □ wheezing □ rhonchi □ crepitation

   Phase □ inspire □ expire □ both

   Site □ generalized □ upper □ middle □lower

   Lung function test

	Pre-bronchodilator			Post-bronchodilator		
FVC						
FEV_1						
FEV_1/FVC						

3. Symptom

   □Y □N cough

   □Y □N sputum

   □Y □N wheeze onset/cause………………………………………

   □Y □N dyspnea onset/cause………………………………………

4. Dyspnea index

□ Class1: if SOB, consistent with activity

□ Class2: SOB climbing hill or stair

□ Class3: can walk at own pace but not at normal pace without SOB

□ Class4: SOB walking 100yrs on level ground, dressing, or talking

5. Medical dosage and frequency.

Oxygen Therapy. □Y □N

Oral medication…………………………………………………………………….

………………………………………………………………………………………

Aerosol therapy……………………………………………………………………….

…………………………………………………………………………………………

6. Smoking history

At present, do you quit or continue smoking?

□Quit date……………..because…………………………………………..

□Continue smoke……………………pack/day

How many packs have you had smoking?

□ 0.5 pack/day □1pack/day □1.5pack/day □>2pack/day

How old are you when began to smoke?……………….years

7. Laboratory test

pH……… PaO_2………mmHg $PaCO_2$………mmHg

SaO_2………..%

8. Medical history

□HT □DM □Cardiac disease □Orthopedic disease

A.2 SIX MINUTES WALK TEST EVALUATION FORM

Name……………………………………………………Group…………Date………..□

Pre-training □ Post-training

Measurement	Resting stage	Post test
Heart rate (beats/min)		
Respiratory rate(beats/min)		
Rating of perceive dyspnea		

NUMBER OF WALK CYCLE	1	2	3	4	5	6	7	8	9	10

1 Cycle = 12 meters

Total distance =…………………………………………………………

A.3 RESPIRATORY MUSCLE STRENTH EVALUATION FORM

Name……………………………………………Group……………..Date………………..

BASELINE DATA

	1st			2nd			Baseline
MIP							
MEP							

INTENSITY FOR STRENGTH TRAINING

Intensity	**1st WK 30%**	**2nd WK 35%**	**3rd WK 40%**	**4th WK 45%**	**5th WK 50%**	**6th WK 55%**
MIP						
MEP						

RESPIRATORY MUSCLE STRENGTH

	1st WK			**2nd WK**			**3rd WK**			**4th WK**			**5th WK**			**6th WK**		
MIP																		
MEP																		

APPENDIX B

B.1 The questionnaire of quality of life

แบบสอบถามคุณภาพชีวิต

แบบสอบถามนี้ใช้สำหรับประเมินคุณภาพชีวิตผู้ป่วยโรคปอดอุดกั้นเรื้อรัง คำถามที่คุณจะถูกถามเกี่ยวข้องกับปัญหาหรือความรู้สึกของผู้ป่วยโรคปอดอุดกั้นเรื้อรังทั้งสิ้น คุณจะถูกถามเกี่ยวกับอาการหายใจขัดหรือหอบเหนื่อย ความรู้สึกเหนื่อยหน่ายและภาวะของอารมณ์และจิตใจในช่วงเวลา 2 สัปดาห์ ที่ผ่านมานี้

ชื่อ...HN......................

A. โปรดบอกกิจกรรมที่คุณเคยทำในช่วง 2 สัปดาห์ที่ผ่านมาที่ทำให้คุณรู้สึกหายใจหอบเหนื่อย (ผู้วิจัยอ่านรายการกิจกรรมที่ทำให้ผู้ป่วยโรคปอดอุดกั้นเรื้อรังเกิดอาการหอบเหนื่อยที่ละข้ออย่างช้าๆ)

☐ขณะที่โกรธหรืออารมณ์เสีย ☐เคลื่อนย้ายเครื่องเรือน
☐กำลังอาบน้ำ ☐เล่นกับลูกหลาน
☐หิ้วหรือถือของ ☐เล่นกีฬา
☐แต่งตัว ☐เอื้อมหยิบของเหนือศรีษะ
☐รับประทานอาหาร ☐ขณะวิ่ง เช่น วิ่งขึ้นรถประจำทาง
☐ขณะเดิน ☐จับจ่ายซื้อของ
☐ขณะเร่งรีบ ☐ขณะพูดคุย
☐นอนราบ ☐เดินรอบๆบ้าน
☐เก็บที่นอน ทำที่นอน ☐เดินขึ้นเนินหรือที่ลาดชัน
☐ถูหรือขัดพื้น ☐เดินขึ้นบันได
☐ขณะนอนหลับ ☐เตรียมอาหารหรือทำกับข้าว
☐ขณะทำงานบ้าน ☐อื่นๆ..........................

B. ระบุกิจกรรมที่สำคัญและทำบ่อยในชีวิตประจำวันแล้วทำให้เกิดอาการหอบเหนื่อย 5 กิจกรรม คุณมีอาการหอบเหนื่อยมากหรือน้อยเพียงใดขณะทำกิจกรรมดังกล่าว(บัตรสีเขียว)

1. ………………………………………………………..☐
2. ………………………………………………………..☐
3. ………………………………………………………..☐
4. ………………………………………………………..☐
5. ………………………………………………………..☐

6. คุณรู้สึกเบื่อหน่าย โกรธ หมดหวัง บ่อยแค่ไหน (บัตรสีฟ้า) ☐

7. คุณรู้สึกหวาดกลัวบ่อยแค่ไหนเมื่อมีอาการหายใจลำบาก (บัตรสีฟ้า) ☐

8. คุณรู้สึกเหนื่อยล้าบ่อยแค่ไหน (บัตรสีฟ้า) ☐

9. บ่อยแค่ไหนที่คุณรู้สึกว่าอาการไอหรืออาการหอบเหนื่อยเป็นอุปสรรค(บัตรสีฟ้า) ☐

10. บ่อยแค่ไหนที่คุณรู้สึกมั่นใจว่าสามารถจัดการกับอาการป่วยของคุณได้ (บัตรสีเหลือง) ☐

11. คุณรู้สึกว่ามีพลังบ่อยแค่ไหน (บัตรสีเหลือง) ☐

12. บ่อยแค่ไหนที่คุณรู้สึกท้อแท้หรือหดหู่ (บัตรสีฟ้า) ☐

13. คุณรู้สึกว่าสามารถควบคุมอาการหอบเหนื่อยได้บ่อยแค่ไหน (บัตรสีเหลือง) ☐

14. บ่อยแค่ไหนที่คุณรู้สึกผ่อนคลายและไม่รู้สึกเครียด (บัตรสีเหลือง) ☐

15. บ่อยแค่ไหนที่คุณรู้สึกหมดเรี่ยวแรง (บัตรสีฟ้า) ☐

16. บ่อยแค่ไหนที่คุณรู้สึกท้อแท้หรือหมดกำลังใจ (บัตรสีฟ้า) ☐

17. คุณรู้สึกอ่อนเปลี้ย เพลียแรงบ่อยแค่ไหน (บัตรสีฟ้า) ☐

18. คุณมีความสุขหรือมีความพอใจมากหรือน้อยแค่ไหนเกี่ยวกับสุขภาพของคุณ (บัตรสีเทา) ☐

19. คุณรู้สึกท้อแท้หรือหวาดกลัวบ่อยแค่ไหนเมื่อมีอาการหอบเหนื่อย (บัตรสีฟ้า) ☐

20. คุณมีความรู้สึกเครียดเกร็งบ่อยแค่ไหน (บัตรสีฟ้า) ☐

B.2 The answer sheet of questionnaire part B

แนวทางเลือกเพื่อตอบแบบสอบถาม

บัตรสีฟ้า

1.	2.	3.	4.	5.	6.	7.
ตลอดเวลา	ส่วนใหญ่	บ่อยครั้ง	บางครั้ง	น้อยครั้ง	ไม่ค่อยมี	ไม่มี

บัตรสีเหลือง

1.	2.	3.	4.	5.	6.	7.
ไม่มี	น้อยครั้ง	บางครั้ง	ปานกลาง	ส่วนใหญ่	บ่อยมาก	ตลอดเวลา

บัตรสีเขียว

1.	2.	3.	4.	5.	6.	7.
หายใจหอบ ตลอดเวลา	หายใจหอบบ่อยครั้ง	หายใจหอบพอประมาณ	หายใจหอบ ปานกลาง	หายใจหอบ บางครั้ง	ไม่ค่อยมี หายใจหอบ	ไม่มี หายใจหอบ

บัตรสีเทา

1.	2.	3.	4.	5.	6.	7.
ไม่พอใจ, ไม่มีความสุข	ส่วนใหญ่ ไม่พอใจ,ไม่มี ความสุข	ไม่ค่อย พอใจ,ไม่มี ความสุข	โดยทั่วไป รู้สึกพอใจ	ส่วนใหญ่ รู้สึกสบาย	มี ความสุขมาก	มี ความสุข ตลอดเวลา

APPENDIX C

หนังสือแสดงเจตนายินยอมเข้าร่วมโครงการวิจัย

วันที่..........เดือน..................พ.ศ............

ข้าพเจ้า....................................อายุ..........ปี อาศัยอยู่บ้านเลขที่...........
ถนน............ตำบล.........อำเภอ.......................จังหวัด.....................โทรศัพท์............

ขอแสดงเจตนายินยอมเข้าร่วมโครงการวิจัยเรื่อง "ผลการฝึกกล้ามเนื้อหายใจต่อความสามารถในการออกกำลัง และคุณภาพชีวิตในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง" โดยข้าพเจ้าได้รับทราบเกี่ยวกับรายละเอียดของโครงการ ดังต่อไปนี้ การศึกษาในครั้งนี้มีวัตถุประสงค์เพื่อศึกษาผลของการฝึกความแข็งแรงของกล้ามเนื้อที่ใช้ในการหายใจ เพื่อใช้เป็นแนวทางในการฟื้นฟูสมรรถภาพปอดในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง และการศึกษาครั้งนี้ไม่ก่อให้เกิดความเสี่ยงหรืออันตรายใดๆ ต่อผู้เข้าร่วมการวิจัย รวมทั้งการตรวจประเมินความแข็งแรงของกล้ามเนื้อหายใจ การวัดความสามารถในการออกกำลัง และการประเมินคุณภาพชีวิต ได้เลือกวิธีการและแบบประเมินที่เหมาะสม ซึ่งได้รับการทดสอบและยอมรับโดยผู้เชี่ยวชาญแล้ว

หากผู้วิจัยมีข้อมูลเพิ่มเติมทั้งด้านประโยชน์และโทษที่เกี่ยวข้องกับการวิจัยนี้ ผู้วิจัยจะแจ้งให้ข้าพเจ้าทราบอย่างรวดเร็วโดยไม่ปิดบัง

ข้าพเจ้ามีสิทธิ์ที่จะของดการเข้าร่วมโครงการวิจัยโดยไม่ต้องแจ้งให้ทราบล่วงหน้า โดยการงดการเข้าร่วมการวิจัยนี้จะไม่มีผลกระทบต่อการได้รับบริการหรือการรักษาที่ข้าพเจ้าจะได้รับประการใด

ข้าพเจ้าได้รับทราบข้อมูลของโครงการข้างต้น และได้ซักถามผู้วิจัยจนหมดข้อสงสัยโดยตลอดแล้ว และข้าพเจ้ายินยอมที่จะเข้าร่วมในโครงการดังกล่าว โดยขอให้ผู้วิจัยงดการเปิดเผยชื่อ ประวัติ ตลอดจนข้อมูลที่เกี่ยวข้องกับข้าพเจ้า แก่ผู้อื่นได้รับทราบ

ลงชื่อ....................................ผู้เข้าร่วมวิจัย

( )

ลงชื่อ....................................หัวหน้าโครงการวิจัย

( )

ลงชื่อ....................................พยาน

( )

APPENDIX D

D.1 Validity test of measurement for record respiratory muscle strength value.

Because the measurement of respiratory muscle strength are no routinely measured by physical therapist in Thailand; then the researcher was needed to be validity of record the values.

Procedure:

1. The Micro MPM device was used for test.
2. Subject: 3 healthy subject who are naïve to these measurements
3. Tester: Tester 1 is chest physiotherapist who had experience of respiratory muscle strength measurement, Tester 2 is the present researcher.
4. Wilcoxon Matched-Paired Signed-Ranks Test was used to compare the values of maximal inspiratory pressure, maximal expiratory pressure between tester.

Table D.1 Comparison of MIP and MEP values between tester

No.	Maximal Inspiratory pressure (cmH_2O)		Maximal Expiratory Pressure (cmH_2O)	
	Tester1	Tester2	Tester1	Tester2
1	65	63	69	64
2	42	55	54	54
3	75	81	77	81
p-value	.285		.655	

D.2 Validity test of measurement for record lung volume values

Because the measurement of lung volume is no routinely, then the researcher was needed to be validity of record the values.

Procedure

1. Spirometer was used for test
2. Subjects: 3 healthy subjects who are naïve to this measurement

3. Tester: Tester1 is technician who had experience of lung volume measurement at least 3 years, Tester2 is the present researcher.
4. Wilcoxon Matched-Paired Signed-Ranks Test was used to compare the values of FVC and FEV_1 between tester.

Table D.2 Comparison of FVC and FEV_1 value between testers

No.	Force Expiratory Volume (FVC)(L)		Force expiratory volume in one second (FEV_1)(L)	
	Tester1	Tester2	Tester1	Tester2
1	2.97	2.92	2.64	2.56
2	3.23	3.25	2.66	2.69
3	2.79	2.74	2.51	2.48
P-value	.276		.414	

APPENDIX E
TEST-RETEST RELIABILITY

The test-retest reliability was determined for the maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), pulmonary function and quality of life questionnaire (CRQ). Ten patients with COPD were included in the reliability studies. The characteristics of all subjects are shown in table E.1. The data from tests were analyzed by SPSS for Window Release 9.0 Intraclass Correlation Coefficients (ICC 3,1) was used to determine the test- retest reliability for all parameters.

Test of respiratory muscle strength

The respiratory muscle strength test protocol was performed 3 trials on 2 occasions both MIP and MEP. The score of all trials were used for reliability calculation. The result demonstrated good reliability with the ICC (3,1) equal to .8963 for MIP and .9034 for MEP

Test of pulmonary function

The subject performed 2 trials of forced expiratory spirometry tests including force vital capacity (FVC) and force expiratory volume in one second (FEV1). The result showed good reliability in both parameters. The ICC (3,1) is showed in table E2.

Test of quality of life questionnaire (CRQ)

Investigator interviewed the subject on 2 occasions. The total score from 2 times were used for reliability calculation. The result demonstrated good reliability in with the ICC (3,1) equal to .9300

Table E.1 Characteristic of subjects for reliability testing

Subjects	Age(yr)	Weight(kg)	Height(cm)
1.	55	57	171
2.	73	60	176
3.	60	35	160
4.	69	60	173
5.	59	67	162

Table E.2 Intraclass correlation coefficients of the pressure generate by respiratory muscles, pulmonary function and quality of life.

Parameter	ICC (3,1)
MIP	.8963
MEP	.9034
FVC	.9964
FEV_1	.9963
CRQ	.9300

APPENDIX F
RESULT OF PILOT STUDY

This aim of this pilot study was to investigate the effect of respiratory muscle training on respiratory muscle function, exercise capacity and quality of life performed by inspiratory and expiratory muscles. Ten COPD patients participated in this pilot study. The characteristics are presented in Table F.1. Respiratory muscle function obtained from pre training and posts six weeks training. Six minute walk distances and quality of life obtained from before and after 6 week training. The mean and stand deviation of all parameters are showed in Table F.1-F.4

Table F.1 Mean and SD of maximum inspiratory pressure (MIP)

Variable	Control group		Exercise group	
	Mean	**SD**	**Mean**	**SD**
MIP pre	79.4	20.51	86.0	15.39
MIP 1	79.8	21.63	92.0	16.17
MIP 2	84.6	18.94	91.2	17.94
MIP 3	78.0	21.13	91.2	14.34
MIP 4	78.2	17.01	94.6	15.5
MIP 5	83.6	20.89	94.0	15.02
MIP 6	84.4	19.96	95.4	14.26

Pre = MIP before training, 1-6 = week 1- week 6

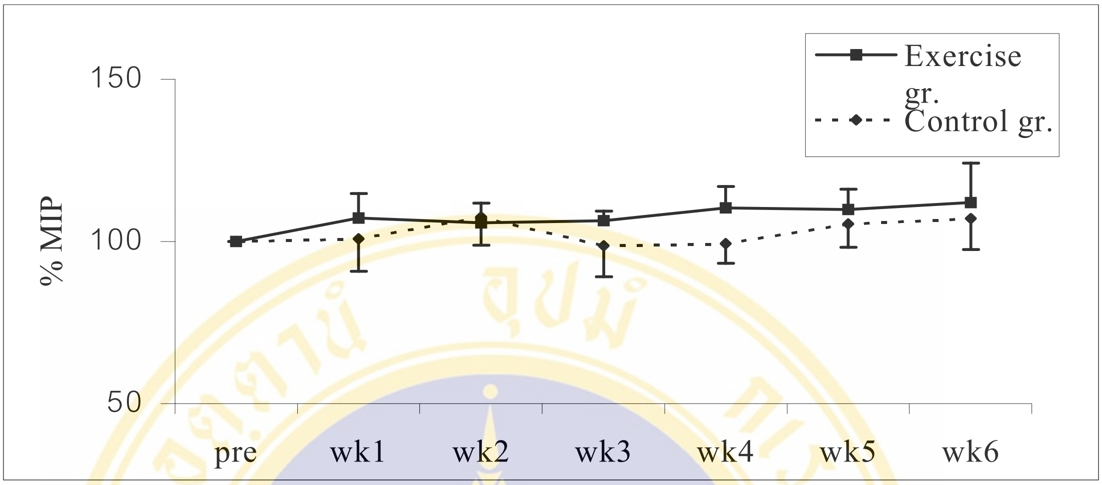

Figure F.1 Show % change of MIP of control and exercise group

Table F.2 Mean and SD of maximum expiratory pressure (MEP)

Variable	Control group		Exercise group	
	Mean	SD	Mean	SD
MEP pre	100.2	44.94	74.2	16.21
MEP 1	90.4	47.46	103.2	28.58
MEP 2	91.6	50.06	97.0	22.47
MEP 3	100.8	60.31	93.0	27.50
MEP 4	94.0	51.28	100.8	29.44
MEP 5	102.0	47.56	102.0	31.47
MEP 6	100.4	34.41	118.0	27.83

Pre = MEP before training, 1-6 = week 1- week 6

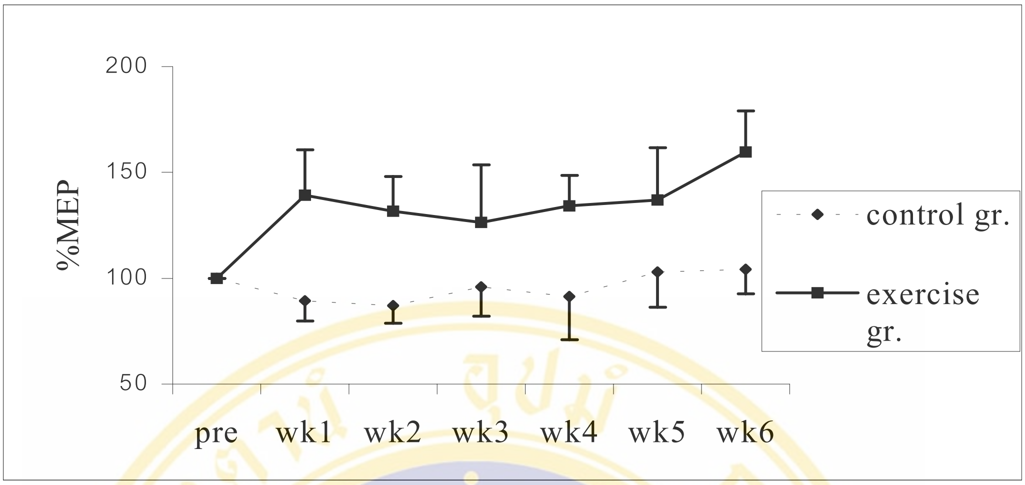

Figure F.2 Show %change of MEP of control and exercise group

Table F.3 Mean and SD of 6 minute walk distance

Vaiable	Control group		Exercise group	
	Mean	**SD**	**Mean**	**SD**
Pre	372.0	101.82	376.8	49.19
Post	424.8	103.44	379.3	50.63

Table F.4 Median and quartile (Q_1 and Q_3) of Quality of life scores

Vaiable	Control group	Exercise group
Pre	102(85,105)	88(82,113.5)
Post	97(88,103.5)	116(109,130)

APPENDIX G
RAW DATA FOR RELIABLITY TESTING

Table G.1 Raw data of MIP, MEP, FVC, FEV_1 and quality of life for reliability testing

subject	MIP		MEP		FVC		FEV_1		Quality of life	
	1	2	1	2	1	2	1	2	1	2
1.	85	72	64	62	3.75	3.66	2.22	2.07	99	106
2.	99	103	91	83	3.48	3.48	1.48	1.43	74	74
3.	85	79	75	77	1.23	1.03	0.48	0.49	93	98
4.	100	109	93	108	1.71	1.84	0.89	0.90	85	80
5.	76	76	75	71	2.36	2.20	1.35	1.39	92	103

APPENDIX H
CALCULATION OF THE SAMPLE SIZE

The main purpose of this pilot study was to investigate the effect of respiratory muscle training on quality of life between control and training group. Therefore, the sample size was calculated by formula of Independent t-test. The following formula was used to determine sample size for the present study.

$N = 2[((Z_{\alpha} + Z_{\beta})\sigma^2) / (Mc\text{-}Mt)^2]$

N/group = sample size of each group

σ^2 = pooled variance

Z_{α} = Z-value when set level of confidence at 90%

= 1.645

Z_{β} = Z-value when set the power of testing at 80%

= 0.842

Mc = the mean of parameters in control group in pilot study

Mt = the means of parameters in study group in pilot study

From the sample size calculation, the score of quality of life is of concern for this study. Below is an example of sample size calculation using score of quality of life after 6 wk of training.

$N = 2[((Z_{\alpha} + Z_{\beta})\sigma^2) / (Mc\text{-}Mt)^2]$

$N = 2[((1.645+0.842)^2(111.5))/(119\text{-}96)^2] = 3$

Thus, the appropriate sample size for each group in the present study is 10

APPENDIX I
RAW DATA OF THE STUDY

Table I.1 Characteristics of subjects

No	Control group (n=8)					Exercise group (n=10)				
	Age (yr)	Ht (cm)	Wt (Kg)	% FEV_1	FEV_1/FVC (%)	Age (yr)	Ht(cm)	Wt (kg)	% FEV1	FEV_1/FVC (%)
1	70	157	61	49	60	75	173	50	58	68
2	70	160	41	57	53	75	157	46	35	49
3	74	159	52	40	48	72	178	74	39	42
4	69	155	55	75	66	69	155	40	37	45
5	76	158	55	36	51	68	161	49	36	51
6	63	159	55	21	33	72	159	53	45	68
7	54	174	65	46	55	53	165	49	48	53
8	65	158	65	27	35	61	165	50	47	58
9						70	159	50	37	53
10						72	162	51	34	58

Table I.2 Maximum inspiratory pressure (MIP) of both groups

No	MIP(cmH_2O)						
	Before	**WK1**	**WK2**	**WK3**	**WK4**	**WK5**	**WK6**
C1	79	83	76	79	74	89	92
C2	79	66	70	66	82	78	74
C3	51	56	58	56	50	52	57
C4	79	82	90	77	82	90	89
C5	91	86	90	82	92	95	88
C6	107	101	96	97	78	87	88
C7	99	90	11	93	98	96	111
C8	67	55	58	67	83	72	71
E1	95	92	100	99	96	102	96
E2	85	87	98	93	99	97	105
E3	103	116	107	106	115	112	113
E4	85	94	90	90	92	86	85
E5	62	71	61	68	72	73	78
E6	76	82	72	67	90	82	82
E7	65	98	96	107	99	106	107
E8	70	88	80	90	91	96	111
E9	88	82	98	96	106	97	104
E10	64	72	82	87	96	89	83

C= subject in control group, E= subject in exercise group

Table I.3 Maximum expiratory pressure (MEP) of both groups

No	MIP (cmH_2O)						
	Before	**WK1**	**WK2**	**WK3**	**WK4**	**WK5**	**WK6**
C1	56	54	48	47	34	59	65
C2	111	92	92	104	106	131	119
C3	60	52	51	52	68	68	67
C4	166	169	172	197	172	171	145
C5	146	128	133	150	103	112	115
C6	52	51	53	53	48	41	42
C7	92	82	76	74	76	99	76
C8	100	97	87	78	69	72	93
E1	87	148	132	141	141	147	152
E2	64	84	80	80	80	72	95
E3	91	101	104	91	91	102	120
E4	77	109	93	78	78	116	130
E5	52	74	76	75	75	73	88
E6	75	100	94	88	88	125	118
E7	86	92	95	106	106	104	94
E8	75	94	127	120	120	140	175
E9	42	32	27	38	38	42	50
E10	62	65	53	60	60	70	100

C = subject in control group, E = subject in exercise group

Table I.4 Six minute walking distance and Quality of life score

No.	6MWD (meter)		Quality of life (score)	
	Before	After	Before	After
C1	420	420	107	97
C2	396	408	107	96
C3	324	324	100	104
C4	324	324	102	103
C5	420	420	111	113
C6	276	288	69	54
C7	336	348	80	101
C8	360	336	100	98
E1	492	540	79	135
E2	240	288	111	114
E3	336	384	88	105
E4	456	516	85	116
E5	336	396	116	125
E6	348	384	85	132
E7	408	444	103	112
E8	456	492	61	72
E9	312	312	95	88
E10	300	396	95	131

C= subject in control group, E= subject in exercise group

Table I.5 The score of quality of life in each dimension

No.	Dyspnea		Emotion		Fatigue		Mastery	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
C1	16	15	46	46	23	17	22	19
C2	25	21	43	38	19	20	20	17
C3	21	23	39	40	17	20	19	21
C4	20	21	45	38	19	23	18	21
C5	16	16	45	48	25	26	25	23
C6	20	16	22	16	15	13	12	9
C7	18	16	30	46	19	21	13	18
C8	21	17	46	43	14	20	19	18
E1	21	34	33	49	12	27	13	25
E2	14	17	49	49	26	26	22	22
E3	17	22	34	38	15	25	22	20
E4	18	24	34	41	15	22	18	22
E5	17	26	48	49	27	27	24	23
E6	18	31	34	48	15	27	18	25
E7	21	23	45	46	17	20	20	23
E8	17	15	21	26	11	16	12	15
E9	13	17	42	33	22	17	18	21
E10	13	32	43	49	22	26	17	24

C = subject in control group, E = subject in exercise group

APPENDIX J
ETHICAL COMMITTEE APPROVAL

เอกสารรับรองคณะกรรมการจริยธรรมการวิจัยในคน
คณะแพทยศาสตร์ศิริราชพยาบาล

เลขที่ 184/2003

ชื่อโครงการ	ผลการฝึกกล้ามเนื้อหายใจต่อความสามารถในการออกกำลังและคุณภาพชีวิตของผู้ป่วยโรคปอดอุดกั้นเรื้อรัง
ชื่อหัวหน้าโครงการ	นางสาวหงษ์ณัฏฐา สิทธิกูล
เลขที่โครงการ/รหัส	--------
สังกัดหน่วยงาน	ภาควิชาศัลยศาสตร์ออร์โธปิดิกส์และกายภาพบำบัด
เอกสารที่รับรอง	- โครงการวิจัย - หนังสือยินยอมและสมัครใจเข้าร่วมโครงการโดยได้รับการอธิบาย

ได้ผ่านการพิจารณาและรับรองโดยคณะกรรมการจริยธรรมการวิจัยในคนเมื่อวันที่ 6 พฤศจิกายน 2546

ลงนาม ....

(ศาสตราจารย์แพทย์หญิงสุมาลี นิมมานนิตย์)

ประธานคณะกรรมการจริยธรรมการวิจัยในคน

ลงนาม ....

(ศาสตราจารย์คลินิกนายแพทย์ปิยะสกล สกลสัตยาทร)

คณบดี คณะแพทยศาสตร์ศิริราชพยาบาล

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The Ethical Committee on Research Involving Human Subject
Faculty of Medicine Siriraj Hospital, Mahidol University

No. 184/2003

Protocol Title	Effects of respiratory muscle training on functional capacity and quality of life in COPD patients.
Protocol Number	----------
Principal Investigator	Miss. Hongnuttha Sittikool
Name of Department	Orthopedic Surgery

The aforementioned project and informed consent have been reviewed and approved by the Ethical Committee, Faculty of Medicine Siriraj Hospital, Mahidol University, based on the Declaration of Helsinki on November 6, 2003

Signature of Chairman ....
(Prof. Sumalee Nimmannit)

Signature of Dean ....
(Clin. Prof. Piyasakol Sakolsatayadorn)

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