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Objective: Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of morbidity and mortality in the United States costing approximately 32 billion dollars yearly. COPD cannot be cured, and existing modalities are limited. This study explored the use of Osteopathic Manipulative Treatment (OMT) on pulmonary function and alveolar ventilation.

Methods: This prospective, randomized single blinded pilot study included 21 subjects with two interventions: OMT and no intervention. Subjects were 40 to 80 years of age with a clinical diagnosis of COPD. Primary outcome measures included pulmonary function values: FVC, FEV1, FEV1/FVC, RV, TLC. Secondary outcome measures included alveolar ventilation measured by pulse oximetry.

Results: No statistically significant results were observed. Clinically relevant trends indicated a potential impact of OMT on COPD subjects. This study was funded by the Osteopathic Research Center (ORC) and approved by the UNTHSC Institutional Review Board.

Conclusions: This study demonstrated the feasibility of conducting research on COPD subjects by the ORC. Because of the small sample size, no conclusive statements can be made determining the efficacy of OMT on pulmonary function and alveolar ventilation.

THE IMMEDIATE EFFECT OF OMT ON A COPD POPULATION: A PILOT STUDY

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THESIS

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TABLE OF CONTENTS

LIST OF FIGURES

Page

CHAPTER 1

BACKGROUND AND SIGNIFICANCE

EPIDEMIOLOGY

Chronic Obstructive Pulmonary Disease, COPD, is the fourth leading cause of morbidity and mortality in the United States.[1] Morbidity and mortality may in fact be underestimated because of failure to diagnose COPD until later stages of the disease.[2] In the year 2000, 119,054 deaths from COPD were recorded. Yearly death rates for the United States for the year 2000 are estimated to be approximately 82.6/100,000 and 56.7/100,000 for males and females respectively. (It is important to note that these data represent ages 25 and above and are not further stratified by age.) It is estimated that of 100,000 yearly deaths in the United States for the year 2000, 70.1 were Caucasian and 42.9 were African American. Geographically, the mountain states were found to have the highest mortality rates of COPD.[3] Quantification of these data proves to be difficult because although COPD is in fact present at the time of death, mortality is derived only from the immediate cause of death and not associated diseases. This suggests that although COPD may have a significant contribution to mortality, it may be underestimated because it is not determined to be the immediate cause of death.[4]

Worldwide prevalence of COPD, as determined by the World Health Organization (WHO) and the World Bank, is estimated to be approximately 9.34/1000

(0.9%) men and 7.33/1000 (0.7%) women. This number does not accurately represent the prevalence of COPD in the older population because of failure to incorporate age stratification of individuals diagnosed with COPD.[1] When chronic bronchitis and emphysema (the two components of COPD) are looked at separately, the majority of the COPD population was found to be in individuals age 65 or older.[3] Also contributing to the difficulty defining worldwide prevalence are the differences in defining COPD.[2]

The burden of disease, as calculated by the Disability-Adjusted Life Year (DALY), measures years of life lost because of premature mortality and years of life lived with disability. Years of life lived with disability is adjusted for the severity of disability. COPD as predicted for the year 2020 will be ranked fifth and comprise 4.1% of the total DALY's, falling behind ischemic heart disease, unipolar major depression, traffic accidents, and cerebrovascular disease.[5]

The National Heart, Lung and Blood Institute (NHLBI) estimated annual costs for the United States to be approximately 32.1 billion dollars with 18.0 billion dollars from direct costs and 14.1 billion dollars from indirect costs in the year 2002. Medicare costs in the year 2000 were 2.5 times that of the expenditures of all other patients. In the year 2000, Emergency Department visits in the United States totaled 1.5 million and hospitalizations totaled 726,000 with an average hospital stay of 11 days.[3] Respiratory disease as a whole ranks third in the most common cause of days of incapacity. Of the respiratory diseases, COPD accounts for 56% of days of incapacitation in males and 26% in females.[6]

RISK FACTORS

Multiple factors play a role in the pathogenesis of COPD, including both host factors and environmental exposures. Of the host factors, a deficiency in α-1 antitrypsin, a protein involved in protecting the lung from common pollutants, predisposes individuals to emphysema at an accelerated rate when compared to those without the deficiency. This acceleration is particularly accentuated if tobacco abuse occurs concomitantly.[1]

Of the environmental exposures, tobacco exposure is the most important risk factor according to the NHLBI.[3] A direct relationship exists between cigarette consumption and the presence of disease.[1] Smokers show greater annual rates of decline in their forced expiratory value at one second (FEV1), a value derived from spirometry, and higher death rates when compared to non-smokers. There is no means of predicting a person's level of deterioration based on tobacco consumption, thus supporting a combination of factors in developing COPD. Occupational exposure can cause COPD in the absence of tobacco exposure and accelerate disease in the presence of smoking. Outdoor pollution shows minimal effect on the development of COPD. Indoor pollution, specifically biomass fuel, has been shown to accelerate the progression of COPD. Socioeconomic status is inversely related to the development of COPD, although this can be related to exposure to indoor and outdoor pollution, crowding, poor nutrition and other factors.[1]

CLINICAL HISTORY AND EXAMINATION

COPD is characterized by airflow limitation, specifically a reduction in maximum expiratory flow and a slow forced emptying of the lungs. Airway limitation is typically progressive in nature and has limited reversibility with provocative measures, specifically bronchodilation. This factor distinguishes COPD from bronchial asthma.[7]

Two disease processes, emphysema and chronic bronchitis, make up COPD. Snider et al with the National Heart and Blood Institute Division of Lung Disease, defines emphysema as a permanent destructive enlargement of airspaces distal to the terminal bronchioles without obvious fibrosis.[8] The Medical Research Council defines chronic bronchitis as the presence of chronic or recurrent increases in bronchial secretions sufficient to cause expectoration. The secretions are present on most days for a minimum of three months a year for at least two successive years.[9]

Multiple physiological changes correspond to the pathological changes that manifest themselves in the individual afflicted with COPD. Increases in the size and number of mucus secreting goblet cells lead to the productive cough and sputum production characteristic of COPD. Injury and repair of airway walls ultimately lead to airway remodeling with the build up of scar tissue causing a limitation in expiratory flow with subsequent lung hyperinflation. Destruction of the pulmonary capillary bed interferes with adequate gas exchange, resulting in hypoxemia.[1] Subsequent pulmonary vascular remodeling can lead to pulmonary hypertension, the most common complication of COPD. Pulmonary hypertension occurs secondary to hypoxia, mechanical stress induced by stretching of hyperinflated lungs and cigarette smoke.[10] A study conducted by

Rutgers University also showed blockage of pulmonary lymphatic vessels secondary to the chronic irritation, exacerbated by tobacco use.[11]

COPD is divided into four stages; stage 0, stage I, stage II, and stage III. Stage 0 (at risk) consists of chronic cough and productive sputum production with pulmonary function values within normal limits as measured by spirometry. Normal values vary based on age, height, sex and race. To correct for these differences, a predicted value is generated with these differences incorporated when pulmonary function is evaluated by spirometry and plethysmography. Any number less than 80% of the predicted value is considered to be abnormal based on the principle that normal lungs can empty more than 80% of their volume in six seconds or less.[12] Stage I (mild COPD), has a Forced Expiratory Value at one second/Forced Vital Capacity (FEV1/FVC) of less than 70% but an FEV1 greater than 80% predicted. Stage II (moderate COPD) has a FEV1 greater than 30% but less than 80% predicted associated with dyspnea. Stage III (severe COPD) has an FEV1 less than 30% predicted or presence of respiratory failure or clinical signs of right sided heart failure.[1]

The first signs of COPD recognized by the patient are shortness of breath, dyspnea, and productive cough. Dyspnea occurs gradually and is first noticed when daily activities become limited. By this point, patients may demonstrate moderate or severe airflow limitation as measured by spirometry. Dyspnea increases as the disease progresses. Sputum production, although present in the majority of patients, does not correlate with severity of disease.[6]

Physical exam, although important in diagnosing COPD, is of limited value. Of the physical signs that may be present in a patient, useful indicators are a prolonged expiratory phase, wheezing, decreased breath sounds with auscultation, and limited excursion of the thorax with breathing. Although these signs are helpful, they cannot quantify the level of severity. Peripheral edema, raised jugular venous pressure and hepatic enlargement can occur if pulmonary hypertension exists, but cannot be used as a sole determinant of COPD.[6]

DIAGNOSTIC TOOLS

SPIROMETRY

Pulmonary function tests, (PFTs), are a recognized tool in diagnosing and managing lung disease, specifically COPD. PFTs incorporate various maneuvers designed to assess lung function and include spirometry, plethysmography, post-bronchodilator spirometry, arterial blood gases and diffusion capacity. Of these, spirometry is most often used by physicians to monitor patients for ease of use, accuracy in measuring lung function, and cost-effectiveness. [13, 12]

Spirometry provides information regarding the rate of movement of air into and out of the lungs with forced breathing maneuvers.[13] The following values are most commonly assessed from spirometric studies: forced expiratory value at one second and forced vital capacity, FEV1 and FVC, respectively. FEV1 is the amount of air forcibly expired in one second. FVC is the amount of air expired in six seconds. A ratio of FEV1

to FVC is generally created and recorded as a percentage. The absolute value of this ratio is the value interpreted as opposed to predicted values.[12]

Although spirometric studies provide more information than FEV1 and FVC, these values show the least amount of intra-subject and inter-subject variability. Thus, other indices do not provide information that is clinically more valuable than FEV1 and FVC. [6] In addition, the Framingham Study identified a low forced vital capacity as a risk factor for premature death.[12]

The American Thoracic Society indicates that using spirometry after bronchodilator treatment provides valuable information regarding prognosis. Bronchodilators, as mentioned previously, provide symptomatic relief by acting on smooth muscle receptors. They are considered to be significant if they produce a response in either the FEV1 or FVC of 12% or greater and .2 L above baseline. [14]

PLETHYSMOGRAPHY

Plethysmography is a tool used to measure thoracic gas volumes. Plethysmography utilizes Boyle's Law which states that pressure and volume of a gas are inversely related if the temperature is held constant. The equation is as follows: $P_1 X V_1 = P_2 X V_2$. [15]

The most important values derived from plethysmography are the total lung capacity (TLC) and residual volume, (RV). These values give the physician an indication of the level of inflation within the lungs, TLC, and the amount of air trapping present, RV.[13]

Functional residual capacity (FRC), TLC and RV are characteristically increased in COPD, in particular TLC.[42]

A study completed by Bates indicates RV levels increase to approximately one liter above predicted values. The ratio of RV to TLC is typically 60% with normal values being approximately 35%.[16]

PULSE OXIMETRY

Oxygen saturation (SaO_2) is defined as the amount of oxygen bound to hemoglobin, an intracellular component of blood that transports oxygen through systemic arterial blood. Each molecule of hemoglobin has a limited ability to carry oxygen molecules, and when that limit is reached, the molecule is considered to be saturated. The level of saturation is expressed as a percentage and represents a ratio of oxygen bound to hemoglobin and the carrying capacity of the hemoglobin molecule.[17] An SaO_2 of 97% simply means that of every 100 hemoglobin binding sites, 97 are occupied with an oxygen molecule. The remaining 3 are unbound or bound by a molecule other than oxygen. SaO_2 is dependent on the amount of oxygen molecules available, described as the partial pressure of oxygen, (P_aO_2.)[18]

The relationship between SaO_2 and P_aO_2, is explained by the oxygen disassociation curve, depicted in Figure 1. As P_aO_2 increases, the amount of oxygen bound to hemoglobin increases to its maximum carrying capacity. As maximum carrying capacity is approached the binding ability of hemoglobin decreases and is reflected by a flattening in the curve.[19]

P_aO_2 is determined by alveolar PO_2. Alveolar PO_2 represents the adequacy of gas exchange occurring at the alveolar-capillary interface of the lung. If there is damage within the architectural structure of the lung causing poor diffusion of oxygen across the interface, P_aO_2 will show a subsequent decline, and hence be manifested by a decrease in SaO_2.[18]

Hemoglobin delivery of oxygen to tissues is largely determined by the partial pressure of oxygen within those tissues (P_aO_2). At high partial pressures, as in the lung, hemoglobin readily binds to oxygen; whereas in the periphery, oxygen is released secondary to the lower partial pressures at these sites.[19]

Pulse oximetry is a tool designed to reflect arterial blood oxygen saturation (S_pO_2). Two components of arterial blood are utilized when measuring S_pO_2, oxyhemoglobin (hemoglobin bound to oxygen) and reduced hemoglobin (non-bound hemoglobin). Oxyhemoglobin and reduced hemoglobin have different absorption spectra at the two wavelengths, 660 nm (red) and 940 nm (infrared), emitted by pulse oximeters. A ratio is produced at the preceding two wavelengths. The ratio is then calibrated empirically against a direct measurement of blood oxygen saturation in volunteers, and a resulting calibration curve is generated. This curve is stored within the pulse oximeter, and consequently enables an estimate of arterial saturation to be attained in percentage form.[20]

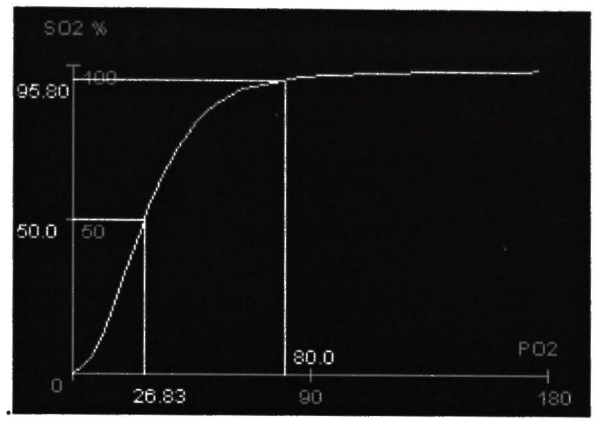


Figure 1: Standard Oxyhemoglobin Disassociation Curve showing the P50 and the SaO2 at PaO2 = 80

Measurements of blood gas tensions are utilized in the COPD patient to follow the impairment of gas exchange at the level of the alveolar-capillary interface. Although arterial blood gases give a better indication of this value, arterial oxygen saturations are an acceptable and non-invasive alternative.[6]

CURRENT TREATMENTS

COPD is a progressive disease with no cure. Treatment is aimed at preserving lung function and preventing further deterioration, improving quality of life, reducing the amount of acute exacerbations experienced, and limiting symptoms.

The most recommended treatment is smoking cessation, the only treatment proven to reduce the progression of disease as measured by spirometry. Practitioners are encouraged to educate patients on the etiology of COPD as the first intervention and then consider progression to a more intense means of support.[6] Nicotine replacement, although helpful in some situations, can prove to be more harmful by continuing to expose the

cardiovascular system to it's adverse effects. Pharmaceutical agents, specifically buproprion, can be used for it's antagonistic properties against the nicotinic receptors.[21] One study suggests that achievement of smoking cessation after administration of seven weeks of buproprion 300 mg was 44% effective in comparison to 19% effective in the placebo group.[22]

Bronchodilators work by relaxing the smooth muscle in the airways and are currently considered the mainstay of treatment. However, they show no effective change in the progression of disease as measured by spirometry. Although there is no reversal in the course of the disease with bronchodilation, their effect on symptomatic control effectively provides functional improvement in some patients. Three groups of bronchodilators exist: β-2 agonists, anticholinergics, and methylxanthines.[6]

Both short acting and long acting inhaled β-agonists provide symptom control.[21] Studies on long acting inhaled β-agonists have not been adequately studied to date. Continued use of β-agonists may lead to a decrease in the response to the medication.[6]

Anticholinergics, although slower in onset in comparison to inhaled β-agonists, prove to be more effective in bronchodilation. Anticholinergics work by blocking the effect of M1and M3 receptors involved in the cholinergic response, specifically bronchoconstriction and mucus production.[21]

Methylxanthines have less effect on bronchodilation than β-agonists and anticholinergics, but show changes in pulmonary vascular dilatation, increased salt and water excretion, and central nervous stimulation. Although this class of drugs have some desired effect on the pathophysiology found in COPD, the array of side effects include

gastric irritation, nausea, diarrhea, headache, tremor, irritability, sleep disturbances, epileptic seizures and cardiac arrythmias. In addition, monitoring therapeutic drug levels is extensive requiring dosage changes for even small lifestyle changes that may affect drug levels.[6]

Evidence indicates that the use of corticosteroids in long-term control of COPD shows minimal benefit. Approximately 10 percent of patients may benefit from inhaled corticosteroid therapy, but those individuals are suspected to have asthma in addition to COPD. It is thought that the asthma component of their disease is what responds to corticosteroid therapy.[23]

A study performed by the Department of Thoracic Medicine, National Lung and Heart Institute showed inhaled steroids to have little anti-inflammatory effect, at least in the short term in this group of patients, and suggests that the inflammatory process in COPD is resistant to the anti-inflammatory effect of glucocorticoids.[23]

No existing evidence supports the use of mucolytic agents and antioxidants in COPD, although the theory behind clearance of sputum reducing symptoms and improving lung function are driving factors in generating support for these agents.[6]

Oxygen Therapy is suggested for people in acute exacerbation or in chronic respiratory failure. With acute exacerbation, the goal is to achieve a S_aO_2 greater than 90 percent or a P_aO_2 of 60 mm Hg. With chronic respiratory failure, patients have a P_aO_2 of 55 mm Hg for approximately three to four weeks at rest during a stable period in their disease (no acute exacerbation present) regardless of optimal therapy.[6]

Individuals who have been diagnosed with COPD and have advancing dyspnea suffer from a decline in activity and subsequently undergo muscle atrophy. Rehabilitation combines muscle training, nutritional therapy, nutritional support and education to promote increased activity and improved quality of life. The effects of respiratory muscle training are not clear, but most studies show an improvement in respiratory muscle function. Malnutrition is associated with an increase in mortality, but high carbohydrate and high calorie diets are associated with an increase in carbon dioxide production and should be avoided.[6]

Lung Volume Reduction Surgery (LVRS) removes about 30% of the most diseased lung tissues so that the remaining healthier portion can perform better. In addition, it allows for the patient to breathe more efficiently by returning the diaphragm to its normal shape. LVRS does not cure COPD and is reserved largely for those with severe emphysema who do not respond to rehabilitation. A large nationwide study, the National Emphysema Treatment Trial (NETT), indicates a potential for improvement in exercise capacity but no definitive survival advantage over medical therapy.[24]

Although current treatments are available for this disease entity, there is little to offer from a medical standpoint for COPD, and therefore, other interventions should be investigated.

OSTEOPATHIC MANIPULATIVE TREATMENT

The underlying pathophysiology of COPD serves as the target for the multiple modalities that exist to provide symptomatic relief of the myriad of clinical manifestations of this disease. Although numerous treatments are incorporated in the care of a patient with COPD, no treatment is curative. Thus, adjunct treatments should be used in order to alleviate the symptoms associated with COPD. Of these adjunctive treatments, Osteopathic Manipulative Treatment (OMT) was the focus of this clinical study.

Based on the principles guiding OMT, a form of manual medicine, restoration of normal physiology and anatomy may serve as a valuable tool in the care and treatment of COPD. OMT is guided by three models: Fluid, Musculoskeletal and Neurological. The fluid model focuses on movement of blood and lymph to enhance cellular metabolism and fluid balance. The musculoskeletal model revolves around the principle that altered structure will interfere with a normally functioning system. The neurological model looks at dysfunction that can in turn alter the autonomic system.[25,26,27,28]

The musculoskeletal model guides the physician in treating changes found in the thorax secondary to pulmonary hyperinflation. Of these structures, the respiratory muscles adapt to the best of their ability to changes that occur throughout the course of the disease. In the presence of sustained labored breathing, as found in COPD due to airway limitation, the respiratory muscles often demonstrate weakness and reduced endurance.[29]

The primary respiratory muscle is the diaphragm, which accounts for 75% of change in intra-thoracic volume during quiet inspiration. The movement of the

diaphragm is often described as piston-like and normally moves on average from 1.5 to 7.0 centimeters with deep inspiration. The diaphragm attaches to three areas: the lower thoracic cage, the lumbar vertebrae and the sternum. The attachments to the thoracic cage are considered the crural portion and are partially innervated by the phrenic nerve which originates at the third, fourth and fifth cervical vertebrae. Transection of the spinal cord above the third cervical vertebrae result in cessation of diaphragmatic motion without the assistance of artificial ventilation.[30]

Pulmonary hyperinflation has several deleterious effects on the diaphragm including reduction in the appositional zone of the diaphragm altering the piston like movement, impedance of normal expansion of the lower rib cage and reduction of the length of the diaphragm. Increased anteroposterior diameter of the chest wall also interferes with normal rib cage motion. Higher Total Lung Capacity (TLC) and Residual Volume (RV) values correlate with the amount of intra-thoracic volume and are indirectly related to sarcomere length. Higher TLC and RV volumes subsequently decrease sarcomere length, shortening the diaphragm muscle and in turn reducing mechanical efficiency of the muscle.[29]

The external costal muscles also assist in inspiration. Contraction of these muscles lift the lower ribs and cause an increase in the anteroposterior diameter of the chest. The sternocleidomastoid and scalene muscles are considered accessory muscles and assist in inspiration during labored breathing.[30]

The internal intercostals muscles are considered expiratory muscles. Contraction of these muscles move the ribcage downward, increasing intra-abdominal pressure and moving the diaphragm upward and enabling forced expiration.[30]

Removing somatic dysfunction at the thorax and surrounding structures will in theory increase the patient's ability to ventilate, reducing the amount of work experienced by the patient and enable the respiratory muscles to properly work.[31] Areas that can be examined are; the thorax which undergoes considerable anatomical changes specifically an increase in anteroposterior diameter and the accessory muscles which suffer from excessive use. In addition, addressing structural dysfunction at the cervical spine may improve ventilation of the diaphragm by removal of impingements of the phrenic nerve. Restoration of normal musculoskeletal attributes will enhance adequate ventilation by enabling the body to perform at an optimal level.

The fluid model deals primarily with improper fluid balance, which can be seen in COPD. Alveolar ventilation is maintained when there is adequate oxygenation at the alveolar capillary bed. Adequate oxygenation cannot occur if the airway becomes infiltrated with secretions, edema or bronchospasms, as can be seen with COPD. Obstruction ultimately causes hypoxemia, leading to dyspnea.[32] Hypoxic vasoconstriction and capillary obliteration lead to pulmonary hypertension. Because hypoxia is a major pulmonary vasoconstrictor, it is important to identify the culprit and reverse it.[33]

By utilizing manipulative techniques to mobilize fluids, specifically removal of restrictions that impede lymphatic flow and restoration of the natural lymphatic pumps of

the body (the respiratory diaphragm), excessive secretions characteristic of this disease can be reduced. Reduction in secretions from the airways will result in improved alveolar ventilation.

The neurological model is closely linked with the autonomic nervous system (ANS) which is divided into the sympathetic and parasympathetic system. Bronchoconstriction and bronchodilation of the lungs are under control of the ANS. The β-adrenergic receptors on the smooth muscle of the lungs, when activated, induce bronchodilation.[32] Sympathetic fibers arise from the spinal cord at the level of the first four thoracic vertabrae and synapse at the costovertebral junction.[34] Stiles suggests that anatomical dysfunction in this region may enable the parasympathetic portion of the ANS to predominate, thus inhibiting bronchodilation that typically comes about with sympathetic stimulation.[31] Adrenergic stimulation conversely when activated, causes bronchoconstriction.[32] Branches of the vagus nerve provide parasympathetic innervation to the pulmonary structures as well as the diaphragm and exit at the condylar portion of the occiput.[35] An imbalance between these two systems can lead to less than optimal conditions to the individual afflicted with COPD.

The use of OMT to address the sympathetic system can be accomplished by treating the area of the costovertebral region of the thoracic spine that innervates the lungs. Dysfunction in this area is likely to occur when considering the anatomical adaptations that occur to compensate for the pulmonary hyperinflation that is seen in this disease process. With an increase in anteroposterior diameter, rib mechanics are changed and the area at which the ribs connect to the thoracic spine are altered. In addressing the

parasympathetic nervous supply to the lungs, the vagus nerve can be freed of structural dysfunction where it exits at the occipital condyles. These two areas provide the supply for normal dilatation and constriction of the lungs. It is imperative to free these areas from restriction to enhance normal activity by the autonomic nervous system.

MANUAL MEDICINE LITERATURE

Although there appears to be a plausible good fit between OMT and it's role in COPD, there have been few documented investigations into the use of OMT as an adjunctive therapy. In addition, there has been only one prospective, randomized, double-blinded, controlled, study looking at the effects of OMT on pulmonary function parameters, the gold standard in measuring the severity of COPD. This suggests that more research needs to be conducted to explore the efficacy of OMT in a COPD population.

An extensive literature search via OSTMED and OVID Medline was performed to find articles that have investigated the use of OMT in a COPD population. In addition to looking for articles that focused on past studies that explored the use of manual medicine as an adjunct therapy, searches were also completed to investigate the use of OMT and it's changes in basic physiological parameters. These papers help to support the use of OMT in COPD in effort to manipulate somatic dysfunction that commonly present and therein lead to the pathological changes that occur throughout the course of the disease.

The most recent study, by Dr. Noll et al, investigated the immediate effects of OMT on pulmonary function. His study was designed as a one-day study that used various manipulative techniques on a COPD population aged 60 or older. Thirty-five subjects were enrolled into the study with 18 subjects randomized to a treatment group and 17 randomized to a sham group. Subjects underwent pulmonary function tests pre- and post-treatment/sham.[36]

The study examined the following parameters: FEF25% (Forced Expiratory Flow during the first 25% of expiratory flow), FEF 25-75% (Forced Expiratory Flow between 25-75% of expiratory flow), IC (inspiratory capacity), RV, TLC and the RV/TLC ratio. Analysis of data was completed using ANCOVA and showed statistically significant changes in the preceding values with all p values less than .05, indicating results could be reported with 95% confidence they did not occur by chance alone. Of the preceding values, FEF25% and FEF 25-75% went in a negative direction; whereas IC, RV, TLC and the RV/TLC ratio went in a positive direction.[36]

It is difficult to determine the details of the study conducted by Dr. Noll because at this time, only a research abstract has been published. The manipulative medicine techniques were not specified, although he mentions in his abstract that treatments were not individualized to tailor to specific dysfunction within the individual. Blinding techniques were not mentioned. Methods to perform sham treatments were not elucidated in this abstract as well.[36]

A study conducted at the Chicago College of Medicine by Dr. Howell et al in 1975 looked at pulmonary function parameters in individuals with objective evidence of

COPD over a nine-month period. Subjects were given standard of care, as well as OMT directed at the spine and paravertebral tissues. Eleven subjects were analyzed. They received one initial pulmonary function test to determine their baseline function and subsequently underwent spirometric examination at one month, three months, six months and nine months. No control group was utilized in this study.[37]

Subjects from this study were assessed for the severity of their disease in the following manner: 11 parameters were used to classify severity of the disease. These parameters were given a score from zero to five, zero being not present in the subject to five severely present. These values were then added to determine overall severity in that subject. The 11 spirometric parameters were also weighted for typical presentation in a patient. If a specific measurement was consistently altered in severe disease, it was given the most weight. Scores were multiplied by their respective weights. Over the nine-month interval, results showed a 10.7% reduction in overall severity. Significant changes in the following individual parameters were also found: PCO2, O2 saturation, TLC and RV with a decrease in PCO2, TLC and RV and an increase in oxygen saturation.[37]

A case study, reported by Mall in a 1973 Journal of the American Osteopathic Association publication examines a 61 year old African American man over the course of six years with the constellation of signs and symptoms consistent with COPD. Spirometric findings supported this diagnosis.This patient was on supportive medications, quit smoking, received instruction on diaphragmatic breathing and received the thoracic pump once a week for approximately three and a half years. During the study

there were specific instances when the subject was receiving medication as his primary treatment with minimal OMT intervention.[38]

Results showed only a ½ liter increase in TLC over the course of three years, a relatively small increase when compared to individuals with similar disease not receiving this treatment regimen. RV values were initially about one liter greater than the expected RV for someone of that age. This value is representative of an individual with moderate emphysema. At the completion of the study, the increase was only ¾ greater than the initial value. It is notable to mention that RV values tended to increase at a more rapid rate when the subject was receiving medication as his primary treatment and decreased when receiving OMT. FEV1 values continued to decrease, but the rate of decline slowed to about half the rate with the addition of OMT when compared to treatment with medication alone.[38]

A pilot study conducted by Dr. Bockenhauer and Dr. Lo in 1998, evaluated 10 subjects with chronic asthma for changes in respiratory excursion (thoracic excursion), peak expiratory flow rates and subjective measures. Although there are fundamental physiological differences in asthma and COPD, both diseases are obstructive in nature and have a common denominator of limited expiratory flow.[34]

In this study, a pretest-posttest crossover design was used so that subjects could be used as their own controls. With this design, subjects were treated with both OMT and sham on different days with at least one week between interventions. The design was intended to look at restoration of compliance to the thoracic cage and it's effect on thoracic excursion. This impediment exists in COPD as well as chronic asthma.[34]

A single session of four techniques was administered; balanced ligamentous tension in the occipitoatlantoid and cervicothoracic junctions, Still technique for the displacement of the first rib and diagphragmatic release. The population was selected in an area where it was thought the subjects were naïve to OMT and would not recognize a sham treatment as opposed to a manipulative medicine treatment. As predicted no subjects had received OMT prior to this study, although one had received chiropractic treatment for lower back pain.[34]

Sham treatments had the subject lay in the same position on the same table as those receiving OMT. They would receive the following: gentle pressure to the thoracic outlet, occipitoatloid and cervicothoracic and epigastric region and partial movement of the upper extremity through range of motion. None of these techniques are recognized OMT techniques.[34]

Fifteen minutes prior to treatment/sham and after, thoracic excursion was measured. Thoracic excursion was measured with a cloth tape held around the thoracic circumference. Upper thoracic excursion was measured at the third intercostal space anteriorly and fifth vertebrae posteriorly, and lower thoracic excursion was measured at the xiphoid process anteriorly and at the tenth vertebrae posteriorly. These areas were marked during the pretest to ensure that measurements would be as close to accurate as possible. Investigators who measured thoracic excursion were blinded to whether or not the subject received OMT or sham intervention.[34]

Results showed significant improvements ($p < .05$) in both upper and lower thoracic excursion in the OMT group, 0.9 cm and 0.8 cm respectively. When considering

the limited motion in an individual with chronic asthma, these changes are notable. Clearly, the study due to it's limited size should be explored further for reproducibility in larger numbers. In addition a double blinded, randomized, controlled study should be encouraged. The similarity between asthma and COPD is limited, but this study should be conducted in a COPD population who also suffers from musculoskeletal changes in the thoracic region.[34]

A 1990 study performed by they Departments of Surgery, Pulmonary Medicine and Family Medicine at the Chicago College of Medicine by Sleszynski et al examined the use of incentive spirometry versus OMT in post-operative atelectasis and rate of return to baseline pulmonary function in a one-year researcher-blinded trial; the analyzing author was blinded to the subjects treatment until all data was entered. The thoracic lymphatic pump (TLP) was the maneuver utilized for this study.[39]

Forty-two low risk patients were entered in the study. Pulmonary function tests (FEV1 and FVC) were performed by a respiratory therapist for both groups, those receiving OMT (21 subjects) and those receiving incentive spirometry (21 subjects). Postoperatively, the OMT group received TLP three times a day while the incentive spirometry group performed incentive spirometry three times a day. Subjects from both groups were evaluated for pulmonary function for three days postoperatively.[39]

Results showed quicker recovery in FVC and FEV1 and were found to be statistically significant for the OMT group. The authors discussed the physiology behind the improvements in their values and attributed them to improved lymphatic flow, deep inspiration, and stimulation of the physiologic reflex in the respiratory center. They

theorized increased lymphatic flow could potentially be a result of increasing intra-thoracic pressure with improved diaphragmatic motion and deeper inspirations. Deep breathing associated with this technique as well as with incentive spirometry provides improved aeration to alveoli not receiving adequate oxygenation. Increased movement of the rib cage during treatment with the thoracic lymphatic pump is also suggested to stimulate the autonomic nervous system by enhancing the peristaltic activity of the larger lymphatic vessels. Finally, pressure to the chest wall induces a stretch in the respiratory muscles and also improves movement in the costo-transvere joints subsequently increasing rib cage motion.[39] These physiological changes could be theorized to work as efficiently in someone with COPD.

A 1971 study conducted by Eshleman et al investigated the changes in blood flow with manipulation, specifically myofascial stretching, to cervical and thoracic regions. Three experiments were conducted to explore this phenomenon. No control groups were utilized in the first two experiments conducted within this study. Experiment 3 served as a control for this study; the subjects within this group received no OMT.[40]

Experiment one had 30 subjects. Blood flow was analyzed, via impedance measurements, for 10 minutes at 2-minute intervals after electrode placement to get a baseline measurement. OMT was administered after the 10-minute standardization period for 5 minutes. After completion of OMT, impedance values were collected for 2-minute intervals for 16 minutes. Results showed a 17.06% average decrease in blood flow.[40]

Experiment two was conducted to determine blood flow changes during manipulation. Fifteen subjects were chosen and underwent the same protocol, with the

exception of measurements during manipulation. Average blood flow decreased 16.61% at one minute and five minutes during OMT intervention.[40]

Experiment three was conducted as a control group, receiving no OMT. Fourteen subjects were chosen. No significant changes were found in blood flow.[40]

This study was intended to show that sympathetic fibers, which arise from specific spinal regions, control vessels by constricting their diameter and reducing blood flow. The effect is considered to be immediate as demonstrated by experiment two and lasting as shown by experiment one.[40]

This literature search provided a sound foundation in pursuing further research into the use of OMT for COPD. This search assisted in creating an OMT intervention model as well as providing useful information in the use of pulmonary function testing in evaluating the efficacy of OMT on a COPD population. Although this search was extremely helpful, it also supported the fact that limited research has been done on this subject. With the growing epidemic of COPD, adjunct therapies like OMT need to be investigated.

CHAPTER II

METHODOLOGY

INTRODUCTION

Several goals guided this study. The first of these goals was to take a step in adding to the treatment armamentarium that is already in existence in the fight against COPD. Current treatments offer limited symptomatic relief, but none provide a cure. Based on the underlying physiology of COPD, OMT may serve as an effective adjunctive therapy. Secondly data from this pilot study could potentially be used as background to justify larger more definitive studies. The implementation and follow through of this pilot study was thus necessary to determine feasibility of larger more definitive studies by the ORC. In addition, the existing knowledge on the use of this treatment is limited. Of the current literature, there are only few prospective, randomized, double-blinded controlled studies. This study will be a randomized, single-blinded, controlled study that could potentially be used as a foundation for future double-blinded studies by the ORC.

Osteopathic manipulative treatment addresses several areas in the COPD population that are altered secondary to the disease process. The following areas are afflicted by this disease and were used to guide in the creation of the OMT protocol:

1. Abnormal rib mechanics and respiratory muscle restriction secondary to pulmonary hyperinflation;

2. Restricted lymphatic drainage secondary to compression of the thoracic duct and inefficient respiration secondary to diaphragmatic restrictions;
3. Dysfunction at the costovertebral junction in the thoracic spine (sympathetics) and the occipitoatlantal junction (parasympathetics) causing autonomic imbalance; and
4. Reduced alveolar ventilation caused by enhanced sputum secretion from airways.

By treating the preceding dysfunctions that are commonly found in the COPD population, the following hypotheses were generated:

1. OMT will improve pulmonary function parameters as measured by spirometry and plethysmography, specifically FEV1, FVC, FEV1/FVC ratio, RV and TLC; and
2. OMT will improve alveolar ventilation as measured by pulse oximetry.

In addition to the above hypotheses, other areas that were explored included demographic characteristics including the following: age, BMI, gender, race, smoking history, comorbidities, inhaler use during the day, inhaler use during the night, total medications as prescribed by the physician, pillows used at night, oxygen use, bronchodilator use, current cough, current sputum production, current wheezing, current dyspnea and steroid use. Demographic information would be collected for the purposes of assessing baseline characteristics of the entire sample set, and then for further investigation of Group tendencies. Data would also be analyzed for clinical trends.

SUBJECT SELECTION AND RECRUITMENT

A preliminary power analysis was performed to give a rough estimate of the sample size that would be required to attain statistical significance. The analysis was conducted in conjunction with the Principal Investigator as well as the Biostatistics Department of the University of North Texas Health Science Center (UNTHSC) School of Public Health. In order to detect a 12% difference in the FEV1 or FVC, with an α of .05 and a β of .2 to achieve a power of 80% approximately 511 individuals would be required to complete the study. A 12% increase in FEV1 and FVC according to the American Thoracic Society constitutes a significant bronchodilator response in a patient with obstructive disease and thus this number was used for power analysis computations.[14] This number was not feasible for the time and resources allocated to the clinical trial.

Therefore, a pilot study consisting of 50 subjects was proposed for the design of this study for initial data collection. This sample size, however, will not protect against type II error. Type II error indicates that the investigator will not find a significant change, when in fact one does exist. Due to difficulty in recruiting and damaged equipment, this number was not attained, and a sample size of 21 was used.

All documents including research protocol, informed consents, questionnaires regarding symptoms and confidence in treatments, and recruit ting materials were approved by the University of North Texas Health Science Center (UNTHSC) Institutional Review Board. Recruiting occurred through the UNTHSC system. Flyers were posted throughout Family Medicine and Internal Medicine Clinics associated with

the University. A publication in a newsletter read specifically by University physicians was also utilized. Charts were screened in the morning by the research team including Pre-Doctoral Fellows and Clinical Research Coordinators for potential subjects.

Once a subject was recruited, they underwent a pre-screening interview where they either entered into the study, or were excluded due to exclusionary factors.

On the day of intervention, the subject was asked to arrive at the Patient Care Center (PCC) on the fourth floor where pulmonary function equipment was available. Selected research team members would review the Informed Consent Document and inclusion and exclusion criteria with the potential subject. If the subject met study requirements, they were consented and proceeded through the course of the study. Inclusion criteria included ages between 40 and 80 years of age and a clinical diagnosis of COPD.

Exclusion criteria included: 1) pneumonia, 2) bronchial asthma, 3) pulmonary fibrosis, 4) neoplasm, 5) bronchiectasis, 6) inability to ambulate, 7) inability to perform pulmonary function tests due to recent heart attack or heart disease, 8) inability to respond to questionnaires or give informed consent, or 9) any contraindication to OMT.

In addition to the Informed Consent Document, subjects were also asked to complete a questionnaire containing demographic information. Demographic information included age, gender, and race. Other pertinent information collected at this time were: referring clinic, other diseases, current medications, recent hospitalizations, recent exacerbations, symptoms that the subject was currently experiencing (coughing, increase

in sputum, wheezing or shortness of breath), smoking history and number of pillows used at night.

After signatures were obtained and subjects completed the demographic questionnaire, they were taken to the Respiratory Therapist for pulmonary function testing. Pulmonary Function data were obtained through plethysmography and spirometry. Three questionnaires followed pulmonary function testing: St. George's Respiratory Questionnaire, the Borg Scale and the American Thoracic Society Dyspnea Index (TDI). The preceding questionnaires were used in a separate arm of this study being conducted in conjunction with pulmonary function exploration. The objectives of this study arm were being investigated by another Pre-Doctoral Fellow.

A six-minute walk followed the questionnaires in which a pre-oxygen saturation value was recorded. Duration and distance during the six-minute walk were also recorded. A post-oxygen saturation value was recorded after the six-minute walk. In addition, the a second Borg Scale and TDI was administered.

Subjects were then taken to a separate room for either OMT intervention (Group 1) or a 30-minute rest period (Group 2), in which they received no treatment. Subjects were pre-determined into their respective groups based on randomization. Groups were determined through randomization to ensure each subject had a known, equal chance of receiving an intervention. Block randomization was used to keep similar sample sizes between groups. Block sizes used were 10, 10 and 6.

Subjects were delivered to the treatment provider who had a sealed envelope containing folded pieces of paper that neither subject nor provider could see. The subject

drew a folded piece of paper. The number of papers contained within the sealed envelope were determined by block randomization as mentioned above. Removal and unfolding of this paper revealed either the number one or two. Number one indicated they would fall into the OMT intervention group; whereas, a two would place them into the no treatment group. Subjects were instructed not to share this information with any other member of the research team. In addition, the treatment provider was not to divulge this information to any other member of the research team.

The two experimental groups are described in full in the Experimental Groups and Intervention section. Both groups underwent identical protocols with the exception of their form of intervention. All members of the research team, with the exception of the treatment provider, were blinded to the randomization. This included the Principal Investigator (PI), Clinical Research Coordinator (CRC), and Respiratory Therapist (RT). A Pre-Doctoral Fellow administered the OMT. Pre-Doctoral Fellows that participated in the OMT intervention were all under guidance of the PI to ensure that treatments were administered in as close to identical fashion as possible. A total of 10 training sessions were administered during the course of this study which included all members of the research team to ensure that subject screening, recruitment, consenting, and flow through protocol was being performed identically.

After intervention, subjects were returned to the Respiratory Therapist for post-treatment pulmonary function tests, identical to the pre-pulmonary function tests. A third Borg Scale and TDI were administered, and subjects completed a second six-minute walk

with pre and post pulse oximetry recordings. The same values were recorded in the second six-minute walk as the first.

Subjects then completed a final Borg Scale and TDI after their second six-minute walk. Subjects were given $25.00 for time and travel expenses.

Figure 2 in appendix A describes the flow through the study.

EXPERIMENTAL GROUPS AND INTERVENTION

Two groups were used in this clinical study: Group 1- OMT with standard of care, and Group 2- No Treatment with standard of care. The OMT provided to Group 1 was administered by a Pre-Doctoral Fellow in the Manipulative Medicine Department at UNTHSC.

Group 1 received a 30-minute Osteopathic Manipulative Treatment (OMT) as their intervention by a Pre-Doctoral Fellow. The treatment protocol is described in detail below. As mentioned above, both groups were to maintain standard of care. This indicates that the subject was to continue all home medications and instructions as provided by their primary care provider.

Treatments focused on five areas that are found to be dysfunctional in the COPD patient. It was theorized that if these specific areas were addressed, improvements in pulmonary function and oxygen saturation would be found. Several types of manipulative medicine modalities were included in the treatment protocol to allow for therapies that may be more suited to the individual's dysfunction.

The following areas were specified, and the rationale for their inclusion in the treatment protocol is described below:

1) Occipitoatlantal Junction: The vagus nerve exits the condylar portion of the occiput. Vagal activity exhibits a secretory and bronchoconstrictive effect on the lungs. Alleviation of dysfunction in this area may assist in normalization of abnormal autonomic activity secondary to the anatomical dysfunction that occurs in COPD. In addition, treatment of this area may assist in decreasing the excessive secretions that are found in patients afflicted with this disease.

2) Cervical Spine, Accessory Muscles and Sibson's Fascia

a. *Cervical Spine:* Innervation to the diaphragm arises from cervical vertebrae three to five, the phrenic nerve. The diaphragm is altered in this disease process secondary to pulmonary inflation and changes in the thorax. If dysfunction also exists in the cervical region at the phrenic nerve, diaphragmatic motion will be further altered with disruption in normal neuroregulatory processes.

b. *Accessory muscles:* Accessory muscles, which assist in respiration, undergo significant changes during the progression of COPD. Viscerosomatic reflexes can be seen in accessory muscles and palpated as rigidity. Treatment to this area may reduce rigidity and encourage less labored, more effective breathing and improvement in alveolar ventilation.

c. *Sibson's Fascia*: Sibson's Fascia surrounds the body's terminal lymphatic thoracic ducts. With recruitment of accessory muscles, first rib elevation is often seen, thus disrupting the normal thoracic inlet and in turn impeding adequate lymphatic drainage. Releasing restriction within this fascia may improve lymphatic flow through this area and

improve alveolar ventilation by helping facilitate removal of excessive mucus and lymph at the pulmonary level.

3) Thoracic Spine and Ribs

a. *Thoracic Spine:* Sympathetic innervation for the lungs arises from the spinal cord in the region of the first four thoracic vertebrae. These nerves synapse at the costovertebral junction, which can suffer from somatic dysfunction as COPD progresses. With an increase in the anteroposterior diameter of the thorax and subsequent alteration in the ribs and their anterior and posterior connections the costovertebral junction can undergo anatomical changes, which will interfere with normal autonomic activity affecting the bronchodilitatory effects of sympathetic stimulation. Correction of anatomical dysfunction in this are may assist in restoring normal autonomic activity hence improving bronchodilitation.

b. *Ribs:* The increased anteroposterior diameter of the thorax restricts normal movement of the ribcage by altering connections anteriorly and posteriorly. In addition to alteration of the ribcage, the diaphragm undergoes flattening with increasing pulmonary inflation. Flattening of the diaphragm alters its normal piston-like movement, which inhibits adequate inhalation and exhalation. In addition, impaired diaphragmatic movement interferes with mobilization of lymphatic fluid. By returning normal mechanics of the ribcage the ability to inhale and exhale will be improved thus improving alveolar ventilation. Restoration of diaphragmatic motion will improve pulmonary function on two levels; more effective inhalation and exhalation with appropriate diaphragm length

and improved lymphatic flow with the return of the diaphragm to a normally functioning pump.

c. Inappropriate thoracic cage mobility can cause dysfunction in lymphatic drainage because the lymphatic system has no intrinsic pump and depends on pressure differences between the thorax and the abdomen to be mobilized. Reduction in this immobility may enhance alveolar ventilation secondary to removal of obstruction.

4) Abdominal Diaphragm: Inadequate excursion of the diaphragm impedes normal alveolar ventilation as well as normal lymphatic drainage. Addressing this area can alleviate this dysfunction.

5) Lymphatic Pumps including Thoracic and Pedal Pumps:

a. *Thoracic Pump:* Enhanced sputum expectoration and increased thoracic mobilization from this technique will improve alveolar ventilation by removal of obstructions caused by excessive secretions accumulating in the airways. In addition, this technique will assist with pulmonary function by normalizing chest wall/rib cage movement.

b. *Pedal Pump:* Mobilization of lymphatics through this technique is accomplished by low frequency oscillatory movement through the lower extremities to encourage excess lymph towards the thoracic duct.

OMT TECHNIQUES

The following techniques were utilized to address the above areas:

1. Muscle Energy (ME): The dysfunctional area is positioned against the restrictive barrier in all planes. The subject is instructed to contract against a resistive force

instituted by the treatment provider for approximately three to five seconds. With muscle relaxation, the subject is repositioned to the new barrier. This is repeated approximately three to five times. Muscle energy was implemented in the cervical and thoracic region.

2. Soft Tissue: Treatment is directed towards restricted tissues and includes lateral stretching, linear stretching, deep pressure, traction and/or separation or muscle origin and insertion while monitoring tissue response. Soft tissue was utilized in the cervical region.

3. High Velocity Low Amplitude (HVLA): Treatment utilizes high velocity and low amplitude forces through a restrictive barrier. This treatment was used in the areas of the cervical and thoracic spine.

4. Myofascial Release (MFR): MFR could be applied to the cervical, thoracic, rib or diaphragm region. Two forms of MFR exist:

a. Direct MFR: A restrictive barrier is palpated and constant pressure is added until tissue release occurs.

b. Indirect MFR: A restrictive barriers is palpated within the tissues and a constant pressure is applied to the area and moved away from until no restriction is palpable.

5. Balanced Ligamentous Tension (BLT): A combination of myofascial release techniques is employed in either a direct or indirect manner until a release is palpated. BLT was used in the cervical region.

6. Springing: A direct technique utilizing gentle and repetitive forces through restrictive barriers in order to improve physiologic motion. Springing was used in the rib region.

7. Thoracic Lymphatic Pump: Oscillatory force at approximately 2Hz is applied to the anterior chest wall with exhalation with the palmer surface of the treatment provider's hands. The operator resists chest expansion during inhalation. This cycle is continued for several cycles. With the last cycle, the subject takes a deep breath and the resistive force is suddenly released at peak inspiratory force.

8. Pedal Pump: A rhythmic force is applied to the lower extremity to encourage lymphatic flow towards the thoracic duct.

The OMT protocol for this study can be found in Appendix B.

A second group, Group 2 received no treatment. The subject was instructed to take a 30 minute rest period, the same amount of time that subjects in Group 1 received OMT. During the rest period, subjects were asked to lie in the supine position and remain relatively motionless. Group 2 also received standard of care as instructed by their primary care provider. The purpose of Group 2 was to demonstrate that OMT does in fact have an impact on pulmonary function and oxygen saturation when compared to a subject that did not receive OMT. It has been theorized that OMT may have an inherent placebo effect by simple patient contact or increased interaction between subject and treatment provider. With this in mind, this study did not incorporate an actual placebo in its design in attempts to demonstrate a change between subjects receiving OMT and subjects receiving no manual treatment and limited subject-provider interaction.

PULMONARY FUNCTION STUDIES

Pulmonary function studies evaluate multiple parameters to give an indication of lung function. Proving or disproving Hypothesis 1 relies on the results of pulmonary function tests. To evaluate pulmonary function, two separate tests, spirometry and plethysmography, were completed by subjects both pre-intervention and post-intervention.

Pulmonary function testing was done identically pre-and post-intervention and conducted by the same Respiratory Therapist (RT). The National Lung Health Education (NLHE) Program indicates that trained technicians who have considerable experience in performing spirometry are acceptable in detecting and determining changes in pulmonary function. The RT, met guidelines as suggested by the NLHE. He demonstrated an appropriate amount of training, experience, motivation, motivational skills, patience and a high number of tests performed per month.[41] The RT has been with the Patient Care Center (PCC) working under two pulmonologists and performs the majority of all pulmonary function exams. It is suggested that pulmonary function data should be interpreted with a trained physician. Although no pulmonologist was available for immediate interpretation all data was reviewed with the PI.[41]

Spirometry was conducted with the Medgraphics 1085 Series with the RT as the performing technician. The PI reviewed and assisted in analyzing all collected data. Spirometry was used to test Hypothesis 1.

Performance of spirometry requires inhalation to a maximum capacity followed by a rapid and forcible exhalation through an inhalation port, which records the amount

of airflow passing through the device. Exhalation continues until lungs are emptied for approximately six seconds or until there is no recorded volume change for one second. Plateaus are calibrated and recorded graphically in a volume/time loop. In addition to creation of a volume/time loop, a flow/volume loop is created which shows a quick expiratory time indicating adequate exhalation effort. Both loops are imperative in assessing effort, which plays a role in collection of usable data.[12]

Spirometry was performed in order to collect data on FEV1, FVC and FEV1/FVC ratio.The FEV1 measures the amount of air forcibly expired in one second and is used for determining the severity of disease. The FVC is the amount expired in six seconds or until a plateau is reached.[41] The FEV1/FVC ratio, when decreased, is typical of obstructive disorders.[14]

All subjects underwent spirometric evaluation pre-and post-intervention in an identical manner. If for some reason they were unable to complete this portion of the study, they were excluded. Data were collected by the RT.

Plethysmography was performed with the Medgraphics 1085 with the RT as the conducting technician. The PI reviewed and assisted in interpreting all collected data. Plethysmography was used to study Hypothesis 1.

Subjects were placed in a large rigid box with a built-in mouthpiece. By inducing rapid shallow breaths against the mouth-piece, small changes in pressure were generated in the box.[42] The inspiratory phase of the breathing maneuver created a volume change within the lung and subsequently reduced the volume and increased the pressure within the box. In addition, the increase in lung volume caused a decrease in the pressure found

within the airway. By using the changes in the volume of the lung and the changes in the pressure of the box and airway, the volume of the lung was calculated by using Boyle's Law.[42] This formula is described in the Diagnostic Tools section of Chapter One.

All subjects underwent plethysmography pre-and post-intervention in an identical manner. If for some reason they were unable to complete this portion of the study, they were excluded. Data were collected by the RT.

Pulse oximetry was performed with the Palco Laboratories Pulse Oximeter Model 305A with the RT as the conducting technician. The PI reviewed and assisted in interpreting all collected data. Pulse Oximetry was used to evaluate Hypothesis 2.

An oximeter probe was placed on the subject's finger sending signals calibrated in the process as described in the Diagnostic Tools Section of Chapter One. An estimate of arterial saturation was thus recorded on the screen connected to the pulse oximeter. This value was given in percentage form and was recorded pre-and post-six minute walk to give an indication of alveolar oxygenation. Values were recorded by the RT.

DATA ANALYSIS

Data in this study were analyzed using analysis of covariance, ANCOVA, as the primary method for data interpretation. For all statistical findings an α value of .05 was utilized to determine significance. Statistical tests were used in order to test the two hypotheses that guided this study: 1) OMT will improve pulmonary function parameters as measured by spirometry and plethysmography and 2) OMT will improve alveolar ventilation as measured by pulse oximetry.

SPSS

The Advanced Statistics Component of SPSS-PC^{TM} version 11.5 was used to integrate collected data for use of the following statistical tools: ANCOVA, Independent Samples T-test, Chi-square, Exploratory Data Analysis (EDA) and Cohen's D.

ANCOVA

The use of Analysis of Covariance (ANCOVA) was to reduce factors that may not be controlled for by randomization between groups, which may affect outcomes of the study. These factors are called covariates and while serving as a control value, they can also act as a variable that may influence the value of the dependent variable. The dependent variable of a study is the outcome believed to be altered by some treatment or exposure. The treatment or experimenter instrumentation implemented in the study is the independent variable, because it has the power to influence the dependent variable. Covariates in this study were pre-intervention pulmonary function and oxygen saturation values, and dependent variables were post-intervention pulmonary function and oxygen saturation value.[43]

INDEPENDENT SAMPLES T-TEST

The Independent samples t-test allows for comparison of differences between two groups that may exist even after randomization. The variables examined using the Independent samples t-test were the following: age, BMI, number of cormobidites, number of times the inhaler was used during the day measured on a weekly basis, number

of times the inhaler was used at night measured on a weekly basis, total medications as prescribed by their physician, number of smoking pack year history, number of pillows used for sleeping, baseline pulmonary function values (FVC, FEV1, FEV/FVC, FEV1 Percent Predicted, RV, TLC) and oxygen saturation.

CHI-SQUARE PROCEDURES FOR TWO DIMENSIONS OF CATEGORIZATION

A Chi-Square test of association is used when determining if two categorical variables are associated. Experimental designs may contain within them two separate dimensions that will have an impact on the outcome. For instance, a population study can be categorized into an intervention group and a non-intervention group (categorical variable one) and further categorized into males or females (categorical variable 2). If multiple categorical variables coexist simultaneously, it is considered to be cross-categorized.

If cross-categorized frequency data exists, a 2X2 contingency table can be created to analyze the data. An example of a contingency table is given below:

	Male	Female
Intervention	Counts	Counts
Non-intervention	Counts	Counts

Figure 3: 2X2 Contingency Table

To determine if the categorical variables are related, a chi square test of association is completed. A null hypothesis is automatically assumed, which states that there is no association between the two categorical variables. If there in fact does appear to be an association, the Chi Square test provides a method to determine if this could have occurred by chance alone.[43] Variables examined using the Chi-Square were gender, oxygen use, steroid use, bronchodilator use, current symptoms including cough, sputum, wheezing and shortness of breath.

COHEN'S D

Cohen's D is a statistical tool that allows for calculation of effect size. The primary use for calculating effect size in this study is to contribute to a body of literature that will make further research in this area possible with guidelines as to study expectations and provide insight into specifics of study features that may have had an impact on outcome results. In addition, it assists in computation of future sample sizes.[44] In this study, direction of change in pulmonary function and oxygen saturation values differed. The following values were expected to increase with OMT intervention: FVC, FEV1, FEV1/FVC and oxygen saturation. The following values were expected to decrease with OMT intervention: RV and TLC. The following equation gives a Cohen's d value: $d = M_1 - M_2 / \sqrt{[(\sigma_1^2 + \sigma_2^2) / 2]}$ (M=mean and σ=standard deviation). Since values in this study were expected to move in different directions, means and standard deviations were arranged to give positive values after computation to indicate a positive impact.

Specifically, post intervention values for FVC, FEV1, FEV1/FVC and oxygen saturation were used as M_1 and $\sigma=_1$, and pre-intervention values for RV and TLC for M_2 and $\sigma=_2$.

EXPLORATORY DATA ANALYSIS (EDA)

Tukey developed Exploratory Data Analysis (EDA) to investigate data in a manner that moves away from the principle of simply confirming or refuting hypotheses. With a smaller data set, like the one that was utilized during this clinical trial, it is imperative to integrate all findings in the study and not be limited by initial assumptions. By incorporating scatter plots, box plots and other descriptive statistical tools, underlying findings can be determined and thus improve on future studies.[45]

CHAPTER III

RESULTS

INTRODUCTION

Subjects for this study were recruited from January 2005 to December 2005 after approval from the University of North Texas Health Science Center (UNTHSC) Institutional Review Board was granted. During these months, 21 subjects were enrolled. Subjects were recruited from Family Medicine and Internal Medicine Clinics affiliated with UNTHSC, primarily the Patient Care Center (PCC). The flow of subjects through this study is depicted in Appendix A.

The 21 subjects accepted in the study were analyzed for results. It is important to mention that although 21 subjects were analyzed for results, one of these subjects was unable to complete pulmonary function tests and another could not complete the six minute walk. Therefore, pulmonary functions were missing on one of these subjects, and oxygen saturations were missing on the other. Both of these subjects belonged to the No Treatment Group, Group 2. The reason for retaining these subjects was based on the small sample size of this pilot study, and although all data could not be collected, these subjects were able to contribute limited data for this study as well as data for another arm of the study performed in conjunction.

Of the 21-subjects, 10 (48%) were randomized to the Treatment group (Group 1) and 11 (52%) were randomized to the No Treatment Group (Group 2).

APPROACH TO DATA MANAGEMENT AND ANALYSIS

As discussed in the Methodology section, various statistical analyses were utilized to interpret data. Few challenges exist in analyzing data. First, the sample size precludes protection against Type II Error; not finding significant data when significant data actually exists. In order to minimize Type II Error, several statistical methods were performed on the data to explore areas in which significance may be found.

DESCRIPTION OF THE SAMPLE DEMOGRAPHICS

Specific demographics were included in this study for their potential impact on outcomes. To assess these differences, a demographic questionnaire was provided to explore similarities and differences that may exist between groups. Questionnaires were administered only after IRB approval. The mean age of subjects enrolled in this study was 58.43 ±10.96 years, and subjects were found to be predominantly female (62%) and Caucasian (90%). This information can be found be in Appendix C.

Due to the different nature of the questions found within the survey, both Independent Sample t-tests and Chi-Square tests were used in analyzing demographic information to look for differences between groups.

Independent Sample t-tests were used to analyze means between intervention groups. Of the findings, no statistically significant differences were noted. These data can be found in Appendix C. The following means were explored: age, BMI, comorbidities, daytime inhaler use, nighttime inhaler use, total medications (as prescribed by physician), smoking pack year history and total number of pillows used at night.

Although no statistically significant differences were found within these data, it is important to note clinical differences in means that may impact outcomes. Of these, the mean age of those in Group 1 was 62.70 ± 11.57 while the mean age in Group 2 was 54.55 ± 9.21 years indicating an older population in the former. The pack year history in Group 1 was 48.56 ± 12.24 and 40.27 ± 24.83 in Group 2. In addition, it is also important to note that statistical significance may not have been found due to the small sample size of this study.

Chi-Square Analysis was used to analyze the following differences between intervention groups: gender, oxygen use, steroid use, bronchodilator use, current cough, current increase in sputum, current wheezing, and current shortness of breath. These data can be found in Appendix C. No statistically significant differences were found between groups.

SPIROMETRY

Hypothesis 1 relies on findings from pulmonary function studies, specifically spirometry and plethysmography. Spirometric values used for data analysis were Forced Vital Capacity (FVC), Forced Expiratory Value at one second (FEV1) and FEV1/FVC. The means ± standard deviations for spirometric values of the 21 subject set were as follows: 2.77 ± 1.05 (FVC), 1.93 ± .86 (FEV1), 69.10 ± 15.88 (FEV1/FVC), and 64.25 ± 23.59 (FEV1 percent predicted).

An Independent Samples T-test was performed to evaluate for spirometric differences existing between groups prior to intervention. Results can be found in Appendix D. None of the values were found to be statistically significant.

Although not statistically significant, three of the four values examined at baseline with spirometry (FEV1, FEV1/FVC and FEV1 Percent Predicted) tended to have poorer results indicated by lower values in Group 1when compared to Group 2. Lower values in FEV1 and FEV1/FVC indicate that this group had a higher level of pulmonary function deterioration as measured by the ability to forcibly exhale. It is also of notable importance that FEV1 values are the gold standard in measuring COPD and it's progression. A lower FEV1 Percent Predicted value indicates that this Group suffered from more severe baseline disease.

Analysis of Covariance, ANCOVA, was used to analyze data between groups after intervention. As mentioned in the Methodology section, subjects in Group 1 received 30 minutes of OMT and subjects in Group 2 received a 30-minute rest period in which they laid supine and relatively motionless. ANCOVA used pre-intervention spirometry values as the covariate, post-intervention spirometry values as the dependent variable and intervention (treatment or no treatment) as the fixed factor. The dependent variables, FVC, FEV1 and FEV1/FVC showed no significant differences between groups. Results can be found in Appendix E.

In addition comparison of mean post-intervention FEV1/FVC values 62.30 ± 15.685 for Group 1 and 66.80 ± 26.216 for Group 2 to pre-intervention means of 64.30 ± 14.55 and 73.90 ± 16.41 for Group 1 and 2 respectively was also noted.

PLETHYSMOGRAPHY

Hypothesis 1 also incorporates pulmonary function findings measured by plethysmography. Plethysmography values used for data analysis were Residual Volume (RV) and Total Lung Capacity (TLC). Baseline findings from plethysmography provided the following means on the 21 subject set sample: 3.66 ± 1.07 (RV) and 6.57 ± 1.51 (TLC).

An Independent Sample T-test was performed to evaluate for lung volume differences as measured by plethysmography to determine if any differences existed between groups prior to intervention. Results can be found in Appendix D. None of these values were found to be statistically significant. Of the baseline plethysmography values, TLC was the only value to violate Levene's Test for Equality of Variance but still gave a p value of .418 indicating non-significant findings. Although findings were not significant both TLC and RV had higher values in Group 1. This indicates that Group 1 suffered from a higher level of pulmonary inflation and air trapping when compared to Group 2.

ANCOVA was used to analyze data between groups after intervention. RV and TLC showed no significant differences and are listed in Appendix E.

PULSE OXIMETRY

Hypothesis 2 is based on information gained from the use of pulse oximetry to determine alveolar ventilation. The baseline oxygen saturation for the 21 subject set was 94.95 ± 2.26 percent.

An Independent Samples T-test was performed to evaluate for alveolar ventilation differences as measured by pulse oximetry between groups prior to intervention. Oxygen saturation values between groups were not statistically different and are depicted in Appendix D. No clinical trends were noticed between groups.

ANCOVA was used to analyze differences in post-intervention oxygen saturations and showed no significant findings. These results are shown in Appendix E.

COHEN'S D

Cohen's d is an analytical tool utilized to calculate effect sizes in regards to the outcome measures. The following outcome measures had small effect sizes (d greater than 0.0 and less than 0.2): FVC and oxygen saturation. The following outcome measures had medium effect sizes (d less than 0.8 and greater than .5): FEV1/FVC, RV and TLC. The following outcome measures had a large effect size (d greater than .8): FEV 1. This information can be found in Appendix F.

EXPLORATORY DATA ANALYSIS (EDA)

Exploratory Data Analysis (EDA) of Group 1 provided further insight into underlying trends that would have otherwise remained unnoticed with such a small sample size. Change in FEV1 was plotted against both age and FEV1 percent predicted. Results for Change in FEV1 vs. Age show a decrease in change in FEV1 with increasing age. Results for Change in FEV1 vs. FEV1 Percent Predicted show an increase in change

in FEV1 with higher initial FEV1 percent predicted values. These results are depicted in Appendix-G.

CHAPTER IV

DISCUSSION

INTRODUCTION

This study was conducted under the guidance of Scott Stoll, D.O., Ph.D., who served as the Principal Investigator. The study was supported by the Osteopathic Research Center of the University of North Texas Health Science Center.

The impact of COPD on the population is significant without entirely effective treatments available. Prevalence continues to grow, as do costs, hospitalizations, emergency room visits, and days of incapacitation. The progressive nature of this disease presents itself as physical and mental deterioration as lung function continues to decline.

As this disease does not show signs of relenting, more tools are required to combat its destructive nature. The Osteopathic profession and philosophy are suited to this type of disease as it is guided by principles that focus on the underlying cause and not simply the symptoms that are manifested by an individual inflicted with COPD. Of the tools that Osteopathy is equipped with, this study focuses on the Manipulative Medicine aspect which directs itself to normalizing anatomical and physiological abnormalities. This modality has been incompletely studied and requires investigation

and supportive literature to incorporate its use everyday in collaboration with modern day medicine.

With completion of this study, it is our hope to have demonstrated feasibility in establishing pilot data that measures the effectiveness of OMT on this population and hence encourage future studies on a larger scale that will incorporate the same principles used in this study.

SAMPLE DEMOGRAPHICS

This pilot study had a total of 21 subjects that were analyzed for pulmonary function and alveolar ventilation as measured by spirometry/plethysmography and pulse oximetry, respectively. Initial power analysis results recommended a sample size of over 500 subjects which was not feasible with time and allocation of resources. Therefore, the use of a pilot study to establish a foundation for future larger studies was utilized.

The 21 subjects recruited for this study were not entirely consistent with epidemiological findings regarding prevalence of COPD in the population. Epidemiological findings indicate that within the population there exists a preponderance of males; whereas in this study, there was a predominance of females: 62% females in comparison to 38% males with COPD. Epidemiologically, the COPD population is mostly Caucasian, which was consistent with our sample, 90.5%. Data indicate that the majority of the population with COPD is 65 years of age or older. Twenty-eight percent of the sample were aged 65 or older. This information suggests that the sample size may not be entirely representative of the general population which shows a male

preponderance and has the majority of their afflicted individuals being age 65 or older. This could potentially be resolved with an increase in sample size.

No statistically significant data were found in regards to demographics, but as mentioned briefly, it is critical not to overlook clinical findings that may have bearing on outcome results. For instance, age and pack year smoking history as analyzed by independent samples t-test, show the treatment group to be older as well as with a more severe smoking history. COPD as measured by FEV1 has been shown to progressively deteriorate with age, suggesting that subjects within Group 1 may have age related changes that were more significant than those in Group 2. In addition, smoking has been shown to be the greatest risk factor for COPD, and smoking cessation is the only current treatment that has been shown to slow yearly decline in FEV1.

Baseline pulmonary function testing showed no significant differences between groups, but of the results three of four values (FEV1, FEV1/FVC and FEV1 Percent Predicted) indicated a higher degree of impaired expiratory flow as measured by FEV1 and FEV1/FVC in Group 1. Although subjects in both groups met criteria for Stage II COPD, the overall FEV1 Percent Predicted was lower for Group 1 when compared to group 2 indicating more severe disease in this group.

Plethysmography values also showed no significant differences between groups at baseline, but had similar clinical findings that would suggest that Group 1 suffered from more extensive disease than Group 2. Both RV and TLC values were increased in Group 1 indicating a higher degree of air trapping and pulmonary inflation.

Since pulmonary function tests are considered the primary tool in diagnosing and monitoring individuals with COPD, it is important to consider clinical trends found within these samples. It appears as if subjects in Group 1 may have poorer pulmonary function as measured by spirometry and plethysmography when compared to Group 2 at baseline.

SPIROMETRY

Hypothesis 1 relied on findings from pulmonary function tests to determine whether it would be proved or disproved. ANCOVA was the primary tool used in determining if a difference was made with OMT as an intervention. No statistically significant findings were discovered with the following spirometry values: FVC, FEV1 and FEV1/FVC.

Results, however, show that there is reduction in the FEV1/FVC ratio in both groups after intervention. The rate of decrease in Group 2 is more substantial when compared to Group 1. Both subjects underwent one set of pulmonary function exams and the six-minute walk prior to attainment of these results. Since both pulmonary function exams and the six-minute walk can be considered an exerting factor, the decreased rate of decline as noticed in Group 1 after activity suggesting that OMT may have been more beneficial than rest alone.

PLETHYSMOGRAPHY AND PULSE OXIMETRY

The lack of significant findings in plethysmography and pulse oximetry values are not necessarily accurate for several reasons. First, the chance of having Type II Error in a study with small sample sizes is high. This suggests that although significant findings were not attained, extreme caution should be taken in accepting the Null Hypothesis, and further studies should be conducted in order to correct for the limitations found within this study. In addition, trends should also be noted and utilized in future study designs.

COHENS D

Effect sizes, as computed by Cohen's D calculations, allow for future estimates for sample sizes required to generate statistically significant data. Small effect sizes (FVC and oxygen saturation) indicate large future sample sizes. Medium effect sizes (FEV1/FVC, RV and TLC) indicate a medium sample size for future studies. Large effect sizes (FEV1) indicate a smaller sample size for future studies to obtain statistically significant data.

EXPLORATORY DATA ANALYSIS (EDA)

With small sample sizes, like the one utilized in this study, it is critical to explore data for underlying findings that will otherwise go unnoticed. Analysis of demographics showed general trends indicating that Group 1 was older and had a higher average smoking history, two important factors in the progression of COPD. In addition, their baseline pulmonary function tended to demonstrate increased impedance in expiratory

flow. With these baseline trends, changes in FEV1 in respect to age and initial severity of disease as measured by the FEV1 percent predicted value were explored. Results indicate the older a subject was the less change was induced with OMT as measured by spirometry. The more significant disease present in a subject (lower FEV1 percent predicted values), the less effect OMT had as measured by pulmonary function. Theoretically, these findings are not unexpected, as this disease has a progressive nature. In addition, tissue elasticity is reduced with increasing age indicating that they may be less responsive to OMT than younger tissues. Also, it is important to realize that as a body adjusts to chronic conditions, it may take longer to reduce structural dysfunction that has been present for longer periods when compared to dysfunction that has been there for less time. There are no current treatments that reverse the decline in FEV1 yearly, so the older an individual gets, the more significant the disease is expected to become. With the irreversible destruction of lung parenchyma, these data suggest that a younger and less afflicted population may benefit more from OMT as measured by pulmonary function.

LIMITATIONS

Limitations of this study need to be explored in order to fully understand the data collected.

One of the most limiting factors was the number of subjects. The number calculated from power analysis was beyond the scope of this study; therefore, a smaller pilot study was designed in effort to determine feasibility of future larger studies and

collect data supporting this endeavor. Data collected from pilot studies run a higher risk of Type II error, not finding statistical significance when in fact it does exist. In addition to reducing the number of subjects recruited to accommodate this study's limited resources, the estimated number of 50 subjects was not reached further reducing the sample size to be analyzed. Several factors contributed to not reaching the desired goal of 50 subjects including: subject ineligibility based on exclusion criteria, failure of subjects to maintain scheduled interventions, limited recruiting facilities, equipment failure, delayed documents and limited time in which recruiting occurred.

In addition to a small sample size, recruiting measures were limited to certain resources, specifically the UNTHSC system. Academic centers, such as this one, may have a larger population that participates in research studies. In addition, most enrolled subjects were recruited by the Research team and did not actively seek out this study thus potentially affecting randomization.

This study was conducted with five Pre-Doctoral Fellows as treatment providers. Although all providers were Pre-Doctoral Fellows who underwent identical training, variability in technique and style may have had an impact of unknown significance with the small sample size of this study. In addition, the level of training may have varied between treatment providers.

OMT is a tool utilized by physicians to target dysfunction at various parts of the body. Physicians, when incorporating OMT in their practice, tailor their treatment plan to specific areas that require addressing. The OMT protocol designed for this study utilized techniques that have been studied in this population as well as techniques that based on

their theorized mechanism of action should have an impact on pulmonary function. However, this does not eliminate the fact that specific areas may suffer from more significant anatomical and physiological changes that require addressing in the individual subject. No time was allocated in the OMT protocol to address these, hence limiting the provider to predetermined sites of dysfunction and possibly decreasing potential treatment efficacy.

Pulmonary Function Tests, including spirometry and plethysmography, are effort dependent on part of the subject. Both exams require the subject to be cooperative and follow instructions explicitly. Although the RT has some indication as to whether or not the subject has successfully accomplished their goal, there is limited knowledge as to whether or not full effort was exerted. Since each subject may demonstrate different levels of effort when performing pulmonary function exams, small differences between subjects effort can have a significant impact on outcome measures, particularly with small sample sizes.

In addition, pulmonary function equipment was not always available for operation. There was an approximate six week period when equipment was being serviced and unavailable for use for this study. This was a crucial time for recruitment and enrollment of subjects, and thus served as a limiting factor to this study.

Few studies like this one exist. In fact, there is only one study that was a randomized, prospective, double-blinded controlled study performed by Dr. Noll. This study also has yet to be published, and important findings may not yet be revealed, as the only literature regarding this study is contained within an abstract. With these limits, it

was difficult to design a study based on current literature. In addition, limited knowledge is available as to specific epidemiological statistics as the disease is difficult to define and diagnose until it has progressed to later stages.

CONCLUSIONS AND FUTURE CLINICAL STUDIES

No conclusive statements can be made regarding the efficacy of OMT on pulmonary function and alveolar ventilation on the COPD population because of small sample size. Trends indicate a possible therapeutic effect with OMT as an adjunct treatment modality for this population and need to be investigated further.

Future studies need to address the limitations encountered during the course of this study. Emphasis needs to be placed on the most limiting factor, low enrollment numbers. The focus of future studies should be guided by the clinical trends that were revealed by exploratory data analysis. Of these clinical trends, an area that perhaps should be further explored is the impact of OMT on a younger COPD population because of possible less impairment in pulmonary function as measured by spirometry and plethysmography. Given the progressive destructive nature of this disease, it could be theorized that a younger less severely impaired sample may benefit more from OMT. In addition the benefit of OMT on sample set with a lower smoking pack year history should be investigated. The link between smoking and COPD has clearly been demonstrated to accelerate the course of disease and therefore should be more thoroughly examined.

LIST OF APPENDICES

APPENDIX A

Flow of Subjects Through Study

APPENDIX A

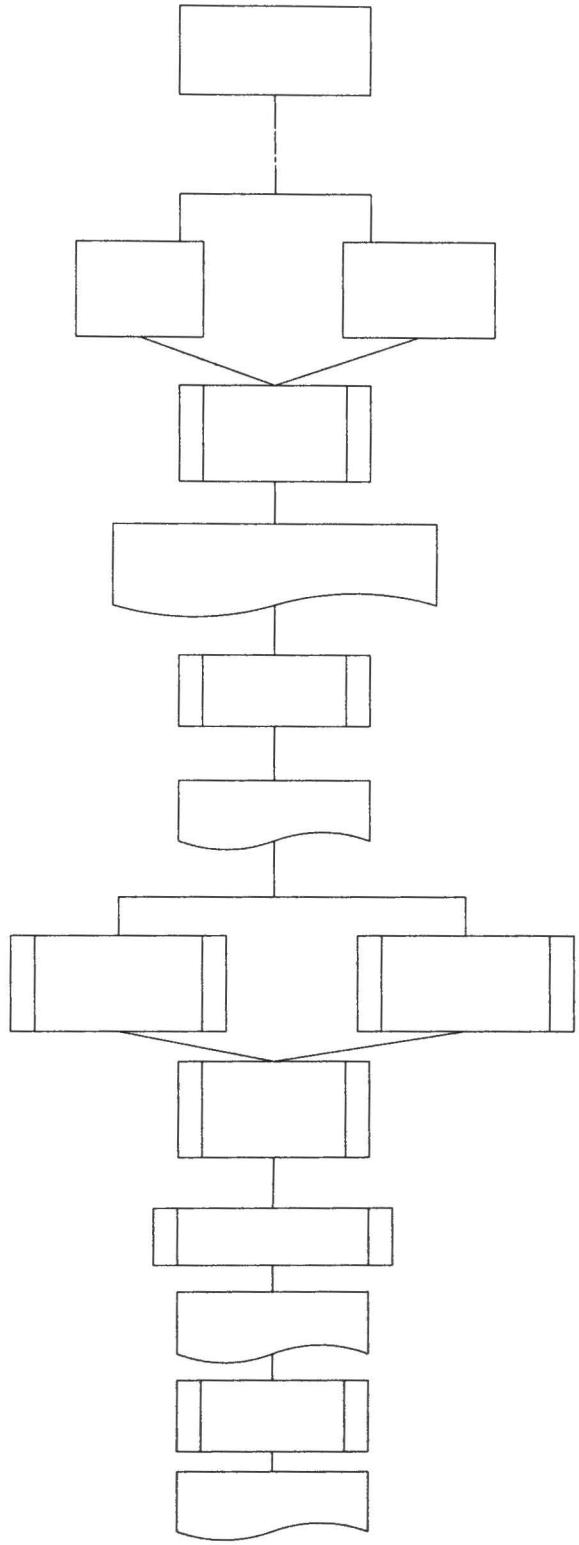


Figure 2: Flow of Subjects Through Study

APPENDIX B

OMT Protocol

APPENDIX B

OMT Protocol – COPD Population

Dose: The duration of the OMT treatment session will not exceed 30 minutes.
Frequency of Treatment: Subjects in treatment group will undergo 1 treatment session.

Subject's Position: All techniques will be performed with the subject supine on the table, unless the patient has difficulty breathing, in which case techniques will be performed with subject sitting.

Note to Providers: Individualization is allowed to increase efficacy. Individualization will include treating what you feel and assessing patient response to specific areas/procedures. When given the option between techniques base your decision on patient's age, ability to relax, and cooperation level.

1. **OA Decompression – approx. 2 min.**
   Superior and cephalad traction will be applied to decompress the joint.
2. **Cervicals – approx. 6 min. (2 min for each a,b,c)**
   a. Accessory muscles of breathing (scalenes)
      Muscle energy: Operator places one hand on shoulder of patient and with other hand the parietal bone is contacted. Scalenes are stretched to barrier, subject is instructed to bring head to midline.
   b. Specific regional dysfunction:
      i. Soft Tissue: Kneading and massaging
      ii. High Velocity/Low Amplitude (HVLA)
      iii. MFR
   c. Sibson's fascia (1 of 2 techniques)
      i. Fingers are placed behind the clavicle bilaterally and brought to a point of balanced ligamentous tension.
      ii. One hand grasps over the clavicle and fingers progress behind the clavicle to the point of fascial tension. The other hand grasps above the subjects elbow and traction is applied inferiorly.
3. **Thoracics/Ribs – approx. 10 min. (5 min. for each a,b)**
   a.. Thoracics
   1) Specific regional dysfunction – MFR, ME or HVLA

b. Ribs (1 and/or 2, and 3)
   1) Lateral recumbent springing:
   Patient lies lateral recumbent with arm abducted over head. Using thumb and index finger, operator creates a horseshoe shape and springs on ribs medially.
   2) Rib Raising – patient supine
   3) MFR – specific ribs

4) 4. Diaphragms – approx. 3 min.

a. Thoracoabdominal (1 of 2 techniques)

1) Doming the diaphragm - bilateral supine
2) AP Central MFR

5. Pumps - approx. 3 min.

a. Thoracic pump

Pedal Pump

APPENDIX C

21 Subject Set Population Demographics

APPENDIX C

21 Subject Set Population Demographics

21 Subject Set Sample Mean Ages

	Age
Mean	58.43
Standard Deviation	10.957

21 Subject Set Sample Percentages by Gender and Race

	Male	Female	Caucasian	Hispanic	African American
Percent	38.1%	61.9%	90.5%	4.8%	4.5%

Demographics Independent Samples T-Test

	Randomization Group	N	Mean	Standard Deviation	Significance
Age	T N	10 11	62.70 54.55	11.57 9.213	.088
BMI	T N	10 10	29.65 31.14	7.81 10.05	.716
Total Comorbidities	T N	10 11	1.50 2.09	1.18 1.81	.393
Inhaler use during day	T N	10 11	20.40 19.18	14.40 14.63	.850
Inhaler use during night	T N	10 11	3.10 3.18	6.65 8.35	.981
Total Meds	T N	8 9	6.00 8.00	3.78 3.12	.251
Smoking Pack Year History	T N	9 11	48.56 40.27	12.24 24.83	.374
Pillows used at night	T N	8 11	1.75 2.09	.89 .95	.433

Demographics Chi-Square Analysis

	Randomization	N	df	Chi Square	Significance
Male	T	5	1	1.147	.387
	N	3			
Female	T	5			
	N	8			
Oxygen Use	T	2	1	.153	1.000
	N	3			
No Oxygen Use	T	8			
	N	8			
Steroid Use	T	3	1	.019	1.000
	N	3			
No Steroid Use	T	7			
	N	8			
Bronchodilator Use	T	10	1	.955	1.000
	N	10			
No Bronchodilator Use	T	0			
	N	1			
Current Cough	T	7	1	.403	.635
	N	9			
No Current Cough	T	3			
	N	2			
Current Increase in Sputum	T	3	1	.531	.659
	N	5			
No Current Increase in sputum	T	7			
	N	6			
Current Wheezing	T	7	1	.403	.635
	N	9			
No Current Wheezing	T	3			
	N	2			
Current Shortness of Breath	T	9	1	.286	1.000
	N	9			
No Current Shortness of Breath	T	1			
	N	2			

* Fisher's Exact Test was utilized if an expected cell count was < 5

APPENDIX D

Between Group Baseline Pulmonary Function and Oxygen Saturation

APPENDIX D

PULMONARY FUNCTION BASELINE DIFFERENCES

Spirometry Values Pre-Intervention Independent Samples T-test

	Randomization	N	Mean	Standard Deviation	df	Significance
FVC	T N	10 10	2.86 2.67	1.03 1.11	18	.687
FEV1	T N	10 10	1.82 2.04	.61 1.08	18	.577
FEV1/FVC	T N	10 10	64.30 73.90	14.55 16.41	18	.183
FEV1 Percent Predicted	T N	10 10	58.70 69.80	18.46 27.67	18	.305

Plethysmography Values Pre-Intervention Independent Samples T-test

	Randomization	N	Mean	Standard Deviation	df	Significance
RV	T N	10 10	3.83 3.49	1.09 1.09	18	.489
TLC	T N	10 10	6.85 6.29	1.80 1.18	18	.418

Pulse Oximetry Values Pre-Intervention Independent Samples T-test

	Randomization	N	Mean	Standard Deviation	df	Significance
O2 Saturation	T N	10 10	95.20 94.70	2.30 2.31	18	.634

APPENDIX E

Between Group Post-Intervention Pulmonary Function and Oxygen Saturation

APPENDIX E

PULMONARY FUNCTION POST INTERVENTION

ANCOVA Spirometry Values

	DV 1	DV 2	C 1	C 2	df	F	Significance
FVC	2.88 ± 1.10	2.68 ± 1.12	2.86 ± 1.03	2.67 ± 1.11	1	.001	.980
FEV1	1.75 ± .59	2.03 ± 1.05	1.82 ± .61	2.04 ± 1.08	1	1.860	.190
FEV1/FVC	62.30 ± 15.69	66.80 ± 26.21	64.30 ± 14.55	73.90 ± 16.41	1	.355	.559

ANCOVA Plethysmography Values

	DV 1	DV 2	C 1	C 2	df	F	Significance
RV	3.83 ± 1.19	3.13 ± 1.26	3.83 ± 1.09	3.49 ± 1.09	1	1.136	.301
TLC	6.90 ± 1.92	5.77 ± 1.211	6.85 ± 1.80	6.29 ± 1.18	1	2.218	.155

ANCOVA Pulse Oximetry Value

	DV 1	DV 2	C 1	C 2	df	F	Significance
O2 Saturation	92.90 ± 4.93	93.70 ± 2.67	95.20 ± 2.30	94.70 ± 2.31	1	.305	.588

*Dependent Variable (DV): Post-Intervention Values
*Covariate (C): Pre-Intervention Values
* 1 indicates Group 1 receiving 30 minutes OMT
* 2 indicates Group 2 receiving no treatment for 30 minutes

APPENDIX F

Cohen's D

APPENDIX F

COHEN'S D Effect Size

FVC_s	OMT Intervention	Rest Period
Means	.0150	-.0222
Standard deviation	.24990	.14351
Cohen's d	.1826 (small effect size)	

FEV1	OMT Intervention	Rest Period
Means	-.0650	-.0356
Standard Deviation	.10190	.06710
Cohen's d	-1.166 (large effect size)	

FEV1/FVC	OMT Intervention	Rest Period
Means	-2.000	-7.5556
Standard Deviation	5.5176	23.054
Cohen's d	.33 (medium effect size)	

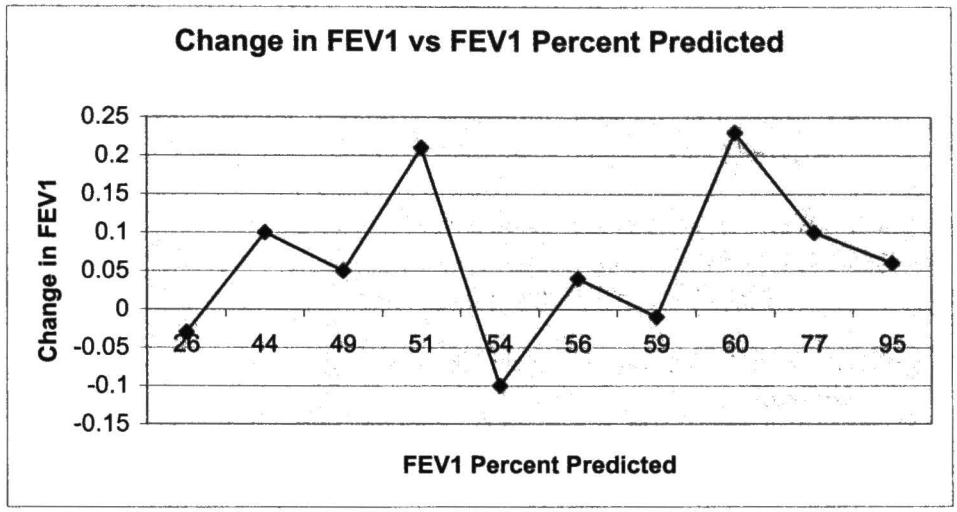
RV	OMT Intervention	Rest Period
Means	-.0050	.3100
Standard Deviation	1.04266	.74064
Cohen's d	-.348 (medium effect size)	

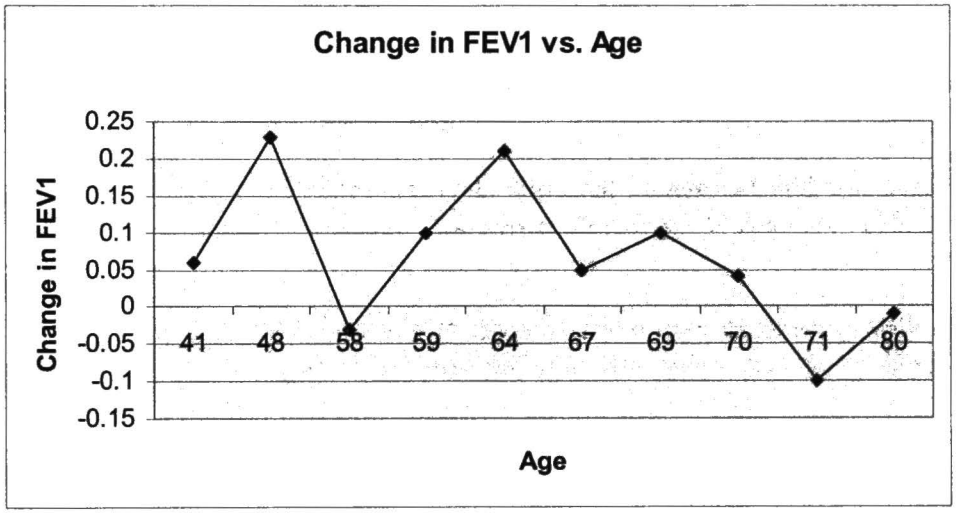
TLC	OMT Intervention	Rest Period
Means	-.0470	.4579
Standard Deviation	1.07966	.81122
Cohen's d	-.529 (medium effect size)	

O_2 Saturation	OMT Intervention	Rest Period
Means	-.4000	-.1111
Standard Deviation	.51640	1.96497
Cohen's d	-.201 (small effect size)	

APPENDIX G

Exploratory Data Analysis Group 1


Change in FEV1 vs FEV1 Percent Predicted
Change in FEV1
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
26
44
49
51
54
56
59
60
77
95
FEV1 Percent Predicted


Change in FEV1 vs. Age
Change in FEV1
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
41
48
58
59
64
67
69
70
71
80
Age

REFERENCES

1. Pauwels RZ, Buist S, Calverley, P.M.' Jenkins, C.R., Hurd SS. Global strategy for the diagnosis, managment and prevention of chronic obstrutice pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 2001;163:1256-1276.

2. Pride NB, Verveire P, Allegra L. Diagnostic labels applied to model case histories of chronic airflow obstruction: Response to questionnaires in 11 north american and western european countries. *European Respiratory Journal*. 1989;2:702-709.

3. National Institutes of Health, National Heart, Lung and Blood Institute. Chronic Obstructive Pulmonary Disease Available at: http://www.nhlbi.nih.gov/health/public/lung/other/copd_fact.pdf2006.

4. Mannino DM, Grown C, Giovinio GA. Obstructive lung disease deaths in the united states from 1979 through 1993: An analysis using multiple cause mortality data. *American Journal of Respiratory and Critical Care Medicine*. 1997;156:814-818.

5. Murray CL, Lopez AD. Evidence-based health policy lessons from the global burden of disease study. *Science*. 1996;274:740-743.

6. Siafakas NM, Vermieire P, Pride NB, et al. Optimal assesment and management of chronic obstructive pulmonary disease. *European Respiratory Journal*. 1995;8:1398-1420.

7. American Thoracic Society. Standards of diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. *American review of Respiratory Disease*. 1987;136:225-244.

8. Snider GL, Kleinerman J, Thurlbeck WM, Bengali ZH. The definition of emphysema: Report of national heart and blood institute, divison of lung disease, workshop. *American Review of Respiratory Disease*. 1985;132:182-185.

9. Medical Research Council. Definition and classification of chronic bronchitis, clinical and epidemiological purposes: A report to the medical research council by thier committee on the etiology of chronic bronchitis. *Lancet*. 1965:775-780.

10. Naeije F, Joan B. Pulmonary hypertension associated with COPD. *Critical Care*. 2001;5:286-289.

11. Mooten SE. Pulmonary lymphatics in relation to pulmonary clearance of interstitial fluids and their possible implication in the pathogenesis of emphysema. *Mt Sinai Journal of Medicine*. 1974:412-429.

12. Barriero TJ, Perillo I. An approach to interpreting spirometry. *American Family Physician*. 2004;69.

13. Crapo RC. Current concepts: Pulmonary function testing. *The New England Journal of Medicine*. 1994;1:25-30.

14. Evans, S.E.' Scanlon, P.D. Current practice in pulmonary function testing. *Mayo Clinic Procedures*. 2003;78:758-763.

15. Coates AL, Peslin R, Rodenstein D, Tocks J. Measurement of lung volumes by plethysmography. *European Respiratory Journal*. 1997;10:1415-1427.

16. Burrows G, Earle RH. Course and prognosis of chronic obstructive lung disease. A prospective study of 200 patients. *New England Journal of Medicine*. 1969;280:397-404.

17. Berne MR, Levy NM. *Principles of Physiology*. Third ed. St. Louis: C.V. Mosby; 1999.

18. Martin L. *All You really Need to Know to Interpret Arterial Blood Gases*. 2nd Edition ed. Lippincot Williams and Wilkins; February 1999.

19. Grippi MA. *Pulmonary Pathophysiology*. Philadelphia: JB Lippincott Company; 1995.

20. Jubran A. Pulse oximetry. *Critical Care*. 1993;3:R11-R17.

21. Barnes PJ. Approaches and targets of treamtment of chronic obstructive pulmonary disease. *American Journal of Respiratory Medicine*. 1999;160:S72-S79.

22. Hurt RD, Sachs DP, Glover E, et al. A comparison of sustained-release buproprion and placebo for smoking cessation. *The New England Journal of Medicne*. 1997;337:1995-1202.

23. Keatings VM, Jatakanon A, Worsdell YM, Barnes PJ. Effects of inhaled and oral glucocorticoids on inflammatory indices in asthma and COPD. *American Journal of Repiratory and Critical Care Medicine*. 1997;155:542-548.

24. National Emphysempa Treatment Trial. A randomized trial comparing lung-volume-reduction surgery with medical therapy for sever emphysema. *New England Journal of Medicine*. 2003;348:2059-2073.

25. Patterson M. Introduction. in: Ward, CX. foundations of OSteopathic medicine. In: ; 1997:24-26.

26. Willard FH. Autonomic nervous system. in: Ward, C. foundations of osteopathic medicine. In: ; 1997:53-80.

27. Towns LC. Rules of anatomy. in: Ward, C. foundations of osteopathic medicine. In: ; 1997:53-80.

28. Jacobs AH, Falls WM. Anatomy. in: Ward, C. foundations of osteopathic medicine. In: ; 1997:27-43.

29. Levi-Orzozco M. Structure and function of the respiratory muscle in patients with COPD: Impairment or adaptation? *European Respiratory Journal.* 2003;22:41S-51S.

30. Ganong WF. *Review of Medical Physiology.* Norwalk: Appleton & Lange; 1993.

31. Stile E. Chronic obstructive pulmonary disease. *Osteopathic Medicine.* 1976:60-63.

32. Shinick JP. Chronic obstructive pulmonary disease-an overview. *Journal of American Osteopathic Association.* 1981;80:s862-s865.

33. Nauser TD, Stites SW. Diagnosis and treatment of pulmonary hypertension. *American Family Physican.* 2001;63.

34. Bockenhauer SE, Lo KS. Quantifiable effect of osteopathic manipulative techniques on patients with chronic asthma. *Journal of American Osteopathic Association.* 2002;7.

35. Gray H. *Anatomy of the Human Body.* 29th ed. Philadelphia: C.M. Goss; 1973.

36. Noll DD, Degenhardt BF, Johnson JC, Burt SA. The immediate effect of OMT on pulmonary function parameters in obstructive pulmonary disease. an abstract. *Journal of American Osteopathic Association.* 2002;12.

37. Howell RK, Allen TW, Kappler RE. The influence of osteopathic manipulative therapy in the managment of patients with chronic obstructive lung disease. *Journal of American Osteopathic Association.* 1975;74:757-760.

38. Mall R. An evaluation of routine pulmonary function tests as indicators of responsiveness of a patient with chronic obstructive lung disease to osteopathic health care. *Journal of American Osteopathic Association.* 1973;73:327-333.

39. Sleszynski SL, Kelso AF. Comparison of thoracic manipulation with incentive spirometry in preventing postoperative atelectasis. *Journal of American Osteopathic Association.* 1993;93:834-845.

40. Eeshleman J, Myers S, Pantle P. Measurement of changes in blood volume as a result of osteopathic manipulation. *Journal of American Osteopathic Research.* 1971;70:1073-1079.

41. Ferguson, GT., Enright, PL., Buist, SA, Higgins MW., Office Spirometry for Lung Health Assessment in Adults. *Chest.* 2000; 117:1146-1161.

42. West, JB. The birth of clinical body plethysmography: it was a good week. *Journal of Clinical Investigation.* 2004; 114:1043-1045.

43. Lowry, Richard. *Concepts of Applications and Inferential Statistics*. 2005

44. Wilkinson & APA Task Force on Statistical Inference, 1999

45. Tukey, J. Exploratory data analysis, 1977, Addison-Wesley.