REVIEW ARTICLE

Osteopathic Considerations in Obstructive Pulmonary Disease: A Systematic Review of the Evidence

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OMM

Background: Since Dr. Still developed osteopathic philosophy many physicians have utilized osteopathic manual medicine (OMM) to treat respiratory disorders and have reported their results in case studies and research projects. With the increasing emphasis on utilizing medical interventions supported by patient-oriented outcomes, it is imperative to evaluate the current evidence regarding the use of OMM in the treatment of respiratory illnesses. The aim of this study is to review the existing evidence regarding the utilization of OMM, specifically in the treatment of patients with chronic obstructive pulmonary disease (COPD). **Method:** In order to perform a review of the existing evidence, comprehensive literature search was conducted to identify investigative studies which enrolled subjects having a diagnosis of COPD and incorporated OMM as an intervention. Articles were chosen based on those containing relevant content and were evaluated for risk of bias using a standardized tool. **Results**: Nine studies met the inclusion criteria and were reviewed for this paper. Overall, incorporating OMM into the treatment of COPD demonstrated inconsistent impact on objective pulmonary measures but when patient assessment of symptoms was included, improvement was noted. **Conclusion**: Current evidence demonstrates inconsistent findings regarding the efficacy of OMM in patients with COPD. Considering that clinical case studies and practice experience suggest this modality provides symptomatic improvement, we encourage researchers to conduct larger studies that minimize bias, incorporate patient-oriented measures, and evaluate the effect on acute exacerbations as the next steps to build the body of evidence regarding the utilization of OMM in COPD.

INTRODUCTION

Since the earliest writings of Andrew Taylor Still, MD, DO, osteopathic literature has included case reports, study proposals, and research articles assessing efficacy in treating respiratory illnesses.[1-5] Case reports have focused on somatic manifestations of respiratory disease, the role of anatomy and physiology in respiratory illness and the utilization of osteopathic manual medicine (OMM) to improve function as well as facilitate patient recovery. Investigations have evaluated the effect on recovery from infectious etiologies[3;6-9] and improvement of pulmonary function in obstructive lung diseases.[10-13]

Chronic obstructive pulmonary disease (COPD) is characterized by a chronic limitation in airflow that is progressive and not fully reversible. It is caused by a chronic inflammatory response to noxious stimuli, including but not limited to tobacco use, and resulting in parenchymal destruction and airway disease. The pathologic changes lead to air trapping and air flow limitation causing breathlessness and other classic COPD symptoms.[14] It represents the third leading cause of death in the United States[15] and fourth leading cause worldwide.[14] In addition to its role in mortality, the morbidity associated with the disease includes decreased exercise capacity and tolerance, as well as the direct and indirect costs of all medical interventions and decreased productivity in the workforce. The challenges that arise when treating the disease take a toll on the patient, the health care system, and the economy. When combined with interventions that impact the disease, such as tobacco cessation, utilization of OMM not only has the potential to slow progression, but to also improve patient functionality and healthcare costs.

When attempting to demonstrate the efficacy of OMM in treating COPD, most investigators consider evaluation and treatment of body regions highly associated with somatic manifestations of pulmonary disease, mainly in the thoracic and cervical regions as well as the ribs and diaphragm. Case reports and investigational studies have shown a correlation in somatic regions associated with viscerosomatic and somatosomatic reflex patterns related to both sympathetic and parasympathetics innervations (Figure 1).[1;2;16-17] Specifically, viscerosomatic changes related to parasympathetic innervation occur at the base of the occiput where the vagus nerve exits the cranium, somatic findings in the upper thoracic region represent changes related to the sympathetic innervation of the lungs, and the classic findings of somatic dysfunction in the region of C3-5 follows with the somatosomatic reflex pattern related to innervation of the diaphragm. Flattening of the respiratory diaphragm, rib restrictions, decreased thoracic compliance, and thoracic outlet obstruction all result from air trapping and decreasing motion of the thoracic cavity as COPD progresses.

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FIGURE 1:
Common somatic dysfunctions noted in obstructive lung disease

Cervical Region	• Suboccipital, scalene hypertonicity • OA, AA dysfunction • C3,4,5 dysfunction
Thoracic Region	• Restrictions in thoracic outlet • Hypertonicity paravertebral musculature T2-7 • Motion restrictions T2-7 • Decreased thoracic compliance, barrel chest
Rib & Other Regions	• Inaled ribs 1,2 affecting thoracic outlet • Motion restriction in ribs 5-8 • Flattened respiratory diphragm • Elevated shoulders/clavicles • Sacral extension

OA: Occipito-atlantal; AA: Atlanto-axial

The body of evidence related to OMM in COPD shows frequent discussion of regional somatic dysfunction without noting types of dysfunction present. Similarly, when case reports and studies mention OMM, some specific techniques are mentioned (thoracic pump, rib raising, doming the diaphragm), but the discussion mainly focuses on the body areas treated (Figure 2). One of the ongoing challenges associated with OMM research is determining the efficacy of an individual technique versus the impact of normalizing somatic function on the disease being evaluated.

When reviewing studies focused specifically on utilization of OMM in COPD, the predominant theory noted was utilizing OMM to decrease chest wall rigidity to improve pulmonary function tests (PFT) and in turn symptoms. Despite lacking overwhelming evidence of improved PFT results, a disease-oriented measure, a consistency is noted in subjective patient improvement. When considering the importance of patient-oriented evidence, subjective improvement in exercise tolerance and work of breathing continue to inspire investigators to explore reasons why this improvement occurs. It is the purpose of this systematic review to summarize the available evidence regarding the manifestations of COPD on the soma, and the effect of OMM on COPD.

METHODS

The objective was to perform a systematic review of the published literature on the effects of OMM in COPD.

Studies were included for review based on the following criteria: participants had a diagnosis of COPD, and use of OMM or a manipulative treatment whose description was found to be similar to OMM and would likely produce similar results. The intervention was compared to either standard care, sham manipulation, minimal touch control or patient's pretreatment baseline. The outcome measures included the effects of OMM on one or more of the following: PFTs, exercise capacity, and subjective reporting of symptoms. Ideal study design would be randomized controlled trials (RCT), however a review of the literature showed a small number of studies available and therefore other study designs were included.

A literature search was conducted using PubMed, IndexCat, OSTMED.DR, Cochrane Central Register of Controlled Trials, Google Scholar, Google Advanced, clinicaltrial.gov and TRIP database in order to identify articles for the purposes of this review. The following search terms or MeSH headings were used: manipulation, osteopathic, manipulation, spinal, lung, pulmonary disease, chronic obstructive, respiratory function test, respiratory tract disease, OMT, OMM, and COPD. The dates searched were from database inception through July 2015. Initial search results were filtered for relevance, according to our inclusion criteria, by the hospital librarian and the reviewers and the subsequent remaining articles were reviewed by two investigators. The bibliographies from relevant articles were scanned and hand searched for additional articles that met inclusion criteria.

Data was extracted using a standard table that included author, year of publication, country, study design, population inclusion criteria, participants, interventions, controls, outcomes measured, main findings, adverse effects, dropouts, comments, and limitations.

Risk of bias in individual studies

Risk of bias was accessed using the Cochrane Collaboration's tool. Individual studies were rated as having a low, high, or unclear risk of bias in the following categories: random sequence generation, allocation concealment, blinding of participants and personnel, incomplete outcome data, selective reporting and other potential sources of bias.[18]

FIGURE 2:
Techniques studied in COPD

Cervical Region	• Suboccipital release • Soft tissue • Mobilization
Thoracic Region	• Thoracic outlet release • Spinal inhibition • Increase thoracic compliance • Mobilization • Chapman's point inhibition
Rib & Other Regions	• Rib raising • Thoracic pump • Doming the diaphragm

RESULTS

Study selection

Initial search of databases was performed by the Wilkes-Barre General Hospital librarian as well as additional records identified by the researchers. Initial filter of results was performed by the hospital librarian. 282 records were reviewed by two researchers. After duplicates, records not studying COPD, records not utilizing OMM or a manipulation technique described similar to OMM, nine studies were included in the systematic review.

Characteristics of studies

The included studies originated from four different countries: four studies from the United States,[16-17;19-20] two studies from Australia,[21-22] two studies from India,[23-24] and one study from Italy.[25] Five of the studies were randomized controlled trials (RCTs), including one crossover RCT. There was one cross sectional study, two pre-test / post-test design, and one randomized cohort study. Three of the studies utilized a sham or minimal touch control.[19-20;25] Three studies had no control group.[16;13;21] Three studies included a control of a standard therapy whether it be a standard pulmonary rehabilitation program or standard medical treatment.[17;22;24] There were a variety of age ranges of included participants and severity of COPD was defined in the inclusion criteria for three of the nine studies.

Seven of the nine studies utilized an intervention that included a single or multiple OMM sessions.[16-17;19-20;23-24] Two of the studies utilized soft tissue, and spinal manipulation interventions with a descriptions that was similar to OMM treatments.[21-22] All studies measured pulmonary function tests as an outcome. Five of the studies collected subjective reports of symptoms either by phone survey or questionnaire.[17;19-22] Three studies measured exercise capacity utilizing the 6 minute walk test.[21-22;25] The specific characteristics of the included studies are presented in Table 1 *(page 32 - 35)*.

Risk of Bias Assessment

Risk of bias for included studies is summarized in Figure 3 (Review Manager version 5.3).[26]

Random sequence generation

Of the nine studies reviewed, five adequately described their method of randomization.[17;20-22;25] Noll et al 2008 stated that they utilized stratified randomization based on disease severity but did not provide a complete description of the randomization process.[19] Mascarenhas et al also did not provide a description of their randomization method.[24] Both Howell et al 16 and Bhilpawar & Arora[23] used a pre-post test design with nonrandomized sampling.

Allocation concealment

Three studies utilized sealed opaque envelopes to conceal allocation[20-22] and one study described the allocation sequence being downloaded, sealed and concealed by an investigator that did not have any clinical involvement. This investigator kept the sequence locked in a room and sequentially assigned patients based on the assignment schedule.[25] Three studies did not describe allocation concealment.[17;19;24] The remaining two studies were non-random pre-posttest design and subject to selection bias.[16;23]

Blinding of participants and personnel

Due to the nature of OMM treatments, it was not possible for the personnel providing the treatments to be blinded. Most studies did not provide a description of participant or personnel blinding therefore the risk of bias was unclear.[17;19;21-22;24] Three studies[16;20;23] did not blind participants. Zanotti et al[25] felt that their patients were adequately blinded and were not able to determine their treatment group.

Blinding of outcome assessment

Five studies provided an adequate description of blinding of personnel involved in assessing the outcome measures.[19-22;25] The remaining four studies did not provide this information.[16-17;23-24]

Incomplete outcome data

Three studies accounted for all outcome data and performed intention to treat analysis.[21-22;25] Two studies did not account for all the participants' data in their outcome analysis.[16-17] Four studies either did not report drop outs or information insufficient to determine if there was an effect on the outcomes.[19-20;23-24]

Selective reporting

Study protocols were not available so there was insufficient information to judge bias.

Other bias

Five studies declared funding sources.[16;19-22] Appropriate information regarding conflict of interest was provided for six studies.[19-23;25] Ethical approval and informed consent was described in all studies except Miller[17] and Howell et al.[16]

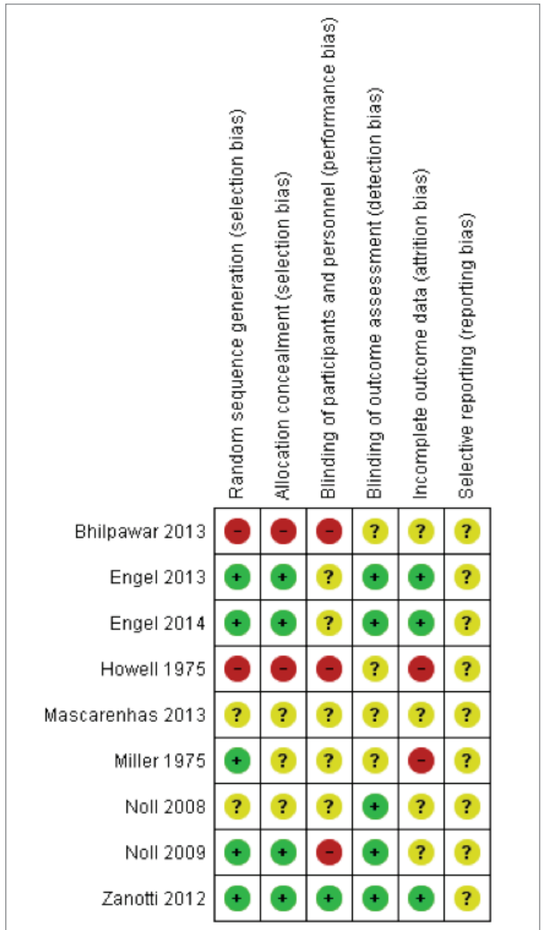
STUDY RESULTS

An overview of the main findings of each study as well as reporting of adverse effects, drop outs and other comments or limitations pertaining to each study is provided in Table 2 *(page 34 - 39)*. All studies used some form of pulmonary function tests as an outcome measure. Some studies also collected participant subjective data and/or assessment of exercise tolerance. There were varying results for PFT outcomes. Mascarenhas et al[24] did not demonstrate a significant difference in testing between the intervention group who received one five minute session of thoracic lymphatic pump (TLP) without activation plus ten minutes of salbutamol nebulization and the control group which only received the nebulization treatment. Both groups showed a significant improvement in vital capacity (VC), forced vital capacity (FVC), forced vital capacity in the first second (FEV1), and their FEV1/FVC ratio from pre to post testing. Miller[17] performed a RCT of 44 patients with COPD and found no significant difference in PFTs between the treatment and control group however some trends showing increase in residual volume (RV), Mean VC, total lung capacity (TLC) and FEV1 and decrease in partial pressure of carbon dioxide (PCO2) for the OMM group were noted. There were no description of dropouts and not all participants were accounted for in the data analysis.

Noll et al (2008)[19] studied 35 patients over age 65 with COPD and compared a single 20-minute session of seven standard OMM techniques to a sham protocol. They also received treatment of specific somatic dysfunction that was found on structural exam. The results revealed an increase in RV, TLC and the ratio of those

FIGURE 3:

Risk of bias for included studies



+, low risk of bias, -, high risk of bias,?, unclear risk of bias

values for the OMM group compared to the sham treatment group. The results suggested a worsening of air trapping in the OMM group when assessed 30 minutes after the treatment sessions compared to the sham group. Subsequently, Noll et al (2009)[20] studied the effect of single OMM treatments and minimal touch on PFTs of patients 50 years or older in a crossover randomized controlled trial. They hoped to demonstrate the effects seen from individual OMM techniques compared with a multi-technique protocol. The results showed that there were varying changes to PFTs for the different techniques. However in all four OMM groups there was a worsening of PFTs post-treatment (*Table 2, pages 34 - 39*).

Two studies utilized a pre-posttest design. Bhilpawar & Arora[23] utilized a pre-posttest design with no control group to study 30 COPD patients selected using non-random convenience sampling and used a single 20 minute OMM session with 7 different techniques. They found that the subjects had an increase in chest expansion at the axillary and xiphisternal levels as well as a decrease in respiratory rate and improvement in peak expiratory flow rate (PEFR). The study methods and baseline characteristics of the subjects were not fully described. And there was no discussion of blinding. Howell et al 16 also used a pre-post test design. They studied 17 patients with COPD over a one year period however only analyzed the 11 patients for which they had nine months of data. They showed statistically significant decrease in PCO2, TLC and RV ($p<0.05$) and increase in O2 ($p=0.05$). A non-validated disease severity score consisting of 11 parameters from spirometry and arterial blood gases (ABGs) was the main outcome. They found an improvement in disease severity scores of 10.7%. However the non-validated nature of the score as well as the exclusion of subject data makes the interpretation of the disease severity score difficult.

Engel et al (2013)[21] performed a randomized cohort pilot study evaluating the short-term effects of these forms of manual therapy. They included 15 subjects with moderate COPD age 40-65. Participants were randomly assigned to one of three groups: soft tissue only (ST), soft tissue and spinal manipulation (ST + SM) or soft tissue, spinal manipulation and exercise (ST + SM + Ex). The pulmonary function tests they studied were FVC and FEV1. Results showed an increase in FVC in the ST + SM + Ex group compared to the ST + SM and ST only groups ($p<0.0001$). Subsequently a randomized controlled trial by Engel et al (2014)[22] studied the effects of manual therapy in conjunction with a pulmonary rehabilitation program. This study included 33 participants, mean age 65.5, with COPD who were in a pulmonary rehabilitation program (PR) and randomly assigned to PR only, ST + PR or ST + SM + PR. They performed treatments two times per week for 8 weeks between weeks 4 and 12 of PR. They assessed outcomes at week 16 and 24 of PR. Results showed that at 24 weeks the ST + SM + PR group had a significant increase in FVC compared to the PR only group ($p=0.03$).

Three studies utilized the 6-minute walk test as an outcome measure. Zanotti et al25 performed a RCT of 20 patients with severe COPD in PR. They compared four sessions of OMM tailored to the individual along with PR to PR plus a soft manipulation sham treatment. Results showed a significant decrease in RV in the OMM + PR group compared to the PR + sham therapy ($p=0.001$) and no significant difference for FEV1. The main outcome measured was results of the 6-minute walk test (6MWT). Both groups showed an increase in their 6-minute walk test, however between group analyses showed a significant increase in the OMM group (48.8m; 95% CI 17-80.6m; $p=0.04$). The two studies by Engel et al (2013 & 2014)[21-22] also utilized the 6MWT. The earlier study showed a statistically significant increase in the 6MWT for the ST + SM (120m) and ST + SM + Ex (168m) groups when compared to ST only ($p<0.0001$). Engel et al (2014)22 demonstrated a significant improvement in the 6MWT between the ST + SM + PR group compared to the ST + PR group at 16 and 24 weeks ($p=0.01$ and $p=0.02$ respectively) but there was no difference when the ST + SM + PR and ST + PR groups were compared to the PR only group.

(Continued on page 38)

TABLE 1:
Characteristics of included studies

Author / Year /Country	Design	Population Inclusion Criteria	Participants	Intervention / Techniques used	Control	Outcomes / Measures
Bhilpawar & Arora, 2013 India	pre-posttest non-random convenience sampling	COPD with FEV1 / FVC <70%	30 patients (28 males) with COPD selected from outpt PT utilizing convenience sampling No specific baseline characteristics Ages 37-81	**Single 20 minute session utilizing 7 techniques:** Soft tissue kneading (paraspinal muscles in lower cervical and thoracic region) Rib raising Redoming the abdominal diaphragm Suboccipital decompression Thoracic inlet myofascial release Pectoral traction Thoracic lymphatic pump with activation	No control group	Chest expansion at axillary and xiphisternal level Peak expiratory flow rate Respiratory rate
Mascarenhas et al. 2013 India	Cross-sectional	Patients with stable COPD grade I-III by GOLD guidelines	50 COPD patients in pulmonary medicine dept. Recruitment not clear	**One 5 minute session** Thoracic lymphatic pump without activation plus ten minutes of Salbutamol nebulization	Control group received only ten minutes of Salbutamol nebulization	Pulmonary function tests: VC, FEV1, FVC, FEV1/FVC ratio, PEF, FEF
Howell et al. 1975 US	pre-posttest case series	COPD according to ATS criteria	17 patients with COPD over a one year period Recruitment not clear	**OMM plus routine management.** OMM "directed toward the mobilization of specific segments of the spinal column at which paravertebral tissue abnormalities were detected and at which restricted intersegmental mobility was evident."[17]	No Control group	Disease severity score derived from 11 parameters from spirometry and ABGs: pre-post testing at periodic intervals (pretreatment, 1 month and 3 months after initiation of OMM and then at 3 month intervals)
Noll et al. 2008 US	Double-blinded RCT	65 years and older with FEV1/FVC ratio <70%	35 patients OMM group: 18 pts (mean age 69.6) Sham group: 17 pts (mean age 72.2)	**Single 20 minute session of 7 standard OMM techniques:** Soft tissue to paraspinal muscles Rib raising Redoming of the abdominal diaphragm Suboccipital decompression Thoracic inlet myofascial release Pectoral traction Thoracic lymphatic pump with activation If applicable additional OMM for specific somatic dysfunctions discovered	Sham (light touch applied to the same anatomic regions for the same duration).	Baseline and post-treatment PFTs Subjective feedback on effects and blinding protocols via phone survey
Noll et al. 2009 US	Cross over RCT	50 years and older with COPD, recruited from the clinical practice, newspaper ad, local talk radio, and COPD support groups	25 subjects: mean age 68	**5 single technique treatment sessions:** 4 OMM, 1 minimal touch control 4 week wash out period **Random order:** Minimal touch control Thoracic lymphatic pump with activation Thoracic lymphatic pump without activation Rib raising Myofascial release	Minimal Touch Control	PFTs at baseline, 30 minutes post treatment Subjective report on a telephone survey
Miller 1975 US	RCT	Ages 36-65 with COPD **Height:** 145-185 cm for females 157-190 cm for males **Weight:** 41-85 kg for females 50-115 kg for males	Treatment group: n=23 Control group: n=21 Matched pairing for sex, age, gender and disease severity	**Standard Treatment plus OMM 2x per week** Methods to hyperextend the dorsal spine Techniques to increase any restrictive motion Techniques to increase lymphatic flow by applying anterior chest compression	Standard Treatment	PFTs: VC, FEV1, FEV2, FEFR, FRC, RV, TLC pH, PO2, PCO2 Diffusion studies Minute ventilation Questionnaire on Respiratory Symptoms Musculoskeletal exam

TABLE 1 (CONT.):

Characteristics of included studies

Author / Year /Country	Design	Population Inclusion Criteria	Participants	Intervention / Techniques used	Control	Outcomes / Measures
Zanotti et al. 2012 Italy	RCT: pilot study	COPD patients consecutively admitted to the pulmonary rehabilitation unit Stage III by GOLD criteria	20 stable patients with severe COPD in pulmonary rehabilitation (PR) Mean age 63, FEV1 26.9%	Pulmonary rehabilitation and 4 sessions of OMT tailored to suit the needs of the individual Treatment sessions once per week lasting 45 minutes each	Pulmonary rehabilitation plus soft manipulation sham treatments	6 minute walk test PFTs: VC, FEV1, RV, FVC
Engel et al. 2013 Australia	Randomized cohort pilot study	Age 40-65 Volunteers with moderate COPD Recruited from the general public by newspaper and radio ads	**15 subjects:** 9 male/6 female mean age 56.1 (range 49-63) moderate COPD, All white	**Subjects randomly assigned to 1 of 3 groups:** Soft Tissue (ST) ST and spinal manipulation (SM) ST, SM and exercise	No control group	FEV1, FVC Chronic respiratory questionnaire 6 minute walk test Monitoring of adverse effects
Engel et al. 2014 Australia	RCT	COPD referred by a respiratory specialist to a PR unit, ages 55-70 Non-smoker for preceding 12 months, ability to complete a 6-minute walk test	33 participants mean age 65.5 with COPD in PR	**Subjects randomly assigned to 1 of 3 groups:** Pulmonary rehabilitation ST + PR ST + SM + PR Each manual therapy session 20 minutes, before the exercise component of PR Two times per week for 8 weeks between weeks 4 to 12 of PR	PR only	BP, FEV1, FVC 6-minute walk test, St. George's respiratory questionnaire hospital anxiety and depression scale

FEV1: forced expiratory volume in 1st second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; VC: vital capacity.

PEF: peak expiratory flow; FEF: forced expiratory function; ATS: American Thoracic Society; ABG: arterial blood gas; PFT: pulmonary function test; RCT: randomized controlled trial; FEFR: forced expiratory flow; FRC: functional residual capacity; RV: residual volume; TLC: total lung capacity

TABLE 2:

Summary of study results

Author / Year /Country	Main Findings	Adverse Effects / Dropout	Comments / Limitations
Bhilpawar & Arora, 2013 India	Mean increase in chest expansion at axillary level of 0.30 post treatment ($p<0.05$) Mean increase in chest expansion at xiphisternal level of 0.29 post treatment ($p<0.05$) Decrease in RR of 2.14/min ($p<0.05$) Improvement in PEFR of 11.73 ($p<0.05$)	Stated patients had no signs of discomfort	Small sample size Baseline characteristics not fully described Methods not fully described No blinding described
Mascarenhas et al. 2013 India	No significant difference in PFTs between groups Both groups showed a significant improvement in VC, FVC, FEV1, FEV1/FVC The experimental group showed an improvement in FEF 75/25	Stated technique is free from side effects	PFTs at baseline similar in both groups No description of randomization Subjects not divided based on disease severity No patient subjective data No blinding described
Howell et al. 1975 US	Improvement in disease severity scores of 10.7% Significant improvement in PCO2, O2, TLC and RV ($p<0.05$)	No description of drop outs or adverse effects	Only 11 of 17 subjects data analyzed Patients admitted at different times No description of statistical tests Missing data/patients unaccounted for Small sample size Non-validated severity score

TABLE 2 (CONT.):
Summary of study results

Author / Year /Country	Main Findings	Adverse Effects / Dropout	Comments / Limitations
Noll et al. 2008 US	Significant improvement between OMT and control groups for 8 out of 21 pulmonary function parameters. FEF 25% (p=0.04), FEF 50% (p=0.008), FEF 25%-75% (p=0.02), and ERV (p=0.02) were significantly lower in the OMT group. RV (p=0.03) and TLC (p=0.02) were significantly increased in the OMT group. RV/TLC ratio (p=0.04) increased in the OMT group. Airway resistance decreased in the OMT group (p=0.04). Phone survey showed that both groups reported an improvement in their breathing. 53% in the OMT group and 41% in the sham group correctly guessed their group assignment.	No severe side effects One subject lost to survey follow-up Two subjects in the OMT group reported muscle soreness Four subjects in the sham group reported adverse effects including palpitations, high BP, muscle soreness and back soreness	Stratified randomization by disease severity not fully described No description of allocation concealment Small sample size Phone survey is not a validated tool
Noll et al. 2009 US	Minimal touch control: Inspiratory capacity showed a decrease from baseline post-treatment (p=0.008) Thoracic lymphatic pump with activation: Post-treatment decrease in FEFmax (p=0.001), MVV (p=0.005), ERV (p<0.0001), and SVC (p=0.04). There was a significant increase in RV (p=0.03) and RV/TLC (p=0.04) Thoracic lymphatic pump without activation: Post-treatment decrease in FVC (p=0.02), FEF25-75% (p=0.006), and MVV (p=0.02). Increase in airway resistance relative to baseline (p=0.04). Rib raising: Post-treatment decrease from baseline in FEFmax (p=0.01) and MVV (p=0.0004) Myofascial release: Post-treatment decrease in FEV1 (p=0.03), FEF25-75% (p=0.007), FEFmax (p=0.007, MVV (p=0.03), and SVC (p=0.008). No significant difference between groups from baseline to 30 minutes post-treatment. Subjects reporting perceived health benefits from the treatment: minimal touch control 41%, TLP with activation 76%, TLP without activation 67%, rib raising 68%, myofascial release 53% Subjects reporting improved breathing after treatment: minimal touch control 44%, TLP with activation 74%, TLP without activation 57%, rib raising 79%, myofasical release 50% Subjects in all group reported enjoying the treatment (71-88%) and would recommend it to others (71-95%)	Side effects were noted in 1/18 patients (6%) in the minimal touch session, 4/23 (17%) after TLP with activation, 4/21 (19%) after TLP without activation, 3/20 (15%) after rib raising, and 2/16 (13%) after myofascial release. Side effects reported were commonly muscle soreness or pain and none were severe. Missed sessions for each group described	Subjects and physicians performing OMT were not blinded Individuals collecting the data, performing the PFTs, and performing the phone survey were blinded Allocation concealment, description of randomization provided Unable to contact all patients for follow up telephone survey
Miller 1975 US	92% of treatment group reported greater walking distances, few cold/URIs, and less dyspnea than prior to treatment. Trends noted: RV: OMT group increased by 0.5L (29%), no change in control (p>0.05) Mean VC: OMT group increased 0.5 L, control group increased 0.1 L (p>0.05) TLC: OMT group increased 1.0L (17%), control group increased 0.1L (2%) FEV1: OMT group increased 2.1 L, control decreased 2.4L PCO2: OMT group decreased 5 mm Hg, control decreased 3.3 mm Hg	No description of drop outs or adverse effects	Recruitment not clear Random allocation with matched pairing No description of allocation concealment Neuromuscular exam performed by 2 physicians who were blinded to treatment group Follow up time not given / Duration of treatment not stated Not all participants/data accounted for No description of statistical analysis Small sample size
Zanotti et al. 2012 Italy	Both groups showed an increased in 6MWT PR group increased 23.7 m and PR + OMT group increased 72.5 m (p = 0.01) Between group analysis showed a significant increase in 6MWT in the OMT group compared to the PR only group (48.8 m; 95% CI 17-80.6m; p = 0.04) Significant decrease in RV in OMT + PR group compared to PR only group (-0.44L; 95% CI -0.26 to -0.62; p = 0.001) FEV1: Between group analysis showed no difference but within group analysis showed a change of FEV 1 from 0.99L to 1.13L (14%) for the OMT+PR group which is noteworthy despite not reaching statistical significance.	Reported no adverse effects or side-effects No drop-outs	Allocation concealment described Data collectors and patients blinded Statistical analysis described No patient subjective data on symptoms or quality of life
Engel et al. 2013 Australia	FVC increase in ST + SM + Ex group compared to ST + SM (1.00L) and ST only (1.01 L) groups (p<0.0001) Increase in walking distance for groups that received ST + SM (120m) and ST + SM + Ex (168m), when compared to ST only (p<0.0001) Decreased dyspnea levels reported in ST + SM (0.64) and ST + SM + Ex (0.44) groups compared to ST only group (p<0.0001)	One participant dropped out for personal reasons No major or moderate adverse effects reported Mild Adverse effects of muscle soreness after 15% of MT sessions	Random allocation described Assessor blinding to intervention ST and SM interventions administered by single clinician who was blinded to all results during the intervention phase of the study Duration 4 weeks (8 sessions at 2 sessions per week) / Small sample size Standardized duration of treatment session for each intervention group Intention to treat analysis performed

TABLE 2 (CONT.):
Summary of study results

Author / Year /Country	Main Findings	Adverse Effects / Dropout	Comments / Limitations
Engel et al. 2014 Australia	Difference between all three groups significant for FVC at 24 weeks (p=0.04) ST + SM + PR group had a significant increase in FVC at 24 weeks compared to PR only (0.40L, 98.33% CI: 0.02, 0.79; p=0.03). No difference between group for HAD or SGRQ scores. There was a difference between all three groups for the 6MWT at 16 and 24 weeks (p=0.01 and p=0.03, respectively). No difference when comparing the ST+SM+PR group or the ST+PR group to the PR only group. Significant improvement noted in the 6MWT between the ST + SM + PR group compared to the ST + PR group at 16 and 24 weeks (p=0.01 and p=0.02 respectively). No difference in blood pressure.	Two participants in the ST + PR group reported mild AE of muscle soreness Withdrawals reported	Randomization and Allocation concealment described Statistical analysis described Intention to treat analysis Baseline characteristics not all similar (gender and HAD scores) Groups not evenly distributed

FEV1: forced expiratory volume in 1st second; FVC: forced vital capacity; VC: vital capacity; PEF: peak expiratory flow; FEF: forced expiratory function; ATS: American Thoracic Society; ABG: arterial blood gas; PFT: pulmonary function test; RCT: randomized controlled trial; FEFR: forced expiratory flow; FRC: functional residual capacity; RV: residual volume; TLC: total lung capacity; MVV: maximum voluntary ventilation; ERV: expiratory reserve volume; TLP: thoracic lymphatic pump; SVC: slow vital capacity; URI: upper respiratory infection; AE: adverse effects; 6MWT: 6 minute walk test; PR: pulmonary rehabilitation; ST: soft tissue; SM: spinal manipulation; MT: manual therapy; HAD: hospital anxiety and depression score; SGRQ: St. George's Respiratory Questionnaire

Five of the studies reported some form of subjective patient data; three utilizing non-validated surveys or questionnaire[17;19-20] and two studies using a validated questionnaire.[21-22] Miller[17] utilized a questionnaire on respiratory symptoms and found that 92% of the OMM treatment group reported greater walking distance, fewer colds or upper respiratory infections, and less dyspnea than prior to treatments. The patients stated they were able to function better in their normal activities than prior to OMM treatment. No data from the questionnaire was provided for the control group, however. Two studies utilized phone surveys following treatments to collect subjective data.[19-20] Noll et al (2008)[19] found that both the OMM and sham treatment groups reported an improvement in their breathing and 53% in the OMM group and 41% in the sham group correctly guessed their group assignment. Noll et al (2009)[20] found that 71% of subjects within the minimal touch treatment group reported enjoying the treatments compared to 80-88% in the four OMM treatment groups. Most subjects would also recommend the treatment to other, ranging from 71% in the minimal touch group to ranging from 91-95% in the four OMM treatment groups. More subjects in the OMM groups reported health benefits from the treatment and improved breathing after treatment (see Table 2).

Two studies utilized validated questionnaires to collect patient subjective data. Engel et al (2013)[21] utilized the Chronic Respiratory Questionnaire (CRQ-SAS) score and found that patients in the ST + SM and ST + SM + Ex groups showed a decrease in their dyspnea levels compared to the ST only group (p<0.0001). Engel et al (2014)[22] utilized the St. George's respiratory questionnaire (SGRQ) and found no difference between the groups for SGRQ scores. They also used a hospital anxiety and depression score and found no significant difference.

One study did not mention any adverse effects.[17] There were no severe adverse effects reported in any studies and the common minor adverse effects reported were mild muscle soreness or pain which mainly resolved on their own without any treatment.[16;19-25]

DISCUSSION

The clinical case reports reviewed in preparation for this systematic review all discussed the positive impact noted when adding OMM to treatment of acute exacerbations of COPD and reinforced the positive clinical experience physicians have expressed as the basis for the studies conducted in this area. The research articles included in this review focused less on acute exacerbations and more on management of the chronic disease process. Most utilized a variation of disease-oriented markers such as PFTs, PEF, ABGs, and chest wall expansion but some also included patient-oriented outcomes such as impact on exercise capacity and frequency of symptom questionnaires. This review found that incorporating OMM into chronic disease management had the highest impact on improving patient-oriented outcomes, such as symptom improvement, while limited effect was demonstrated on disease-oriented outcomes. We also found that most of the studies had limitations associated with small study size, study design, and the potential for bias.

Previous discussions looking to explain the impact of OMM on COPD have focused on the mechanical aspect of breathing but the results of this systematic review would indicate that other means of impacting the disease should be considered as well. Techniques such as the thoracic pump and doming the diaphragm decrease congestion and improve lymphatic flow within minutes of the treatment and the evidence supports that when applied, patients report feeling better regardless of the results of lung function measurements. This may also explain the improvement noted in the case studies reviewed for this article. Improving lymphatic flow and minimizing pulmonary congestion allows the body to maximize its ability to resolve the acute disease process.

This review ran into challenges associated with limited studies that were not consistently of high quality and built from information garnered from reviewing case studies that is outside the usual spectrum of a literature review. Considering the relative infancy of osteopathic medicine and the challenges associated with performing research in OMM, case studies still serve a role in defining the impact OMM may have in treating a disease process. As knowledge and understanding of OMM study limitations increase, future investigation of OMM and COPD should minimize the challenges noted here and incorporate well-designed studies that provide evidence regarding the effects on patient-oriented outcomes. It is our hope that this review will stimulate thought regarding study design that will demonstrate the impact OMM has on treating patients with this disease process.

Considering the impact that this disease has on patients and society, continuing to explore how to best utilize OMM within the context of treating it has the potential to impact the health care system on multiple levels. Further studies might wish to focus on treatment in acute exacerbations and longer, larger studies utilizing techniques that address lymphatic flow in addition to maximizing thoracic cage function and using patient-oriented outcomes to demonstrate the value OMM can add to managing COPD.

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