

Review Article

Efficacy of Osteopathic Manipulative Treatment (OMT) with Lymphatic Pump Treatment (LPT), Adjuvant to Conventional Antibiotic Therapy in Hospitalized Patients with Pneumonia: A Systematic Review of Randomized Controlled Trials (RCTs)

Bledar Gjikolaj^{1,2}, Bruno Morabito^{3,4,5}, Alberto Castellan⁵, Dario Silvestri³

¹Sapienza University of Rome, Italy

²Catholic University Our Lady of Good Counsel of Tirana, Albania

³Asomi College of Sciences Research Department, Block D Giorgio Mitrovich Street, Malta

⁴Department of Cardiology and Cardiac Surgery, U.C.S.C. Rome A. Gemelli Italy University Hospital Foundation, Italy

⁵CRESO, School of Osteopathic Centre for Research & Studies, Gorla Minore (VA) Italy

***Corresponding author:** Bruno Morabito, CRESO, School of Osteopathic Centre for Research & Studies, Gorla Minore (VA) Italy

Citation: Gjikolaj B, Morabito B, Castellan A, Silvestri D (2022) Efficacy of Osteopathic Manipulative Treatment (OMT) with Lymphatic Pump Treatment (LPT), Adjuvant to Conventional Antibiotic Therapy in Hospitalized Patients with Pneumonia: A Systematic Review of Randomized Controlled Trials (RCTs). Chron Pain Manag 6: 142. DOI: 10.29011/2576-957X.100042

Received Date: 10 May 2022; **Accepted Date:** 19 May 2022; **Published Date:** 24 May 2022

Abstract

Introduction: Pneumonia is a prevalent problem that generates huge social and economic burdens. Osteopathic manipulative treatment OMT with lymphatic pumping treatment LPT in immune, lymphatic and respiratory system disorders has been used for many years. **Objectives:** Summarize the results of experimental clinical studies, which investigate the effect of Osteopathic Manipulative Treatment OMT in patients hospitalized with Pneumonia. **Methods:** The search was performed through nine electronic databases: MEDLINE, Cinhal, PEDro, Cochrane library, PsycINFO, sciELO, Science Direct, SCOPUS e Web of Science - from inception to March 2022, using the following keywords: Osteopathic Manipulative Treatment or Osteopathic Manipulative Medicine or Osteopathic Physicians or Lymphatic Pump Treatment AND Pneumonia or Pneumoniae or Pneumonias or Pneumoniae's. Randomized controlled trials have been selected that evaluate the effect of osteopathic manipulative treatment OMT with lymphatic pump treatment LPT in people hospitalized with pneumonia, which had as outcome: Duration of hospital Length of Stay (LOS), ventilator-dependent respiratory failure rate, in-hospital mortality rate, duration of Intravenous antibiotic use (days), duration of oral antibiotic use (days) and duration of total (intravenous+oral) antibiotic use (days). **Results:** Four RCTs meet the inclusion criteria, three are of high methodological quality and one is of medium quality, all studies have low risk of bias according to the analysis through the Pedro score and the Risk of Bias Cochrane tool. **Conclusions:** Manipulative treatment osteopathic OMT adjuvant to conventional care can reduce the use of intravenous antibiotics, the duration of hospitalization, the rate of ventilator-dependent respiratory failure and mortality rate in hospitalized patients with pneumonia, according to well-conducted RCTs with high methodological quality and low risk of bias.

Keywords: Osteopathic manipulative treatment; Osteopathic manipulative medicine; Osteopathic Physicians; Lymphatic pump treatment; Pneumonia; Pneumoniae; Pneumonias; Pneumoniae's

Introduction

Pneumonia is one of the main infectious diseases that afflicts elderly patients. Antibiotic therapy is the mainstay of treatment, although the appearance of resistant bacteria is worrisome [1-3]. The elderly are a vulnerable population: the majority of hospital admissions for pneumonia occur in people aged 60 or over, the elderly have a longer hospital Length of Stay (LOS) and an increased severity of lung infection disease, also have higher mortality than younger age groups [4]. Community-acquired pneumonia is the most common among potentially fatal infectious diseases, *Streptococcus pneumoniae* remains the main etiological pathogen. While antibiotic treatments have reduced the rate of death from pneumococcal pneumonia, the prevalence of organisms resistant to antimicrobial therapy has increased substantially, increasing the possibility that these pharmacological treatments become less effective for the treatment of infectious diseases in the future. Therefore, it is necessary to examine the advantages of additional methods that can help in the treatment and prevention of infectious diseases [5].

Osteopathic Manipulative Treatment (OMT) is an additional treatment that can be used for patients with pneumonia, is a non-pharmacological manual therapy, developed in the late XIX century before the use of antibiotics. It was used by osteopathic physicians the osteopathic manipulative treatment OMT with lymphatic pump treatment LPT in the era of the Spanish flu pandemic of 1918-1919 [6]. During the Spanish flu pandemic, patients treated with standard medical care had an estimated 33% mortality rate, compared to a 10% mortality rate of patients treated by osteopathic physicians [7]. The OMT includes a series of manipulative techniques aimed at improving the patient's defenses and physiological functions [8]. When applied to the management of pneumonia, manual manipulation techniques strengthen the flow of the lymphatic system, respiratory function and immunological defense, aiming at the anatomical structures involved in these systems [9-11]. Clinical studies report that LPT improves antibody responses to bacterial vaccines [12,13], reduces the duration of coughing in patients with respiratory diseases [11], shortens the duration of intravenous antibiotic therapy and reduces hospital Length of Stay (LOS) in patients with pneumonia [14]. Animal studies show that LPT promotes the absorption of interstitial antigens into the lymphatic system [15], increases the lymphatic flow [16,17], increases the lymphatic concentration of leukocytes [18-19] and increases the lymphatic flow of inflammatory cytokines, also reduces bacterial load in rat lungs [20]. Osteopathic manipulative treatment OMT with lymphatic pump treatment LPT can protect

against pneumonia by inhibiting bacterial growth in the lungs, LPT can be optimally applied in patients with pneumonia, which can substantially reduce morbidity, mortality and frequency of hospitalization [21]. Many techniques included in OMT can treat a multitude of disorders, including the lymphatic system. Problems within this system lead to the accumulation of lymph, decreased immune responses, accumulation of fat, swelling of tissues and accumulation of connective tissue [22]. Osteopathic manipulative treatment OMT is used to treat somatic dysfunction. OMT focuses on improving neuromuscular connection, improving biomechanical balance, reducing pain, and increasing movement [23]. Many of these techniques, rib raising, doming of the diaphragm with myofascial release and, thoracic lymphatic pump treatment, have been developed specifically for the treatment of pneumonia [24]. Some manual medicine procedures have been designed to increase lymphatic flow or to prevent the accumulation of fluid in the tissues, these procedures can be used for the treatment of edema and infectious diseases. These procedures include the connective compression of certain tissues and body districts [25]. Osteopathic doctors use manual medicine techniques called Lymphatic Pump Techniques (LPT) they use them to improve lymphatic flow and improve immunity. These manipulations can be applied to the rib cage (thoracic pump), abdomen (abdominal pump), feet and legs (pedal pump), spleen and liver areas [25,26]. Randomized controlled clinical trials suggested that OMT in elderly patients hospitalized with pneumonia reduced the hospital length of stay LOS and the duration of intravenous antibiotic therapy [27,28]. A randomized multicenter study, with the creation of a detailed experimental protocol called MOPSE, reported together with the results of the trial, tried to evaluate the effectiveness of OMT as a complementary treatment for pneumonia in elderly hospitalized patients. These have highlighted significant improvements of length of stay LOS, In- hospital mortality rate, duration of intravenous antibiotic therapy and in the ventilator- dependent respiratory failure, in favor of the experimental group OMT [14,24].

Material and Methods

Search Strategy and Eligibility Criteria

The research was performed on nine electronic databases- MEDLINE, Cinhal, PEDro, Cochrane library, PsycINFO, sciELO, Science Direct, SCOPUS and Web of Science – from inception to March 2022. The keywords used to search on databases were: Osteopathic Manipulative Treatment or Osteopathic Manipulative Medicine or Osteopathic Physicians or Lymphatic Pump Treatment AND Pneumonia or Pneumoniae or Pneumonias or Pneumoniae's (Pneumonia Mesh terms). The combination of search terms was defined using the population, intervention, comparison, and outcome (PICO) model. Randomized controlled trials have been selected that evaluate the effect of osteopathic manipulative

treatment OMT with lymphatic pump treatment LPT in people hospitalized with pneumonia, which had as outcome: Duration of hospital Length of Stay (LOS), ventilator-dependent respiratory failure rate, in-hospital mortality rate, duration of Intravenous antibiotic use (days), duration of oral antibiotic use (days) and duration of total (intravenous+oral) antibiotic use (days). Through the search in the electronic databases, emerge altogether 708 articles. In the research carried out through other sources (as in the gray literature), 3 additional articles are taken. So the total number of articles identified through the search strategy is 711. Of these 520 remain after the elimination of duplicates. Then 191 remain after deleting all titles with different arguments. After reading, the abstracts there are 20 articles that are read the full tests to check if they met the criteria of inclusion. At the end, 4 studies are included in the qualitative summary of the review, as they are the only studies dealing with the topic according to the inclusion criteria. These included studies shall be extrapolated to the data, the results, the materials, methods used, and the characteristics of the samples. Always these 4 studies are carried out the evaluation of methodological quality through the Pedro score and the risk of bias through the Risk Of Bias Tool Chocrane.

Studies Selection and Quality Assessment

Two authors independently researched the articles using the search terms and independently screened titles and abstracts

according to the eligibility criteria to select relevant studies. The quality of the included studies was assessed by using Cochrane Collaboration's tool for assessing risk of bias by RevMan [29] and by extracting PEDro (Physiotherapy Evidence Database) scores from the PEDro website. Each score on the PEDro website is generated by two accredited raters scoring the trial; any discrepancies in rating are resolved by a third accredited rater (<https://www.pedro.org.au/>).

Outcome Measures

The primary outcomes of interest included: hospital Length of Stay (LOS), ventilator-dependent respiratory failure rate and in-hospital mortality rate, duration of Intravenous antibiotic use (days), duration of oral antibiotic use (days) and duration of total (intravenous+oral) antibiotic use (days).

Results

Search Results

The study selection process is diagrammed in (Figure 1). A total of 411 records were identified and screened through the initial search strategy, and a total of 707 records were excluded based on irrelevant titles and abstracts. Four RCTs (randomized controlled trials) met the eligibility criteria.

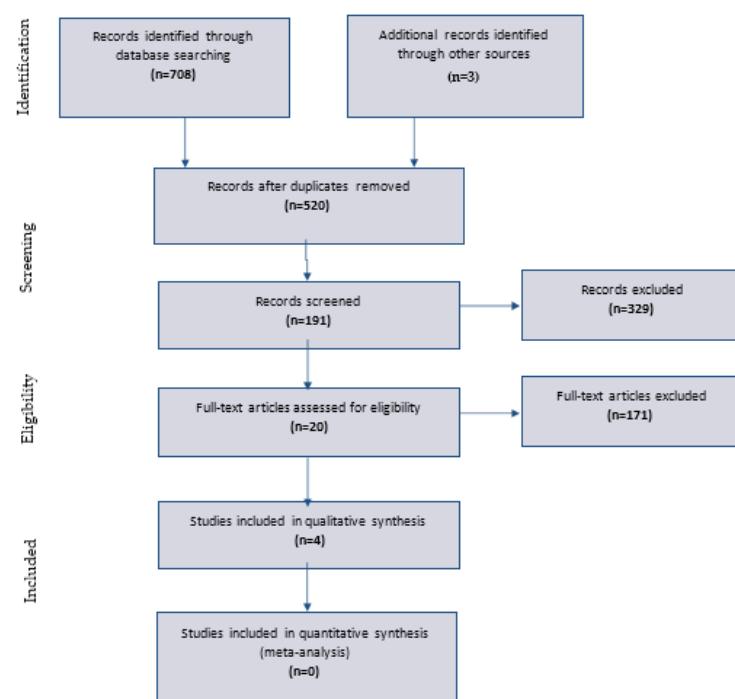


Figure 1: PRISMA flow diagram.

Characteristics of Included Studies

A summary of studies characteristics is shown in (Table 1). All studies are RCTs and recruit elderly patients hospitalized with pneumonia, among them there are two multicenter studies with triple control arm. All as intervention group carry out the standard protocol of manipulative treatment osteopathic OMT in addition to conventional antibiotic therapy treatment. All studies have a standard protocol control group of dummy LT light touch in addition to conventional antibiotic therapy. The LT protocol occurs at the same points and in the same positions of the OMT intervention protocol, in this group unlike the intervention group, the actual manipulation of the districts is not carried out. Two studies (DR Noll 2016 and DR Noll 2010) also have a third group, which is given only the conventional antibiotic wiper CCO. In all RCTs the standard protocol OMT and LT are performed for 15 minutes, twice a day, for 6 hours away. All protocols begin within 24 hours of admission or nosocomial infection and have as end point: hospital discharge, cessation of antibiotic therapy, ventilator- dependent respiratory failure, death or withdrawal from the study (Tables 1-4).

| Authors (condition of RCT and participants) | n. total; n. male; n. female. | Age mean | Subgroups Age | Subgroups PSI class | SAPS score Treatment group – Control group (Mean) | Subgroups Type of Pneumonia |
|--|---|---|---|--|---|---|
| Donald R. Noll et al. 2016 Randomized controlled multicenter double-blind trial on patients with PSI-class pneumonia I-II-III-IV-V, triple arm: 1) experimental group of antibiotic therapy + OMT 2) control group of antibiotic therapy + LT 3) control group of conventional care only CCO | ITT analysis n tot. 387 n 174 male n 213 female PP analysis n tot. 318 n 141 male n 177 female | ITT analysis 73,7 PP analysis 73,8 | ITT analysis: • Age 50-74 (n 186) • Age ≥75 (n 201) PP analysis: • Age 50-74 (n 153) • Age ≥75 (n 165) | ITT analysis: I-II (n 73) III (n 109) IV (n 149) V (n 56) PP analysis: I-II (n 64) III (n 90) IV (n 125) V (n 39) | It is not measured. | ITT analysis: Community-acquired (n 306) Nursing home-acquired (n 81) PP analysis: Community-acquired (n 253) Nursing home-acquired (n 65) |
| Donald R. Noll et al. 2010 Randomized controlled multicenter double-blind trial on patients with PSI-class pneumonia I-II-III-IV-V, triple arm: 1) experimental group of antibiotic therapy + OMT 2) control group of antibiotic therapy + LT 3) control group of conventional care only CCO | ITT analysis n tot. 387 n 174 male n 213 female PP analysis n tot. 318 n 141 male n 177 female | ITT analysis 73,7 PP analysis 73,8 | There is no stratification by age groups. | ITT analysis: I-II (n 73) III (n 109) IV (n 149) V (n 56) PP analysis: I-II (n 64) III (n 90) IV (n 125) V (n 39) | It is not measured. | ITT analysis: Community-acquired (n 306) Nursing home-acquired (n 81) PP analysis: Community-acquired (n 253) Nursing home-acquired (n 65) |
| Donald R. Noll et al. 2000 Randomized controlled double-blind trial in hospitalized patients with pneumonia | n total 58; n 30 male n 28 female | 77,35 | There is no stratification by age groups. | There is no stratification according to the severity class groups of PSI pneumonia. | Treatment group: 9.4 Control group: 9.6 | Community-acquired (n 31) Nursing home-acquired (n 25) Hospital-acquired (n 2) |
| Donald R. Noll et al. 1999 Randomized controlled pilot study on hospitalized patients with pneumonia | n total 21 n 6 male n 15 female | 80,6 | There is no stratification by age groups. | There is no stratification according to the severity class groups of PSI pneumonia. | Treatment group: 9.7 Control group: 9.4 | Community-acquired (n 8) Nursing home-acquired (n 9) Hospital-acquired (n 4) |

Table 1: Characteristics of the included studies according to the PICO strategy. Number of participants; Age mean; Subgroups Age; Subgroups PSI class; SAPS score; Subgroups Type of Pneumonia. PSI: Pneumonia Severity Index; SAPS: Simplified Acute Physiology Score; ITT: Intention-To-Treat analysis; PP: Per-Protocol analysis; OMT: Osteopathic Manipulative Treatment; LT: Light Touch Treatment; CCO: Conventional Care Only; LOS: Hospital Length of Stay.

| Authors (condition of participants) | Duration of the experimental protocol | Intervention; (n) | Comparison; (n) |
|--|--|--|--|
| Donald R. Noll et al. 2016 Randomized controlled multicenter double-blind trial on patients with PSI-class pneumonia I-II-III-IV-V, triple arm: 1) experimental group of antibiotic therapy + OMT 2) control group of antibiotic therapy + LT 3) control group of conventional care only CCO | Start within 24 hours of hospitalization or nosocomial infection. End point= hospital discharge, cessation of antibiotic therapy, ventilator dependent respiratory failure, death or withdrawal from the study. | Standart protocol of OMT for 15 minutes, twice a day (6 hours away, for 7 days a week), starting within 24 hours of admission and continuing until the End Points. In addition to the OMT protocol received conventional antibiotic therapy; • ITT analysis (n 130) • PP analysis (n 96) | Light Touch LT control group: Light touch standart protocol at the same points of the experimental protocol, for 15 minutes, twice a day (7 days a week). In addition to the LT protocol received conventional antibiotic therapy; • ITT analysis (n 124) • PP analysis (n 95) Control group conventional care only CCO; • ITT analysis (n 133) • PP analysis (n 127) |
| Donald R. Noll et al. 2010 Randomized controlled multicenter double-blind trial on patients with PSI-class pneumonia I-II-III-IV-V, triple arm: 1) experimental group of antibiotic therapy + OMT 2) control group of antibiotic therapy + LT 3) control group of conventional care only CCO | Start within 24 hours of hospitalization or nosocomial infection. End point= hospital discharge, cessation of antibiotic therapy, ventilator dependent respiratory failure, death or withdrawal from the study. | Standart protocol of OMT for 15 minutes, twice a day (6 hours away, for 7 days a week), starting within 24 hours of admission and continuing until the End Points. In addition to the OMT protocol received conventional antibiotic therapy; • ITT analysis (n 130) • PP analysis (n 96) | Light Touch LT control group: Light touch standart protocol at the same points of the experimental protocol, for 15 minutes, twice a day (7 days a week). In addition to the LT protocol received conventional antibiotic therapy; • ITT analysis (n 124) • PP analysis (n 95) Control group conventional care only CCO; • ITT analysis (n 133) • PP analysis (n 127) |
| Donald R. Noll et al. 2000 Randomized controlled double-blind trial in hospitalized patients with pneumonia | Start within 24 hours of hospitalization or nosocomial infection. End point= hospital discharge, cessation of antibiotic therapy, ventilator dependent respiratory failure, death or withdrawal from the study. | Standart protocol of OMT for 15 minutes, twice a day (7 days a week), starting within 24 hours of admission and continuing until the End Points. In addition to the OMT protocol received conventional antibiotic therapy; (n 28) | Light Touch LT control group: Light touch standart protocol at the same points of the experimental protocol, for 15 minutes, twice a day (7 days a week). In addition to the LT protocol received conventional antibiotic therapy; (n 30) |
| Donald R. Noll et al. 1999 Randomized controlled pilot study on hospitalized patients with pneumonia | Start within 24 hours of hospitalization or nosocomial infection. End point= hospital discharge, cessation of antibiotic therapy, ventilator dependent respiratory failure, death or withdrawal from the study. | Standart protocol of OMT for 15 minutes, twice a day (6 days a week), starting within 24 hours of admission and continuing until the End Points. In addition to the OMT protocol received conventional antibiotic therapy; (n 11) | Light Touch LT control group: Light touch standart protocol at the same points of the experimental protocol, for 15 minutes, twice a day (6 days a week). In addition to the LT protocol received conventional antibiotic therapy; (n 10) |

Table 2: Characteristics of the included studies according to the PICO strategy. Duration of the experimental Protocol; Intervention (number participants); Comparison (number participants). PSI: Pneumonia Severity Index; SAPS: Simplified Acute Physiology Score; ITT: Intention-To- Treat analysis; PP: Per-Protocol analysis; OMT: Osteopathic Manipulative Treatment; LT: Light Touch Treatment; CCO: Conventional Care Only; LOS: Hospital Length of Stay.

| Authors (condition of participants) | Outcome measures | Main Findings |
|---|--|---|
| Donald R. Noll et al. 2016 Randomized controlled multicenter double-blind trial on patients with PSI-class pneumonia I-II-III-IV-V, triple arm: 1) experimental group of antibiotic therapy + OMT. 2) control group of antibiotic therapy + LT. 3) control group of conventional care only CCO. | Primary outcome: <ul style="list-style-type: none">• Hospital length of stay LOS ;• Ventilator-dependent respiratory failure rate;• In-hospital mortality rate; | Hospital length of stay LOS was shorter for the OMT group than for the LT and CCO groups, For the 50-74 age subgroup, from the PP analysis ($P=0.006$); For the ≥ 75 age subgroup, an improvement of the OMT intervention group, In-hospital mortality rate, was found from ITT and PP analysis ($P=0.005$). The PSI Class IV subgroup of the experimental OMT group had a statistically significant improvement in the hospital length of stay LOS ($P=0.01$). The OMT intervention group had a statistically lower mortality rate than the conventional care only CCO group, in the PSI V pneumonia class subgroup ($P=0.05$), also in the ventilator-dependent respiratory failure rate for subgroup PSI IV ($P=0.05$) from PP analysis. In the ITT and PP analysis of the subgroups of community-acquired pneumonia, results a reduction in the rate of ventilator-dependent respiratory failure of the experimental OMT group was found in the analysis of the subgroup class PSI IV ($P=0.05$) compared to the conventional care only CCO control group. Statistically significant reduction in the mortality rate of the OMT experimental group for the subgroup PSI V class ($P=0.05$) compared to the conventional care only CCO control group, both from ITT and PP analysis. |
| Donald R. Noll et al. 2010 Randomized controlled multicenter double-blind trial on patients with PSI-class pneumonia I-II-III-IV-V, triple arm: 1) experimental group of antibiotic therapy + OMT. 2) control group of antibiotic therapy + LT. 3) control group of conventional care only CCO. | Primary outcome: <ul style="list-style-type: none">• Hospital length of stay LOS;• Duration of clinical stability (in days);• Symptomatic and Functional RecoveryScore; Secondary outcome: Duration of Intravenous Antibiotic Use (days); Duration of oral antibiotic use (days); Duration of Total (Intravenous+Oral) Antibiotic Use (days); Ventilator-dependent respiratory failure rate; In-hospital mortality rate; Maximum daily temperature; Maximum daily respiratory rate; | The result of the PP analysis is a lower hospital length of stay LOS, for the experimental group OMT in comparison to the control group CCO ($P = 0.01$ OMT>CCO). Results from PP analysis show a shorter duration of intravenous antibiotic therapy, for the OMT experimental group compared to the CCO control group ($P = 0.05$ OMT>CCO). The PP analysis shows a significant difference of lower in-hospital mortality rate for the experimental group OMT, in comparison to the control group CCO ($P = 0.006$). |
| Donald R. Noll et al. 2000 Randomized controlled double-blind trial in hospitalized patients with pneumonia | Duration of intravenous antibiotic use (days), duration of oral antibiotic use (days) and duration of total (intravenous+oral) antibiotic use (days); hospital length of stay LOS; In-hospital mortality rate; Chest X-ray; Leukocyte count; Duration of leukocytosis; Body temperature; Duration of fever; Number of Tachypnea and Tachycardia Events. | Average duration of the use of intravenous antibiotics ($P 0.002$), total antibiotic therapy ($P 0.003$), hospital length of stay ($P 0.14$) were significantly shorter for the OMT intervention group. |
| Donald R. Noll et al. 1999 Randomized controlled pilot study on hospitalized patients with pneumonia | Duration of intravenous antibiotic use (days), duration of oral antibiotic use (days) and duration of total (intravenous+oral) antibiotic use (days); hospital length of stay LOS; In-hospital mortality rate; Leukocyte counts; Duration of leukocytosis; Body Temperature; Duration of Fever; Number of Tachypnea and Tachycardia Events . | The experimental OMT group lasted less than days of fever, duration of leukocytosis, duration of antibiotic intra-venous therapy, total duration of antibiotic therapy and days of hospitalization. Although the results of this pilot study did not reach statistical significance, the only outcome that has reached statistical significance is the duration of oral antibiotic therapy ($P=0.04$) in favour of the control group. Authors think this is due to a direct improvement of the intervention group in the duration of intravenous antibiotic therapy. |

Table 3: Characteristics of the included studies according to the PICO strategy. Outcome measures; Main Findings. PSI: Pneumonia Severity Index; SAPS: Simplified Acute Physiology Score; ITT: Intention-To-Treat analysis; PP: Per-Protocol analysis; OMT: Osteopathic Manipulative Treatment; LT: Light Touch Treatment; CCO: Conventional Care Only; LOS: Hospital Length of Stay.

| | Dr. Noll 2016 | Dr. Noll 2010 | Dr. Noll 2000 | Dr. Noll 1999 |
|----------------------------|---------------|---------------|---------------|---------------|
| Eligibility Criteria | Yes | Yes | Yes | Yes |
| Random allocation | Yes | Yes | Yes | Yes |
| Concealed allocation | Yes | Yes | Yes | Yes |
| Groups similar at baseline | Yes | Yes | Yes | Yes |
| Participant blinding | Yes | Yes | Yes | Yes |
| Terapist blinding | No | No | No | No |
| Assessor Blinding | Yes | Yes | Yes | Yes |
| <15% dropouts | Yes | Yes | Yes | No |

| | | | | |
|---|-----|-----|-----|-----|
| Intention to treat analysis | Yes | Yes | Yes | Yes |
| Between-group difference reported | Yes | Yes | Yes | No |
| Point estimate and variability reported | Yes | Yes | Yes | Yes |
| Total (0-10) | 9 | 9 | 9 | 7 |

Table 4: Pedro scores for included papers (n=4) extracted from website www.pedro.org.au

Trial Quality

The Cochrane collaboration's tool for assessing risk of bias was used to assess risk of bias of each study (Figure 2). All included and evaluated studies are of low risk of bias. All studies were assigned high risk in blinding of participants and personnel (performance bias) due to the nature of treatment; on the other hand, risk of all other bias was low, apart from incomplete outcome data (attrition bias risk), which was unclear in DR Noll1999 trial because of a missing adequate description of outcome data. We also used the PEDro scores to assess the quality of included studies (Table 2). According to the PEDro criteria, the quality of the studies can be classified as three ranges: low quality (scores 0-3), medium quality (scores 4-7), and high quality (scores 8-10). The score of 10 reflects the best quality. The score of our papers was: 9 for three RCTs (DR Noll 2016, DR Noll 2010, DR Noll 2000) and an RCT scored 7 (DR Noll 2010). Three RCTs were rated as high-quality studies and one medium-quality study. The quality assessments were initially completed by a single reviewer and then checked for accuracy by one other reviewer.

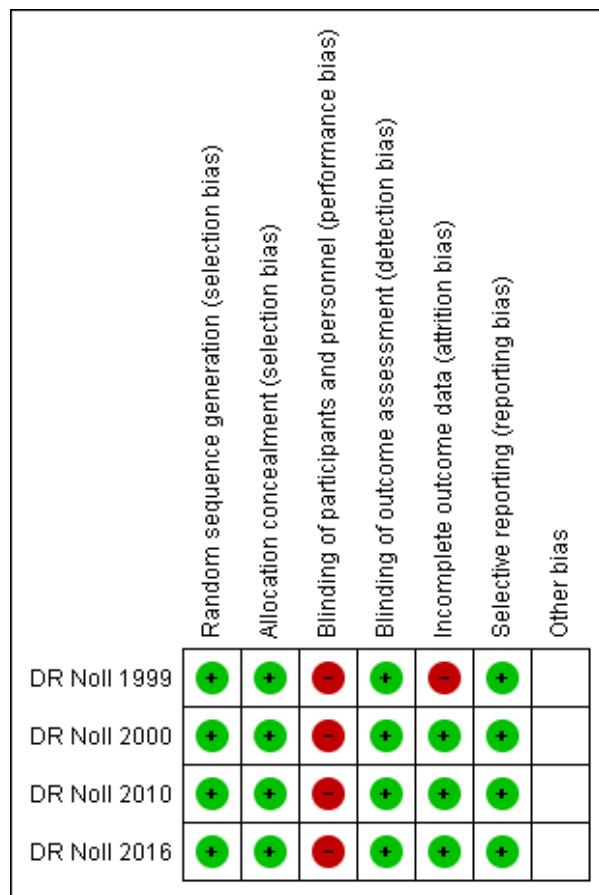


Figure 2: Cochrane risk of bias of the included studies. Quality appraisal. + (green), low risk of bias; ? (yellow), unclear risk of bias; - (red), high risk of bias.

Discussion

A significant number of diseases and conditions can be treated or improved with the OMT by integrating LPT maneuvers. The following list includes many, but not all, conditions that can be treated: upper respiratory infections, Chronic Obstructive Pulmonary Disease (COPD), asthma, atelectasis, bronchitis, otitis, pharyngitis, sinusitis, after a myocardial infarction, congestive heart failure, pericarditis, myocarditis, constipation, gastrointestinal infections, Crohn's disease, colitis, cirrhosis of the liver, chronic hepatitis, nephrotic syndromes, pancreatitis, uterine fibroids, uterine contractions, premenstrual syndrome, endometriosis, cystitis, tendinitis, joint infection and hospitalized patients with pneumonia [30]. The lymphatic system functions as a part of the circulatory system maintaining fluids in the body at balanced levels and as a part of the immune system by playing a role in the body's defense system against infections. The lymphatic system is comprised of lymphoid organs, lymph tissues, lymph ducts, lymph capillaries, and lymphatic vessels that transport lymph and miscellaneous materials throughout the body [31]. Doctor of Osteopathic Medicine DO have commonly used OMT to remove impediments, or augment lymph flow, and stimulate the body's immune system defenses [32]. The main functions attributed to the lymphatic system are: the reabsorption and return of excess interstitial fluids into the circulatory system [33], also through the lymphatic capillaries that are located within the villi of the small intestine, are able to absorb fats and fat-soluble vitamins for metabolism or storage in the bloodstream and finally participation in the body's immune response and prevention of infectious pathogens [34]. The crucial task attributed to the lymphatic system is the transport of lymphatic fluid from the interstitium to the central circulatory system. The energy for this process comes by way of pumping mechanisms that propel the lymph along with the lymphatic network of vessels. These pumping mechanisms are extrinsic and intrinsic. The extrinsic pump produces cyclical compression and expansion of lymphatic vessels by such actions as joint movements, muscular contractions, myofascial flexibility, mechanical respiration, and postural changes. The intrinsic pump relies on the rhythmic, spontaneous contractions of lymphatic muscle, and neural modulation via the autonomic nervous system [35]. In osteopathy somatic dysfunction SD is defined as "impaired or altered function of related components of the somatic (body framework) system: skeletal, arthrodial and myofascial structures, and their related vascular, lymphatic, and neural elements". SDs that result in restricted joint motion, hypertonic musculature (including restricted thoracoabdominal or pelvic diaphragm motion), abnormal myofascial tension, and/or decreased rib cage motion, may inhibit the cyclical expansion and contraction of the lymphatic vessels, resulting in less than the optimum flow of lymphatic fluid in those regions where SD is

present. Any conditions that result in abnormally altered autonomic activity may also reflexively affect the optimum functioning of the intrinsic lymphatic pumping mechanism in segmentally related body regions [36]. The osteopathic manipulative treatment OMT and integration of lymphatic pumping techniques LPT, are indicated in the treatment of conditions of lymphatic system disorders related to pneumonia infections. Treating SD somatic dysfunction that hinders the optimal function of the lymphatic system, secretly related autonomic nervous system areas and lymphatic pumping techniques LPT. OMT techniques can help optimize the functioning of the lymphatic system through changes in muscle tone, attenuation of myofascial restrictions, modulation of neural reflexes, maintaining the balance of autonomic tone and beneficial effects on breathing [14,24,28,36,37]. The mechanisms and principles, for which the OMT can intervene for the benefit of the population with polomintis, as well as other multitudes of pathologies, are analyzed. There appears to be support for the application of OMT osteopathic principles for pulmonary infections and some conditions involving the lymphatic and immune system [25,38,39]. The safety and efficacy of osteopathic lymphatic treatments have been demonstrated in many publications without any significant complications [25,37]. A review evaluates pump and pumping techniques in a multitude of pathologies including also RCTs with pumping techniques, with objective and subjective parameters. They highlighted the possible benefits of such techniques even in patients with pneumonia [40]. This systematic review has a rational and targeted strategy, researching in the international literature, through electronic databases and manual search, all RCTs articles experimenting OMT treatment with LPT, adjuvants to conventional therapy in patients with pneumonia. The specific inclusion criteria allowed us to identify RCTs carried out strictly according to a single research and intervention protocol (MOPSE). The studies that have met the inclusion criteria, result from the qualitative evaluation, overall be of high methodological quality and low risk of bias [14, 24, 27, 28]. It is important to continue research in this field, as OMT treatment can be an excellent support to conventional antibiotic therapy in patients with pneumonia. We recommend future research according to the MOPSE protocol, which is of high methodological quality, effective and respects the principles of osteopathy. So we need future double- blind, triple-arm RCTs. Stratification of patients will also be important: depending on the severity class PSI, depending on whether pneumonia contracted in hospital, nursing home or community, depending on the age of patients from 50 to 74 years and from ≥ 75 years of age, bringing definite results by stratification in the different subclasses. Prolonging the study in addition to the end points (cessation of antibiotic therapy, discharge from the hospital and death) will allow us to verify whether OMT treatment could bring benefits even in home or outpatient regimen.

Study Limits

It has not been possible to bring the data in meta-analysis because the clinical trials that met the inclusion criteria have differences in the analysis and stratification of the sample. The strictly targeted research strategy allowed us to incorporate RCTs that treated OMT treatment adjuvant to conventional antibiotic therapy or compared to LT light touch in patients with pneumonia, as a result, it has not allowed us to analyze other populations and other pathologies, which could be extended this reasoning.

Conclusions

Well-conducted research with high methodological quality and with low risk of bias, brings important statistically significant evidence regarding the effectiveness of OMT treatment compared with conventional antibiotic only therapy CCO. L'OMT reduced the hospital length of stay LOS, ventilator-dependent respiratory failure rate, the duration of total antibiotic therapy, the duration of intravenous antibiotic therapy and mortality rate compared to the control group CCO. These findings suggest a potential role for OMT in increasing the effectiveness of conventional antibiotic therapy in treating pneumonia. This role can become important with increased antibiotic resistance, the existence of new emerging pathogens, the aging of the world's population, the cost of health care and the likelihood of another flu pandemic. These results of study of high methodological quality and low risk of bias, involve the need for further research in order to implement the current international scientific evidence.

References

- Yoshikawa TT (2002) Antimicrobial resistance and aging: beginning of the end of the antibiotic era? *J Am Geriatr Soc* 50(7 suppl): S226-S229.
- Chung DR, Song JH, Kim SH, Thamlikitkul V, Huang SG, et al. (2011) High prevalence of multidrug- resistant nonfermenters in hospital-acquired pneumonia in Asia. *Am J Respir Crit Care Med* 184: 1409-1417.
- Balsalobre LC, Dropa M, Matté MH (2014) An overview of antimicrobial resistance and its public health significance. *Braz J Microbiol* 45: 1-5.
- Fry AM, Shay DK, Holman RC, Curns AT, Anderson LJ (2005) Trends in hospitalizations for pneumonia among persons aged 65 or older in the United States, 1988-2002. *JAMA* 294: 2712- 2719.
- Fuller JD, McGeer A, Low DE (2005) Drug-resistant pneumococcal pneumonia: Clinical relevance and approach to management. *Eur J Clin Microbiol Infect Dis* 24: 780-788.
- Baroni F, Mancini D, Tuscano SC, Scarlata S, Lunghi C, et al. (2021) Osteopathic manipulative treatment and the Spanish flu: a historical literature review. *J Osteopath Med* 121: 181-190.
- Smith RK (2000) One hundred thousand cases of influenza with a death rate of one-fortieth of that officially reported under conventional medical treatment. *J Am Osteopath Assoc* 100:320-323.
- Facto LL (1947) The osteopathic treatment for lobar pneumonia. *J Am Osteopath Assoc* 46: 385- 392.
- Saggio G, Docimo S, Pilc J, Norton J, Gilliar W (2011) Impact of osteopathic manipulative treatment on secretory immunoglobulin a levels in a stressed population. *J Am Osteopath Assoc* 111: 143-147.
- Measel JW, Kafity AA (1986) The effect of the lymphatic pump on the B and T cells in peripheral blood. *J Am Osteopath Assoc* 86: 608.
- Allen TW, Pence TK (1967) The use of the thoracic pump in treatment of lower respiratory tract disease. *J Am Osteopath Assoc* 67: 408-411.
- Jackson KM, Steele TF, Dugan EP, Kukulka G, Blue W, et al. (1998) Effect of lymphatic and splenic pump techniques on the antibody response to Hepatitis B vaccine: A pilot study. *J Am Osteopath Assoc* 98: 155-160.
- Measel JW (1982) The effect of lymphatic pump on the immune response: Preliminary studies on the antibody response to pneumococcal polysaccharide assayed by bacterial agglutination and passive hemagglutination. *J Am Osteopath Assoc* 82: 28-31.
- Noll DR, Degenhardt BF, Morley TF, Blais FX, Hortos KA, et al. (2010) Efficacy of osteopathic manipulation as an adjunctive treatment for hospitalized patients with pneumonia: a randomized controlled trial. *Osteopath Med Prim Care* 4: 2.
- Dery M, Winterson BJ, Yonuschot G (2000) The effect of lymphatic pump manipulation on the healthy and injured rat. *Lymphology* 33: 58-61.
- Knott EM, Tune JD, Stoll ST, Downey HF (2005) Increased lymphatic flow in the thoracic duct during manipulative intervention. *J Am Osteopath Assoc* 105: 447-456.
- Hodge LM, King HH, Williams AG, Reder SJ, Belavadi T, et al. (2007) Abdominal lymphatic pump treatment increases leukocyte count and flux in thoracic duct lymph. *Lymphat Res Biol* 2: 127-133.
- Hodge LM, Bearden MK, Schander A, Huff JB, Williams A, et al. (2010) Abdominal lymphatic pump treatment mobilizes leukocytes from the gastrointestinal associated lymphoid tissue into lymph. *Lymphat Res Biol* 2: 103-110.
- Huff JB, Schander A, Downey HF, Hodge LM (2013) Lymphatic pump treatment enhances the lymphatic release of lymphocytes. *Lymphat Res Biol* 11: 219-226.
- Hodge LM (2012) Osteopathic lymphatic pump treatments to enhance immunity and treat pneumonia. *Int J Osteopath Med* 15: 13-21.
- Creasy C, Schander A, Orlowski A, Hodge LM (2013) Thoracic and Abdominal Lymphatic Pump Techniques Inhibit the Growth of *S. pneumoniae* Bacteria in the Lungs of Rats. *Lymphat Res Biol* 11: 183-186.
- Alitalo K (2011) The lymphatic vasculature in disease. *Nat Med* 17: 1371-80.
- Bodine WA (2019) Osteopathic Manipulative Treatment: A Primary Care Approach. *Am Fam Physician* 99: 214.
- Noll DR, Degenhardt BF, Johnson JC (2016) Multicenter Osteopathic Pneumonia Study in the Elderly: Subgroup Analysis on Hospital Length of Stay, Ventilator Dependent Respiratory Failure Rate, and In- hospital Mortality Rate. *J Am Osteopath Assoc* 116: 574-587.
- Degenhardt BF, Kuchera ML (1996) Update on osteopathic medical concepts and the lymphatic system. *J Am Osteopath Assoc* 96: 97-100.

26. Seffinger MA, King HH, Ward RC, Jones JM, Rogers FJ, et al. (2003) Osteopathic philosophy. In: Ward RC eds. *Foundations for osteopathic medicine*. Philadelphia: Lippincott Williams and Wilkins 3-12.
27. Noll DR, Shores J, Bryman PN, Masterson EV (1999) Adjunctive osteopathic manipulative treatment in the elderly hospitalized with pneumonia: a pilot study. *J Am Osteopath Assoc* 99: 143-146, 151-152.
28. Noll DR, Shores JH, Gamber RG, Herron KM, Swift J (2000) Benefits of osteopathic manipulative treatment for hospitalized elderly patients with pneumonia. *J Am Osteopath Assoc* 100: 776-782.
29. Higgins JPT, Green S (2011) *Cochrane Handbook for Systematic Reviews of Interventions*. The Cochrane Collaboration.
30. Remien K, Vilella RC (2022) Osteopathic Manipulative Treatment: Lymphatic Procedures. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing.
31. Olszewski WL (2003) The lymphatic system in body homeostasis: physiological conditions. *Lymphat Res Biol* 1: 11-21.
32. Seffinger MA (2018) *Foundations of Osteopathic Medicine*. Philadelphia: Lippincott Williams & Wilkins pp: 178-179.
33. Ozdowski L, Gupta V (2022) In: *StatPearls*. Treasure Island (FL): StatPearls Publishing. Treasure Island: StatPearls Publishing. *Physiology, Lymphatic System*.
34. Cohen SR, Payne DK, Tunkel RS (2001) Lymphedema: strategies for management. *Cancer* 92: 980- 987.
35. Zawieja DC (2009) Contractile physiology of lymphatics. *Lymphat Res Biol* 7: 87-96.
36. Hruby RJ, Martinez ES (2021) The Lymphatic System: An Osteopathic Review. *Cureus* 13: 7.
37. Sandhouse M (2015) *A Teaching Guide for Osteopathic Manipulative Medicine*. Chevy Chase: American Association of Colleges of Osteopathic Medicine. Hensel K, Cymet T (Authors).
38. Yao S, Hassani J, Gagne M, George G, Gilliar W (2014) Osteopathic Manipulative Treatment as a Useful Adjunctive Tool for Pneumonia. *J Vis Exp* 87: 50687.
39. Pelosi P, Quintel M, Malbrain ML (2007) Effect of intra- abdominal pressure on respiratory mechanics. *Acta Clin Belg Suppl* 1: 78-88.
40. Vanti C, Golfari M, Pellegrini G, Panizzolo A, Turone L, et al. (2021) The Effectiveness of Pump Techniques and Pompages: A Systematic Review. *Journals Applied Sciences* 11: 9.