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Adjunctive osteopathic therapy for hospitalized COVID-19 patients: A feasibility-oriented chart review study with matched controls

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ABSTRACT

Background: Osteopathic manipulative treatment (OMT) may improve outcomes during COVID-related respiratory distress – the most common cause of death from novel coronavirus (SARS-CoV-2). Outcomes from OMT treatments of respiratory distress during the COVID-19 pandemic have not been reported.

Objective: Assess adjunctive OMT in hospitalized patients with SARS-CoV-2 and respiratory distress.

Design: Feasibility oriented retrospective observational cohort study.

Setting: COVID-19 (non-ICU) ward in a tertiary academic medical center.

Methods: Inpatients received daily OMT treatments of rib raising, abdominal diaphragm doming, thoracic pump and pedal pump. Primary outcomes were procedural acceptance, satisfaction, side effects, and adverse events. Secondary outcomes were patient-reported clinical change after therapy; number of hospital days; need during hospitalization for high-flow oxygen, C-PAP/BiPAP or intensive care; need for supplementary oxygen at discharge; and discharge disposition.

Participants: Hospitalized adults with SARS-CoV-2 infection and respiratory distress.

Results: OMT (n = 27) and Control (n = 152) groups were similar in demographics and most laboratory studies. 90% of patients accepted OMT and reported high satisfaction (4.26 ± 0.71 (maximum 5)), few negative effects, no adverse events, and positive clinical change (5.07 ± 0.96 (maximum 7)). Although no significant differences were found in secondary outcomes, OMT patients trended towards fewer hospital days than Controls (p = 0.053; Cohen’s d = 0.22), a relationship that trended towards correlation with number of co-morbidities (p = 0.068).

Conclusion: Hospitalized patients with respiratory distress and COVID-19 reported acceptance, satisfaction, and greater ease of breathing after a four-part OMT protocol, and appear to have a shorter length of hospitalization. Randomized controlled trials are needed to confirm these results.

Implications for practice

- OMT for hospitalized COVID-19 patients in respiratory distress is well accepted by patients, who perceived value in OMT treatments and experienced no adverse events.
- OMT for hospitalized COVID-19 patients in respiratory distress showed marginally significant reductions in length of hospital stay.
- OMT for hospitalized COVID-19 patients in respiratory distress appear to have better effect on patients with more comorbidities.
- OMT for hospitalized COVID-19 patients in respiratory distress did not have an impact on mortality or hospital disposition in our patients.

1. Introduction

Infection with SARS-CoV-2 often presents with mild to moderate lower respiratory symptoms, but severe infections can lead to respiratory distress and death [1]. Disease severity is associated with age and numerous co-morbidities including heart disease [2]. The U.S. and worldwide case number, morbidity and death rates are well-reported; the cost to society is incalculable. While vaccines are expected to limit infection and spread of SARS-CoV-2, there is no cure for active disease. Care is supportive, high case rates are expected to continue, and there is now concern that SARS-CoV-2 may become endemic, with annual surges of COVID-19 similar to influenza [3]. Effective adjunctive therapy is therefore urgently need for severe SARS-CoV-2 infections characterized by respiratory distress.
Osteopathic medical care, a medical tradition dating to the mid-1800s, has become progressively integrated into U.S. conventional care in the past 20 years [4]. Osteopathic manipulative treatment (OMT) is the foundational therapy in osteopathy and has a long history of reported efficacy for a variety of conditions [5–8], including as adjunctive therapy for respiratory disease [9–11]. During the Spanish influenza pandemic of 1918–1919, osteopaths reported better outcomes than did allopaths [12–15]. While those reports are controversial [12,14], they document a history of use. However, comparative effectiveness studies for OMT often lag behind reported efficacy [4], and OMT for respiratory distress follows this pattern. In spite of the efficacy reported during Spanish flu, nearly a century passed before a randomized controlled trial (RCT) demonstrated how effective OMT may be when used as an adjunctive treatment for respiratory distress. That RCT reported that elderly patients with pneumonia who received a complete OMT protocol had significantly reduced hospital length of stay, duration of antibiotics, and respiratory failure and death rates [16]. Older, sicker patients were more likely to benefit from OMT [17]. Content experts have called for assessment of OMT for respiratory distress in the context of the COVID-19 pandemic [18,19]. We (*blinded author initials*) treated patients with respiratory distress stemming from a variety of conditions with OMT, and have used OMT to treat patients with respiratory distress from infection with SARS-CoV-2. However, no formal treatment protocol or systematic study has been undertaken in a hospital setting. We therefore conducted a feasibility study using retrospective chart review methodology comparing two groups of hospitalized patients receiving usual care for presumed SARS-CoV-2 infection: those who also received adjunctive OMT and those who did not.

2. Methods

This is a feasibility-oriented retrospective cohort study using electronic health record review, determined to be exempt from formal review by the *blinded* Institutional Review Board. Reporting is consistent with published CONSORT guidelines and adapted for our retrospective design [20,21]. Inclusion criteria were age ≥18 years, infection with SARS-CoV-2 (laboratory confirmed or presumed based on symptom constellation), evidence of respiratory distress (increased work of breathing, elevated respiratory rate, need for new or increased oxygen), and admission to our COVID-19-dedicated inpatient service (Service) between May 5, 2020 and June 7, 2020. Exclusion criteria were injury or condition preventing safe receipt of OMT procedures.

2.1. Cohort selection

All patients treated on the Service were identified using the Penn State Health Electronic Health Record. One study team member (*blinded*) reviewed charts of adults. All parts of the patient medical record, including physician notes, laboratory and other diagnostic studies, were used to identify those patients who received OMT (OMT) and those who did not (Control).

During the study period, all adult patients on the COVID-19 Service received guideline-driven routine supportive care (usual care). When the Service was staffed by an attending physician trained to perform OMT for respiratory distress, all patients seen by that clinician and eligible for OMT were offered OMT in addition to usual care at the first encounter, and were offered OMT daily for as long as that patient and an OMT physician were on the Service. Conversely, all patients seen by a clinician not trained in OMT received usual care alone. In this way, patients who did not receive OMT served as a control for the OMT group.

Like most osteopathic practitioners, we typically select OMT procedures based on individual patient presentation. However, because of the limitations of time and invasiveness, our providers used an iterative consensus-based process to determine a set of procedures most likely to yield benefit. From this process, they applied each of the following four treatments to each patient: rib raising, abdominal diaphragm doming, thoracic pump and pedal pump. See Appendix 1 for a description of each technique. Treatments were given with the clinician dressed in personal protective equipment due to COVID-19, and with the patient supine in bed, except in the presence of orthopnea or dyspnea, in which case the patient’s head was elevated to 45°. Detailed discussion [22,23] and video of the first three techniques [24] and pedal pump [25] are described elsewhere. The entire procedure requires approximately 5 min.

2.2. Outcome measures

Demographic data extracted from patient charts included age, sex, race, and ethnicity. Where race was not identifiable in the chart, “Other” was recorded. Where ethnicity was not identified as “Hispanic, Latino, or Spanish Origin” in the chart, “Not Hispanic, Latino, or Spanish Origin” was recorded. We determined the presence or absence of comorbidities Diabetes Type 2, Cardiovascular Disease, Chronic Renal Disease, Chronic Obstructive Pulmonary Disease, Obesity, Sickle Cell Disease, or Immunocompromised Status (See Appendix 2). Admission temperature, presence of fever (temperature ≥38° Celsius), admission oxygen saturation, and the presence of pneumonia on chest x-ray were also documented. Test results for SARS-CoV-2, D-Dimer, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C reactive protein (CRP), ferritin, and procalcitonin, if drawn within the first 24 h of admission, were also recorded.

We assessed four primary clinical outcome measures associated with administration of OMT: rate of procedural acceptance, satisfaction (5-point ordinal scale, –2 = “very unsatisfied” to +2 = “very satisfied”, later converted to a 1–5 point scale), side effects, and adverse events. We assessed six secondary outcomes: patient-reported clinical change after therapy was assessed using the Global improvement item of the Clinical Global Impression Scale, a 7-point ordinal scale (–3 = “very much worse” to +3 = “very much improved”, later converted to a 1–7 point scale) [26]; and number of hospital days, need for high-flow oxygen or CPAP/BiPAP during hospitalization (yes/no), intensive care unit stay during hospitalization (yes/no), need for supplementary oxygen at discharge (yes/no), and discharge disposition (home, rehabilitation facility, death).

The time point during hospitalization at which OMT was first delivered was assessed in two ways: first, the days from admission on which OMT was first delivered; second, the relative time point during admission as a whole when OMT was first applied was expressed as a fraction of days from admission to first OMT/total number of days hospitalized. We extracted and summarized qualitative physician comments from the charts of OMT-treated patients related to OMT treatment.

2.3. Sample size

Feasibility and effects of OMT for symptoms associated with presumed or laboratory-proven SARS-CoV-2 infection in hospitalized patients have not been reported, so it was not possible to rigorously calculate a sample size. A longer period of collection offers greater power to identify positive clinical outcomes and explore subgroup analysis, but needed to be balanced with a need to determine acceptability to patients and general efficacy to address the urgent need for care during the pandemic. With those considerations, we chose a convenience sample of patients enrolled to the Service during a one-month time period.

2.4. Statistical methods

Statistical analyses were performed in R [27] with packages knitr, Hmisc, gtsummary to generate reproducible statistical analyses and tables. Non-parametric statistical tests, and Wilcoxon rank sum test were performed for comparing continuous variables between OMT and
control groups, while Chi-square test or Fisher exact test were conducted for comparing categorical variables between two groups. A multiple linear regression analysis controlling for age, gender, ethnicity and number of co-morbidities was applied to compare the length of hospital days between OMT and control groups. Statistical significance is defined as p < 0.05. Cohen’s d effect size was calculated: d = 0.2 is considered a ‘small’ effect size, 0.5 a ‘medium’ effect size and 0.8 a ‘large’ effect size.

3. Results

3.1. Baseline characterization and hospital course

179 patients (27 OMT and 152 Control) were treated on the Service and were included in the analysis; the study sample consisted of 54% women, was 62.7 ± 18.3 years old and had a body mass index of 31.8 ± 9.02 kg/m²; 65.5% were White. The groups were similar at baseline in demographics, vital signs, co-morbidities, and laboratory studies, with significant differences only in Control having lower AST (34.8U/L versus 49.6U/L, p = 0.041) and lower ferritin (429 ng/mL versus 965 ng/mL, p < 0.001; Table 1). There was no difference between the percent of patients in the OMT group versus Control for patients needing supplemental high flow oxygen (33.3% versus 33.6%, p = 1.00), mechanical ventilation (0% versus 12.8%, p = 0.081), or CPAP/BiPAP (3.7% versus 10.5%, p = 0.476) during their hospital stay.

3.2. OMT receipt and patient-reported effects

Nine patients seen by OMT providers were not offered OMT due to being under 18 years old (n = 7), leaving the hospital against medical advice (n = 1) or recent motor vehicle accident involving trauma to the chest (n = 1). 29 patients were offered a first OMT procedure, of whom 27 accepted and received a treatment session. The number of daily subsequent sessions per patient decreased by hospital day depending on patient and OMT provider presence on the Service and patient preference; 15 patients received a second session, five received a third, three received a fourth and two received a fifth, for a total of 52 sessions (Fig. 1). Forty-eight of 52 treatment sessions included all four procedures; three patients either shortened or declined one procedure during one session (three diaphragmatic doming and one thoracic pump) due to procedure-related pain. One patient declined diaphragmatic doming due to pre-existing musculoskeletal abdominal pain. Two patients who had an initial session declined a subsequent session, one for unrelated psychological reasons, the second because of pain on the prior day from the thoracic pump procedure. Completed OMT elements were done in accordance with planned procedures description (Appendix 1). Sessions were performed relatively early in patients’ hospitalization; the hospitalization ratio was 0.32 ± 0.22 and their first OMT session was provided within 2.07 ± 1.73 days of admission. Patients reported satisfaction with the OMT sessions of 4.33 ± 0.68 points per session (“satisfied”; Table 2). They reported clinical change after OMT sessions therapy of 5.13 ± 1.05 points per session (“improved”) (Table 2). Side effects included two procedure-related and self-limited episodes of pain with diaphragmatic doming, and one of pain with thoracic pump. There were no adverse events.

3.3. Hospitalization days, ICU stays, new home oxygen, discharge status

In our unadjusted statistical model, OMT patients trended towards fewer hospital days than Control patients (6.93 ± 3.02days versus 8.63 ± 7.97 days (p=0.053; Cohen’s d = 0.23 (small effect size) (Table 3). There were no significant differences between groups regarding the presence of ICU care, new home oxygen requirement, or discharge status (Table 3).

To explore the relationship between hospital days and OMT receipt, we performed a log transformation of hospital days to reduce data skewness. The results from subsequent linear regression analysis showed no significant difference in hospital days between OMT and Control patients (p = 0.2). However, as the number of patient comorbidities increased, OMT patients trended toward fewer hospital days compared with Control group patients (p = 0.068) (Fig. 2).

3.4. Qualitative comments

OMT-treated physicians noted that OMT was well tolerated by almost all patients; they felt that the limited treatment options available may have predisposed them to trying OMT. The few patients that reported side effects still found some value in OMT, even if they decided to discontinue all or part of the treatment. OMT was easily performed, though the degree of contact with the patient (particularly with rib raising) was significantly greater than that of a general physical exam; appropriate personal protective equipment was available and used. Physicians reported that patients considered OMT to be a respite from an otherwise isolating and frightening hospital course. Providers reported

### Table 1

| Demographics                        | OMT (N = 27) | Control (N = 152) | p |
|-------------------------------------|--------------|-------------------|---|
| **Age (years), mean (SD)**          | 61.8 (17.3)  | 62.3 (18.5)       | 0.885 |
| **Female Sex, % (N)**               | 16 (59.3%)   | 76 (50.0%)        | 0.498 |
| **Race, % (N)**                     |              |                   | 0.901 |
| Asian                               | 1 (3.70%)    | 11 (7.24%)        |     |
| Black or African American           | 2 (7.41%)    | 18 (11.8%)        |     |
| Other                               | 4 (14.8%)    | 24 (15.8%)        |     |
| White                               | 20 (74.1%)   | 99 (65.1%)        |     |
| **Hispanic, Latino, or Spanish Origin, % (N)** | 5 (18.5%) | 21 (13.8%) | 0.554 |
| **Presence of selected comorbid conditions, % (N)** |       |                   |       |
| Diabetes Type 2                      | 9 (33.3%)    | 57 (37.5%)        | 0.844 |
| Cardiovascular Disease               | 5 (18.5%)    | 41 (27.0%)        | 0.492 |
| Chronic Renal Disease                | 5 (18.5%)    | 50 (32.9%)        | 0.206 |
| COPD                                | 4 (14.8%)    | 20 (13.2%)        | 0.764 |
| Immunocompromised Status             | 0 (0.00%)    | 2 (1.32%)         | 1.000 |
| Obesity (BMI ≥30 kg/m²)              | 19 (70.4%)   | 74 (48.7%)        | 0.062 |
| Sickle Cell Disease                  | 0 (0.0%)     | 0 (0.0%)          | 1.000 |
| **Status on Admission**              |              |                   |       |
| BMI (kg/m²), mean (SD)              | 33.2 (7.53)  | 31.6 (9.26)       | 0.338 |
| Temperature (Celsius), mean (SD)     | 37.4 (0.94)  | 37.8 (5.08)       | 0.328 |
| Presence of fever on admission       | 6 (22.2%)    | 28 (18.4%)        | 0.843 |
| Admission O2 saturation, % (SD)      | 93.4 (7.03)  | 94.9 (5.81)       | 0.304 |
| Pneumonia on Chest X-Ray, % (SD)     | 16 (61.5%)   | 105 (71.4%)       | 0.221 |
| **Laboratory studies**               |              |                   |       |
| Positive test for SARS-CoV-2, % (SD) | 19 (70.4%)   | 128 (85.3%)       | 0.090 |
| D-dimer (mcg/mL), mean (SD)         | 2.30 (5.15)  | 2.11 (2.79)       | 0.896 |
| ALT (U/L), mean (SD)                | 29.8 (17.9)  | 40.2 (90.5)       | 0.207 |
| AST (U/L), mean (SD)                | 34.8 (20.0)  | 49.6 (72.0)       | 0.041 |
| CRP (mg/dL), mean (SD)              | 6.07 (5.97)  | 7.33 (6.61)       | 0.373 |
| Ferritin (ng/mL), mean (SD)         | 423 (466)    | 963 (1430)        | 0.001 |
| Procalcitonin (ng/mL), mean (SD)    | 0.21 (0.22)  | 0.44 (1.05)       | 0.038 |

SD = standard deviation; AST = aspartate aminotransferase; ALT = alanine aminotransferase; CRP = C reactive protein; COPD = chronic pulmonary obstructive disease; OMT = osteopathic manipulative treatment.

- Wilcoxon rank sum test was used for comparing continuous variables; Chi-square test or Fisher exact test were conducted for comparing categorical variables; all to 95% confidence. Bold value are significant.
- Gender was not to be identified from the medical record. Sex (M/F) was found for all patients in the medical record.
- Race and ethnicity were documented as recorded in the medical record. Where race was unclear or missing, “Other” was documented, where ethnicity was not documented as “Hispanic, Latino, or Spanish Origin,” “Not Hispanic, Latino, or Spanish Origin” was documented.
- See Appendix 2 for details.
- These are patients with positive findings diagnostic of pneumonia. One patient in the OMT group and one patient in the Control group had an undetermined chest x-ray, the remainder in each group had no findings suggestive of pneumonia.
- Laboratory confirmed positive SARS-CoV-2 test.
6

benefit in being able to offer OMT as a personal management option in an otherwise challenging environment with limited therapeutic options.

4. Discussion

4.1. Main findings

This chart review of hospitalized patients with laboratory proven or presumptive COVID-related respiratory distress, and who were treated with routine care or routine care with OMT, has several important findings. Patients accepted and were satisfied with OMT care. Physicians reported that OMT was easily performed in the inpatient setting, but that the procedures, especially rib raising, resulted in more contact than routine physical exams. There were few side effects and no adverse events. Patients reported improvement in overall breathing status and OMT patients trended towards fewer hospital days, a finding that may be correlated with number of co-morbidities. To our knowledge, these data are the first to assess the feasibility and effect of OMT in COVID patients.

While such findings are suggestive, caution is warranted. Consistent with the retrospective nature and small sample size of our study, we are not able to assign causality. In addition, while we have made efforts to control for as many non-specific factors as possible, we have not been able to control for elements such as time required to perform OMT or the therapeutic nature of a physician’s healing touch [28].

4.2. Comparison to literature

Reduction in hospital stay with OMT is consistent with the MOPSE trial [11]. In that multicenter RCT, per-protocol analysis showed a one day decrease in length of stay (LOS) among patients with pneumonia treated with OMT compared to those receiving conventional care only [11], which supports the marginal significance with small effect size of our OMT cohorts’ shorter stay of 1.7 days. With an average daily cost of $836 for patients hospitalized with pneumonia [29], a 1.7 day decrease in LOS for COVID-19 patients saves $1,420 per patient. Across the 161,266 patients admitted in the U.S. for COVID-19 between March 2020 and March 2021 [30], this represents a potential cost savings of over $229,000,000.

Other therapies for COVID-19 have yielded mixed results regarding LOS. Among high-profile treatments that showed no impact on LOS are vitamin D [31] and hydroxychloroquine [32]. Dexamethasone use has been controversial as a treatment during the COVID-19 pandemic, with studies showing mortality benefits in patients requiring mechanical

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ventilation, but not in those receiving no respiratory support [33]. Results of studies on LOS with steroid treatment are mixed, so no firm conclusions can be drawn [34]. Treatments shown to decrease LOS in COVID-19 patients include tocilizumab (1 day) [35], anticoagulation (2 days) [36], convalescent plasma (3.3 days) [37], and the only FDA-approved therapy for COVID-19, remdesivir (5 days) [38].

Benefits of OMT compared to other effective treatments include low cost and an absence of side effects. In low resource areas or patients intolerant of specific drug therapies, OMT alone may provide significant benefit. In high resource settings, OMT may serve as a useful adjunct for care, potentially providing effects synergistic to existing effective treatments.

Greater effect on LOS reduction with increasing comorbidities is also consistent with the MOPSE trial, which found that OMT had greater benefit in older adults with more severe pneumonia [10].

4.3. Mechanism of action

The precise mechanism of action of osteopathic therapy in general and OMT in particular is not well understood. A multifactorial mechanism with both direct and indirect effects, is possible. Many osteopathic techniques, including those used in this study, were designed to remove restriction to tissues, drain pooled fluid from diseased tissue, and enhance the entry of lymph into systemic circulation. While the exact mechanism of protection offered by OMT during the treatment of COVID-19 has not been identified, it is possible that OMT enhances the immune response to respiratory pathogens. Animal studies support this hypothesis and have provided insight into the mechanisms by which OMT enhance immunity. For example, both abdominal and thoracic pumps were documented to increase thoracic duct lymph flow in dogs [39]. In subsequent studies, abdominal pump increased lymph flow and the flux of leukocytes, protein, cytokines, chemokines, and reactive oxygen and nitrogen species in both the intestinal and thoracic lymph of dogs [40–44]. In a rat model of bacterial pneumonia, the application of thoracic and abdominal pumps decreased the concentration of pulmonary bacteria [45]. Therefore, increasing lymph flow during OMT may redistribute immune cells and protective lymph-borne factors to the lung which aid the clearance of respiratory pathogens. Cytokines such as interleukin (IL)-1, IL-6, IL-8 and tumor necrosis factor-alpha (TNF-a) contribute to the cytokine storm in patients with COVID-19 infection [46]. The additional lymph mobilized by OMT may contain bioactive mediators that protect the lung against the immunopathology that is associated with COVID-19, such as the cytokine storm. In support of this theory, the transfusion of lymph into rats alleviated endotoxin-induced lung injury [47]. Lymph has also been reported to suppress the secretion of TNF-a by endotoxin-activated macrophages [44]. In addition to clinical endpoints, future studies could measure the impact of OMT on inflammatory biomarkers which may help elucidate the mechanism of protection offered by OMT during the treatment of COVID-19.

4.4. Strengths and limitations

A strength of this study is its pragmatic assessment of outcomes from actual practice. Another is that, consistent with clinical trials, each patient received uniform care. While osteopathic care often appropriately tailors care to individual patient needs, the uniformity of our approach increases the ability of others to reproduce the intervention. Limitations include the retrospective nature of the study, which limits the extent to which we can control for confounding variables including non-specific effects of osteopathic care. Also limiting is our small intervention group sample size; while the Cohen’s effect size suggests a meaningful treatment effect, more formal prospective basic science and clinical studies are needed to assess the impact of OMT for respiratory distress. Rib raising resulted in greater physical contact than usual care; this may limit generalizability in areas with inadequate personal protective equipment, or for application in diseases with higher infectivity and mortality. Using a standard protocol for all patients is a limitation when viewed from the osteopathic medical tradition, a cornerstone of which is treatment tailored to each patient. However, it is unclear whether results would change with individualized care. The reproducibility associated with a standard protocol is important when assessing research outcomes and to wider dissemination should OMT for respiratory distress be found efficacious in more rigorous trials.

These results have implications for clinical practice and research. Incorporating OMT in the routine care of hospitalized patients infected with SARS-CoV-2 who are experiencing respiratory distress may increase hospital throughput, increasing available beds and decreasing cost. Research to determine clinical utility and optimize the OMT procedural protocol is urgently needed. Given the proposed mechanism of action, this benefit may also exist for other sources of respiratory distress. Over time, research exploring the range of conditions for which a standardized, reproducible protocol is effective may reveal opportunities to improve care in both the inpatient and outpatient setting.

5. Conclusions

Among these hospitalized patients with SARS-CoV-2 with respiratory distress, OMT appears to be a feasible, well-tolerated and effective adjunctive therapy. Prospective studies are needed to confirm these results and explore the extent of benefit of OMT alone and in combination with other treatments, mechanisms of action, and application to other respiratory conditions.

Conflict of interest

The authors declare no conflicts of interest.

Funding sources

Funding for this project was provided by the Pennsylvania State University Huck Institutes of the Life Sciences. The funding source had no role in study design, collection and analysis of data, or in the writing of this report.

Ethical approval

This study was approved by the Pennsylvania State College of Medicine Institutional Review Board. Clinical Trial Registration was not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.josm.2022.05.004.

References

[1] Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. J Med Virol 2020. https://doi.org/10.1002/jmv.25748.
[2] Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in wuhan, China. JAMA Cardiology 2020;5 (7):982–10. https://doi.org/10.1001/jamacardio.2020.0950.
[3] Scudellari M. How the pandemic might play out in 2021 and beyond. Nature (London) 2020;584(7819):22–3. https://doi.org/10.1038/s41586-020-02279-3.
[4] Steel A, Sundberg T, Reid R, et al. Osteopathic manipulative treatment: a systematic review and critical appraisal of comparative effectiveness and health economics research. Man Ther 2016;27:165–75. https://doi.org/10.1016/j.math.2016.10.067.
[5] Cerritelli F, Ginevri L, Mesi G, et al. Clinical effectiveness of osteopathic treatment in chronic migraine: 3-Armed randomized controlled trial. Compl Ther Med 2015; 23(2):149–56. https://doi.org/10.1016/j.ctim.2015.01.011.
[6] Crow WT, Gorodinsky L. Does osteopathic manipulative treatment (OMT) improves outcomes in patients who develop postoperative ileus: a retrospective chart review.
International Journal of Osteopathic Medicine 44 (2022) 3–8

[7] Gros A, Langevin P, Burnie SJ, et al. Manipulation and mobilization for neck pain contrasted against an inactive control or another active treatment. Cochrane library 2015;2015(9):CD004249. https://doi.org/10.1002/14651858.CD004249.

[8] Orrock PJ, Myers SP. Osteopathic intervention in chronic non-specific low back pain: a systematic review. BMC Musculoskel Disord 2013;14(1):129. https://doi.org/10.1186/1471-2474-14-129. 129.

[9] Goyal M, Goyal K, Narkeesh K, et al. Efficacy of osteopathic manipulative treatment approach in the patient with pulmonary fibrosis in critical care outpatient department. Indian J Crit Care Med Jul 2017;21(7):469–72. https://doi.org/10.4103/0972-5229.210648.

[10] Noll DR, Degenhardt BF, Johnson JC. 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 Sep 1 2016;116(9):574–87. https://doi.org/10.7556/jaoa.2016.117.

[11] Noll DR, Degenhardt BF, Morley TF, et al. Efficacy of osteopathic manipulation as an adjunctive treatment for hospitalized patients with pneumonia: a randomized controlled trial. Osteopath Med Prim Care Mar 19 2010;42. https://doi.org/10.1186/1750-4732-4-2.

[12] Hruby RJ, Hoffman KN. Avian influenza: an osteopathic component to treatment. Osteopath Med Prim Care 2007;1(1):10. https://doi.org/10.1750-4732-1-10. 10.

[13] Magoun JHI. More about the use of OMT during influenza epidemics. J Am Osteopath Assoc 2004;104(10):406.

[14] Mueller DM. The 2012-2013 influenza epidemic and the role of osteopathic manipulative medicine. J Am Osteopath Ass 2013;113(9):703–7. https://doi.org/10.7556/joa.2013.036.

[15] Walter G. The first school of osteopathic medicine. The Thomas Jefferson University Press at Northeast Missouri State University; 1992.

[16] Noll DR, Degenhardt BF, Morley TF, et al. Efficacy of osteopathic manipulation as an adjunctive treatment for hospitalized patients with pneumonia: a randomized controlled trial. Osteopath Med Prim Care 2010;4(1):2. https://doi.org/10.1186/1750-4732-4-2.

[17] Noll DR, Degenhardt BF, Johnson JC. 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 Sep 1 2016;116(9):574–87. https://doi.org/10.7556/jaoa.2016.117.

[18] Martinez E, Redding D. Osteopathic response to the COVID-19 pandemic. J Am Osteopath Assoc Sep 1 2020;119(7):455.

[19] Colon M, Wilkins; 2011. p. 1056.

[20] Hodge LM, King HH, Williams Jr AG, et al. Abdominal lymphatic pump treatment as an adjunctive treatment for hospitalized patients with pneumonia: a randomized controlled trial. Osteopathy Med Prim Care Mar 19 2010;42. https://doi.org/10.1186/1750-4732-4-2.

[21] Hodge LM, Bearden MK, Schander A, et al. Lymphatic pump treatment mobilizes leukocytes from the gut associated lymphoid tissue into lymph. Lymphatic Res Biol 2013;11(4):219. https://doi.org/10.1089/lrb.2012.0021.

[22] Schander A, Downey HF, Hodge LM. Lymphatic pump manipulation mobilizes inflammatory mediators into lymphatic circulation. Exp Biol Med Jan 2012;237(1):58–63. https://doi.org/10.1258/ebm.2011.011220.

[23] Schander A, Padro D, King HH, Downey HF, Hodge LM. Lymphatic pump treatment repeatedly enhances the lymphatic and immune systems. Lymphatic Res Biol Dec 2013;11(4):219–26. https://doi.org/10.1089/lrb.2012.0021.

[24] Castilho R, Schander A, Hodge LM. Lymphatic pump treatment mobilizes bioactive lymph that suppresses macrophage activity in vitro. J Am Osteopath Assoc Jul 1 2018;118(7):455–61. https://doi.org/10.7556/joa.2018.099.

[25] Hodge LM, Creasy C, Carter K, Orlowski A, Schander A, King HH. Lymphatic pump treatment as an adjunct to antibiotics for pneumonia in a rat model. J Am Osteopath Assoc May 15 2015;115(5):306–16. https://doi.org/10.7556/joa.2015.061.

[26] Soy M, Keser G, Atagündüz I, Tabak F, Atagündüz I, Kayhan S. Cytokine storm in COVID-19: pathogenesis and overview of anti-inflammatory agents used in treatment. Clin Rheumatol Jul 2020;39(7):2085–94. https://doi.org/10.1007/s10067-020-05195-5.

[27] Cheng AM, Moore EE, Masuno T, et al. Normal mesenteric lymph blunts the pulmonary inflammatory response to endotoxin. J Surg Res Dec 2006;136(2):166–71. https://doi.org/10.1016/j.jss.2006.05.013.