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Manual therapy is effective in reducing VAS pain scores in patients with osteoarthritis

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Abstract

Osteoarthritis (OA) affects more than 30 million American adults over the age of 40. Current physical therapy treatment regimes to treat OA do not always include manual therapy and the efficacy of manual therapy remains controversial. Additionally, pain associated with OA can lead to increased stress and cortisol exposure. Our goal was to determine if manual therapy, in addition to prescriptive exercise and ultrasound, is more effective in reducing OA- associated pain and cortisol exposure as compared to prescriptive exercise and ultrasound alone. We hypothesized that the addition of manual therapy would promote an increased reduction in pain and cortisol. Participants were randomly assigned to either a control group (n=19) receiving ultrasound (US) and prescriptive exercise or to an experimental group (n=24) receiving manual therapy in addition to US and prescriptive exercise over a 6-week treatment period. Outcome measures included change in visual analogue scale (VAS) pain level and change in basal salivary cortisol levels. Participants who received the manual intervention experienced a significantly greater reduction in pain level and this was more evident among women, participants with low or normal BMI scores and participants with affected weight-bearing joints. No correlation between change in pain-level and change in basal cortisol was found. Limitations of this study include the small sample size, the length of the study follow up and extrinsic factors that are difficult to control for including stressors in the environment and timing of medication ingestion as it related to cortisol collection time. Overall our data support the efficacy of manual therapy in a physical therapy plan of care to promote the reduction of OA associated pain.

Keywords: Osteoarthritis, manual therapy, ultrasound, pain

Introduction

Osteoarthritis (OA) is the most common form of arthritis, affecting more than 30 million American adults over the age of 40. Risk factors for OA include age, gender, obesity, joint stress, and genetics [1]. OA is characterized by articular cartilage decline [2] in synovial joints throughout the body. Pain, as a result of inflammation and degeneration, is a significant symptom of OA. In response to pain, the stress-axis is activated, resulting in increased circulating cortisol levels [3]. Over time, chronic pain associated stress can lead to cortisol dysfunction and widespread inflammation, thus exacerbating inflammation-associated joint degeneration [4].

Physical Therapy (PT) is often used to treat patients with OA [5]. The standard plan of care, as described by The Brigham and Women's Hospital, includes exercise, joint preservation through assistive devices or bracing, education, and modalities one to two times per week for four to six weeks [6]. Ultrasound (US) and manual techniques are both conventional PT modalities.

Ultrasound has been used for many decades in the management of OA pain and has been shown to enhance stress protein

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production in arthritic chondrocytes [7]. Low-level therapeutic ultrasound (0.125-3 watts/cm2) is used to stimulate a normal physiology response which enhances cartilage repair in early OA, and arrest deteriorative damage in later stages [8,9].

Manual therapy also results in a significant improvement in pain, general health, and functional disability [10] through a mechanism akin to that associated with massage therapy. Massage therapy can lead to pain relief by breaking down subcutaneous adhesions, which promotes blood and lymph circulation, increases serotonin levels, and stimulates the release of endorphins into the bloodstream. An increased level of serotonin "may inhibit the transmission of noxious nerve signal to the brain" [11]. In line with this, studies demonstrate that manual therapy, along with supervised exercise in OA management, added greater pain relief than a home exercise program alone [12].

The need for additional investigation on the use of modalities such as US and manual therapy has been identified [5,13,14]. Recently, the healthcare industry is facilitating and encouraging the treatment of more patients in less time, which could inhibit the inclusion of time-consuming manual therapy in a care plan. Additionally, the efficacy of manual therapy in treatment of musculoskeletal disorders remains controversial and it has been suggested that the goal of manual therapy is to provide a window of opportunity for achieving a change in the neuromuscular system [15].

Our goal was to determine if manual therapy, in addition to prescriptive exercise and ultrasound, is more effective in reducing OA- associated pain and cortisol exposure as compared to prescriptive exercise and ultrasound alone. The hypothesis was that the addition of manual therapy would further promote an increased reduction in pain and cortisol.

Methods

Study Participants

Approval to carry out the study with human subjects was approved by the Molloy College Institutional Review Board (IRB). Physical therapy patients that were referred by a physician for treatment of osteoarthritis to a local outpatient clinic were asked to participate in the study, all of whom signed an informed consent. Inclusion criteria were the diagnosis of OA in male and female patients ages 40-90. Subjects were excluded from the study if they had an intra-articular injection in the associated joint within six weeks of the study start or surgical intervention at the site. Also excluded were patients with comorbidity of inflammatory, rheumatic, hypothalamic, pituitary or adrenocortical disease, or any contraindications to ultrasound or manual therapy.

Randomization and Blinding

After consent, participants were identified by a number between 1 and 45, randomly chosen out of a blinded bag of numbers by a clerical staff member not involved in the study. Participants were alternately assigned to the experimental group, and then the control group. The construction of treatment plans for subjects occurred after all participants received a thorough evaluation of their condition. These plans included prescriptive exercises and ultrasound for the affected joint, typical in any standard therapy Plan of Care. Patients that were randomly assigned to the experimental group received manual therapy in addition to conventional practices. All clinical and demographic information was collected and recorded. BMI was determined at the initial visit using a hand-held monitor (Fat Loss Monitor Model HBF-306C, distributed by Omron Healthcare, Inc.). All participant data was assigned a number by a staff member not involved in the study. No unique identifiers were used. To control for the placebo effect and bias, the control group also received superficial manual touch, not to affect beyond the epidermis. The provider that carried out the manual treatment in the study has practiced PT for over 25 years, holds an advanced degree in manual therapy, and is an Orthopedic Certified Specialist.

Interventions

Ultrasound was used for all patients in both the experimental and control group at 1.2 w/cm2 for 8 minutes as per previous protocols [2,9] and applied over the joint line of the affected articulation. Patients in the experimental group received manual therapy in addition to the ultrasound. The definition of manual therapy in the context of this study includes massage, stretching, soft tissue techniques at the muscular and connective tissue level, and joint mobilization. The five grades of mobilization as described by Maitland are Grade 1=Gentle movements of small amplitude done at the beginning of the available range.

Grade 2=Gentle movements of larger amplitude done into available mid-range of a joint.

Grade 3=Moderate movements of large amplitude done through the available range of the joint and into the resistance.

Grade 4=Oscillating movements of small amplitude done at the end of range and into the resistance.

Grade 5=Thrusting movements done to the anatomical limit of the joint [16].

Massaging of the affected area lasted for 5 - 10 minutes to increase blood flow and warm the soft tissue. Stretching the smaller, non-weight bearing (NWB) joints consisted of holding the muscles at the end of the pliable/available range for 10 seconds whereas stretching the larger, weight-bearing (WB) joints consisted of holding the muscles at the appropriate point for 20 seconds. Low amplitude joint mobilization (grade 1 and 2) was implemented if there were capsular restrictions or high pain level preventing mobility. The use of grade 3 end-range mobilization was for cases of restricted joint mobility. The majority of joint mobilization was grade 3 into the restricted range unless pain level was higher than 6. In those instances, grade 1 and 2 oscillation mobilization at the beginning of the available range was utilized to reduce pain. Distraction of the articulations occurred before any joint glide, roll, or rock technique. This study did not use high-velocity

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manipulation, to maintain a level of care that most therapists could replicate in the future, without the expertise of advanced manual training. All patients received approximately the same amount of time of manual care (15-20 minutes). Patients in the control group received treatment with superficial touch only for approximately 1-2 minutes.

All participants in both the experimental and the control group were prescribed exercises. The therapeutic exercises were limited to active range of movement (AROM) of the involved joint, joint preserving exercises, and a functional activity appropriate to the joint. The prescribed exercises were performed at a level that was challenging to the subject, at a level that they could not complete more than 2 sets of 15 reps without experiencing fatigue of the primary muscle group. Exercise routines were carried out during each appointment over the 6-week period and were limited to 5-10 exercises that were specifically intended to promote range of motion, stabilization, and joint preservation, and reduce the functional limitation of the before joint treatment.

Outcome assessment

Pain scores

Pain scores were assessed at baseline and the end of the treatment period using a visual analog scale 0-10. The subject's pain was measured using a standard visual analog scale (VAS), with numbers and pictures of facial expression in multiple languages. The reliability and validity of the VAS scale in the measurement of OA pain has been demonstrated using psychometric analyses [17]. In order to reduce reporting bias, the participants were asked to report their perceived pain to a staff member not involved in the study, and who did not have access to group assignment.

Cortisol Measurements

Cortisol levels were measured in saliva samples collected at the baseline and the end of the treatment period. Saliva was collected via the passive drool method and samples stored at -20 C until assay. Cortisol was measured using the DetectX Enzyme Immunoassay Kit from Arbor Assays according to the manufacturer's directions. Samples were diluted 4X in assay buffer before assay.

Statistical analysis

Statistical significance to the data was determined by independent t-test, two-way ANOVA or Pearson correlation where appropriate, with α=0.05. Parametric assumptions were tested using Levene's Test for equality of variances. Multiple comparisons after 2-way ANOVA were carried out using Sidak's multiple comparisons test. All analyses were carried out using Prism 8.0 (GraphPad).

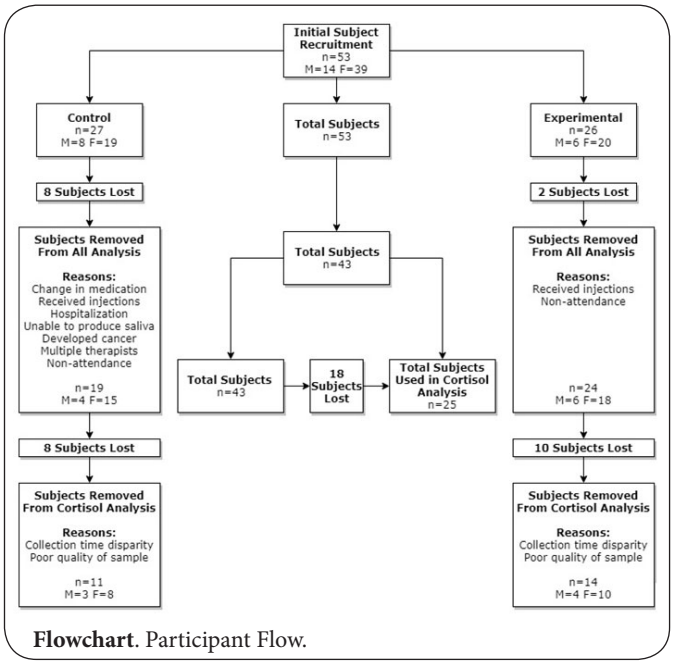
Comparability

(**Table 1** and **Flowchart**).

Table 1. Participant Baseline Characteristics.

	Male	Female	Total
Subjects	10	33	43
Age Range	53-79	42-91	42-91 years of age
Experimental group	6	18	24
Control group	4	15	19
Participants with affected weight bearing joints	9	21	25
Participants with affected non-weight bearing joints	4	9	18
Total Low/Normal BMI Subjects	3 (range: 24 to 24.7)	28 (range: 17.8 to 35.9)	31
Total High/Very High BMI Subjects	7 (range: 24.1 to 35)	5 (range: 30.7 to 39.9)	12

*Note BMI categories are based on NIH/WHO criteria as stated in [18] and reflect accepted ranges for both gender and age.



Flowchart. Participant Flow.

Results

Manual intervention reduced pain as measured by VAS

Subjects who received the manual intervention experienced a significantly greater reduction in pain level as measured by the VAS (**Figure 1A**) when compared to those receiving only ultrasound and prescriptive exercise. Our subject pool consisted of more than twice as many females as males which is consistent with risk factors as reported by the CDC [1]. They report that 52% of all adults with arthritis are women. Therefore using two-way ANOVA with gender and treatment as factors, we examined the effect of manual therapy based on gender. Results revealed a trend toward an interactive effect but it

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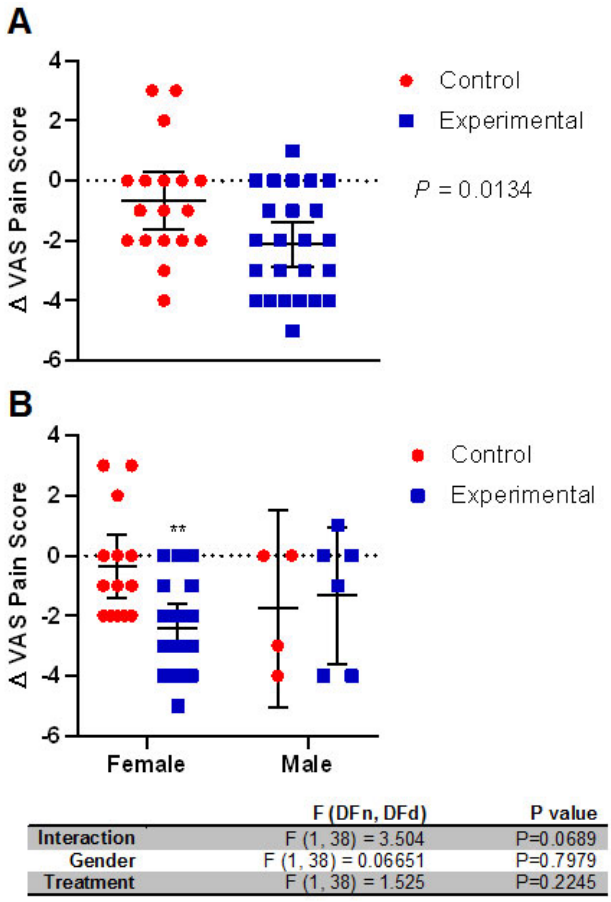
was not statistically significant (**Figure 1B**). However, multiple comparisons analysis detected a significant effect in manual intervention among the female subjects (*P*=0.0053).

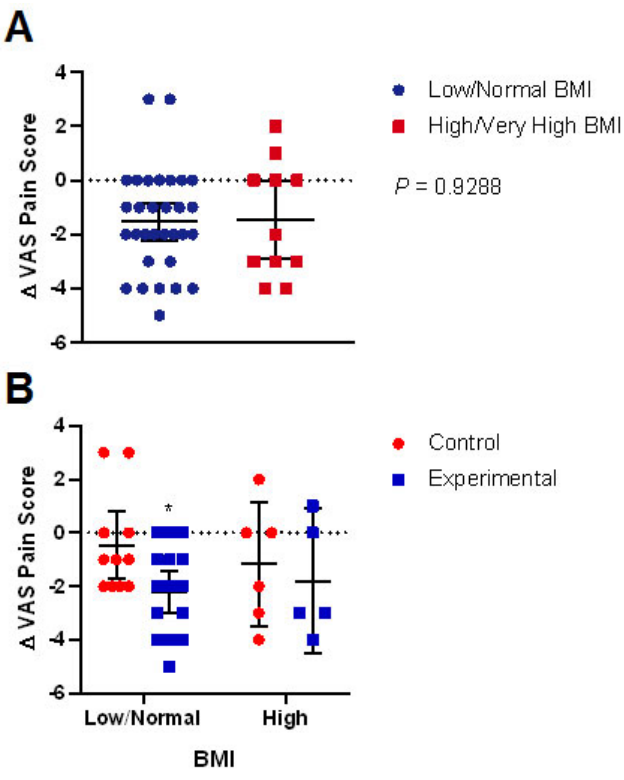
Subjects with a low to normal BMI experienced a greater reduction in pain with manual therapy as measured by VAS

An elevated body mass index is another risk factor associated with greater risk for developing OA [1]. Therefore we also examined if BMI status played a role in response to therapy. When comparing the response to all therapy, no significant difference in low/normal BMI and high/very high BMI was found (**Figure 2A**). However when using two-way ANOVA with BMI and treatment as factors there was a trend toward a significant effect of treatment due to the significant response of the low/normal BMI group to manual intervention (**Figure 2B**).



	F (DFn, DFd)	P value
Interaction	F (1, 38) = 3.504	P=0.0689
Gender	F (1, 38) = 0.06651	P=0.7979
Treatment	F (1, 38) = 1.525	P=0.2245

Figure 1. Manual therapy reduces pain scores in osteoarthritic patients.
In (**A**) patients were treated with standard therapy (Control) or treated with standard therapy and manual therapies (Experimental) are compared and data analyzed using t-test. In (**B**) two-way ANOVA (gender X treatment) is used to determine the effects of gender. ** P=0.0053 using Sidak's multiple comparisons test. Data are presented as mean with 95% CI.



	F (DFn, DFd)	P value
Interaction	F (1, 37) = 0.7168	P=0.4027
BMI	F (1, 37) = 0.05173	P=0.8213
Treatment	F (1, 37) = 3.247	P=0.0797

Figure 2. Subjects with low to normal BMI report lower pain levels with manual therapy.
In (**A**) no difference in response to all therapy is seen when comparing pain scores between subjects with low/normal to high/very BMI using t-test. In (**B**) 2-way ANOVA (BMI X Treatment) is used to determine the response to manual therapy in subjects with low/normal and high/very high BMI. * P=0.0339, using Sidak's multiple comparisons test. Data are presented as mean with 95% CI.

Subjects with affected non-weight-bearing joints experienced greater reduction in pain as measured by VAS

We also determined that non weight bearing subjects reported a greater decrease in pain levels when compared to the WB subjects, regardless of treatment regime (**Figure 3A**). When using two-way ANOVA to determine the effect of manual intervention, a significant effect of joint bearing was found due to a greater response from the subjects with affected weight-bearing joints (**Figure 3B**).

Reported changes in pain (VAS) did not correlate with change in cortisol

Pain has been associated with elevations in cortisol and increased cortisol exposure [3]. When examining the correlation between the change in pain level and the relative percentage change in cortisol no significant correlation was found (**Figure 4A**).

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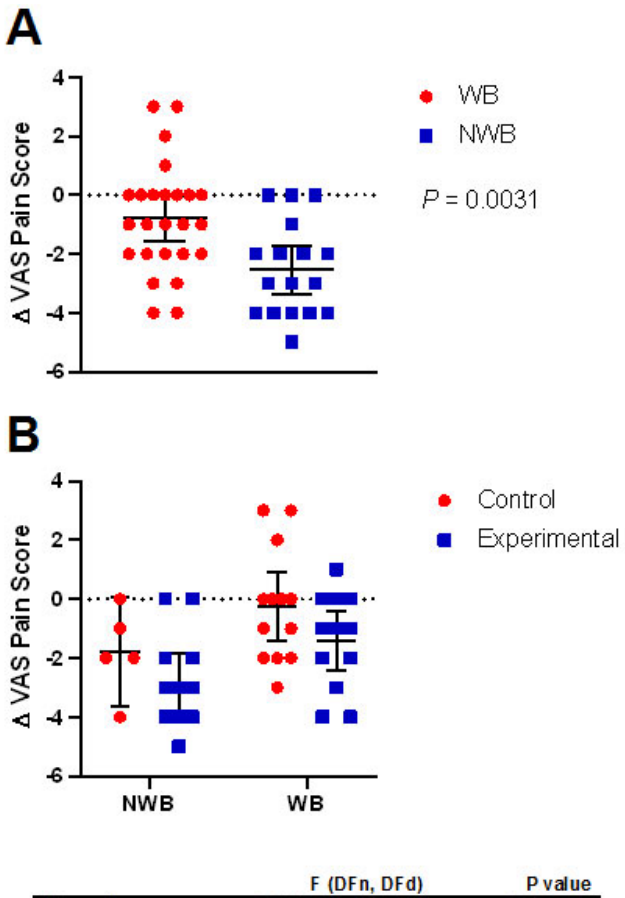

	F (DFn, DFd)	P value
Interaction	F (1, 38) = 0.01818	P=0.8935
Bearing	F (1, 38) = 6.963	P=0.0120
Treatment	F (1, 38) = 3.846	P=0.0572

Figure 3. The bearing of the affected joint impacts pain scores.
In (**A**) a significant difference in response to therapy is greater with subjects with affected non-weight bearing joints. In (**B**) 2-way ANOVA (Bearing x Treatment) results reveal a significant effect of the joint bearing in the response to manual therapy. Data are presented as mean with 95% CI.

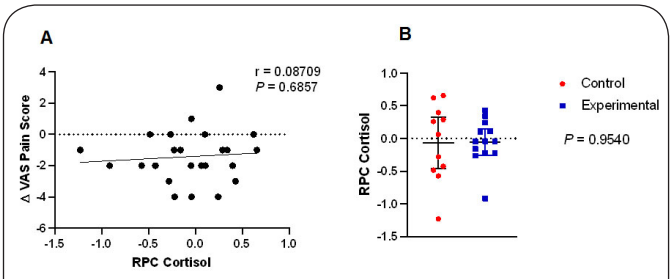

Figure 4. Relative percentage change in cortisol does not correlate with change in VAS pain scores after six weeks of therapy.
In (**A**) Pearson's correlation of change in pain scores with relative percentage change in cortisol was not significant. In (**B**) no significant change in cortisol occurred in the experimental group vs the control group. Data are presented as mean with 95% CI.

Additionally, no significant reduction in cortisol level was observed in subjects receiving manual therapy compared to ultrasound and exercise alone (**Figure 4B**).

Discussion

Human touch has been long known to facilitate the healing processes of the human body and manual therapy promotes healing and health [16,19]. Although manual skill training is a component of Physical Therapy education and intervention recently, the healthcare industry is facilitating and encouraging the treatment of more patients in less time, which hinders its inclusion in current care plans. In an effort to provide additional data regarding its efficacy our goal was to determine if manual therapy, in addition to prescriptive exercise and ultrasound, is more effective in reducing OA- associated pain and cortisol exposure as compared to prescriptive exercise and ultrasound alone. Patients receiving manual intervention along with ultrasound and prescriptive exercise over a six week period reported significantly greater reduction in pain compared to subjects receiving only ultrasound and prescriptive exercise, which substantiates its use in a Physiotherapy plan of care. These data are supported by previous works. Sharma et al. examined the effectiveness of manual therapy combined with exercise in reducing knee OA associated pain. They found that subjects receiving manual therapy in addition to clinical exercise experienced the greatest improvement [20]. In another randomized trial, effects of manual therapy and exercise therapy were measured based on patient-reported pain levels using the 100-mm VAS, an Oswestry low back pain disability questionnaire, and Dartmouth COOP. Significant improvement was apparent in all of these measurements after treatment with manual therapy. While improvements occurred in both groups, the improvement was twice as successful for the group treated with manual therapy as the group treated with exercise therapy [10].

It must be noted that the majority of participants in our study were women and when gender was accounted for in the analysis, the significance of the impact of manual intervention was increased in this group. This finding supports the use of manual care in the treatment of OA, in this population. The small number of men in this study makes it difficult to assess whether or not this trend would be observed among men. Future studies examining gender and the reduction in pain in response to manual therapy are warranted.

Although a greater BMI score is also a significant risk factor for the development of OA, our study population included a greater number of subjects with normal and low BMI. This was also the group that reported the largest decrease in pain with manual therapy. This isn't to suggest that manual therapy is ineffective with high BMI patients. However, it could be said that lower-

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ing one's BMI may assist in improving outcomes with therapy.

Participants with affected non-weight-bearing joints responded with a greater decrease in pain, regardless of treatment regime, than participants with affected weight-bearing joints. This may be related to the repeated exposure to stress that weight-bearing joints undergo daily. Bracing and unloading techniques are common in standard practice [5,6,12]. Consideration during Plan of Care development for reduction of joint stress and weight-bearing pressure for the larger lower extremity articulations is supported by this study. Additional study will determine if the intensity, duration, or frequency of manual interventions or therapeutic exercise modalities may need modification for the treatment of weight-bearing versus non-weight-bearing joints.

It is possible that the manual mobilization stimulated an acute discomfort or inflammatory response, which in turn would activate the stress axis and cortisol release. This situation might, in effect, serve to reduce the chronic pain cycle in the longer term. The acute versus chronic phase of reporting was controlled for by obtaining cortisol and VAS measures before therapy sessions. There is limited data on joint pain and cortisol correlation, more so classifying any difference in acute versus chronic processes. Cortisol is a measure of overall stress activation [21]. Although higher levels of cortisol did not correlate to VAS reduction in this study, it is noteworthy that pain-inducing stress may elevate cortisol temporarily [4]. Manual therapy stimulates joint receptors, which may include nociceptors [11]. This, in turn, may elevate cortisol, and play a role in the reduction of chronic OA pain. Cortisol and stress axis activation may still correlate to manual therapy. We postulate the possibility that the acute receptor activation by joint mobilization may increase cortisol as a direct result of the treatment. What is not clear is whether there is an overall systemic reduction in cortisol over a longer time frame with the treatment.

Additional limitations of this study include the small sample size and the length of the study follow up. Other extrinsic factors that are difficult to control for included stressors in the environment and timing of medication ingestion as it related to cortisol collection time. More time may have shown more cortisol change to allow for natural systemic processes. The loss of cortisol participant data impacted the sample size for effective cortisol assessment.

Future studies should include better control for cortisol collection, and a longer follow up period, perhaps after the completed trial. A further longitudinal study would be advantageous, as would study of how acute and sub acute pain from treatment differs from the chronicity of the osteoarthritis process, and how this relates to cortisol. Testing erythrocyte sedimentation rate or other inflammatory markers more specifically may be an idea for future study. Alternative treatment protocols may be necessary to treat weight-bearing versus non-weight-bearing joints. There is limited research that compares how osteoarthritic weight-bearing and non-weight-bearing joints respond differently to therapeutic intervention. Studies have shown that manual therapy provides a mechanical stimulus to alter the neuromusculoskeletal system through various neurophysiological mechanisms and reflexes [15,22]. Our data suggests that manual therapy can contribute to breaking the pain cycle and benefit other interventions. Evidence-based practice is the current standard of care, and therefore, this and further studies to establish efficacious treatment protocols that include manual care are warranted.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	MS	JE
Research concept and design	✓	✓
Collection and/or assembly of data	✓	✓
Data analysis and interpretation	✓	✓
Writing the article	✓	✓
Critical revision of the article	✓	✓
Final approval of article	✓	✓
Statistical analysis	--	✓

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