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A Feasibility Study of Acupuncture for Chronic Pain in Patients with Osteoporotic Thoracolumbar Compression Fracture: A Prospective Case Series

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ABSTRACT

Background: The aim of this study was to assess the feasibility of conducting a clinical study of using acupuncture for chronic pain in patients with osteoporotic thoracolumbar vertebral compression fractures (VCFs) in the outpatient setting.
Methods: A prospective case-series attempting to recruit 20 participants was performed from February 11, 2016, to December 31, 2016. We provided Manual and electrical acupuncture was provided one 1 to three 3 times a week, for 6 weeks, up to 18 sessions. The primary clinical outcome was the average pain intensity as measured by the visual analog scale (VAS) at 6 weeks. Secondary outcomes included back-specific dysfunction (Oswestry disability index), quality of life (quality of life questionnaire-26), patient-reported improvement, use of other healthcare resources, and adverse events at 6 weeks. Use of healthcare resources and adverse events were additionally followed-up at 12 weeks by telephone.
Results: Of 33 patients screened, a total of 7 were enrolled in the study. Manual and electrical acupuncture was provided 1 to 3 times a week, for 6 weeks, up to 18 sessions. We observed reduced pain intensity at 6 weeks in all participants. The change in the quality of life and back-specific dysfunction was inconsistent among participants. Mild, temporary adverse events were observed in three patients.
Conclusion: In our clinical setting, it was not feasible to recruit sufficient participants and to assess the efficacy of acupuncture for chronic pain after osteoporotic thoracolumbar VCFs under a year. Strategies to improve recruitment and to identify barriers to participation are required for future clinical trials.

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Introduction

Vertebral compression fractures (VCF) are one of the common degenerative spinal diseases without vertebral posterior column fracture and spinal cord injury [1]. Osteoporosis is the most frequently reported etiology for VCF [2,3]. In Korea, 22.4% of adults over 50 years old had osteoporosis, 47.9% had osteopenia, and women were 3 times more likely to have osteoporosis than men [4]. The Korean Health Insurance Review and Assessment Service also reported that the number of patients with pathologic fractures accompanied by osteoporosis in the past 7 years was more than 57,000 per year [5].

Patients with osteoporotic VCF may present with pain, dysfunction, and impaired quality of life. Acute symptoms usually subside within 6 weeks without any complication under standard care including both surgical and non-surgical management [6]; however, up to one-third of patients are known to experience chronic pain, poor quality of life, depression, lower self-esteem, and subsequent spinal deformity [6,7]. Possible interventions to manage chronic pain in osteoporotic patients, and may be also in patients with VCF, consist of physical exercise, physical therapy (magnetic fields, vibration, and so on). Other possible interventions include pharmacological therapy (non-steroidal anti-inflammatory drugs, opioids, vitamin D, bisphosphonates, calcitonin and raloxifene), and surgical treatment (vertebroplasty). However, none of these are known to provide sufficient pain

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relief as a stand-alone intervention and surgery is often not a realistic option for patients with other comorbidities or older age. Therefore, multimodal pain management is recommended for patients with chronic pain in patients with osteoporosis, and those possibly with VCF [8].

Acupuncture is regularly practiced for chronic pain management in South Korea. Mounting evidence suggests its effectiveness in the management of chronic musculoskeletal pain [9] and the safety when handled by qualified practitioners [10]. However, little is known about benefits and harms of acupuncture for chronic pain management in patients with VCF. In a systematic review, we found a low quality of evidence for the role of Korean medicine in patients with VCF, and any recommendation for or against the use of Korean medicine was unlikely to be drawn with the current evidence [11]. Therefore, we performed a clinical study to determine if acupuncture for chronic pain in patients with osteoporotic VCF would provide evidence to support the use of acupuncture in current clinical practice.

Materials and Methods

Study design and recruitment

This was a pilot, prospective case series study. Participants were recruited from February 11, 2016, to December 31, 2016, through hospital postings, flyers, advertisements in local newspapers, and on the hospital website. At the protocol stage, we intended to recruit 20 participants. However, the study was terminated early with the inclusion of 7 participants due to the unexpected low recruitment process and the limited resources (i.e., time and funding).

Inclusion criteria

The patients were to be at least 19 years old and radiologically diagnosed with osteoporotic vertebral compression fractures at one or more thoracolumbar spinal levels for at least 1 month. To be eligible, the average back pain intensity was to be 4 points or more on a 0 to 10 point visual analog scale (VAS) score over a 1-week period after baseline screening.

Exclusion criteria

Exclusion criteria included non-osteoporotic pathological fractures (e.g., cancer, metabolism, other), spinal dorsal column defects or deformity, pregnancy, or other clinical conditions (e.g., local or systemic infection or cognitive impairment, which may interfere with study participation). Other exclusion criteria included the history of sensitive reaction to acupuncture; conditions deemed eligible for surgical intervention (neurological defects due to spinal cord injury, cauda equina syndrome, unstable fractures, kyphotic angles of more than 30 degrees or compression ratios of more than 50%).

Acupuncture treatments

Acupuncture treatment was provided 1 to 3 times a week for a total of 12–18 times for 6 weeks. Disposable, stainless-steel acupuncture needles (0.25 x 30mm, 0.25 x 40mm, 0.35 x 40mm, and 0.30 x 60mm), from Dongbang Inc., Korea, were inserted on the nearby tender points around the fractured site, Back-Shu points, and distal points on the extremities. For needles that were inserted on bilateral Back-Shu points near the fractured vertebral body, manual stimulation eliciting de-qi sensation and electrical stimulation with 2 to 100 alternating frequency, biphasic square waves at intensities tolerable to the patients were provided. Other points were manually stimulated. Full information on the acupuncture treatments according to the Standard for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [12] is provided in Table 1.

Outcomes

The primary clinical outcome was the average pain intensity assessed during the last 24 hours after 6 weeks, measured by VAS scores (ranged 0 to 10; higher scores reflect worse pain). The secondary clinical outcomes included back-specific dysfunction and quality of life measured by the Oswestry disability index (ODI) [13] questionnaire and quality of life questionnaires-26 [14], respectively. The patient-reported overall improvement was assessed by the Patient Global Assessment. Information about names, doses, the frequency of drugs used to control pain, and the number of patients who needed surgery during the study period were recorded. Patients were asked to report any adverse events experienced at each visit or contact. All the discomforts or complications related to acupuncture treatment, such as bleeding and pain around needled sites were considered as adverse events.

An independent assessor not involved in the treatment process assessed the outcomes to avoid the risk of social desirability bias during measurements [15]. All outcomes were measured after 6 weeks from the baseline. Use of healthcare resources and adverse events were additionally followed-up at 12 weeks by telephone.

Simple descriptive analyses were performed. Data were presented as median with range or frequency and/or percentage where appropriate, using Microsoft Office Excel 2007.

Ethics

The institutional review boards of Pusan National University Korean Medicine Hospital approved this study (approval number: 2015002). The protocol was registered after the study was terminated (NCT03359941). Written informed consents were obtained from all participants.

Results

Patient recruitment and feasibility

A total of 33 patients were screened for 11 months; 25 of them did not meet the selection criteria, and one refused to participate. A total of 7 patients (35% of target recruiting) were eligible and participated in the study; one patient reported the acupuncture was too painful and withdrew from the study after one session (Fig. 1). Six patients completed the measurement of the primary clinical outcome at 6 weeks.

Characteristics of participants

Patients were aged between 37 and 76 years old (median 67 years). Three out of 7 patients were female. Table 2 shows further characteristics of enrolled patients.

Clinical outcomes

At least a one-point reduction in pain intensity on the VAS score was observed after treatment in all patients (Fig. 2). All patients showed mild or minimal back-specific dysfunction at baseline. The median reduction of the ODI score was 4.4 (range -11.2 to 8.9). Two patients who had minimal dysfunction (i.e., an ODI score of 4.4) showed worsened dysfunction at 6 weeks. Change in quality

Table 1. Standard for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA).

1) Acupuncture rationale	
1a) Style of acupuncture	Classical acupuncture with manual and electrical stimulation
1b) Reasoning for treatment provided	A group of expert Korean medicine doctors developed the protocol of acupuncture treatment based on the systematic review and a textbook of acupuncture.
1c) Extent to which treatment was varied	Semi-individualized selection was adopted.
2) Details of needling	
2a) Names of points	1. Essential points on the first line of the Bladder meridian were selected based on the location of pain, tenderness or fractured vertebral bodies. Possible points include Gan-su(BL18), Dam-su (BL19), Bi-su (BL20), Wi-su (BL21), Samcho-su (BL22), Sin-su (BL23), Gihae-su (BL24), Daejang-su (BL25),etc. 2. Additional points on the extremities commonly used for pain relief were chosen as required. They include Sok-gol (BL65), Wi-jung (BL40), Gol-lyun (BL60), Gok-ji (LI11), So-bu (HT8), Hap-gok (LI4), Joksam-ni (ST36), Jogim-eup (GB41) and Tae-chung (LR3). 3. Use of tender or A-shi points on low back, buttock and lower extremities were also possible. Most points were needled bilaterally unless hematomas or pain was presented.
2b) Number of needle insertions per session	Overall 20 to 30 needles were inserted at the Korean medicine doctor's discretion.
2c) Depth of insertion	0.5 – 6.0cm according to acupoints
2d) Responses sought	De-qi or local muscle twitch response
2e) Needle stimulation	Manual stimulation: rotation, lifting and thrusting for 30 seconds just after the insertion of needles. Electro-stimulation: 2-100Hz alternating frequency, adjusted to intensity within the patient's pain threshold. Trans-vertebral electrical stimulation (i.e., clips across the both side of the vertebrae) was applied for the BL meridian points on the level of the fractured vertebrae. For other points on the first BL meridian line, ipsilateral electrical stimulation (i.e., clips longitudinally on the same side) was employed.
2f) Needle retention time	15-20 minutes
2g) Needle type	0.25×30mm, 0.25×40mm, 0.35×40mm, 0.30×60mm Dong bang Sterilized stainless steel disposable needle
3. Treatment regimen	
3a) Number of treatment sessions	Total 12-18 times (according to patients' symptoms and conditions)
3b) Frequency and duration of treatment sessions	1-3 times a week, total 6 weeks
4) Other components of treatment	
4a) Details of other interventions administered to the acupuncture group	1. Medication related to vertebral compression fractures (analgesics, osteoporosis treatment, other) 2. Patient self-management (bed rest, exercise therapy, orthosis) 3. Treatment for stable management of chronic diseases (hypertension, diabetes, etc.) 4. Other medicinal treatment needed for the judgment of the medical staff or the patient wants
5) Practitioner background	
5a) Description of participating acupuncturists	A study KMD should have at least 2 years of clinical experience of acupuncture.

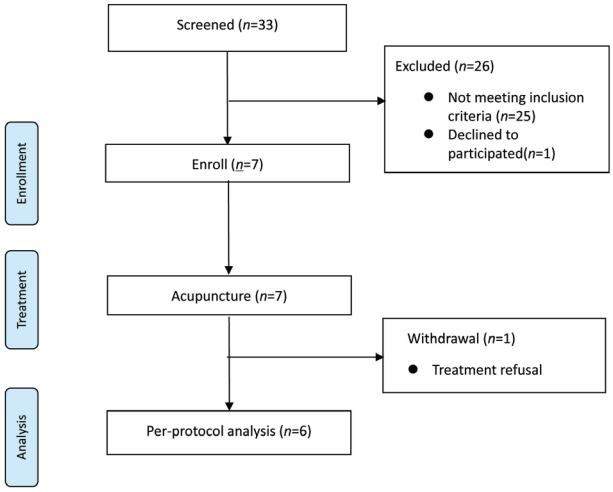

Fig. 1. Flow chart.

Table 2. Characteristics of Included Patients.

	Patients (n = 7)
Age (y)	63.4 (37.0 – 76.0)
Female (n, %)	3 (43)
BMI (kg/㎡)	23.4 (21.2 – 25.4)
Osteoporosis (n, %)	4 (57)
Duration of disease (mo)	35 (10 – 112)

BMI, body mass index.
Data are presented with median (range) or count (%).

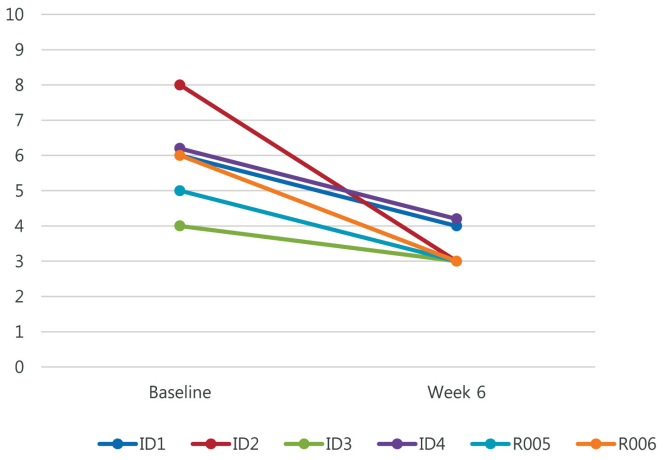

Fig. 2. Primary outcome.
Detailed numbers are given in the Table 3. The smallest decrease is 1, and the largest decrease is 5.

of life was not clinically meaningful and was inconsistent between patients. Five patients (71%) reported that they felt significant (*n*=2) or slight (*n*=3) improvement, and one reported results as not improved. Table 4 presents individual data for the above outcomes. Four patients (57%) took osteoporosis medication and one (14%) took cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs (Celecoxib 200mg / capsule 3 times daily). Use of medication did not alter during the study period, and no patient underwent surgery related to compression fractures during the study period.

Adverse events

A total of 81 acupuncture sessions were performed on 7 patients, and a total of 6 adverse events were reported in 3 patients. One patient complained of purulent blisters on the buttocks away from the acupuncture site but continued to participate in the study as the study Korean medicine doctor and the patient, deemed this event as unrelated to the acupuncture treatments. Mild and temporary local bruising (*n*=1) and pain (*n*=2) at needled sites, increased back pain (*n*=1), fatigue (*n*=1), and the blisters distally located from the needled site (*n*=1) were reported.

Discussion

In this single-center feasibility study, only one third of the anticipated number of participants were enrolled during the 11-month study period. Six of 7 patients completed a series of acupuncture treatments for 6 weeks. Measurement of the primary and secondary outcomes was possible at 6 weeks. Patients reported mild to moderate pain relief following acupuncture treatment in patients with VCF, although measurement of functional outcomes and quality of life did not show a clinically relevant benefit. This inconsistency between different outcome parameters makes interpretation difficult. Lack of consistent beneficial improvements in the patients was unexpected and discordant with previous findings as well as our clinical experiences, although the small number of participants did not allow further inference. Adverse events were not common and deemed acceptable. Overall, our pilot study implies there may be unknown barriers to the recruitment of participants in our setting (i.e., outpatient clinic of Korean medicine hospital).

The failure to enroll the anticipated number of participants was a major factor that needs to be addressed for the design of future trials. In a systematic review of barriers to participation in randomized controlled trials, additional demands of the trial, patient preferences, and concerns on the uncertainty or consent process in the trial context were identified as patient-level barriers [16]. Patients with osteoporotic fractures may have more impaired mobility requiring additional resources (e.g., private transportation) and possibly interfere with participation in the treatment courses of the study compared with non-VCF patients. The process of acupuncture treatments, which requires regular visits to the study hospital, might be bothersome to patients who prefer simple, self-intervention modalities, such as analgesic

Table 3. Primary and Secondary Outcomes.

	Pain Intensity VAS		ODI*		QUALEFFO-26†								PGA‡
					Pain		Physical function		Cognitive function		Total		
	Baseline	6 wks	Baseline	6 wks	Baseline	6 wks	Baseline	6 wks	Baseline	6 wks	Baseline	6 wks	6 wks
ID1	6	4	33.3	28.9	43.8	25.0	25.0	18.5	33.3	36.1	31.3	25.6	Slightly improved
ID2	8	3	28.9	24.4	37.5	56.3	17.3	19.8	33.3	25.0	26.3	27.2	Significantly improved
ID3	4	3	4.4	15.6	62.5	37.5	6.3	7.7	44.4	52.8	28.2	27.9	No change
ID4	6	4	28.9	20.0	56.3	18.8	5.8	5.0	69.4	61.1	36.2	26.5	Slightly improved
ID5	5	3	4.4	6.7	25.0	12.5	1.9	5.8	25.0	22.2	13.5	12.5	Slightly improved
ID6	6	3	31.1	26.7	31.3	31.3	25.0	30.8	61.1	58.3	39.5	40.4	Significantly improved
ID7	4	None	24.4	None	18.8	None	1.9	None	19.4	None	10.6	None	None

* ODI: Score ranges from 0 to 100%. Higher scores mean worse outcome. It consists of 10 topics such as intensity of pain, walking, lifting, sitting, sleeping, social life and travel [13].
† QUALEFFO-26: A total of 26 items can be evaluated in terms of pain, physical function, social function, general health perception, and cognitive function. The higher the score, the higher the disability [14].
‡ PGA: Patients can choose from 5 items: "significantly improved", "slightly improved", "no change", "slightly worse", "significantly worse"
ODI, Oswestry Disability Questionnaire; PGA, Patient Global Assessment; QUALEFFO-25, Quality-of-Life Questionnaire of the European Foundation of Osteoporosis-26; VAS, Visual Analog Scale.

intake or wearing a brace. Needle sensation might produce discomfort and be intolerable in some patients. The process of obtaining written informed consents and information on a pre-planned study schedule may have influenced potential participants' perceptions and attitudes toward participation in a clinical study. Whether these factors are potential barriers to the clinical study of acupuncture in patients with VCF requires further investigation. Qualitative studies or surveys, which explore patients' views on the clinical study of acupuncture, are also warranted. Trial-level barriers may have limited the feasibility of our study. For instance, the 11-month recruitment period may not have been enough time to find sufficient participants for our trial although we expected that recruiting at least 20 participants would be feasible. Other Korean medicine hospitals that already have a population of patients with VCF, may have potential hospital-level facilitating factors for better recruitment than ours.

In our systematic review concerning the role of Korean medicine, including acupuncture, we found a low quality of evidence for benefits for patients with VCF. Based on our retrospective audit, other studies had large numbers of participants, used unvalidated outcomes, and employed multiple combinations of several types of Korean medicine (e.g., acupuncture, herbal, cupping, and Chuna) [11]. In the current study, we attempted to test the feasibility of conducting a clinical study that serves to inform future study designs, which would overcome the limitation of previous studies. However, different study designs, characteristics of clinical components of interventions, and context (real practice versus prospective clinical trial) in our setting may be partly responsible for the unsuccessful recruitment. In a sham-controlled randomized trial conducted in Germany, both real and sham acupuncture produced pain relief in 53 patients with osteoporosis but not necessarily those having VCF, showing both types of acupuncture were associated with the relief of pain. The difference between the eligible population in our study (i.e., participants should have a history of VCF) and the German trial (i.e., participants with osteoporosis, but not necessarily with VCF), may be one of the factors associated with different recruitment efficiency and study feasibility [17].

There have been several mechanisms that have been suggested as possible therapeutic pathways for acupuncture treatment for chronic pain. 1) Segmental analgesia: In the dorsal horn of the spinal cord, there are cells (substantia gelatinosa) that act as switches between afferent nerve impulses from different fibers. Chronic pain is carried by C fibers. Acupuncture stimulates the A delta nerve fiber and closes the gate to the C fiber impulse. 2) The release of endogenous opioid peptides in the central nervous system: Electroacupuncture stimulates the central nervous system and induces various endogenous opioid peptides (endorphin, enkephalin, dynorphin, and orphanin) in the brain and spinal cord. 3) Diffuse noxious inhibitory control: It has been proposed that in this pathway, any painful and noxious stimulus (including acupuncture) will relieve existing pain even in extra-segmental areas. 4) Serotonin: Serotonin is an important transmitter of pain control. It is released in a descending pain control system and inhibits the nociceptive pathway. Acupuncture increases serotonin levels and achieves pain relief [18]. Whether these potential mechanisms of acupuncture analgesia are associated with clinical improvement of chronic pain in patients with VCF requires further research.

This study has the following limitations. As a case-series study with a short-term observation period, the possibility of natural symptom fluctuation, which may be irrelevant to the given intervention, cannot be ruled out. The patients who were enrolled in this study had a willingness to participate in the acupuncture treatment, and it is sensible to assume that participants may have anticipated beneficial effects for the acupuncture treatment. High expectations of trial participants are associated with increased risks of selection and information bias, which may overestimate the changes after acupuncture sessions in our study [19]. Unblinded assessments of subjective outcomes, may influence the results thereby increasing information bias, another caveat of this study.

Conclusion

In our setting, it was not feasible to recruit a pre-specified number of participants for an uncontrolled observational study of acupuncture for chronic pain after osteoporotic thoracolumbar compression fractures within a 1-year period. Strategies to improve recruitment and identify barriers to participation in the acupuncture trial are required to plan future clinical trials of acupuncture for this population. Observed short-term changes after treatments should not be regarded as the effects of acupuncture because of the high risk of selection and information bias.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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