TESIS DOCTORAL

Effectiveness of Electrical Dry Needling for Lower Extremity Pain Disorders

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Preface

I am deeply grateful to Professor César Fernández-de-las-Peñas for his willingness to guide in a direct fashion and share knowledge in support of this academic journey.

Although neither of my parents had the opportunity to attend college or university, they nevertheless realized the importance of education for their children. During my childhood and early adult years, they devoted much of their time and means to support me in academic achievement. Therefore, I dedicate this work to both of them - Geoffrey and Suzette. Nevertheless, the lasting influence of the devoted teachers at Lockington Primary School, Beverley Grammar School and Cardston High School must also be recognized.

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Abstract

Abstract

Study Design: Randomized, single-blinded, multi-center, parallel-group trial.

Background: Manual therapy, exercise and acupuncture have been found to be moderately effective for knee osteoathrtitis (OA) when applied in isolation. No study has previously investigated the effectiveness of the combination of electrical dry needling in addition to manual therapy and exercise in patients with knee OA. Similarly, the isolated application of electrical dry needling, manual therapy, exercise, and ultrasound has been found to be effective for plantar fasciitis (PF). However, no study has investigated the combined effect of these interventions in patients with PF.

Objectives: 1, To compare the effects of adding electrical dry needling into a manual therapy and exercise program on pain, stiffness, function, and disability in individuals with painful knee OA; 2, To compare the effects of adding electrical dry needling into a program of manual therapy, exercise and ultrasound on pain, function and related-disability in individuals with PF.

Methods: For study 1, two hundred and forty-two participants (n=242) with painful knee OA were randomized to receive electrical dry needling, manual therapy and exercise (dry needling group, n=121) or manual therapy and exercise (non-dry needling group, n=121). The primary outcome was the related-disability as assessed by the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index at 3 months. Secondary outcomes were knee pain intensity as measured by the Numeric Pain Rating Scale (NPRS), WOMAC subscales (pain: WOMAC-P; stiffness: WOMAC-S; and physical function: WOMAC-PF) medication intake, and the Global Rating of Change (GROC). The treatment period was 6 weeks with follow-up assessments at 2 weeks, 6 weeks, and 3 months after the first

treatment session. Both groups received between 8-10 sessions of manual therapy (passive joint mobilizations and muscle stretching) and exercise (riding a stationary bicycle, range of motion and strengthening exercises to the lower extremity). In addition, the dry needling group also received electrical dry needling using a standardized 9-point protocol for 30 minutes on each treatment session. For study 2, 111 patients with PF were randomized to receive electrical dry needling, manual therapy, exercise and ultrasound (n=58) or manual therapy, exercise and ultrasound (n=53). The primary outcome was first-step pain in the morning as measured by the Numeric Pain Rating Scale (NPRS). Secondary outcomes included resting foot pain (NPRS), pain during activity (NPRS), the Lower Extremity Functional Scale (LEFS), the Foot Functional Index (FFI), medication intake, and the Global Rating of Change (GROC). The treatment period was 4 weeks with follow-up assessments at 1 week, 4 weeks, and 3 months after the first treatment session. Both groups received 6 sessions of impairment-based manual therapy directed to the lower limb, self-stretching of the plantar fascia and the Achilles tendon, strengthening exercises for the intrinsic muscles of the foot, and therapeutic ultrasound. In addition, the dry needling group also recieved 6 sessions of electrical dry needling using a standardized 8-point protocol for 20 minutes. The primary aims were examined with a 2-way mixed-model ANCOVA with group as the between-subjects variable and time as the within-subjects variable after adjusting for baseline outcomes.

Results: For study 1, the analysis revealed that individuals receiving the combination of electrical dry needling, manual therapy and exercise experienced significantly greater improvements in related-disability (WOMAC: $F=35.504$; $P<0.001$) than those receiving manual therapy and exercise alone at 6 weeks and 3 months. The dry needling group also experienced greater improvements in all the secondary outcomes (knee pain intensity:

F=29.094, P<0.001; WOMAC-P: F=30.13, P<0.001; WOMAC-S: F=39.665, P<0.001, WOMAC-PF: F=30.114; P<0.001). In addition, patients receiving electrical dry needling were 1.7 times more likely to have completely stopped taking medication for their pain at 3 months than individuals receiving manual therapy and exercise (OR: 1.6; 95%CI: 1.24-2.01; P=0.001). Based on the cutoff score of +5 on the GROC, significantly (X^2=14.887; P<0.001) more patients (n= 91, 75%) within the electrical dry needling group achieved a successful outcome compared to the manual therapy and exercise group (n=22, 18%) at 3 months follow-up. Effect sizes were large (SMD>0.82) for all outcome measures in favor of the electrical dry needling group at 3 months. For study 2, the 2X4 ANCOVA revealed that individuals with PF receiving the combination of electrical dry needling, manual therapy, exercise and ultrasound experienced significantly greater improvements in first-step morning pain (F=22.021; P<0.001), resting foot pain (F=23.931; P<0.001), pain during activity (F=7.629; P=0.007), LEFS (F=13.081; P<0.001), FFI Pain Subscale (F=13.547; P<0.001), FFI Disability Subscale (F=8.746; P=0.004), and FFI Total Score (F=10.65; P<0.001) than those who received manual therapy, exercise and ultrasound at 3 months No differences in FFI Activity Limitation Subscale (F=2.687; P=0.104) were observed. Patients in the electrical dry needling group were 1.2 times more likely than patients receiving manual therapy, exercise and ultrasound to have completely stopped taking medication for their pain at 3 months (OR: 1.22; 95%CI: 1.02-1.51; P=0.01). Based on the cutoff score of ≥+5 on the GROC, significantly (X^2=45.582; P<0.001) more patients within the electrical dry needling group (n=45, 78%) achieved a successful outcome compared to the manual therapy, exercise and ultrasound group (n=11, 21%). Effect sizes were medium to large (0.53<SMD<0.85) at 3 months in favor of the electrical dry needling group.

Conclusions: The inclusion of electrical dry needling into a manual therapy and exercise program was more effective for improving pain, function and related-disability than the application of manual therapy and exercise alone in individuals with painful knee OA at mid-term (3 months). Similarly, the inclusion of electrical dry needling into a program of manual therapy, exercise and ultrasound was more effective for improving pain, function and related-disability than the application of manual therapy, exercise and ultrasound alone in individuals with PF at mid-term (3 months).

Resumen

Resumen

Diseño: Ensayo clínico aleatorizado, a simple ciego, multicéntrico, con grupo paralelo.

Antecedentes: Se ha encontrado que la aplicación de manera aislada de terapia manual, ejercicio y acupuntura tiene eficacia moderada en la artrosis de rodilla. Ningún estudio ha investigado previamente la eficacia de combinar electro-punción, terapia manual y ejercicio en pacientes con artrosis de rodilla. De igual modo, la aplicación aislada de electro-punción seca, terapia manual, ejercicio y ultrasonido ha resultado ser eficaz en la fascitis plantar. Sin embargo, ningún estudio ha investigado el efecto combinado de estas intervenciones en pacientes con fascitis plantar.

Objetivos: 1, Comparar los efectos de añadir electro-punción seca a un programa de terapia manual y ejercicio para el dolor, rigidez, función y discapacidad en pacientes con artrosis de rodilla; 2, Comparar los efectos al añadir electro-punción a un programa de terapia manual, ejercicio y ultrasonido para el dolor, función y discapacidad en pacientes con fascitis plantar.

Métodos: Para el estudio 1, se eligieron de manera aleatoria doscientos cuarenta y dos participantes (n=242) con artrosis de rodilla, que recibieron electro-punción, terapia manual y ejercicio (grupo de punción seca, n=121) o terapia manual y ejercicio (grupo sin punción seca, n=121). La variable principal fue la discapacidad-relacionada a los 3 meses según el Western Ontario y McMaster Universities (WOMAC). Las variables secundarias fueron la intensidad de dolor de rodilla medida por la escala numérica de dolor (NPRS), las subescalas WOMAC (dolor: WOMAC-P; rigidez: WOMAC-S; y función física: WOMAC PF), la toma de medicación y la puntuación global de cambio (GROC).

El periodo de tratamiento fue de 6 semanas con evaluaciones de seguimiento a las 2 semanas, 6 semanas y 3 meses desde la primera sesión de tratamiento. Ambos grupos recibieron entre 8-10 sesiones de terapia manual (movilizaciones articulares pasivas y estiramientos musculares) y ejercicio (bicicleta estática y ejercicios de movilidad y fortalecimiento de la extremidad inferior). Además, el grupo de punción seca también recibió electro-punción seca utilizando un protocolo estandarizado de 9 puntos durante 30min en cada sesión de tratamiento. Para el estudio 2, se seleccionaron de manera aleatoria 111 pacientes con fascitis plantar que recibieron electro-punción seca, terapia manual, ejercicio y ultrasonido (n=58) o terapia manual, ejercicio y ultrasonido (n=53). La variable principal fue el dolor al primer paso por la mañana, medido por la escala numérica de dolor (NPRS). Las variables secundarias incluyeron el dolor en reposo (NPRS), el dolor durante la actividad (NPRS), la escala funcional para la extremidad inferior (LEFS), el índice funcional del pie (FFI), la toma de medicación y la puntuación global de cambio (GROC). El periodo de tratamiento fue de 4 semanas con evaluaciones de seguimiento a 1 semana, 4 semanas y 3 meses desde la primera sesión de tratamiento. Ambos grupos recibieron 6 sesiones de terapia manual basada en las deficiencias y dirigidas al miembro inferior, auto estiramientos de la fascia plantar y el tendón de Aquiles, ejercicios de fortalecimiento de la musculatura intrínseca del pie y ultrasonido terapéutico. Además, el grupo de punción seca también recibió 6 sesiones de electro-punción seca utilizando un protocolo estandarizado de 8 puntos durante 20min. Se empleó un modelo mixto ANCOVA con el grupo como variable entre-sujetos y el tiempo como variable intra-sujeto, después de ajustar las variables al inicio.

Resultados: Para el estudio 1, el análisis reveló que los individuos con artrosis de rodilla que recibieron combinación de electro-punción seca, terapia manual y ejercicio experimentaron mejorías significativamente mayores en la discapacidad a las 6 semanas y a los 3 meses (WOMAC: F=35.504; P<0.001) que aquellos que recibieron solo terapia manual y ejercicio. El grupo de punción seca también experimentó mejorías mayores en todos los resultados secundarios (intensidad del dolor de rodilla: F=29.094, P<0.001; WOMAC-P: F=30.13, P<0.001; WOMAC-S: F=39.665, P<0.001, WOMAC-PF: F=30.114; P<0.001). Además, los pacientes que recibieron punción seca tuvieron una probabilidad 1.7 veces mayor de haber dejado de tomar la medicación para su dolor a los 3 meses, comparados con los individuos que recibieron terapia manual y ejercicio (OR: 1.6; 95%CI: 1.24-2.01; P=0.001). Basándonos en la puntuación de corte de +5 del GROC, en el grupo de electro-punción seca, mayor número de pacientes (n=91, 75%) consiguieron resultados de éxito (X^2=14.887; P<0.001) comparado con el grupo de terapia manual y ejercicio (n=22, 18%) a los 3 meses de seguimiento. Los tamaños del efecto fueron grandes (SMD>0.82) para todas las medidas de resultado a los 3 meses, a favor del grupo de electro-punción seca. Para el estudio 2, el 2X4 ANCOVA reveló que los individuos con fascitis plantar que recibieron la combinación de electro-punción seca, terapia manual, ejercicio y ultrasonido experimentaron mejorías significativamente mayores a los 3 meses en el dolor al primer paso (F=22.021; P<0.001), dolor en reposo (F=23.931; P<0.001), dolor durante la actividad (F=7.629; P=0.007), LEFS (F=13.081; P<0.001), escala FFI para dolor (F=13.547; P<0.001), subescala FFI para discapacidad (F=8.746; P=0.004) y puntuación total del FFI (F=10.65; P<0.001) que aquellos sujetos que recibieron terapia manual, ejercicio y ultrasonido. No se observaron diferencias en la subescala de limitación de la actividad del FFI (F=2.687; P=0.104).

Los pacientes en el grupo de electro-punción seca tuvieron 1.2 mayor probabilidad de haber abandonado totalmente la toma de medicación para su dolor a los 3 meses que aquellos pacientes que recibieron terapia manual, ejercicio y ultrasonido (OR: 1.22; 95%CI: 1.02-1.51; P=0.01). Basándonos en la puntuación de corte ≥+5 en el GROC, significativamente (X^2=45.582; P<0.001) más pacientes del grupo de electro-punción seca (n=45, 78%) consiguieron resultados exitosos comparados con el grupo de terapia manual, ejercicio y ultrasonido (n=11, 21%). Los tamaños del efecto fueron intermedios a grandes.

Conclusiones: La inclusión de electro-punción seca en un programa de terapia manual y ejercicio fue más eficaz para mejorar el dolor, la función y la discapacidad que la aplicación de sólo terapia manual y ejercicio en individuos con artrosis dolorosa de rodilla a medio plazo (3 meses). Igualmente, la inclusión de electro-punción seca en un programa de terapia manual, ejercicio y ultrasonido fue más eficaz para la mejoría del dolor, la función y la discapacidad que la aplicación de sólo terapia manual, ejercicio y ultrasonido en individuos con fascitis plantar a medio plazo (3 meses).

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Introduction

Epidemiology of Knee Osteoarthritis

Osteoarthritis (OA) of the knee affects up to 37% of adults in the United States between 45 and 60 years of age.[1] A recent meta-analysis found that the crude prevalence of knee OA was 25% in subjects aged >20 years and 39% in people aged >30 years.[2] In addition, hip and knee OA are ranked as the 11th highest contributors to global disability in patients with chronic pain.[3] The physiological changes in OA have been well documented and are characterized by degeneration of the articular cartilage with osteophyte formation, microfractures, subchondral sclerosis and plate thickening, and exposure of the articular end of the bone.[4-6] The clinical manifestations of knee OA are joint pain, stiffness in the morning or after rest, restricted/limited joint motion, night pain, and/or joint deformity. The categorization or diagnosis of knee OA is typically made using the American College of Rheumatology clinical criteria developed by Altman, which has been found to be 89% sensitive and 88% specific,[7,8] or those who self-report knee OA on the basis of chronic joint pain (with/without radiographic confirmation).[9] The pathogenesis and temporal relationship of subchondral bone damage, chronic inflammation of synovial tissue, and cartilage erosion is largely unknown, and there are currently no curative treatments for osteoarthritis.[10,11]

Management of Knee Osteoarthritis

Long-term use of oral non-steroidal anti-inflammatory (NSAIDs) drugs has been discouraged, and many subjects with chronic pain want non-pharmacological management options.[12,13] Notably, exercise therapy[9,14-18] and acupuncture[19-25] are two of the main non-pharmacological interventions recommended for people with knee OA in meta-analyses and international clinical guidelines.

In a randomized controlled trial of 134 subjects with radiographically confirmed knee OA, Deyle et al[26] found that a 4-week program of manual therapy and supervised exercise was more effective than a home exercise program for increasing function and decreasing pain and stiffness at 4-weeks and 8-weeks; however, no significant between group differences were evident in WOMAC scores or medication intake at 1-year outcome. While Deyle et al[26] utilized specific manual therapy techniques (i.e. passive physiological and accessory joint mobilizations, static muscle stretching, and soft tissue mobilization interventions) and a semi-standardized approach to the type, dosage and progression of exercise prescribed (i.e. active range of motion exercises, weight and non-weight bearing muscle strengthening exercises, static muscle stretching, and riding a stationary bicycle), a recent systematic review and meta-analysis[14] of 12 randomized controlled trials concluded that the duration of the treatment period, the treatment frequency, and the type of exercise (weight bearing versus non-weight bearing) each had no significant influence on the size of the effects for pain and physical function in knee OA patients Exercise therapy plus manual mobilization showed a moderate effect size (SMD 0.69) which was significantly higher than the small effect sizes for exercise alone (SMD 0.34), i.e., the combination of strength training, aerobic activity exercises, and strength training alone (SMD 0.38).[14]

In a Cochrane review of 44 trials (n=3537 subjects) that examined the effectiveness of various forms of exercise in individuals with mild to moderate knee OA, Fransen et al[9] concluded that the pooled results demonstrated a statistically significant benefit, with moderate effect sizes for pain (SMD 0.49) and physical function (SMD 0.52) immediately after treatment. This was equivalent to an immediate post-treatment reduction of 12 points (on a 0 to 100-point VAS pain scale) for pain and 10 points (on a 0 to 100-point scale) for physical function.[9] In addition, the pooled results from 12 trials (n=1468 participants)

demonstrated statistically significant benefit for exercise at 2-6 months' post-treatment initiation; nevertheless, small effect sizes were found for pain (SMD 0.24) and physical function (SMD 0.15) that were equivalent to 6% and 3% improvements in pain and physical function, respectively.[9] Notwithstanding the favourable immediate and medium term results for exercise in individuals with knee OA, the pooled results of 6 longer term studies (n=1104 subjects) demonstrated a non-significant effect (SMD 0.08) for pain; that is, the pain-relieving benefit of exercise was not maintained 6 or more months after treatment, but improvements in physical function were maintained with a small effect size (SMD 0.20).[9] Notably, the meta-analysis by Fransen et al[9] found no significant differences in the magnitude of treatment effects for pain and physical function between different types of exercises (i.e. weight bearing vs. non-weight bearing quadriceps strengthening, general lower extremity muscle strengthening, aerobic exercise, concentric-eccentric strengthening exercises versus isometric strengthening exercises) and their delivery modes (home-based, class-based program or individually physiotherapy-led exercise sessions). Furthermore, specific recommendations cannot be made regarding the optimal exercise dosage (i.e. frequency, duration and intensity of treatment sessions) in patients with knee OA.[9]

The mechanisms by which exercise favourably affects pain and physical function in patients with knee OA remains unclear; however, it is suggested that regular exercise is able increase bone morphogenetic proteins (i.e., modify structural disease progression),[9,27] elongate restricted periarticular and muscular connective tissue,[26,28] and alter synovial fluid cytokine levels.[29] In addition, enhanced strength of the lower extremity muscles may lessen the forces around the knee, modify the biomechanics and improve the arthrokinematics in the knee, to reduce loading rates and stress on the articular cartilage, and thereby reduce pain and improve physical function in patients with knee OA.[27,29-36]

Epidemiology of Plantar Fasciitis

Plantar fasciits (PF) is the most common cause of heel pain and is estimated to affect 10% of the general population during their lifetime.[37] During the years 1995 to 2000, PF accounted for 1 million patient visits per year to medical physicians in the United States.[38] In 2007, the cost of treatment for PF in the United States was between $192 and $376 million.[39] There is an ongoing debate regarding the proper nomenclature, mainly as to whether the disorder should be referred to as plantar fasciitis, plantar fasciosis or plantar heel pain. Imaging and histological findings support the premise that plantar "fasciitis" is actually a degenerative "fasciosis" without inflammation;[40,41] thus, several studies have used the broader and nonspecific term plantar heel pain.[42-45] Nevertheless, many trials,[46-53] literature reviews[54-57] and clinical practice guidelines[58] have reverted back to the "well established phrase"[55] and more common clinical term of plantar fasciitis; therefore, we will use the term 'plantar fasciitis' (PF).

The plantar fascia is a tight band of connective tissue that supports the medial longitudinal arch of the foot like a windlass.[59] The plantar fascia extends from the medial tubercle of the calcaneus to the plantar plates of the metatarsal phalangeal joints, the bases of the proximal phalanges and the flexor tendon sheathes.[60] PF is characterized by intense sharp pain over the medial plantar heel with intial steps in the morning or after inactivity that increases with prolonged weightbearing activities; in addition, localized pain on palpation occurs primarly where the plantar fascia attaches to the medical calcaneal tubercle.[44,54,56,58] PF can be mainly categorized as an enthesopathy, i.e. an attachment dyfunction of ligament or tendon to bone, with the enthesis being the interface between the periosteum and ligament (plantar aponeurosis) or tendon (flexor digitorum brevis).[44,55,56]

According to the clinical practice guidelines from the Orthopaedic Section of the American Physical Therapy Association (APTA),[58] the diagnosis of PF is made using the following history and physical examination findings: plantar medial heel pain (most noticeable with initial steps after inactivity, but also worse following prolonged weight-bearing activities); heel pain precipitated by a recent increase in weight-bearing activity; pain with palpation of the proximal insertion of the plantar fascia at the medical calcaneal tubercle; limited active and passive ankle dorsiflexion range of movement; abnormal Foot Posture Index score; high body mass index in nonathletic individuals; positive windlass test; and negative tarsal tunnel tests. Most of time the diagnosis of PF is straightforward;[55] however, in cases where pain localization is poor, differential diagnosis may include: tarsal tunnel syndrome, entrapment of the first branch of the lateral plantar nerve, subtalar arthritis, S1 nerve root impingement, central heel pain syndrome, fat pad atrophy, proximal plantar fibroma, fat pad contusion, calcaneal bruise, or calcaneal stress fractures.[44,55,56,58] Diagnostic imaging can be also used for PF; however, it usually is not necessary and rarely changes management. That is, although heel spurs on x-ray,[61,62] thickened plantar fascia on ultrasound,[63] and "hot" bone scan on the calcaneus bone are more common in patients with PF, many asymptomatic subjects can have the same imaging findings.

The etiology of PF remains unclear; however, it appears multi-factorial with several risk factors.[54] Obesity is thought to be a factor in 70% of cases of PF,[64] but the condition seems to be most common in younger people, predominately male athletes and middle-aged women.[60] Reduced ankle dorsiflexion,[61] prolonged standing,[61] and tightness of the calf and hamstrings[65] appear also to be factors associated with the development of PF.

Management of Plantar Fasciitis

The 2008 Clinical Practice Guidelines for PF proposed by the Orthopedic Section of the APTA did not recommend one treatment over another.[66] However, based on "strong evidence" from level I and II studies, the revised 2014 APTA guidelines recommend the following interventions for the management of PF: manual therapy (joint and soft tissue mobilization), plantar fascia-specific and gastrocnemius/soleus stretching, antipronation taping, prefabricated or custom orthoses, and night splints. In addition, iontophoresis with dexamethasone or acetic acid, rocker bottom-shoes in conjunction with a foot orthosis, ultrasound, phonophoresis with ketoprofen gel, low-level laser are supported by "weak" or "conflicting evidence" in the same guidelines.[58]

A Cochrane review on PF concluded that high quality evidence of efficacy for any one treatment modality is still lacking.[67] Treatment options for PF remain controversial and the preferred or recomemended method of intervention is inconsistent.[44,54,55,58,68] There is limited evidence for the effectiveness of dorsiflexion night splints in reducing pain.[67] Several trials have observed that manual therapy, i.e., passive joint mobilization, soft tissue mobilization, stretching, when included in a multimodal rehabilitation program, to be more effective at reducing pain and improving function in patients with PF than comparative interventions.[42,43,69,70] Furthermore, the findings of a recent systematic review suggest that manual therapy (i.e. joint mobilization/manipulation, soft tissue mobilization, manual stretching, trigger point release) may be effective in treating patients with PF; however, the dosing (i.e. frequency, intensity, duration) of the manual therapy remains unclear.[71]

Further, according to a another systematic review,[72] stretching is no more effective than other interventions, including sham or control groups, in relieving plantar heel pain. No clear conclusions can be drawn regarding the most effective stretch position, duration, frequency or optimum number of repetitions; however, plantar fascia stretching may be more effective than tendon Achilles stretching in the short term.[72] Moreover, in a recent randomized controlled trial of 83 patients with PF, eight weeks of strengthening exercises of the intrinsic and extrinsic muscles of the feet and the abductors and lateral rotators of the hip combined with stretching exercises were no better than application of stretching alone for improvements in pain, function and quality of life.[48] Nevertheless, a 2017 systematic review suggested strength training of the intrinsic foot musculature may be effective for improving pain and function in patients with plantar fasciitis;[73] however, this conclusion was based primarly on the findings of a single trial.[74] Notably, in a randomized controlled trial, Cleland et al found manual therapy and exercise to be superior to iontophoreiss with dexamethasone and exercise for the treatment of plantar fasciitis.[42]

Although the APTA clinical practice guideline does not recommend ultrasound therapy for PF,[58] a recent trial found the addition of ankle and foot joint mobilization aimed at improving dorsiflexion range of motion was not more effective than stretching and ultrasound alone in treating PF;[49] furthermore, a recent trial in individuals with calcaneal spurs reported mean decreases in first-step morning pain of 3.72 points (NPRS 0-10) in those receiving 10 sessions of ultrasound therapy and soft-tissue therapy.[75] Moreover, a recent systematic review concluded that "the available higher-quality evidence suggests that patients with persistant plantar fasciitis may benefit from ultrasound"[76] and it is still commonly used by many physical therapists in the USA as part of a multimodal approach in PF.[77,78]

The 2010 revised clinical practice guidelines for PF by the American College of Foot and Ankle Surgeons (ACFAS),[44] recommend treatment options be graded according to 3 progressive tiers. The first treatment tier includes: padding and strapping of the foot, prefabricated arch support insoles/heel cup, oral anti-inflammatory medication, cortisone injections, home-based physical therapy, Achilles and plantar fascia stretching. The second tier of the treatment ladder includes continuation of the tier 1 treatment options with the consideration of adding night splints, custom orthotics, repeat corticosteroid injections, botox injections, a course of physical therapy, cast immobilization for 4 to 6 weeks or use of walking boot, and referral for an appropriate weight loss program. It is thought that a positve clinical response to tier 2 options will usually occur within 2 to 3 months in 85% to 90% of the individuals.[44] After 6 months of failed conservative treatments, the third tier of treatment begins with the consideration for extracorporeal shock wave therapy (ESWT) or surgical plantar fasciotomy with or without nerve release.

Most non-invasive treatments have demonstrated limited effectiveness; therefore, invasive and novel approaches have been investigated for PF. For cases of persistent plantar fasciitis, physicians often recommend corticosteroid injections;[44,79] however, while steroid injections may be useful for managing the symptoms of plantar fasciitis in the short-term, long-term outcomes appear to be lacking.[67,80,81] Moreover, steroid injections have been linked with plantar fat pad atrophy, calcaneal osteomielitis, plantar fascia weakening and rupture.[82-84] While a meta-analysis found extracorporeal shock wave therapy (ESWT) to be an "ideal alternative" for treating plantar fasciitis,[85] a number of trials have led to inconsistent results[86-88] and its effectiveness remains equivocal.[67,76] Platelet rich plasma treatment was found to be a superior alternative to corticosteroid injections for PF,[89] and it may be one of the preferred treatment options for long term outcomes.[80]

Nevertheless, platelet rich plasma injections are considered controversial, expensive and are not normally covered by insurance plans.[90] In addition, the injection of botulinum toxin type A has been shown to yield superior results for pain associated with PF compared to placebo[91] and corticosteroid injections.[92]

Needling Therapies

Pain may be a potential barrier leading to underdosage of strength training and aerobic exercise stimulus in individuals with painful knee OA; therefore, needling therapies may be a reasonable non-pharmacologic adjunct intervention for the reduction of chronic pain in people participating in exercise programs for knee OA.[19,20,22,23] Similarly, needling therapies may be a reasonable adjunct therapy for the reduction of pain in individuals who are already receiving manual therapy, exercise, or electrophysical agents for the treatment of PF.

Needling therapy refers to the insertion of thin monofilament needles, as used in the practice of acupuncture, without the use of any injectate.[93-97] Dry needling is typically used to stimulate muscles, ligaments, tendons, subcutaneous fascia, scar tissue or peripheral nerves for management of pain and related-disability associated with neuromusculoskeletal disorders.[93,96-98] Interestingly, the most common term used to describe dry needling is "acupuncture", i.e., "acu" literally translates to needle and "puncture" to penetration.[97] On the contrary, injection therapies, often referred to as "wet needling", use hollow-bore needles to deliver corticosteroids, anaesthetics, sclerosants, botulinum toxins, or any other agents.[99,100]

Physiotherapists and/or medical physicians within both government administered national health services and mainstream university health systems[101-109] in the United Kindogm,[25,110-116] Canada,[105] USA and Germany[101-104,106-109] use the term ”acupuncture” to describe dry needling methodologies. The same is true in articles published in mainstream, highly respected journals, such as *British Medical Journal*,[110,113,116-119] *European Journal of Pain*,[111,120] *Archives of Physical Medicine & Rehabilitation*,[68,121-125] *Pain*,[96,104,108,126-131] *Annals Internal Medicine*,[94,114,132-135] *Headache*,[136,137] *Rheumatology*,[25,138-140] *Spine*,[95,105,141-146] and *Cochrane Database of Systematic Reviews.*[147,148] It would be therefore a mistake to ignore findings of high-quality, randomized clinical trials,[103,105-107,110,113,114,119,131,132,144,149-156] systematic reviews,[24,101,121,142,145,157-159] meta-analyses,[120,140] Cochrane reviews,[147,148,160] the British practice guidelines,[118] the European practice guidelines,[161,162] or the joint clinical practice guidelines from the American College of Physicians/American Pain Society[133] simply because they used the term “acupuncture” instead of the term “dry needling” in their title or methods sections.

The terminology, theoretical constructs and philosophies may differ; however, dry needling and acupuncture overlap in some terms of needling technique with the use of thin monofilament needles.[163] Notably, several previous meta-analyses and literature reviews have chosen to consider “acupuncture and dry needling” as one (the same) category of interventions.[120,142,147,159,164] Therefore, from a technical perspective, and for evaluating and comparing the efficacy and effect sizes within the literature on the use of needling without injectate in individuals with knee OA published by acupuncturists, medical physicians and physiotherapists, “electroacupuncture” and “electrical dry needling” will be considered as interchangeable terms, but not rely on diagnoses from Oriental medicine (e.g. *bi* syndrome, blood stagnation, or kidney *yang* deficiency[149,165]), or theoretical movement of *qi* along

traditional Chinese acupuncture meridians.[166,167] Importantly, none of the knee OA studies cited herein used injectate in conjunction with their needling procedure; therefore, all studies fit within the definition of dry needling, acupuncture, or "noninjection needling" (as opposed to "injection needling" or "wet needling"), regardless of the used terminologies, theoretical constructs, or philosophies.[93,97,163]

Chinese Acupuncture Points vs Western Dry Needling

Neither dry needling attempts to move energy or "*qi*" along meridians, nor does it rely on diagnoses from traditional Chinese acupuncture or Oriental medicine.[166,167] Dry needling also relies on Western medical diagnoses such as chronic neck pain[168,169-176], plantar fasciitis[177,178,179], knee OA[106,110,119,128,180-189], and carpal tunnel syndrome,[190-194] instead of traditional Chinese, Oriental or East Asian medicine diagnoses such as *bi* syndrome, *qi*, blood stagnation, and kidney *yang* deficiency.[166,167]

The Chinese originally established a set of 349 acupoints between 259 and 282 AD, while trigger points were first described as "nodular tumors or thickenings" by Balfor[195] in 1816 and "fibrosis" by Gowers[196] in 1904. While Steindler is widely recognized as coining the term "trigger point" in 1940, Dr. Karel Lewit, a medical physician and physiatrist from Czechoslovakia, published the first article on dry needling in 1979, noting that the needle insertion itself rather than the injectate appeared to be the cause of the analgesic response.[96] Despite the unique developmental lineage of acupoints and trigger points, a number of journal articles have noted significant anatomical and clinical similarities between the phenomena.

In 1977, Melzack et al[197] compared 48 known trigger points locations to acupoints for pain, giving a 100% anatomic correspondence and a 71% clinical correlation to pain patterns. While 48 trigger points is certainly less than the 255 myofascial trigger points documented by Travell and Simons,[198] Dorsher et al[199,200] provided a more comprehensive comparison of trigger points and acupoints, reporting 92% agreement for location and 79.5% agreement for pain referral patterns. Moreover, another recent study reported a 70% correlation between trigger points and classical acupoints.[201]

Following a 3-part analysis for the anatomical location, pain location and referred pain patterns of acupoints and trigger points, and using graphic software, Dorsher[44,45] superimposed 255 of the most common myofascial trigger points from the Travell and Simons Trigger Point Manual[43] with 361 classical acupoints. Dorsher concluded that 238 of the classical acupoints matched with the 255 myofascial trigger points, with 89, 107 and 32 acupoints falling within 1, 2 and 3cm of myofascial trigger points, respectively.[44,45] Dorsher then took the 238 corresponding anatomical points and cross-referenced their indications for pain with the Travell and Simons Trigger Point Manual[43] and classical acupuncture texts. Dorsher found 221 of 238 points (93%) had myofascial trigger point pain indicators, 208 of 221 points (94%) had similar regional pain indicators, and 180 of 238 points (81%) had complete or near complete pain referral patterns.[44,45]

Notably, recent investigations by Western-based medical practitioners report a lack of robust evidence validating the clinical diagnostic criteria for trigger point identification and/or diagnosis. In a systematic review on the reliability of physical examination for the diagnosis of myofascial trigger points, Lucas et al[202] concluded, "There is no accepted reference standard for the diagnosis of trigger points, and data on the reliability of physical examination for trigger points is conflicting."

Lew et al[203] further reported that the inter-examiner agreement was only 21%, and Sciotti et al[130] reported error rates of 3.3-6.6 cm among examiners attempting to identify the specific location of trigger points in the upper trapezius muscle. In another literature review, Myburgh et al[204] found poor inter-examiner reliability of manual palpation of trigger points in various muscle groups. Only 'tenderness' of the upper trapezius, not the actual location of the trigger point, was found to be moderately reliable. Therefore, high-quality evidence suggests that manual examination for identification of the specific location of the trigger point is not a valid[204-206] or reliable[130,202-204] process between-examiners. This is perhaps a potential reason why medical physicians and physical therapist researchers have chosen to use the acupoint nomenclature to more reliably identify the exact insertion location, angulation and depth of the needle placement, which is of course required when using standardized interventions or needling protocols in the confines of randomized controlled trials.

In review paper on similarities and differences between dry needling and acupuncture, Zhu et al[207] recommended "collaboration and integration should be strengthened between dry needling practitioners who are not physicians and acupuncturists so that the patients can receive safe and high quality acupuncture treatment". Consistent with the remarks of Zhou et al,[163] several healthcare providers, i.e. physical therapists, chiropractors, nurse practitioners, naturopaths, osteopaths, or medical physicians, should possess a fundamental and working knowledge of the acupoint nomenclature so as to more reliably treat myofascial pain located throughout the body. Therefore, that is, without using the principles or theories of traditional Chinese acupuncture or Oriental medicine (i.e. movement of *qi* or energy along Chinese meridians to alter function of all 10 organ systems; use of tongue and pulse diagnosis; use of Oriental medicine diagnoses such as *bi*

syndrome, kidney *yang* deficiency, blood stagnation etc), physical therapists can achieve greater accuracy in needle placement (due to the poor inter-examiner reliability associated with localizing muscle trigger points) by becoming more familiar with the location of acupoints that correspond, in the main, to the same trigger point locations.[41-47] In the words of Zhou et al, **"**Because of the close relationship between dry needling and acupuncture, collaboration rather than dispute between acupuncturists and other healthcare professionals should be encouraged with respect to education, research, and practice for the benefit of patients with musculoskeletal conditions who require needling therapy."[163]

Attorney General Opinions

Dry needling and acupuncture dramatically differ in their origins, theoretical and scientific underpinnings; however, "dry needling and acupuncture overlap in terms of needling technique with solid filiform needles."[121] Notably, in response to an Attorney General Opinion request made by the Texas State Board of Acupuncture Examiners in 2016, the Attorney General of Texas opined, "it should not be assumed that the practice scope of physical therapy and the scope of practice of acupuncture are mutually exclusive; that is, overlap between the scopes of practice of acupuncture and physical therapy may exist (recognizing that the scopes of practice of medicine and physical therapy overlap with regard to a procedure called needle electromyography)."[208]

Moreover, at the request of the Chiropractic Examining Board, the Attorney General of Wisconsin concluded that "chiropractors do not have a monopoly on the application of therapeutic touch to the neck, back and joints"; furthermore, "even if nearly identical physical motions were performed by a chiropractor", the "terms such as adjustment and manipulation have a variety of appropriate meanings to various healing disciplines", that is, it is "the principles of physical therapy science" versus "chiropractic science" that separates the two disciplines, not the actual performance of the manipulation technique itself.[209]

Acupuncture and Dry Needling for Knee Osteoarthritis

The current body of evidence strongly supports the use of acupuncture for treating pain, stiffness and disability associated with knee OA; that is multiple high quality RCTs, systematic reviews and meta analyses have concluded such.[19,23,25,97,106,119,128] Zhang et al[210] cited a 69% consensus following a Delphi study recommending the use of acupuncture for the symptomatic treatment of joint OA and reported a moderate effect size for the modality (i.e. acupuncture). Witt et al[211] reported on the data from 304,674 patients with knee or hip OA, and in short follow-up, those treated with acupuncture in addition to usual care showed significantly greater improvements in pain compared to patients who received usual care only, demonstrating acupuncture is an effective adjunct to usual care alone. Additionally, the acupuncture group showed significantly greater pain reduction compared to the waiting-list control group.

In a comprehensive network meta-analysis, Corbett et al[19] evaluated 22 treatment interventions across 114 RCTs for treatment of pain due to knee OA, and based on a primary sensitivity analysis of better quality studies, acupuncture was found to be one of the more effective physical treatments for reducing pain at short-term. Moreover, verum or real acupuncture was significantly superior for reductions in pain when compared to standard care and sham acupuncture. In addition, acupuncture was significantly better than muscle strengthening exercise, weight loss, aerobic exercise or no intervention.[19] Notably, Corbett et al[19] alluded to the pitfalls of sham controlled acupuncture trials and reported that the effects of acupuncture in their study may have been *underestimated* due to the inclusion of 2 large sham controlled studies that used a placebo that likely was physiologically active.

There are 8 systematic reviews and/or meta-analyses,[19,21,24,134,140,212-214] 1 Cochrane review,[21] and 7 randomized controlled trials[106,119,128,183,184,189,211] that have reported some positive effects for acupuncture in patients with joint OA.[215] Of the 8 reviews, Manheimer et al provide the weakest support for the use of acupuncture in patients with knee OA.[21,134] Notably, the two reviews[21,134] reported statistically significant and clinically meaningful improvements in pain and function compared to usual care and a wait-list control; however, these were clinically irrelevant improvements when compared to sham acupuncture. The Manheimer reviews highlight the verum versus sham acupuncture debate. Certainly, patient expectations and values concerning acupuncture may play a critical factor,[216] especially if patients are able to distinguish the difference between real and sham acupuncture. However, as Dincer et al[217] points out, designating sham acupuncture interventions as placebo controls is "misleading and scientifically unacceptable". In addition, Lundeberg et al[218] remind us, the danger of placebo acupuncture is to assume that it is a true, non-inert control and conclude that, in many trials, acupuncture is either no better than or modestly

better than sham, thereby committing a type 2 error, i.e., accepting a false null hypothesis or falsely concluding that the treatment is useless.[218] Corbett et al[19] further alluded to the pitfalls of sham controlled acupuncture trials and reported that the effects of acupuncture in their study may have been *underestimated* due to the inclusion of 2 large sham controlled studies that used a placebo that likely was physiologically active.[219]

Of the 8 systematic reviews on acupuncture for knee OA, one of the strongest came from White et al.[25] Interestingly, White et al combined the results of 5 RCTs and found that acupuncture for knee OA resulted in significant reductions in pain and disability (WOMAC subscale) compared to sham acupuncture and no treatment at both short-term (12 weeks) and at long-term follow-up (26-52 weeks).[25] Importantly, White et al[25] only included studies with a "true sham", defined as a treatment that avoided stimulating neural structures in the same neurological segments of the knee joint. As White stated, "even superficial penetration with needles is regarded as unacceptable because it has the potential to be physiologically active." In fact, White et al[25] only included studies that adequately treated knee OA with a sufficient dosage of acupuncture. White et al defined "adequate" dosage of acupuncture for knee OA as at least 6 treatments (1 treatment per week) that incorporated 4 points in the region of the knee for at least 20 minutes with either manual stimulation (de qi) or electric stimulation. Given that these parameters of "adequate" acupuncture are also supported by other investigators,[220,221] it begs the question of whether previously published RCTs on acupuncture for individuals with knee OA have incorporated suboptimal needling protocols, thereby "watering down" the results reported in some of the systematic reviews and meta-analyses. For example, although Hinman et al[222] concluded that "needle and laser acupuncture were no more efficacious that sham laser acupuncture" for knee pain, it should be noted that they did not standardize the number and placement of needles, did not report

whether the needles were manual manipulated, and did not use electric current stimulation. Furthermore, and of major importance, unlike 11 of the 13 randomized controlled trials in the Cochrane Database systematic review[21] that found acupuncture effective in patients with knee OA, Hinman et al[222] did not radiographically confirm the clinical diagnosis of knee OA.[7] Importantly, these trials are in agreement with the large scale Cochrane review on acupuncture for knee OA by Manheimer et al[21] that compared the effects of verum acupuncture with sham acupuncture, another active treatment, and waitlist control from 12 RCTs. Although the effects of verum acupuncture vs. sham acupuncture were statistically significant in the short-term and at 6 months; however, the benefits were considered as clinically irrelevant.[21] A subgroup analysis found that the effects of verum acupuncture were clinically relevant when compared to several active treatments and waitlist controls, and the authors suggest that patients with OA will find meaningful benefits from acupuncture.[21]

Statistical significance is one thing and effect size is another; however, the OARSI guidelines[223] for hip and knee OA reported a moderate effect size for pain (0.51), stiffness (0.41), and function (0.51). In addition, Zhang et al[223] reported a pooled effect size for acupuncture compared to usual care and wait lists from the data provided by Manheimer et al of 0.58.[134] MacPherson further reported a 0.27 larger effect of acupuncture with electric stimulation compared to controls.[221] As expected, the effect size of acupuncture versus sham acupuncture was less (0.35 to 0.40), but this effect size is still comparable to that of NSAIDs (0.32) for knee OA.[25] While it is not always appropriate to compare effect sizes among various treatments,[223] to our knowledge, a pooled standard effect size of 0.58 for acupuncture in individuals with knee OA is higher than any other treatment traditionally

provided by a physical therapist, to include strengthening exercises (0.32) and aerobic exercises (0.52).[210,223]

Although the mechanisms by which electroacupuncture improves pain and physical function in knee OA remain to be elucidated; Zhang et al[224] found significantly lower T2 values at the anteromedial and anterolateral tibial areas of 100 knees following 20min sessions over 4weeks of low frequency electroacupuncture, that is, electroacupuncture appears to play a role in cartilage repair in individuals with knee OA.[224] Many researchers articulate that the general effect of acupuncture for patients with OA is due to increased blood flow to the peri and intra-articular tissues. For example, following acupuncture, Loaiza et al measured a significant increase in vasodilation over the medial aspect of the knee.[225]

Electroacupuncture may improve vascularity of the joint via CGRP and nitric oxide, thereby inhibiting and/or reversing symptoms associated with OA. A number of studies have also shown a significant reduction in inflammatory cytokines in the synovial fluid of osteoarthritic joints following acupuncture. The increased blood flow likely facilitates the recruitment of opioid producing immune cells required to reduce the level of inflammatory cytokines. Furthermore, Ahsin et al reported a significant increase in plasma β-endorphin levels after electroacupuncture to local points at the knee that correlated with reductions in pain, stiffness and disability, which is likely due to vasodilation.[126] Electroacupuncture further blocks the local release of IL-1 β and TNF-α in the synovia of osteoarthritic joints[226] and the systemic release of IL-1 β and TNF-α by inhibiting melanocortin-4 in the periaqueductal gray of the brain stem.[227] Lastly, there is limited evidence suggesting acupuncture may stimulate an increase in hyaluronic acid, allowing the synovial fluid to better lubricate the joint.[228]

Acupuncture and Dry Needling for Plantar Fasciitis

Although the 2014 clinical practice guidelines[58] concluded that "the use trigger point dry needling cannot be recommended for people with PF," a recent meta-analysis of seven trials concluded that trigger point dry needling is effective in patients with PF, and reported a pooled estimate of -15.5 points (VAS 0-100) for pain reduction.[229] Furthermore, in a recent randomized controlled trial of 84 patients with PF, Cochett et al[45] reported statistically significant differences in first-step pain and foot pain in favor of trigger point dry needling over sham dry needling.

Nevertheless, the palpatory methods used by Cochett et al[45] to identify the location of trigger points, and therefore the entry point, angulation, and depth of needle insertion, have not yet been found to possess accurate diagnostic validity[68,181,230] or acceptable inter-examiner reliability[68,130,158,231] for muscles in the foot or lower leg. In addition, although the etiology of PF remains unclear, the proximal attachment of the plantar aponeurosis at the medial tubercle of the calcaneus is the most often reported by the patients as the origin of symptoms and the site of greatest discomfort.[60,232,233] That is, had Cotchett et al[45] targeted the insertion of the plantar fascia at or near the medial tubercle of the calcaneus[234-236] and left the needles in place for 15 minutes,[112] 20 minutes,[236,237] or 30 minutes[235] as previous studies have done in chronic PF patients, perhaps the between-group difference in first-step pain (i.e., the primary outcome measure at the primary end-point of 6-weeks) of -14.4mm (VAS 0-100) would have shown a larger effect size and exceeded the minimum clinically important difference for that measure.[238-240] Moreover, according to Lucas et al, "It is not yet evident that examiners can agree on the precise location of an active TrP; hence, they cannot be relied upon to accurately insert the needle into the nodule of the taut band."[202]

Given the 21% inter-examiner agreement[203] and 3.3 cm to 6.6 cm error rate of locating trigger points within the upper trapezius,[130] it is doubtful that Cotchett was able to reliably needle trigger points in muscles such as the quadratus plantae, flexor digitorum brevis and abductor hallicus. Notably, when Cotchett et al compared his consensus driven dry needling model[241] for a prospective randomized controlled trial, they reported statistically significant improvements in pain and function.[242] However, neither the 14.4 mm improvement in first-step morning pain nor the 10.0 point improvement on the pain subscale of the Foot Health Status Questionnaire (FHSQ) reported by Cochett et al[45] exceeded the 19 mm[243] (VAS 0-100 mm) and 13-point[243] minimum clinically important difference (MCID), respectively.

Notably, a randomized controlled trial of patients with chronic PF reported a 69% reduction in foot pain and an 80% success rate following 10 sessions of electroacupuncture over 5 weeks targeting the most tender points over the medial plantar aspect of the calcaneus with 2 to 6 needles left in place for 30 minutes.[235] It is perhaps worth noting that periosteal "pecking" or "peppering", a technique that stimulates bleeding via multiple penetrations at or near the proximal attachment of the plantar fascia at the medial tubercle of the calcaneus, has also been performed in conjunction with injection therapies for PF.[244,245] In the case of corticosteroid injections, peppering resulted in significantly greater reductions in pain secondary to PF than corticosteroid injection alone.[246,247] Moreover, a trial found miniscalpel-needle release ("over the most painful tender point at the medial calcaneal tubercle") was superior to steroid injections in the short and long-term (1-, 6- and 12-month outcomes) for improving first-step morning pain in recalcitrant PF patients.[47]

Objectives

Electrical dry needling and the combination of manual therapy and exercise have each been found to be moderately effective for knee OA. However, no previous study has investigated the combination of the effectiveness of electrical dry needling in addition to manual therapy and exercise in patients with knee OA. Similarly, although there is limited evidence upon which to base clinical practice, and in the absence of high-quality evidence for any one treatment modality, it may still be possible to achieve a high success rate with a combination of the treatments for PF. Electrical dry needling, manual therapy and exercise, and combination of stretching and ultrasound, when applied separately, have been found to be moderately effective for PF. However, again no study has investigated the effectiveness of combining electrical dry needling, manual therapy, exercise and ultrasound in PF.

Therefore, the objectives of this PhD thesis were:

1. To compare the effects of adding electrical dry needling, into a manual therapy and exercise program on pain, stiffness, function and disability in people with knee OA.
2. To compare the effects of adding electrical dry needling, into a program of manual therapy, exercise and ultrasound on first-step pain and related-disability in people with chronic PF.

The hypotheses of this PhD thesis were:

1. Individuals with knee OA receiving electrical dry needling combined with manual therapy and exercise would exhibit greater improvements in pain, stiffness, function and disability than those receiving only manual therapy and exercise.
2. Subjects with PF receiving electrical dry needling combined with manual therapy, exercise and ultrasound would exhibit greater improvements in pain and related-disability than those receiving only manual therapy, exercise and ultrasound.

Methods

Study 1 - Knee OA

Study Design

This randomized, single-blinded, multi-center, parallel-group trial compared two treatment protocols for the management of painful knee OA: manual therapy and exercise vs. manual therapy and exercise plus electrical dry needling. The primary outcome was related-disability as assessed by the Western Ontario and McMaster Universities (WOMAC total score) Osteoarthritis Index at 3 months. Secondary outcomes included knee pain intensity as measured by the Numeric Pain Rating Scale (NPRS), all WOMAC subscales (pain: WOMAC-P; stiffness: WOMAC-S; physical function: WOMAC-PF), medication intake, and the Global Rating of Change (GROC). The current clinical trial was conducted following the Consolidated Standards of Reporting Trials (CONSORT) extension for pragmatic clinical trials.[248] The study was approved by the ethics committee at Universidad Rey Juan Carlos, Madrid-Spain (URJC) and the trial design was prospectively registered (ClinicalTrials.gov: NCT02373631).

Participants

Consecutive individuals with painful knee OA from 18 outpatient physical therapy clinics in 10 different states (Arizona, Florida, Georgia, Illinois, New Hampshire, New York, North Carolina, Rhode Island, South Carolina, Virginia) were screened for eligibility criteria and recruited over a 24-month period (from February 2015 to February 2017). For patients to be eligible, they had to have met the American College of Rheumatology criteria for the diagnosis of knee OA[7,8] and have had chronic pain in the knee joint for more than 3 months.

Patients had to have at least 3 of the following criteria[7,8,248] to be included in the study: 1, >50 years of age; 2, less than 30 minutes of morning stiffness; 3, crepitus on active motion; 4, bony tenderness; 5, bony enlargement; and 6, no palpable warmth of synovium.[7] In addition, participants had to have a minimum knee pain intensity score of 2 points and be older than 18 years of age. Patients were excluded if they exhibited: 1, a history of surgery in the knee; 2, a history of surgery to either of the lower extremities in the last 6 months; 3, any red flags to manual therapy, dry needling or exercise; 4, had received physical therapy, acupuncture, massage therapy, chiropractic or intra-articular injections for the painful knee in the last 3 months; 5, presented with 2 or more positive neurologic signs; or 6, had involvement in litigation or worker's compensation regarding their knee pain. Patients were also excluded if they were pregnant. All participants signed an informed consent prior to their participation in the study. All participants were naïve to the use of dry needling procedures and had not previously experienced needling without injectate for their knee pain.

Treating Therapists

Eighteen physical therapists (mean age, 38.4 years, SD 10.44) participated in the delivery of treatment for patients in this study. They had an average of 12.5 (SD 9.54) years of clinical experience, an average of 4.3 (SD 1.88) years using dry needling, and all had completed a 54-hour post-graduate certification program that included practical training in electrical dry needling for knee OA. All participating physical therapists were required to study a manual of standard operating procedures and participate in a 6-hour training session with the principal investigator.

Randomization and Blinding

Following baseline examination, patients were randomly assigned to receive manual therapy and exercise alone or in combination with electrical dry needling. Concealed allocation was conducted using a computer-generated randomized table of numbers created by a statistician who was not otherwise involved in the trial and did not participate in analysis or interpretation of the results. Individual and sequentially numbered index cards with the random assignment were prepared for each of the 18 data collection sites. The index cards were folded and placed in sealed opaque envelopes. Blinded to the baseline examination, the treating therapist opened the envelope and proceeded with treatment according to the group assignment. The examining therapist remained blind to the patient's treatment group assignment at all times; however, based on the nature of the interventions it was not possible to blind patients or treating therapists.

Interventions

All participants received between 8 and 10 treatment sessions at a frequency of 1-2 times per week over a 6-week period. Both groups received manual therapy (passive joint mobilizations and muscle stretching) and exercise (riding a stationary bicycle, range of motion and strengthening exercises to the lower extremity) on each session. In addition, the dry needling group also received electrical dry needling using a standardized 9-point protocol for 20-30 minutes on each treatment session.

Although specific recommendations cannot be made regarding the type of exercise[14] or the optimal exercise dosage in patients with knee OA,[9] patients received the following interventions at all treatment sessions: 30 minutes of lower extremity strengthening (weight bearing, non-weight bearing, concentric, eccentric), range of motion (riding a stationary bicycle), stretching exercises (static muscle stretching) and passive accessory/physiological joint mobilizations.[26] The exercise program was taught to the patient by an experienced physical therapist on the first session and supervised on subsequent sessions. Strengthening, range of motion and stretching exercises were gradually progressed according to tolerance of each individual patient. That is, progression only occurred if patients reported a decrease in symptoms and in the absence of excessive soreness. Details regarding the exercise and manual therapy program have previously been described by Deyle et al.[26]

All patients in both groups were asked to complete a daily home exercise program.[26] The home exercise program consisted of the same strengthening, range of motion and stretching exercises that were prescribed and supervised in the clinic.[26] Patients were asked to complete the home exercise program during all days that they did not receive supervised physical therapy in the clinic. Patients were asked to monitor their compliance with the home exercise program by maintaining a home exercise program logbook.

In addition to manual therapy and exercise, patients allocated to the dry needling group also received 8-10 sessions of periosteal electrical dry needling at a frequency of 1-2 times/week over 6 weeks. Electric dry needling included a 9-point standardized protocol as depicted in **Figure 1**.

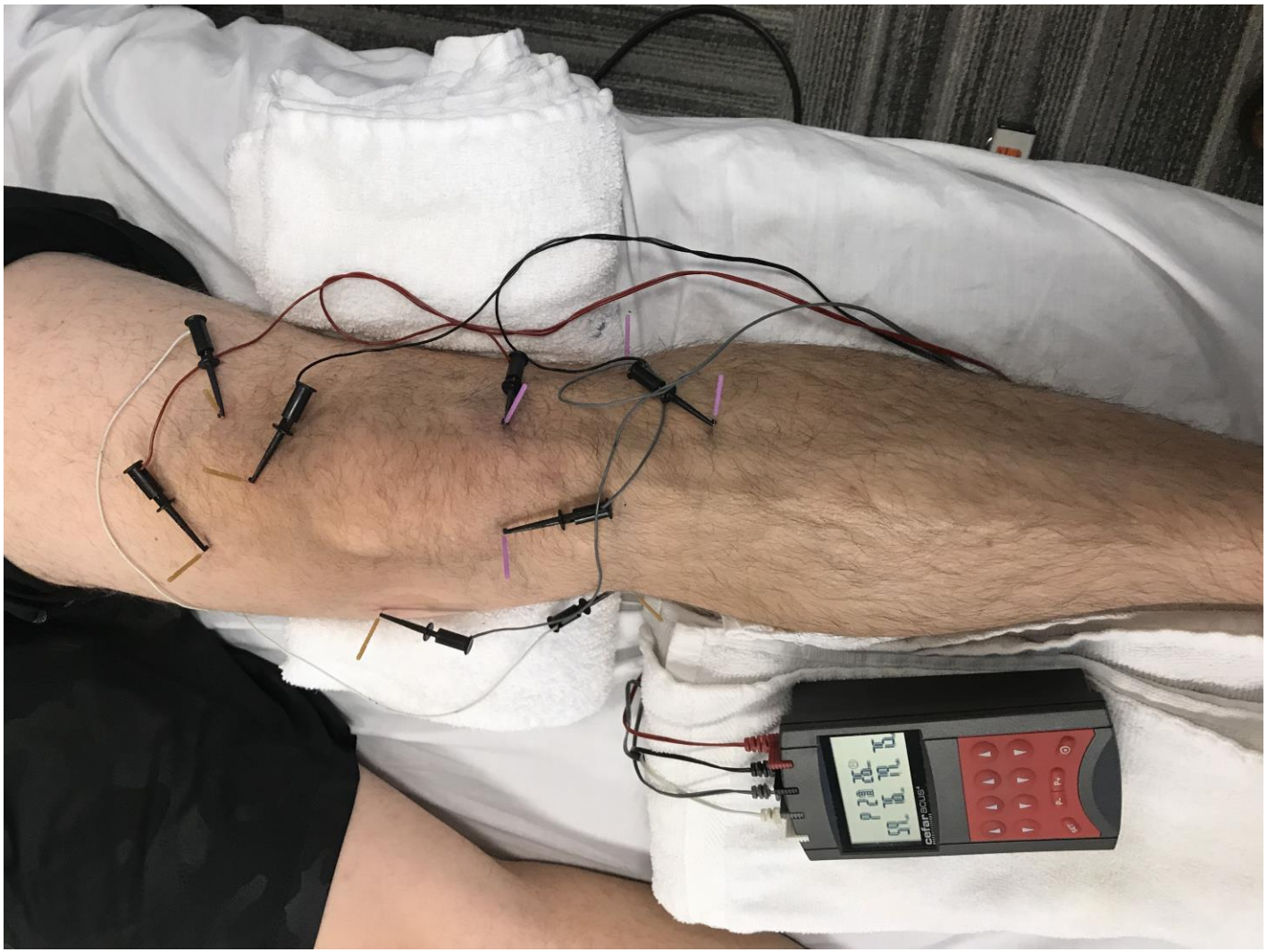


Figure 1: Standardized 9-point protocol of periosteal electrical dry needling for knee OA

Description of 9-point electrical dry needling intervention for knee OA

The technique is performed with the patient supine with the treated knee slightly flexed over a towel roll. The following 9 needles were inserted:

(1) superolateral and anterior insertion within the popliteus, with periosteal stimulation over the posteromedial aspect of the medial tibial condyle;

(2) inferolateral insertion angle within the distal adductor magnus, with periosteal stimulation within the depression posterosuperior to the femoral epicondyle;

(3) perpendicular insertion within the tibialis anterior, with periosteal stimulation over the anterolateral crest of the tibia one fingerbreadth lateral to the tibial tuberosity;

(4) perpendicular insertion within the quadriceps tendon, one fingerbreadth proximal to the superior border of the patella;

(5) perpendicular insertion within the vastus lateralis, three fingerbreadths proximal to the superolateral border of the patella;

(6) perpendicular insertion within the vastus medialis, three fingerbreadths proximal to the superomedial border of the patella;

(7) perpendicular insertion at the level of the tibiofemoral joint margin within the medial infrapatellar sulcus;

(8) perpendicular insertion at the level of the tibiofemoral joint margin within the lateral infrapatellar sulcus; and

(9) perpendicular insertion within the extensor digitorum longus, one thumb width distal and anterior to the fibula head.

Unlike the first 8 needles that were electrically connected in pairs, and for the purpose of standardization, the last ninth needle was not paired with one of the 4 electrical channels; nevertheless, it was manually manipulated and left in situ for the duration of the treatment **(Figure 1).** In addition to the obligatory 9-point standardized protocol, clinicians were also permitted to insert needles at up to 4 additional locations based on the presence of the symptoms.

Sterilised disposable stainless steel Seirin J-type acupuncture needles were used with three sizes: 0.25 mm x 30 mm, 0.30 mm x 40 mm, and 0.30 mm x 50 mm. The depth of needle insertion ranged from 15mm to 45mm and depended on the point (intramuscular, periosteal, joint line, intra/periarticular) and the patient's constitution (i.e. size and bone depth, muscle or connective tissue thickness). Following topical skin cleansing with sterile alcohol prep pads, all needles were inserted and then manipulated bi-directionally to illicit a sensation of aching, tingling, deep pressure, heaviness or warmth.[249,250] In addition, at least 3 of 9 obligatory needles (i.e. over the posteromedial aspect of the medial tibial condyle, within the depression posterior to the femoral epicondyle, and over the anterolateral crest of the tibia one fingerbreadth lateral to the tibial tuberosity) were repeatedly thrusted and tapped on to the respective bone using a "periosteal stimulation" technique.[251] Notably, with the exception of the 2 obligatory needles inserted at the level of the tibiofemoral joint margin within the medial or lateral infrapatellar sulcus, and depending on the patient's physical constitution, the needle length selected by the practitioner and the patient's tolerance to such, the remaining obligatory needles were also advanced towards the underlying bone to facilitate direct mechanical and electrical "periosteal stimulation".[251]

The needles were then left in situ for 20-30 mins[106,119,128,252-254] with electric stimulation (ES-160 electrostimulator ITO co.) in pairs (crossing through the knee joint in a superior-inferior and diagonal orientation) using 4 channels to 8 of the needles using a low frequency (2 Hz), moderate pulse duration (250 microseconds), biphasic continuous waveform at a maximum tolerable intensity.[253,254] In cases of bilateral knee OA, both knees were treated, but only the most painful side at baseline was recorded and analyzed throughout the study to satisfy the assumption of independent data.[255]

Outcome Measures

The primary outcome was the related-disability as assessed with the WOMAC total index score, whereas each WOMAC subscale [pain (WOMAC-P), stiffness (WOMAC-S) and physical function (WOMAC-PF)] were considered secondary outcomes. The WOMAC is a valid and reliable instrument and has been used extensively to evaluate 3 dimensions (pain, stiffness, and physical function) in patients with hip or knee OA.[256-258] In patients with OA of the lower extremities participating in rehabilitation programs, the minimum clinically important difference (MCID) for the WOMAC has been calculated to range from 9% to 12% of the baseline score.[259-261] However, in our study, we used 36% change in the WOMAC (i.e. triple the value of the 12% MCID) to represent a successful outcome.

Secondary outcomes included the intensity of knee pain, the 3 WOMAC subscales, medication intake, and the GROC. A Numeric Pain Rating Scale (NPRS) measured knee pain intensity. Patients were asked to indicate the average intensity of knee pain over the past week using an 11-point numerical scale ranging from 0 (“no pain”) to 10 (“worst pain imaginable”) at baseline, 2 weeks, 6 weeks, and 3 months following the initial session.[262]

The NPRS is a reliable and valid instrument to assess pain intensity.[263-265] The MCID for the NPRS has been shown to be 1.74 in patients with chronic pain conditions;[265] however, the MCID for knee-related pain has not yet been established. Nevertheless, a change of 2 points or a 30% decrease in pain from baseline can be considered as a MCID in subjects with chronic musculoskeletal pain.[265,266]

Medication intake was measured as the number of times that the patient had taken prescription or over-the-counter analgesic or anti-inflammatory medication in the past week for their knee pain, with five options: (1) not at all, (2) once a week, (3) once every couple of days, (4) once or twice a day, or (5) three or more times a day. Medication intake was assessed at baseline and at 3 months after the first treatment session.

At 2 weeks, 6 weeks and 3 months following the initial treatment session, patients completed a 15-point GROC question based on a scale described by Jaeschke et al[267] to rate their self-perceived improved function. The MCID for the GROC has not been specifically reported but scores of +4 and +5 have typically been indicative of moderate changes in patient status.[267]

Treatment Side Effects

Patients were asked to report adverse events that they experienced during any part of the study. In the current study, an adverse event was defined as a sequelae of one-week duration with any symptom perceived as distressing and unacceptable to the patient that required further treatment.[268] Particular attention was given to the presence of ecchymosis and post-needling soreness within the group receiving electrical dry needling.

Sample Size Determination

The sample size calculations were based on detecting a between-groups moderate effect size of 0.4 at 3 months, assuming a 2-tailed test, an alpha level (α) of 0.05 and a desired power (β) of 90%. The estimated desired sample size was calculated to be 105 subjects per group. A dropout percentage of 15% was expected, so 120 patients were included.

Statistical Analysis

Statistical analysis was performed using SPSS software, version 24.0 (Chicago, IL, USA) and it was conducted according to intention-to-treat analysis. We performed Little's Missing Completely at Random (MCAR) test[269] to determine if missing data associated with dropouts were missing at random or missing for systematic reasons. Intention-to-treat analysis was performed by using Expectation-Maximization whereby missing data was computed using regression equations. The effects of treatment on pain, stiffness, physical function and related-disability were each examined with a 2-by-4 mixed model analysis of covariance (ANCOVA) with treatment group as the between-subjects factor, time as the within-subjects factor, and adjusted for baseline data. Separate ANCOVAs were performed with each outcome as the dependent variable. For each ANCOVA, the main hypothesis of interest was the 2-way interaction (group by time) with a Bonferroni-corrected alpha level of 0.0125 (4 time points). We used $\chi 2$ tests to compare self-perceived improvement with GROC and changes in medication intake. To enable comparison of between-group effect sizes, standardized mean differences (SMDs) were calculated. Numbers needed to treat (NNT) and 95% confidence intervals (CI) were also calculated at the 3-months follow-up period using each definition for a successful outcome.

Study 2 - Plantar Fasciitis

Study Design

This randomized, single-blinded, multi-center, parallel-group trial compared two treatment protocols for the management of PF: manual therapy, exercise and ultrasound vs. manual therapy, exercise and ultrasound plus electrical dry needling. The primary end-point was first-step pain in the morning as measured by the Numeric Pain Rating Scale (NPRS). Secondary outcomes included mean resting foot pain intensity (NPRS), pain during activity (NPRS), the Lower Extremity Functional Scale (LEFS), the Foot Functional Index (FFI), medication intake, and the Global Rating of Change (GROC). The current clinical trial was conducted following the Consolidated Standards of Reporting Trials (CONSORT) extension for pragmatic clinical trials.[248] The study was approved by the ethics committee at Universidad Rey Juan Carlos, Madrid, Spain and the trial was prospectively registered (ClinicalTrials.gov: NCT02373618).

Participants

Consecutive individuals with PF from 10 outpatient physical therapy clinics in 6 different states (Arizona, Florida, Georgia, Kentucky, North Carolina, Texas) were screened for eligibility criteria and recruited over a 27-month period (from February 2015 to February 2017). For patients to be eligible, they had to meet the following criteria: 1, a clinical diagnosis of PF in accordance with the clinical practice guidelines from the Orthopaedic Section of the American Physical Therapy Association (APTA);[58] 2, plantar heel pain for longer than 3 months; 3, first-step pain in the morning during the previous week rated at least 2 on the numeric pain rating scale (NPRS 0-10);[270] and 4, aged 18 years or older.

Patients were excluded if any of the following criteria were present: 1, a history of surgery to the ankle, foot or lower leg; 2, potential contraindications to manual therapy, dry needling, exercise or ultrasound; 3, had received conservative treatment (i.e. physical therapy, acupuncture, massage therapy, chiropractic treatment or local steroid injections) for PF within the previous 4 weeks; 4, presented with 2 or more positive neurologic signs consistent with nerve root compression (muscle weakness involving a major muscle group of the lower extremity, diminished lower extremity deep tendon reflex, or diminished or absent sensation to pinprick in any lower extremity dermatome); 5, other causes of heel pain (including tarsal tunnel syndrome, calcaneal fracture, ankle or foot instability, arthritis of the foot or ankle, rheumatioid arthritis, neurogenic claudication, peripheral neuropathy); or 6, had involvement in litigation or worker's compensation regarding their heel pain. Patients were also excluded if they were pregnant. All participants signed an informed consent prior to their participation in the study.

Treating Therapists

Ten physical therapists (mean age, 34.5 years, SD 5.4) participated in the delivery of treatment for patients in this study. They had an average of 8.0 (SD 4.4) years of clinical experience and all completed a 54-hour post-graduate certification program that included practical training in electrical dry needling for PF. All therapists delivering treatment were Fellows-in-Training within the APTA-accredited American Academy of Manipulative Therapy Fellowship in Orthopaedic Manual Physical Therapy post-graduate program. To ensure all examination, outcome assessments, and treatment procedures were standardized, all participating physical therapists were required to study a manual of standard operating procedures and participate in a 6-hour training session with the principal investigator.

Examination Procedure

All patients provided demographic information and completed a number of self-reported measures followed by a standardized history and physical examination at baseline. The primary self-rated outcome was first-step pain (when getting out of bed in the morning) as measured by the Numeric Pain Rating Scale (NPRS). Secondary outcomes were resting pain intensity (NPRS), pain during activity (NPRS), the Lower Extremity Functional Scale (LEFS), the Foot Functional Index (FFI), medication intake (number of times the patient had taken prescription or over-the-counter analgesic or anti-inflammtory medication for their PF during the last week), and the Global Rating of Change (GROC). Participants recieved a standardized physical examination during which the affected foot, ankle and lower extremity were examined for conditions other than PF; that is, other causes of heel pain were ruled out. The physical examination included, but was not limited to, assessments for the impairments of reduced ankle dorsiflexion range of motion[61] and tightness of the calf and hamstrings musculature.[65] Most of time the diagnosis of PF is straightforward;[55] however, in cases where pain localization is poor, differential diagnosis includes tarsal tunnel syndrome, entrapment of the first branch of the lateral plantar nerve, subtalar arthritis, S_1 nerve root impingement, central heel pain syndrome, fat pad atrophy, proximal plantar fibroma, fat pad contusion, calcaneal bone bruise, or calcaneal stress fractures.[44,55,56,58]

Randomization and Blinding

Following baseline examination, patients were randomly assigned to receive manual therapy, exercise and ultrasound alone or combined with electrical dry needling. Concealed allocation was conducted using a computer-generated randomized table of numbers created by a statistician who was not otherwise involved in the trial and did not participate in analysis or interpretation of the results. Individual and sequentially numbered index cards with the random assignment were prepared for each of the 10 data collection sites. The index cards were folded and placed in sealed opaque envelopes. Blinded to the baseline examination, the treating therapist opened the envelope and proceeded with treatment according to the group assignment. Patients were instructed not to discuss the particular treatment procedure received with the examining clinician. The examining clinician remained blinded to the patient's treatment group assignment at all times; however, based on the nature of the interventions it was not possible to blind patients or treating therapists.

Interventions

All participants received up to eight treatment sessions at a frequency of once or twice per week over a 4-week period. Both groups received an impairment-based manual therapy approach directed to the lower limb,[42,49,66,71,271] an exercise program[43,48,49,72-74] including self-stretching of the plantar fascia, gastrocnemius, soleus and Achilles tendon and strengthening exercises for the intrinsic muscles of the foot, and therapeutic ultrasound[42,75,76] (3 MHz, 1.5 W/cm^2, 20% duty cycle for 5min to the most tender region of the proximal portion of the plantar fascia).

Therefore, both groups received an impairment-based manual therapy approach directed primarily to the foot/ankle, but also to the hip and knee, including but not limited to passive anterior to posterior talocrural joint mobilizations in weight-bearing and non-weight-bearing positions and/or distraction thrust talocrural joint manipulation to improve ankle dorsiflexion, subtalar joint lateral glide mobilizations for eversion and inversion, and anterior and posterior first tarsometatarsal joint glide mobilizations for pronation and supination of the midfoot.

While not required, clinicians were permitted to apply ice to the plantar fascia over its proximal insertion in the region of the medial calcaneal tubercle for a period of 10min at the completion of the treatment session.[42] The exercise program was taught to the patient by an experienced physiotherapist on the first treatment session and supervised on subsequent sessions. Strengthening and stretching exercises were gradually progressed according to tolerance of each individual patient. That is, progression only occurred if patients reported a decrease in symptoms associated with PF and in the absence of excessive soreness, defined as soreness lasting longer than a few hours post-treatment. Notably, the findings of a recent systematic review suggest that manual therapy (i.e. joint mobilization and/or manipulation, soft tissue mobilization, stretching, trigger point pressure release) may be effective in treating people with PF; however, the dosing (i.e. frequency, intensity, duration) of manual therapy remains unclear.[71] Further, no clear conclusions can be drawn regarding the most effective stretch position, duration, frequency or optimum number of repetitions; however, plantar fascia stretching may be more effective than tendo Achilles stretching in the short term.[72]

All patients in both groups were instructed to complete a home exercise program during the 4-week treatment period. The home exercise program consisted of the same strengtheing and stretching exercises that were prescribed and supervised in the clinic, but without the supervision. Patients were told to complete the home exercise program 3 times daily on the days that they did not receive supervised physical therapy in the clinic.[42,66,235] Patients were asked to monitor their compliance with the home exercise program by maintaining a home exercise program logbook.

In addition to manual therapy, exercise and ultrasound, patients allocated to the dry needling group also recieved up to 8 sessions of electrical dry needling at a frequency of 1-2 times/week for 4weeks using a standardized protocol of 8 points for 20min.[112,229,235,237,241] Electrical dry needling included an 8-point standardized protocol as depicted in **Figure 2**.

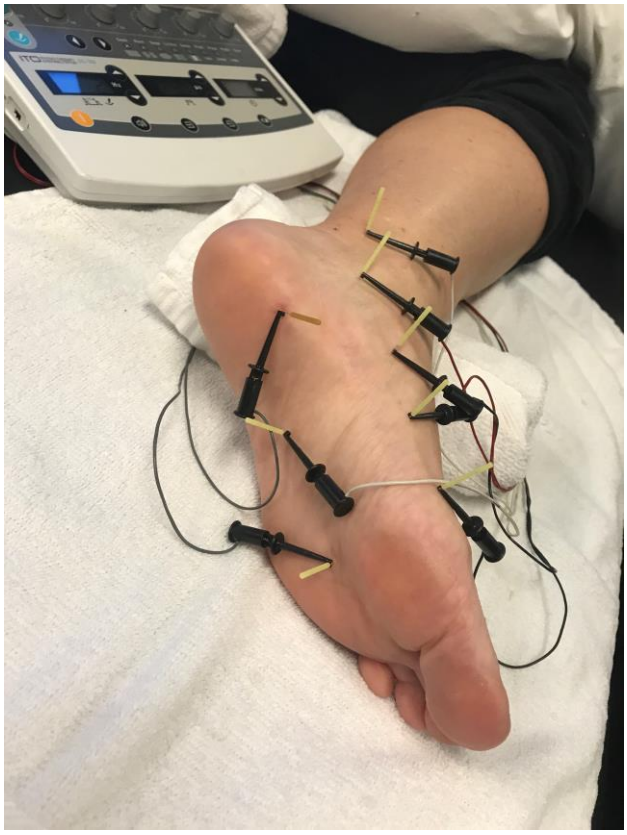


Figure 2: Standardized 8-point protocol of electrical dry needling for PF

Description of 8-point electrical dry needling intervention for PF

The technique is performed with the patient in prone or side lying. The plantar and medial surface of the foot and ankle were cleaned with alcohol. The following 8 needles were inserted:

(1) superoposterior and slightly lateral insertion angle toward the proximal attachment of the plantar fascia at the medial tubercle of the calcaneus. PF has been categorized as an enthesopathy, with the enthesis being the interface between the periosteum and ligament (plantar aponeurosis) or tendon (flexor digitorum brevis); thus, the primary target for dry needling was the insertion of the plantar fascia at or near the medial tubercle of the calcaneus. Therefore, “periosteal stimulation” or “periosteal pecking” at or near the proximal attachment of the plantar fascia at the medial tubercle of the calcaneus, was performed for 30sec over the most painful tender point at the medial calcaneal tubercle;

(2) medial to lateral perpendicular insertion within the distal abductor hallucis, immediately plantar and proximal to the head of the first metatarsal, common myofascial trigger point location and perineural for the medial plantar nerve;

(3) medial to lateral perpendicular insertion within the abductor hallucis, immediately plantar and distal to the base of the first metatarsal, common myofascial trigger point location and perineural for the medial plantar nerve;

(4) medial to lateral perpendicular insertion, immediately inferior to the sustentaculum tali (approximately two fingerbreadths inferior to the inferior apex of the medial malleolus), near the bifurcation point of the tibial nerve and posterior tibial artery;

(5) medial to lateral perpendicular insertion in the depression midway between the prominence of the medial malleolus and the Achilles tendon, perineural point for the tibial nerve at the ankle;

(6) plantar to dorsal perpendicular insertion in the mid belly of flexor digitorum brevis and quadratus plantae muscles, two to three fingerbreadths distal to the anterior and plantar border of the calcaneus, common myofascial trigger point within the flexor digitorum brevis and perineural stimulation for the lateral plantar nerve;

(7) plantar to dorsal perpendicular insertion within the distal plantar aponeurosis near its attachment at the metatarsophalangeal plates, within the depression on sole of the foot one third of the distance from the tip of the second toe to the posterior calcaneus;

(8) medial to lateral perpendicular insertion within the abductor hallucis, within the depression immediately plantar to the navicular tuberosity, common myofascial trigger point and perineural for the medial plantar nerve.

Notably, PF has been categorized as an enthesopathy, with the enthesis being the interface between the periosteum and ligament (plantar aponeurosis) or tendon (flexor digitorum brevis);[44,55,56] thus, the primary target for dry needling was the insertion of the plantar fascia at or near the medial tubercle of the calcaneus bone.[47,234-236] Therefore, "periosteal stimulation" or "periosteal pecking" at or near the proximal attachment of the plantar fascia at the medial tubercle of the calcaneus,[244,245] was performed for 30 seconds over the most painful tender point at the medial calcaneal tubercle.[47,246,247] In addition to the obligatory 8-point standardized protocol, clinicians were also permitted to insert needles at up to 4 additional locations in the foot and/or lower leg based on the presence of trigger points or presence sensitivity by the patient. Notably, the medial head of the gastrocnemius was recommended as one of the four optional needle insertion sites.[112,234]

Sterilized disposable stainless-steel acupuncture needles were used (Seirin®, City, State) with three sizes: 0.18 mm x 15 mm, 0.25 mm x 30 mm, 0.30 mm x 40 mm. The plantar and medial surface of the foot and ankle were cleaned with alcohol. The depth of needle insertion ranged from 10mm to 35mm and depended on the point selected (intra-muscular, periosteal, perineural) and the patient's constitution (i.e. size and bone depth, muscle and/or connective tissue thickness). Following insertion, needles were manipulated bi-directionally to ellicit a sensation of aching, tingling, deep pressure, heaviness or warmth.[112,241,249,250] The needles were then left in situ for 20 mins[112,235-237] with electric stimulation (ES-160 electrostimulator ITO co.) in pairs to all 8 of the obligatory needles using a low frequency (2 Hz), moderate pulse duration (250 microseconds), biphasic continuous waveform at an intensity described by the patient as "mild to moderate".[235,237] In cases of bilateral PF, both feet were treated, but only the most painful side at baseline was recorded and analyzed through-out the study to satisfy the assumpton of independent data.[45,255]

Outcome Measures

As a modification of the trial registration, we considered just one primary outcome. Among all outcomes included in the clinical trial registry, the primary outcome of the current trial was first-step pain[45,48,49,75,237,272] during the morning as measured by the Numeric Pain Rating Scale (NPRS). Patients were asked to indicate the average intensity of first-step pain when getting out of bed in the morning over the past week using an 11-point scale ranging from 0 ("no pain") to 10 ("worst pain imaginable") at baseline, 1 week, 4 weeks, and 3 months following the initial treatment session.[262]

The NPRS is a reliable and valid instrument to assess pain intensity.[263-265] The MCID for the NPRS has been shown to be 1.74 in patients with a variety of chronic pain conditions;[265] thus, a change of 2 points or a 30% decrease in pain from baseline can be considered as a MCID in individuals with chronic musculoskeletal pain.[265,266] Furthermore, the MCID in individuals with PF for the VAS (0-100 mm) has been found to be 19 mm for first-step pain and 8 mm for average pain.[243] When compared with the VAS, the NPRS has higher compliance rate, responsiveness and ease of use, and less practical difficulties;[273,274] thus, for these reasons we used the NPRS and chose to only include patients with a score of 2 points or greater for first-step pain.[45]

Secondary outcomes included resting mean foot pain (NPRS), pain during activity (NPRS), the Lower Extremity Functional Scale (LEFS), the Foot Functional Index (FFI), medication intake, and the Global Rating of Change (GROC) and were each collected at baseline, 1 weeks, 4 weeks and 3 months after the initial treatment. The Lower Extremity Functional Scale (LEFS) is a commonly used outcome measure in patients with PF[42,49,58] and has been found to have excellent validity, test-retest reliability, and responsvieness to change in patients with lower extremity disorders.[275-277] The LEFS consists of 20 questions involving everyday functional activities each worth 0-4 points; therefore, the range for the LEFS is 0-80 points, with higher scores indicating greater levels of function.[276] The MCID for the LEFS has been reported to be 9 points.[276]

The FFI was developed to measure the impact of foot pathology on pain, disability and activity limitation.[278] The FFI is the most widely used foot-specific self-reporting measure[279] and is a commonly used outcome measure in patients with PF.[58,80,235] The FFI has been shown to be valid, reliable and sensitive to change in various populations with a variety of foot and ankle disorders.[279,280] Subscale scores range from 0% to 100%, with

higher scores indicating lower levels of function and poorer foot health-related quality of life.[278] The FFI Total Score is derived by calculating the mean of the 3 subscale scores.[278] In patients with PF, the MCID (on a 0 to 100 scale) has been reported to be 12.3%, 6.7% and 6.5% for the Pain Subscale, Disability Subscale, and Total Score, respectively.[281] Notably, the MCID for the FFI Activity Limitation Subscale was reported to be 0.5%, indicating that for PF, interpretation of this subscale alone is likely inappropriate.[281]

Medication intake was measured as the number of times the patient had taken prescription or over-the-counter analgesic or anti-inflammatory medication in the past week for their heel pain, with five options: (1) not at all, (2) once a week, (3) once every couple of days, (4) once or twice a day, or (5) three or more times a day. Medication intake was assessed at baseline and at 3 months after the first treatment session.

In addition, 1 week, 4 weeks and 3 months following the intial treatment session, patients completed a 15-point GROC question based on a scale described by Jaeschke et al.[267] The scale ranges from -7 (a very great deal worse) to zero (about the same) to +7 (a very great deal better). Intermittent descriptors of worsening or improving are assigned values from -1 to -6 and +1 to +6, respectively. The MCID for the GRC has not been specifically reported but scores of +4 and +5 have typically been indicative of moderate changes in patient status.[267] The GROC may not correlate with changes in function in populations with hip and ankle injuries;[282] nevertheless, it has been used in a number of PF studies.[42,283,284]

Treatment Side Effects

Patients were asked to report adverse events that they experienced during any part of the study. In the current study, an adverse event was defined as a sequelae of one-week duration with any symptom perceived as distressing and unacceptable to the patient that required further treatment.[268] Particular attention was given to the presence of ecchymosis and post-needling soreness within the group receiving electrical dry needling.

Sample Size Determination

The sample size calculations were based on detecting treatment differences of 2 points on the main outcome (MCID for NPRS on first-step pain), assuming a standard deviation of 3 points, a 2-tailed test, an alpha level (α) of 0.05 and a desired power (β) of 90%. The estimated desired sample size was calculated to be at least 49 subjects per group. A dropout percentage of 10% was expected, so 53 patients were included in each group.

Statistical Analysis

Statistical analysis was performed using SPSS software, version 24.0 (Chicago, IL, USA) and it was conducted according to intention-to-treat analysis for patients in the group to which they were first allocated. Mean, standard deviations and/or 95% confidence intervals were calculated for each quantitative variable. The Kolmogorov-Smirnov test revealed a normal distribution of the variables ($P>0.05$). Baseline demographic and clinical variables were compared between both groups using independent Student t-tests for continuous data and $\chi 2$ tests of independence for categorical data.

The effects of treatment on first-step pain intensity, resting foot pain, pain during activity, physical function, and related-disability were each examined with a 2-by-4 mixed model analyses of covariance (ANCOVA) with treatment group (manual therapy, exercise and ultrasound versus manual therapy, exercise and ultrasound plus electrical dry needling) as the between-subjects factor, time (baseline, 1 week, 4 weeks and 3 months follow-up) as the within-subjects factor, and adjusted for baseline data for evaluating between-groups differences in the outcomes. Separate ANCOVAs were performed with first-step pain intensity (NPRS), mean heel pain at rest (NPRS), pain during activity (NPRS), the Lower Extremity Functional Scale (LEFS), the FFI Total Score, the FFI Pain Subscale, the FFI Disability Subscale, and the FFI Activity Limitation Subscale as the dependent variable. For each ANCOVA, the main hypothesis of interest was the 2-way interaction (group by time) with a Bonferroni-corrected alpha of 0.0125 (4 time points). We used $\chi 2$ tests to compare self-perceived improvement with GROC and changes in medication intake. To enable comparison of between-group effect sizes, standardized mean score differences (SMDs) were calculated by dividing mean score differences between groups by the pooled standard deviation. Numbers needed to treat (NNT) and 95% confidence intervals (CI) were also calculated at the 3-months follow-up period using each definition for a successful outcome.

Results

Study 1 - Knee OA

Participants

Between February 2015 and February 2017, 431 consecutive individuals with knee pain were screened for eligibility criteria. Two hundred forty-two (56.15%) satisfied all the inclusion criteria, agreed to participate, and were randomly allocated into the manual therapy and exercise (n=121) or manual therapy and exercise plus electrical dry needling (n=121) group. Randomization resulted in similar baseline characteristics for all variables (**Table 1**).

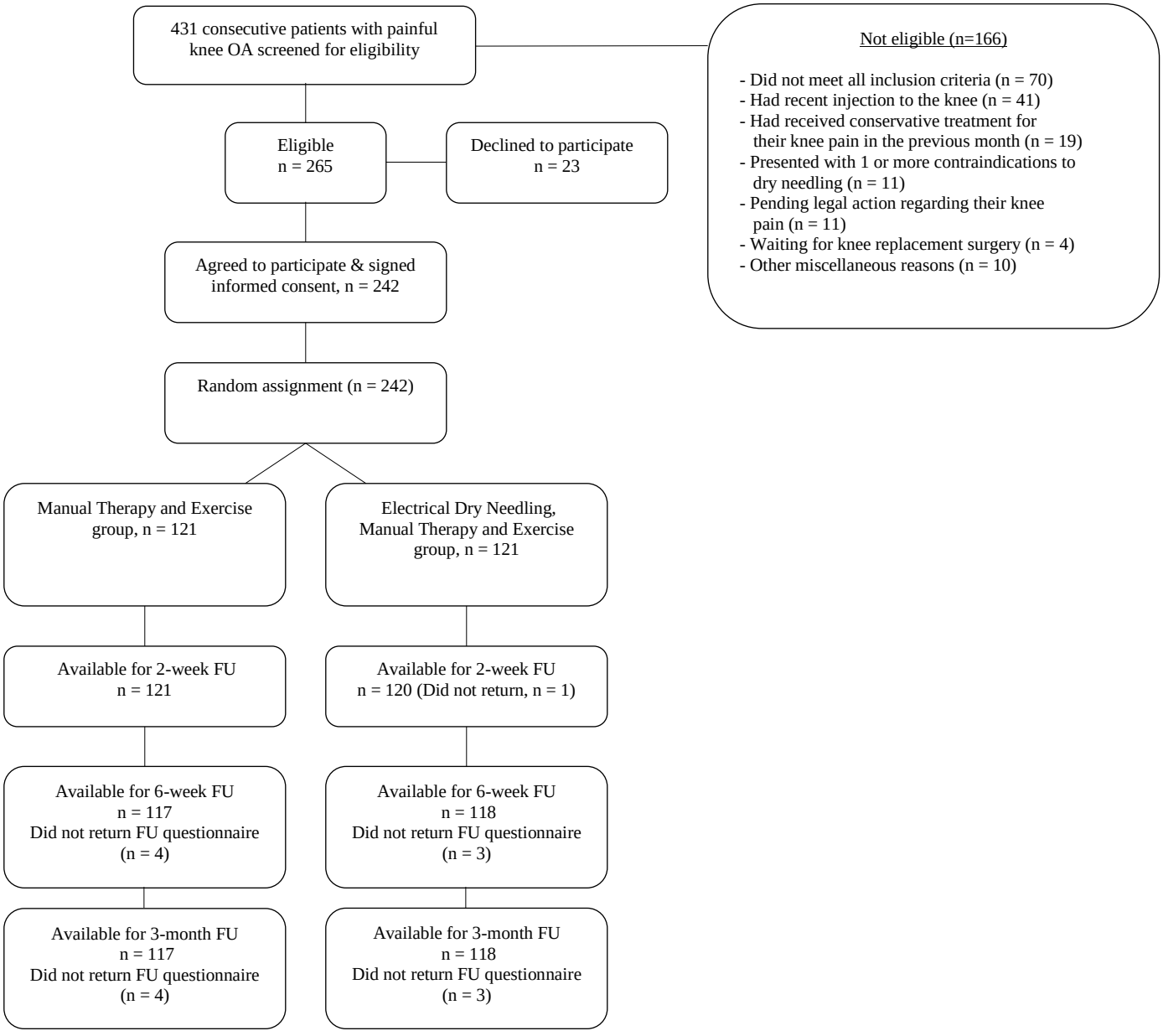
Table 1: Baseline characteristics by treatment assignment

Baseline Variable	Manual Therapy + Exercise (n=121)	Manual Therapy + Exercise + Electrical Dry Needling (n=121)
Gender (male/female)	55/56	56/55
Age (years)	58.1 ± 13.1	57.1 ± 13.2
Weight (kg)	83.8 ± 16.6	83.4 ± 15.6
Height (cm)	172.0 ± 8.9	172.1 ± 8.6
Years with knee pain	4.6 ± 5.1	4.5 ± 4.7
Medication intake n (%) **Not at all** **Once a week** **Once every couple of days** **Once or twice a day** **Three or more times a day**	 39 (32%) 13 (11%) 29 (24%) 37 (31%) 3 (2%)	 36 (30%) 13 (11%) 28 (23%) 40 (33%) 4 (3%)
Number of treatment sessions	8.9 ± 1.9	8.7 ± 1.8
Mean intensity of knee pain (NPRS, 0-10)	5.4 ± 1.8	5.7 ± 1.6
WOMAC Pain Scale (0-20) **WOMAC Stiffness Scale (0-8)** **WOMAC Physical Function Scale (0-68)** **WOMAC Total Score (0-96)**	8.0 ± 3.3 3.8 ± 1.4 28.1 ± 11.1 39.9 ± 14.6	8.7 ± 3.2 4.0 ± 1.6 28.9 ± 10.6 41.6 ± 14.3

Data are mean (SD) except for gender and medication intake. NPRS= Numeric Pain Rating Scale, 0-10, lower scores indicate less pain; WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index, 0-96, lower scores indicate less pain and related-disability.

The reasons for ineligibility are found in **Figure 3**, which provides a flow diagram of patient recruitment and retention.

Figure 3: Flow diagram of patient recruitment and retention**.**



There were no significant differences (P=0.468) between the number of completed treatment sessions for the manual therapy, exercise plus electrical dry needling group (mean: 8.7±1.8) and the manual therapy and exercise group (mean: 8.9±1.9). Two hundred thirty-five of the 242 patients completed all outcome measures through 3 months (97% follow-up). Of the 7 patients that dropped out or failed to complete outcome measures, 3 were from the electrical dry needling group and 4 were from the manual therapy and exercise group (see Figure 3).

Adverse Events

Eighty-seven patients assigned to the manual therapy and exercise plus electrical dry needling group (71.9%) experienced post-needling muscle soreness and 57 (47.1%) experienced mild bruising (ecchymosis) which most commonly resolved spontaneously within 48 hours and 2-4 days, respectively. In addition, 6 patients (4.9%) in the electrical dry needling group experienced drowsiness, headache or nausea, which spontaneously resolved within several hours. No other adverse events were reported.

Changes in WOMAC Index

Adjusting for baseline outcomes, the mixed-model ANCOVA revealed a significant Group*Time interaction for the primary outcome (WOMAC: F=35.504; P<0.001): patients with painful knee OA receiving electrical dry needling experienced significantly greater improvements in related-disability at 6 weeks (Δ -10.4, 95%CI: -13.7, -7.1, P<0.001) and 3 months (Δ -13.9, 95%CI: -17.4, -10.4, P<0.001) than those receiving manual therapy and exercise alone (**Figure 4**).

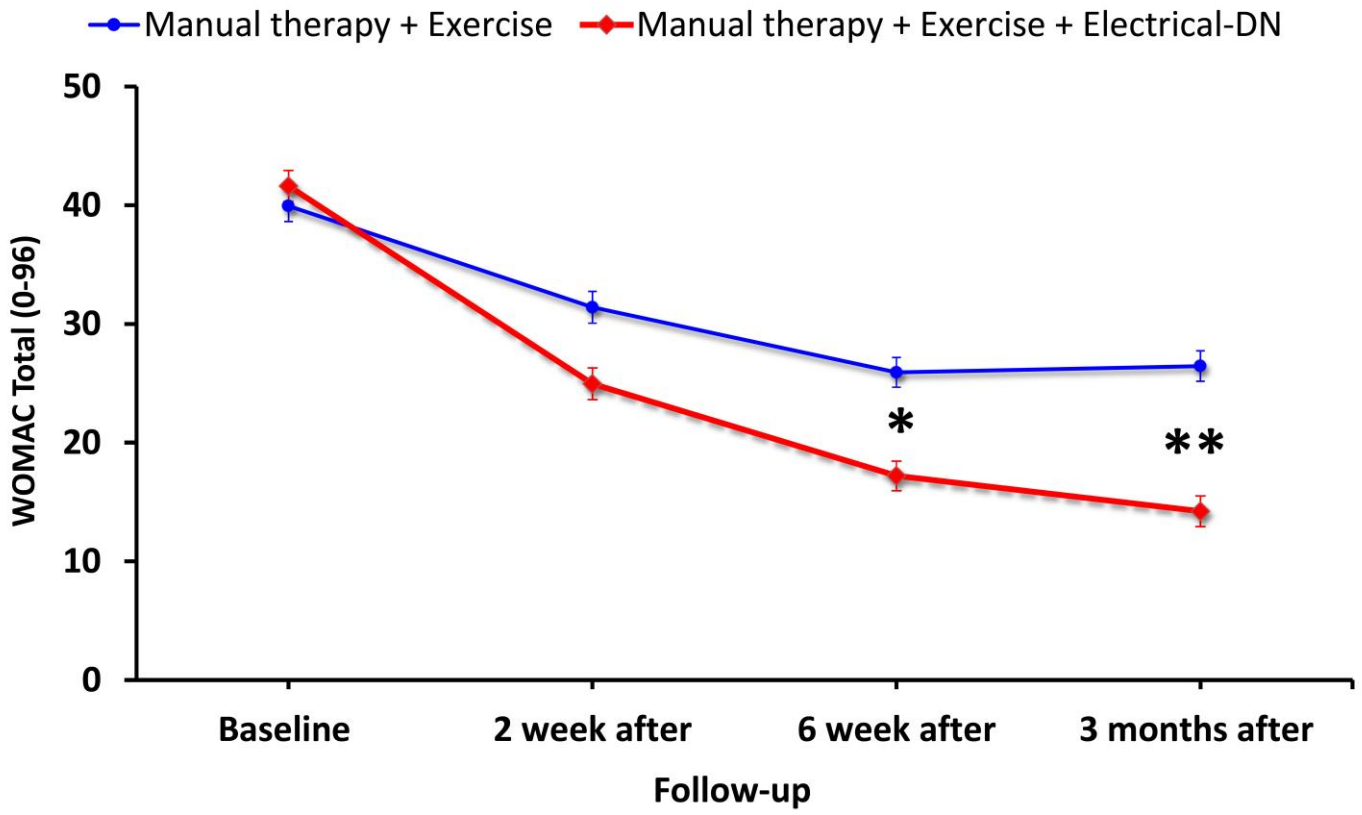


Figure 4: Evolution of the WOMAC throughout the course of the study stratified by randomized treatment assignment. Data are means (standard error).

Similarly, significant Group*Time interactions were also found for all WOMAC subscales (WOMAC-P: F=30.131, P<0.001; WOMAC-S: F=29.665, P<0.001; WOMAC-PF: F=30.114, P<0.001) in favor of the dry needling group (**Table 2**).

Table 2: Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index at baseline, 2-weeks, 6-weeks and 3-months after the first treatment sessions as well as within-group and between-groups mean scores by randomized treatment assignment

Outcomes	**Timeline Scores: Mean ± SD (95% CI) Within-Group Change Scores: Mean (95% CI)**		**Between-Group Differences: Mean (95% CI)**
	MT + EX (n=121)	**MT + EX + EDN (n=121)**	
WOMAC-P: Pain (0-20)			
Baseline	8.0 ± 3.3 (7.4, 8.6)	8.7 ± 3.2 (8.1, 9.3)	
2 weeks	6.1 ± 3.0 (5.6, 6.6)	5.4 ± 3.2 (4.8, 6.0)	
Change baseline → 2 weeks	-1.9 ± 2.5 (-1.5, -2.3)	-3.3 ± 2.6 (-2.8, -3.8)	- 1.4 (-2.1, -0.7)
6 weeks	4.8 ± 2.8 (4.3, 5.3)	3.4 ± 2.6 (2.9, 3.9)	
Change baseline → 6 weeks	-3.2 ± 3.1 (-3.8, -2.6)	-5.3 ± 3.0 (-5.9, -4.7)	-2.1 (-2.9, -1.3)
3 months	5.2 ± 3.2 (4.7, 5.7)	2.8 ± 2.5 (2.3, 3.3)	
Change baseline → 3 months	-2.8 ± 3.2 (-3.4, -2.2)	-5.9 ± 3.3 (-6.5, -5.3)	-3.1 (-3.9, -2.3)
WOMAC-S: Stiffness (0-8)			
Baseline	3.8 ± 1.4 (3.6, 4.0)	4.0 ± 1.6 (3.7, 4.3)	
2 weeks	3.0 ± 1.5 (2.7, 3.3)	2.5 ± 1.4 (2.2, 2.8)	
Change baseline → 2 weeks	-0.8 ± 1.4 (-1.1, -0.5)	-1.5 ± 1.3 (-1.8, -1.4)	-0.7 (-1.0, -0.4)
6 weeks	2.4 ± 1.5 (2.1, 2.7)	1.7 ± 1.4 (1.5, 1.9)	
Change baseline → 6 weeks	-1.4 ± 1.6 (-1.7, -1.1)	-2.3 ± 1.5 (-2.6, -2.0)	-0.7 (-1.0, -0.4)
3 months	2.4 ± 1.5 (2.2, 2.6)	1.3 ± 1.3 (1.1, 1.5)	
Change baseline → 3 months	-1.4 ± 1.6 (-1.8, -1.2)	-2.7 ± 1.5 (-3.0, -2.4)	-1.3 (-1.6, -0.9)
WOMAC-PF: Physical Function (0-68)			
Baseline	28.1 ± 11.1 (26.1, 30.1)	28.9 ± 10.6 (27.0, 30.8)	
2 weeks	22.3 ± 11.6 (20.3, 24.3)	17.1 ± 10.6 (15.1, 19.1)	
Change baseline → 2 weeks	-5.8 ± 8.7 (-7.0, -4.6)	-11.8 ± 9.6 (-13.6, -10.0)	-6.0 (-8.4, -3.6)
6 weeks	18.7 ± 10.9 (16.8, 20.6)	12.1 ± 9.8 (10.2, 14.0)	
Change baseline → 6 weeks	-9.4 ± 9.0 (-11.0, -7.8)	-16.8 ± 10.2 (-18.7, -14.9)	-7.4 (-9.9, -4.9)
3 months	18.7 ± 11.7 (16.8, 20.6)	10.1 ± 9.3 (8.2, 12.0)	
Change baseline → 3 months	-9.4 ± 9.8 (-11.1, -7.7)	-18.8 ± 10.6 (-20.7, -16.9)	-9.4 (-12.0, -6.8)
WOMAC: Total Index (0-96)			
Baseline	39.9 ± 14.6 (37.4, 42.4)	41.6 ± 14.3 (39.0, 44.2)	
2 weeks	31.4 ± 15.1 (28.8, 34.0)	25.0 ± 14.3 (22.3, 27.7)	
Change baseline → 2 weeks	-8.5 ± 11.0 (-10.5, -6.5)	-16.6 ± 12.3 (-18.9, -14.3)	-8.1 (-11.1, -5.1)
6 weeks	25.9 ± 14.3 (23.5, 28.3)	17.2 ± 13.1 (14.7, 19.7)	
Change baseline → 6 weeks	-14.0 ± 12.4 (-16.2, -11.8)	-24.4 ± 13.4 (-26.9, -21.9)	-10.4 (-13.7, -7.1)
3 months	26.4 ± 15.6 (23.9, 28.9)	14.2 ± 12.5 (11.7, 16.7)	
Change baseline → 3 months	-13.5 ± 13.3 (-15.9, -11.1)	-27.4 ± 14.1 (-29.9, -24.9)	-13.9 (-17.4, -10.4)

For the WOMAC total score and all its subscales, between-groups effect sizes were moderate (0.53<SMD<0.76) at 6-weeks and large (0.82<SMD<0.94) at 3-months after the first treatment session in favor of the electrical dry needling group (**Table 3**). Within-group percentage change from baseline to 3 months for the primary outcome (WOMAC) was 67.0% and 32.9% for the electrical dry needling group and non-dry needling group, respectively.

Table 3: Between-group effect sizes (SMD) in favor of the dry needling group when compared to the combination manual therapy and exercise

Outcome	WOMAC Total	WOMAC Pain	WOMAC Stiffness	WOMAC Function	NPRS Pain
6 weeks	0.76	0.67	0.53	0.74	0.60
3 months	0.94	0.90	0.82	0.87	0.96

Large between-group effect size: Cohen's *d* = .8 or greater. Medium effect size: Cohen's *d* = .5 or greater. Small size: Cohen's *d* = .2 or greater. Effect size provides information about the magnitude or strength of the difference between the two groups.

Changes in Pain Intensity

The intention-to-treat analysis also revealed a significant Group*Time interaction for knee pain (NPRS) intensity (F=29.094; P<0.001): individuals receiving electrical dry needling experienced significantly greater decrease in knee pain at 6 weeks (Δ -1.2, 95%CI: -1.7, -0.7, P<0.001) and 3 months (Δ -2.7, 95%CI: -3.4, -2.0, P<0.001) than those receiving manual therapy and exercise alone (**Figure 5**).

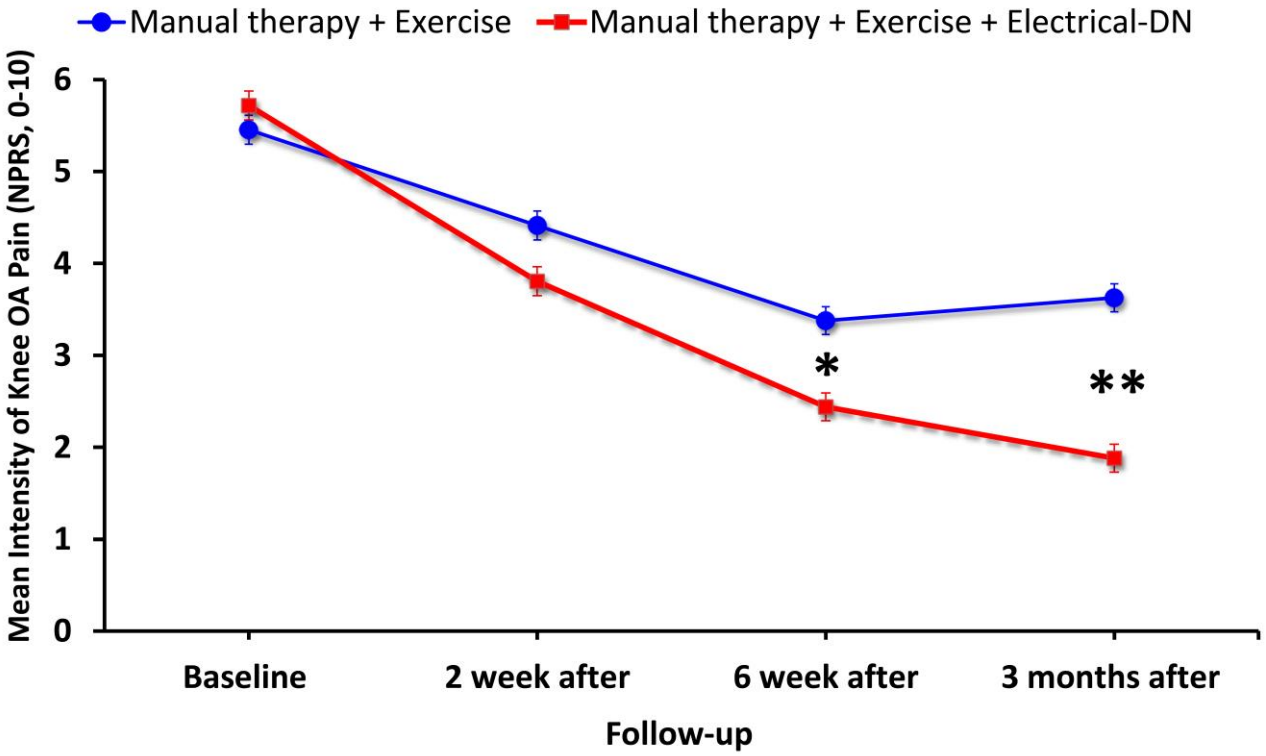


Figure 5: Evolution of knee pain intensity (NPRS, 0-10) throughout the course of the study stratified by randomized treatment assignment. Data are means (standard error).

For knee pain intensity (NPRS), between-groups effect sizes were moderate (SMD: 0.60) at 6 weeks and large (SMD: 0.96) at 3 months in favor of the dry needling group (see table 3). Within-group percentage change from baseline to 3 months for knee pain intensity (NPRS) was 67.2% and 28.9% for the electrical dry needling group and non-dry needling group, respectively.

Changes in Medication Intake

Patients with knee OA receiving electrical dry needling were 1.7 times more likely to have completely stopped taking medication for their pain at 3 months than individuals receiving manual therapy and exercise alone (OR: 1.6, 95%CI: 1.24, 2.01; P=0.001).

Self-perceived Improvement

Based on the cutoff score of ≥+5 on the GROC, significantly (X^2=14.887; P<0.001) more patients (n= 91, 75%) in the electrical dry needling group achieved a successful outcome compared to the non-dry needling group (n=23, 19%) at 3 months (**Table 4**).

Therefore, based on the cutoff score of ≥+5 on the GROC, the NNT was 1.78 (95% CI: 1.50, 2.18) in favor of the electrical dry needling group at 3-month follow-up. Likewise, based on the cutoff score of 36% improvement (i.e. triple the MCID) on the WOMAC, the NNT was 2.37 (95% CI: 1.89, 3.19) in favor of the electrical dry needling group at 3-month follow-up.

Table 4: Self-perceived improvement with Global Rating of Change (GROC) in both groups [n (%)]

Global Rating of Change (GROC, -7 to +7)	Manual Therapy + Exercise (n=121)	Manual Therapy + Exercise + Electrical Dry Needling (n=121)
2 weeks after first treatment session		
Moderate changes (+4 / +5)	18 (14.9%)	49 (40.5%)
Large changes (+6 / +7)	2 (1.7%)	11 (9.1%)
6 weeks after first treatment session		
Moderate changes (+4 / +5)	39 (32.2%)	59 (48.8%)
Large changes (+6 / +7)	8 (6.6%)	36 (29.8%)
3 months after first treatment session		
Moderate changes (+4 / +5)	27 (22.3%)	45 (37.2%)
Large changes (+6 / +7)	10 (8.3%)	57 (47.1%)

Study 2 - Plantar Fasciitis

Participants

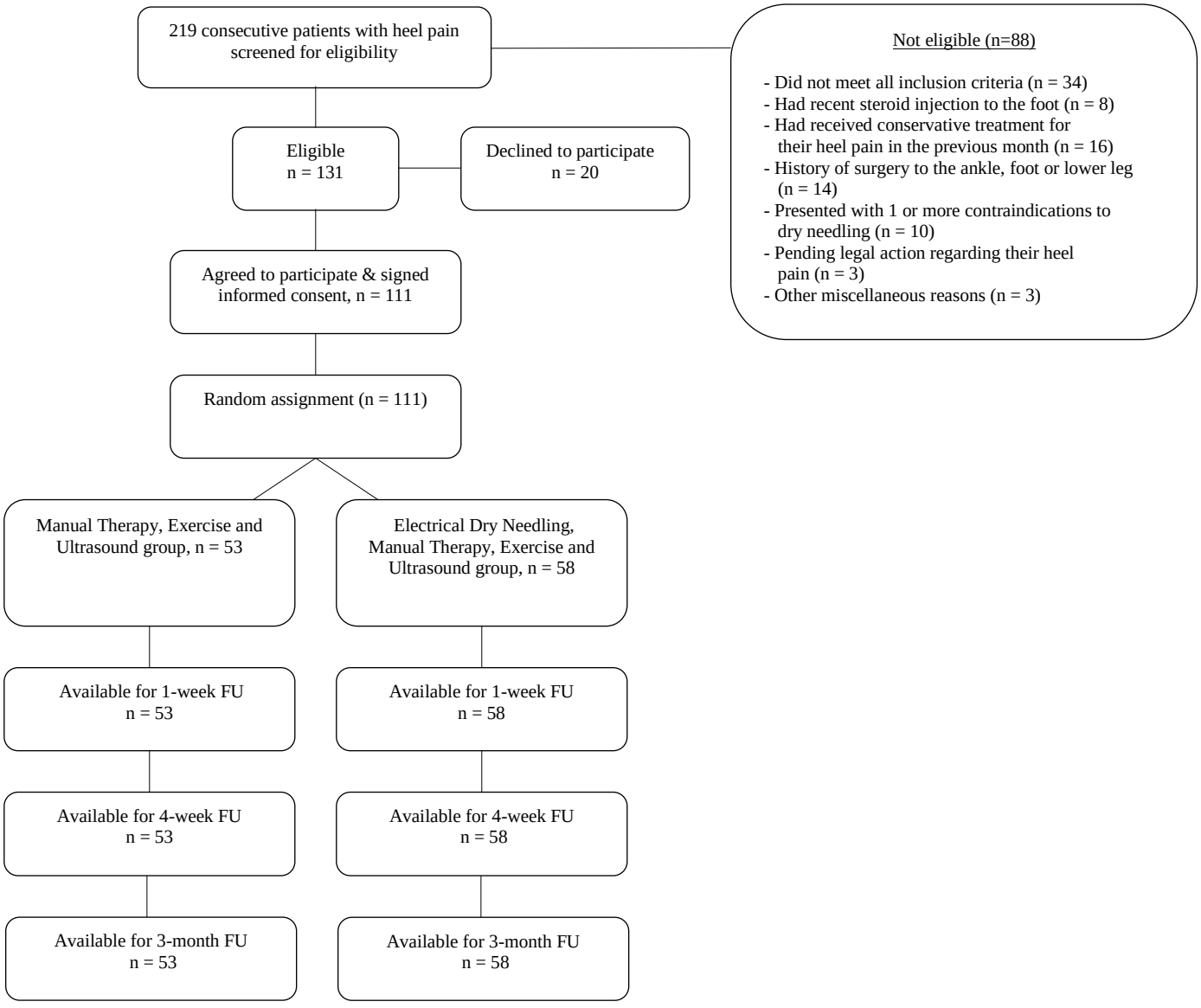
Between February 2015 and February 2017, 219 consecutive patients with PF were screened for eligibility criteria. One hundred eleven (50.7%) satisfied all the inclusion criteria, agreed to participate, and were randomly allocated into the manual therapy, exercise and ultrasound (n=53) or manual therapy, exercise, ultrasound plus electrical dry needling (n=58) group. Randomization resulted in similar baseline features (**Table 5**).

Table 5: Baseline characteristics by treatment assignment

Baseline Variable	Manual Therapy + Exercise + Ultrasound (n=53)	Manual Therapy + Exercise + Ultrasound + Electrical Dry Needling (n=58)
Gender (male/female)	27 / 26	37 / 21
Age (years)	42.6 ± 11.6	39.1 ± 10.4
Weight (kg)	81.6 ± 16.3	81.9 ± 14.3
Height (cm)	172.0 ± 9.1	173.4 ± 9.2
Duration of symptoms (days)	336.4 ± 288.8	386.1 ± 451.1
Medication intake n (%) **Not at all** **Once a week** **Once every couple of days** **Once or twice a day** **Three or more times a day**	 28 (52.8%) 2 (3.8%) 15 (28.3%) 8 (15.1%) 0 (0%)	 26 (44.8%) 5 (8.5%) 18 (31%) 7 (12.2%) 2 (3.5%)
Number of treatment sessions	6.2 ± 2.4	5.9 ± 2.5
Mean intensity of heel pain (NPRS, 0-10)	6.1 ± 1.6	5.8 ± 1.8
First step pain intensity (NPRS, 0-10)	6.4 ± 1.8	6.3 ± 2.0
Pain intensity during activity (NPRS, 0-10)	5.8 ± 2.1	5.5 ± 2.1
LEFS (0-80)	48.9 ± 13.1	50.4 ± 12.8
FFI Pain Scale (0-100) **FFI Disability Scale (0-100)** **FFI Activity Limitation Scale (0-100)** **FFI Total Score (0-100)**	59.3 ± 16.2 50.7 ± 18.4 16.3 ± 12.2 42.1 ± 12.7	57.8 ± 19.8 44.9 ± 24.3 15.1 ± 12.6 39.3 ± 16.9

The reasons for ineligibility are found in **Figure 6**, which provides a flow diagram of patient recruitment and retention.

Figure 6: Flow diagram of patient recruitment and retention



No patients were lost at any of the follow-up periods in either group. None of the participants in any group reported receiving other interventions during the study, excluding the use of NSAIDs, as needed and recorded. There was no significant difference (P=0.432) between the mean number of completed treatment sessions for the manual therapy, exercise and ultrasound group (mean: 6.25) and the manual therapy, exercise and ultrasound plus electrical dry needling group (mean: 5.88). One hundred three patients (92.8%) reported compliance with the home exercise program.

Adverse Events

Thirty-nine patients assigned to the manual therapy, exercise and ultrasound plus electrical dry needling group (67.2%) experienced post-needling muscle soreness and 15 (25.9%) experienced mild bruising (ecchymosis) which most commonly resolved spontaneously within 48 hours and 2-4 days, respectively. In addition, 1 patient (1.7%) in the electrical dry needling group experienced drowsiness, headache or nausea, which spontaneously resolved within several hours. No other adverse events were reported.

Changes in Pain Intensity and Relaed-Disability

Adjusting for baseline outcomes, the mixed-model ANCOVA revealed a significant Group*Time interaction for the primary outcome (F=22.021; P<0.001): patients with PF receiving electrical dry needling experienced significantly greater improvements in first-step morning pain at 4 weeks (Δ -1.6, 95%CI -2.4 to -0.8, P<0.01) and 3 months (Δ -2.2, 95%CI -3.0 to -1.6, P<0.001) than those receiving manual therapy, exercise and ultrasound alone (**Figure 7**).

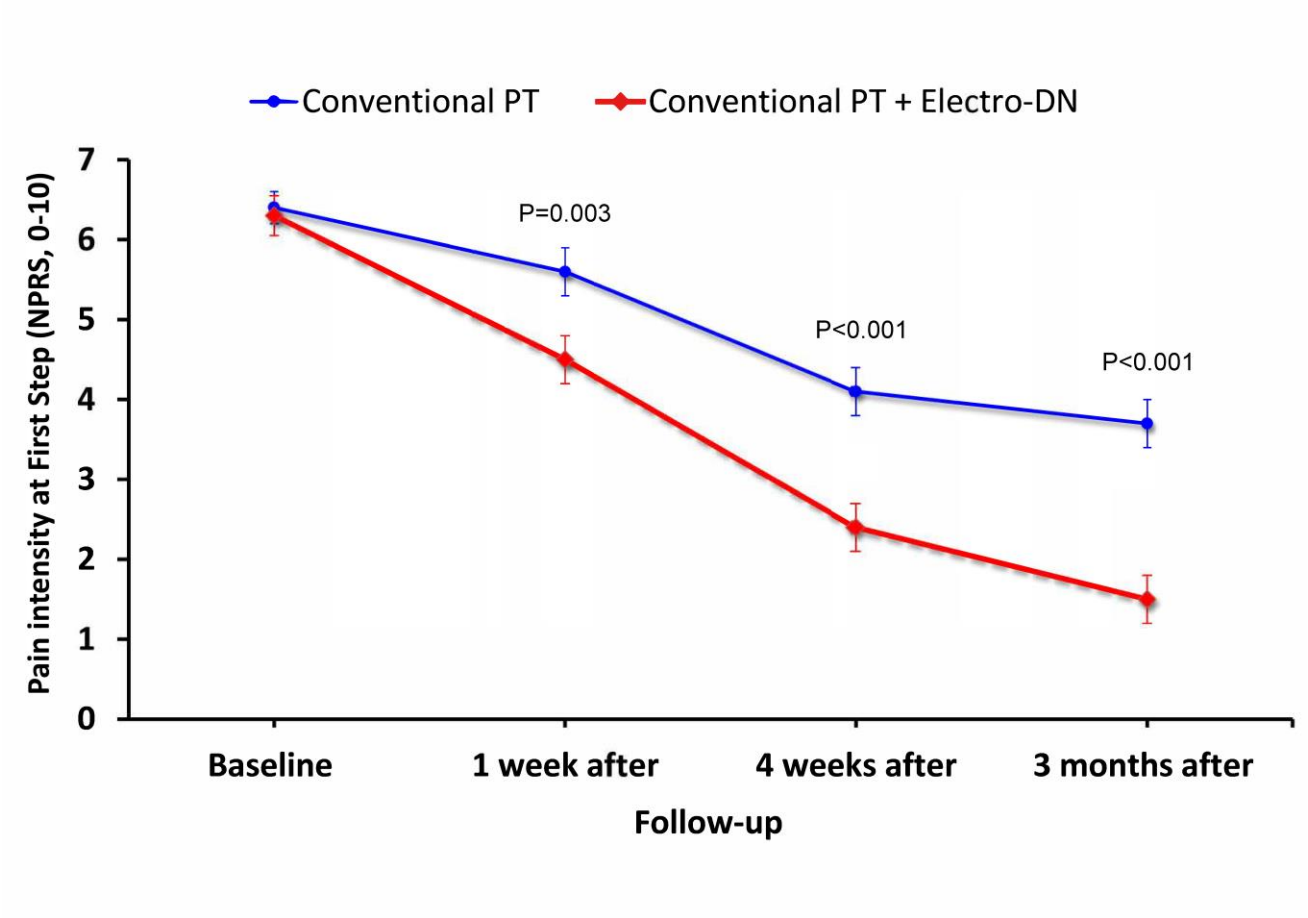


Figure 7: Evolution of first step pain intensity (NPRS) throughout the course of the study stratified by randomised treatment assignment. Data are means (standard error).

Between-groups effect sizes were medium (SMD: 0.68) at 4 weeks and large (SMD: 0.85) at 3 months after the first treatment session in favor of the dry needling group.

Similarly, significant Group*Time interactions were also found for resting foot pain ($F=23.931$; $P<0.001$), pain during activity ($F=7.629$; $P=0.007$), LEFS ($F=13.081$; $P<0.001$; **Figure 8**), FFI Pain Subscale ($F=13.547$; $P<0.001$), FFI Disability Subscale ($F=8.746$; $P=0.004$), and FFI Total Score ($F=10.676$; $P<0.001$), but not for FFI Activity Limitation Subscale ($F=2.687$; $P=0.104$), in favor of dry needling (**Table 6**).

For the LEFS, FFI Total and all significant FFI Subscales, between-groups effect sizes were small to medium ($0.32<SMD<0.55$) at 4 weeks and medium ($0.53<SMD<0.66$) at 3 months after the first treatment session in favor of the dry needling group (**Table 7**).

Table 6: Foot Functional Index (FFI) within-group and between-groups mean scores by randomized treatment assignment

Outcomes	Timeline Scores: Mean ± SD (95% CI) Within-Group Change Scores: Mean (95% CI)		Between-Group Differences: Mean (95% CI)
	MT + EX + US (n=53)	MT + EX + US + EDN (n=58)	
Foot Functional Index - Pain Scale (0-100)			
Baseline	59.3 ± 16.2 (54.3, 64.3)	57.8 ± 19.8 (53.0, 62.6)	
1 week	51.5 ± 17.9 (45.9, 57.1)	48.7 ± 22.9 (43.3, 54.1)	
Change baseline → 1 week	-7.8 ± 15.0 (-11.9, -3.7)	-9.1 ± 14.6 (-12.9, 5.3)	-1.3 (-6.9, 4.3)
4 weeks	40.3 ± 21.6 (34.9, 45.7)	27.4 ± 18.6 (22.1, 32.7)	
Change baseline → 4 weeks	-19.0 ± 20.4 (-24.6, -13.4)	-30.4 ± 19.3 (-35.5, -25.3)	-11.4 (-18.8, -4.0)*
3 months	34.6 ± 22.2 (28.9, 40.3)	19.2 ± 20.1 (13.7, 24.7)	
Change baseline → 3 months	-24.7 ± 21.0 (-30.5, 18.9)	-38.6 ± 21.4 (-44.2, -33.0)	-13.9 (-21.8, - 6.0)*
Foot Functional Index - Disability Scale (0-100)			
Baseline	50.7 ± 18.4 (44.8, 56.6)	44.9 ± 24.3 (39.3, 50.5)	
1 week	41.3 ± 18.9 (35.2, 47.4)	37.6 ± 25.2 (31.8, 43.4)	
Change baseline → 1 week	-9.4 ± 16.3 (-13.9, -4.9)	-7.3 ± 14.7 (-11.2, -3.4)	2.2 (-3.6, 9.0)
4 weeks	30.9 ± 20.2 (25.9, 35.9)	18.4 ± 16.5 (13.6, 23.2)	
Change baseline → 4 weeks	-19.8 ± 19.0 (-25.0, -14.6)	-26.5 ± 22.0 (-32.3, -20.7)	-6.7 (-14.4, 1.0)
3 months	29.3 ± 21.0 (24.3, 34.3)	11.5 ± 15.6 (6.7, 16.3)	
Change baseline → 3 months	-21.4 ± 20.8 (-27.2, -15.6)	-33.4 ± 23.2 (-39.5, -27.3)	-12.0 (-20.3, -3.7)*
Foot Functional Index - Activity Limitation Scale (0-100)			
Baseline	16.3 ± 12.2 (12.9, 19.7)	15.1 ± 12.6 (11.9, 18.3)	
1 week	13.3 ± 11.4 (10.2, 16.4)	12.9 ± 11.2 (9.9, 15.9)	
Change baseline → 1 week	-3.0 ± 7.0 (-4.9, -1.1)	-2.2 ± 7.5 (-4.2, -0.2)	0.8 (-1.9, 3.5)
4 weeks	8.1 ± 7.6 (6.0, 10.2)	5.5 ± 7.9 (3.5, 7.5)	
Change baseline → 4 weeks	-8.2 ± 9.9 (-10.9, -5.5)	-9.6 ± 11.4 (-12.6, -6.6)	-1.4 (-5.5, 2.7)
3 months	8.5 ± 11.8 (6.1, 10.9)	3.7 ± 5.4 (1.3, 6.1)	
Change baseline → 3 months	-7.8 ± 12.8 (-11.3, -4.3)	-11.4 ± 11.9 (-14.6, -8.2)	-3.6 (-8.3, 1.1)
Foot Functional Index – Total Score (0-100)			
Baseline	42.1 ± 12.7 (38.0, 46.2)	39.3 ± 16.9 (35.3, 43.3)	
1 week	35.4 ± 13.5 (30.9, 39.9)	33.1 ± 18.6 (28.8, 37.4)	
Change baseline → 1 week	-6.7 ± 10.7 (-9.7, 3.7)	-6.2 ± 9.9 (-8.8, -3.6)	0.5 (-4.4, 3.4)
4 weeks	26.5 ± 14.6 (22.7, 30.3)	17.2 ± 12.8 (13.5, 20.9)	
Change baseline → 4 weeks	-15.6 ± 14.2 (-19.6, -11.6)	-22.1 ± 15.4 (-26.2, -18.0)	-6.5 (-12.1, -0.9)*
3 months	24.2 ± 16.3 (20.2, 28.2)	11.5 ± 12.9 (7.6, 15.4)	
Change baseline → 3 months	-17.9 ± 16.0 (-22.4, -13.4)	-27.8 ± 16.8 (-32.2, -23.4)	-9.9 (-16.0, -3.8)**

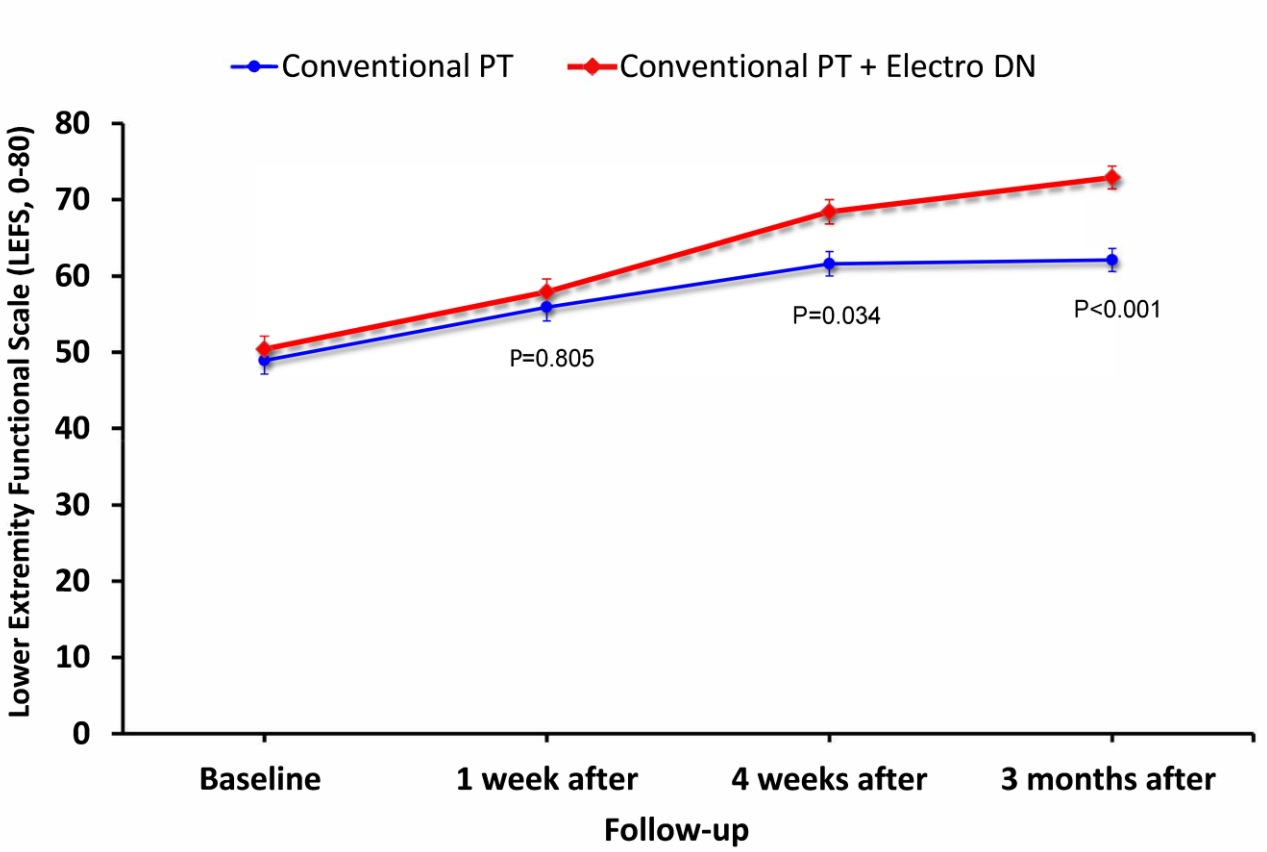


Figure 8: Evolution of lower extremity funtion (LEFS, 0-80) throughout the course of the study stratified by randomised treatment assignment. Data are means (standard error).

Table 7: Between-group effect sizes (SMD**)** in favor of the dry needling group when compared to conventional physical therapy

Outcome	1st Step Pain	LEFS	FFI Total	FFI Pain	FFI Disability	FFI Activity Limitation
4 weeks	0.68	0.40	0.43	0.55	0.32	0.13
3 months	0.85	0.66	0.58	0.62	0.53	0.30

Changes in Medication Intake

Participants with PF in the electrical dry needling group were 1.2 times more likely to have completely stopped taking medication for their pain at 3 months than patients receiving manual therapy, exercise and ultrasound (OR: 1.22; 95%CI: 1.02-1.51; P=0.01).

Self-perceived Improvement

Based on the cutoff score of +5 or higher on the GROC, significantly (X^2=14.887; P<0.001) more patients with PF in the electrical dry needling group (n=45, 77%) achieved a successful outcome compared to manual therapy, exercise and ultrasound group (n=11, 21%) at 3 months follow-up (**Table 8**). Therefore, based on the cutoff score of ≥+5 on the GROC at 3-month follow-up, the NNT was 1.76 (95%CI: 1.39, 2.41) in favor of the electrical dry needling group. Likewise, based on a 50% improvement from baseline to 3 months in first step morning pain on the NPRS, the NNT was 2.44 (95%CI: 1.75, 4.02) in favor of the electrical dry needling group.

Table 8: Self-perceived improvement with Global Rating of Change (GROC) in both groups [n (%)]

Global Rating of Change (GROC, -7 to +7)	**Manual Therapy + Exercise + Ultrasound (n=53)**	**Manual Therapy + Exercise + Ultrasound + Electrical Dry Needling (n=58)**
1 week after first treatment session		
Moderate changes (+4 / +5)	8 (15%) / 3 (5.5%)	5 (8.5%) / 4 (7%)
Large changes (+6 / +7)	1 (2.0%) / 0 (0%)	3 (5.5%) / 1 (1.5%)
4 weeks after first treatment session		
Moderate changes (+4 / +5)	7 (13.5%) / 5 (9.5%)	9 (15.5%) / 15 (26%)
Large changes (+6 / +7)	3 (5.5%) / 1 (2.0%)	15 (26%) / 5 (8.5%)
3 months after first treatment session		
Moderate changes (+4 / +5)	8 (15%) / 4 (7%)	6 (10.5%) / 13 (22.5%)
Large changes (+6 / +7)	6 (11.5%) / 1 (2.0%)	19 (32.5) / 13 (22.5%)

Discussion

Study 1 - Knee OA

Findings

To our knowledge, this is the first randomized clinical trial comparing compare the effectiveness of manual therapy and exercise plus electrical dry needling to manual therapy and exercise alone in patients with painful knee OA. The results suggest that a mean of 9 sessions of manual therapy and exercise plus electrical dry needling, using a 9-point standardized protocol targeting the knee locally at a frequency of 1-2 times per week over 6 weeks, resulted in greater improvements in pain, stiffness, function, related-disability, and medication intake than manual therapy and exercise alone[223]. For the primary outcome (WOMAC), between-groups effect sizes were moderate at 6 weeks and large at 3 months in favor of the dry needling group. The between-groups difference for change in related-disability, as measured by the WOMAC (34.1%, 95%CI: 26.6, 41.4) exceeded the reported MCID (i.e. 12%[259]) at 3 months. In addition, for knee pain intensity, the between-groups change (3.23 points, 95%CI: 2.4, 4.0) also exceeded the reported MCID (i.e., 1.74 points[265,266]) at 3 months. Finally, the NNT suggests for every 2 patients treated with electrical dry needling, rather than manual therapy and exercise alone, one additional patient with painful knee OA achieves clinically important reductions in related-disability at 3 months follow-up.

Three previous studies found non-superior results when adding acupuncture as an adjunct therapy to exercise-based physical therapy in knee OA.[110,135,285] Notably, Foster et al[110] reported no significant between-groups difference in WOMAC pain subscale scores after adding a course of acupuncture to exercise in knee OA. Nevertheless, in the Foster et al[110] trial, the acupuncture points were not standardized but selected based on the "clinical opinion" of 67 different physiotherapists at different centers.

Considering the recent findings regarding the influence of acupuncture on cartilage repair[224] and the efficacy of periosteal stimulation[251] in patients with knee OA, it is possible that the needles in the Foster et al (0.5 to 2.5cm[110]), Chen et al (0.2 to 3cm[285]) and Scharf et al (0.5 to 3.5cm[135]) trials were not inserted deep enough.

A meta-analysis concluded electroacupuncture is superior to manual acupuncture for improving pain and function in knee OA.[286] Eleven RCTs with 695 participants were included. The meta-analysis indicated that electroacupuncture was more effective than pharmacological treatment (RR=1.14; *P*=0.03) and manual acupuncture (RR=1.12; *P*=0.02) for pain reduction and functional improvement in patients with knee OA. Likewise, in a secondary analysis that pooled data from the Manheimer et al Cochrane review,[21] Langevin et al[287] concluded that electroacupuncture was superior to the use of manual acupuncture (pooled effect of 5 trials; n=1215; p=0.042).[287] Notably, this may be one reason why the Foster et al[110] and Chen et al[285] studies found unfavorable results when investigating the effects of acupuncture in knee OA.

Physiology of Electrical Dry Needling

According to Weiner et al, periosteal stimulation with needles inhibits peripheral pain processing, stimulates local vasodilation and alters vascular sympathetics.[251] More specifically, electroacupuncture has been shown to activate Aδ, C and Aβ pain fibers, facilitating diffuse noxious inhibitory control and gate control within the dorsal horn of the spine.[288-290] Electroacupuncture has also been shown to facilitate endogenous anandamide, increasing local opioid production while decreasing pro-inflammatory factors such as TNF-α, IL-4, IL-6, IL-8 and IL-10.[227,291]

In addition, electroacupuncture can also cause the release of substance-P and CGRG predominantly from non-neural structures, facilitating a negative feedback loop to neural and neuroactive components of the target tissue.[292,293] In the case of periosteal needling, this may lead to decreased inflammation of the densely innervated periosteum. Notably, CGRP in high quantities causes inflammation, but the concurrent release of substance-P combined with electric stimulation in the vicinity of the periosteum may provide sustained, low levels of CGRP required for an anti-inflammatory effect.[294-297] CGRP also initiates a cascade of events mediated by protein kinase A (PKA) in vascular smooth muscle, leading to vasodilation.[298] Moreover, PKA stimulates nitric oxide synthase, increasing the production of nitric oxide, thereby exaggerating the vasodilation effect.[298] The improved vasodilation enhances the microcirculation of degenerative joints, resulting in increased opioid delivery and decreased inflammatory factors in the synovia.[126,226]

Limited evidence suggests that acupuncture may stimulate an increase in hyaluronic acid, allowing the synovial fluid to better lubricate the joint.[299] Mechanical and electric needle stimulation at, or close to, the periosteum may be particularly advantageous in joint OA, as acupuncture has been shown to reduce IL-6 mRNA expression in bone marrow, limiting inflammation and inhibiting myelogenic osteoclast activity driving degeneration.[300]

At a cellular level, electroacupuncture has been found to stimulate immune cells, fibroblasts and keratinocytes to release CGRP and substance-P,[295] altering CGRP stimulation of TTX receptors to reverse hyperalgesia.[294] Furthermore, acupuncture encourages the supraoptic nucleus to release oxytocin to quiet ASIC receptors peripherally and stimulate opioid interneurons spinally.[301-303] Moreover, acupuncture facilitates mechanotransduction of fibroblasts and peripheral nerves via TRPV1[304] and P2X/Y-mediated intercellular Ca^{2+} wave propagation and subsequent activation of the nucleus

accumbens, and this inhibits spinal pain transmission via glycinergic and opioidergic interneurons.[305,306] The increased ATP is metabolized to adenosine, which activates P1 purinergic receptors, events considered key to acupuncture mediated analgesia and rho kinase-based tissue remodeling.[307]

Electroacupuncture to local points at the knee has been found to modulate knee joint microcirculation, significantly increase endogenous opioid levels, and significantly reduce plasma cortisol levels.[126,308] In addition, electroacupuncture has been found to block the local release of inflammatory cytokines (i.e. IL-1 β and TNF-α) in the synovia of osteoarthritic joints[226] and the systemic release of inflammatory factors in the periaqueductal gray of the brain stem.[227] Acupuncture may also stimulate an increase in hyaluronic acid, allowing the synovial fluid to better lubricate the joint.[299]

Mechanisms of Intra-articular Dry Needling

Given the physiologic mechanisms at play in periosteal needling, it is perhaps worth noting that the needle insertions at the medial and lateral eye of the knee, consistent with acupoints Xiyan and ST35, are widely considered the two most important points for knee OA.[309-311] Taechaarpornkul et al. found that electroacupuncture performed only at the medial and lateral eye of the knee resulted in equivalent therapeutic outcomes as a 6-point, local needling protocol.[309] While generally considered a precaution in the acupuncture profession to contact bone or enter the joint capsule with the needle at these locations, the angle and depth (25-30mm) of insertion described in most acupuncture textbooks[166] is consistent with the depth used by physicians to perform intra-articular joint injections.[312] Therefore, acupuncture at these locations are likely intra, or at a minimum, peri-articular.[313]

Moreover, needle insertions at the medial and lateral eye of the knee are at the joint line, facilitating stimulation of the periosteum of the articulating bones at the source of degeneration.[313] Needling at these locations also allows access to the anterior cutaneous branch of the femoral nerve, the recurrent articular nerve from the common peroneal nerve and the infrapatellar branch of the saphenous nerve along with the medial and lateral anastomosis, connecting the superior medial and lateral genicular arteries.[313,314] Interestingly, Liu et al. reported a quicker and more robust therapeutic effect after deep needling with electricity at Xiyan and ST35 compared to more traditional, superficial needling with electricity at the same locations.[311] Thus, needling at the medial and lateral eye of the knee area may be particularly advantageous because of their close anatomical relationship with peri-osteal, neural and vascular structures that support the knee and may help explain the robust short-term and long-term outcomes reported in the present study.

Mechanisms and Effects of Periosteal Dry Needling

The underlying mechanisms as to why the electrical dry needling group in the current study experienced greater improvements than the manual therapy and exercise group remains to be elucidated. However, appropriate needle depth may be an important component to consider when using dry needling therapies for knee joint OA. A number of studies have demonstrated that periosteal needling, i.e., getting the needle close to the bone, cartilage or joint line, or tapping the needle repeatedly on to the bone, leads to significant and clinically meaningful improvements in pain and disability in hip and knee OA.[251,315,316] Periosteal needling is a needle technique originally described by Felix Mann that targets the richly innervated periosteum of bone, typically with electric stimulation.[317] Zhang et al[224]

recently reported significantly lower T2 values on MRI at the anteromedial and antero-lateral tibial sub-regions of 100 knees following 20 minute sessions over 4 weeks of 7-point, low frequency electroacupuncture; that is, electroacupuncture appears to play a role in cartilage repair in individuals with knee OA.[224] Similarly, 10 sessions of periosteal electric stimulation (i.e. 4 acupuncture needles touching the bone of the tibiofemoral joint) with monthly "booster" sessions have been found in the medium and long term (9 months post treatment initiation) to significantly decrease WOMAC pain, stiffness and function scores in patients with severe (i.e. Kellgren-Lawrence grade 3 or 4) knee OA.[251]

A number of studies have attempted to delineate physiologic processes responsible for pain reduction following acupuncture. While needling muscle tissue with trigger points in an effort to elicit local twitch responses has been shown to reduce pain and inflammation in the short-term,[318,319] it has also been found to systemically reduce pain by activating opioid-based pain reduction[227,320-322] that is mediated by endogenous cannabinoids[291,323,324] and the sympathetic nervous system,[325,326] and to activate non-opioid pain relief via serotonin and norepinephrine pathways in the brain stem.[227,228,288,327] Further, acupuncture triggers the HPA-axis centrally[328] and the CRH-POMC-corticosteroid axis locally[329] to inhibit cox-2 and reduce inflammatory cytokines.

In the Cochrane review on acupuncture for knee OA, Manheimer et al[21] compared the effects of verum acupuncture with sham acupuncture, another active treatment, and waitlist list from 12 randomized controlled trials. Although the effect of verum acupuncture versus sham acupuncture was statistically significant in the short term and at 6 months, the benefits were considered clinically irrelevant.[21] Nevetheless, a subgroup analysis found the effects of verum acupuncture were clinically relevant when compared to several active

treatments and waitlist controls, and the authors suggest that patients with OA will find meaningful benefits from acupuncture.[21]

In addition, and according to the study by Vickers et al[4] that evaluated data from 17,922 individual patients with non-specific back/neck pain, OA, shoulder pain or chronic headache, acupuncture was found to be superior to sham acupuncture and no-acupuncture controls. Notably, Vickers et al[4] concluded that while there are specific effects of acupuncture beyond placebo, non-specific effects also exist. Furthermore, it should be noted that several of the largest trials in this study had a sham intervention arm that likely was active.[330] Therefore, according to the findings of multiple trials and systematic reviews, acupuncture demonstrates both effectiveness and efficacy for the treatment of pain.

Biochemical Changes Following Electrical Dry Needling

The physiological changes in OA have been well documented and are characterized by degeneration of articular cartilage with osteophyte formation and subchondral plate thickening.[4,5] Yet, the pathogenesis and temporal relationship of subchondral bone damage, chronic inflammation of synovial tissue, and cartilage erosion is largely unknown, and there are currently no curative treatments for OA.[10]

However, pro-inflammatory cytokines have been implicated as a major causal factor of cartilage destruction and the inflammatory cascade, particularly involving Interleukin (IL)-1β and tumor necrosis factor alpha (TNF-α), among others.[4,10]

Given that most occurrences of OA are mechanically based (i.e. “wear and tear” related), it is ironic that manual therapy and exercise are useful in relieving pain and disability.[223] Movement stimulates synthetic chondrocyte activity and internal tissue

remodeling, resulting in a reduction of proteoglycan synthesis and loss of cartilage.[331] As Burr et al reported, intramuscular stimulation of the quadriceps in immobilized rabbit knees resulted in a significant reduction of cartilage atrophy compared to controls.[332] However, therapeutic modalities that decrease the spatial summation of nociceptive input associated with low grade, C-fiber mediated chronic inflammation may also be useful in relieving pain. As Schaible suggested, reducing peripheral inflammation to stop and or reverse central mediated chronic changes may be key to effectively treating the pain associated with osteoarthritis.[333] In this regard, dry needling may be a powerful intervention for physical therapists to utilize in conjunction with exercise and manual therapy to additively treat OA conditions.

The mechanical stimulation from needling without injectate has been shown to cause the early release of substance P and CGRP from both neural and non-neural cells, which may contribute to peripheral sensitization and inflammation.[292,293] There are two primary theories for the early increase in substance P and CGRP following acupuncture (i.e. "needle puncture" or dry needling without injectate without the intent of moving *qi* along traditional Chinese acupuncture meridians). First, the additional neuropeptides provided by non-neurologic sources could provide negative feedback onto auto receptors located on nerve endings.[293] Second, the increase in substance P may function to regulate peripheral levels of CGRP.[294] The latter is particularly intriguing, given that CGRP has been shown to propagate inflammation in high quantities but provides potent anti-inflammatory actions in low concentrations via tetrodotoxin (TTX) channel inhibition.[294,295]

The fact that CGRP promotes inflammation acutely is somewhat of a paradox, as the ability of CGRP to increase blood flow through vasodilation has been shown to contribute to tissue healing.[298] Moreover, a study demonstrated that acupuncture is able to

promote tendon healing via angiogenesis and fibroblast migration via CGRP release from sensory nerve endings and mechanical stimulation of collagen fibers, respectively.[334,335] In short, CGRP causes vasodilation by binding to CGRP1 receptors on vascular smooth muscle, resulting in the increase of phosphokinase-α (PKA). The subsequent opening of K^+ channels and reduction of Ca^{2+} results in smooth muscle relaxation and vasodilation.[298] The increase in PKA also stimulates nitric oxide synthase, an enzyme responsible for producing nitric oxide, thereby enhancing the response.[298] Zhang et al further hypothesized that acupuncture may directly stimulate the sympathetic nervous system to release nitric oxide by creating an "axon reflex" within densely innervated tissue.[293]

The role of CGRP in OA is particularly counterintuitive, as the pain associated with OA has been linked to an upregulation of vascular and neural tissue (with CGRP and substance P) in the vicinity of joint structures that are typically aneural.[336] The CGRP expression has been shown to increase in animals injected with monosodium iodoacetate, a model of OA pain;[337] however, the effects of acupuncture for OA have also been shown to increase blood flow. While the effects of acupuncture on OA have yet to be fully realized, a previous study demonstrated an equivalent positive outcome of needling at acupoint and non-acupoint locations around the hip joint.[338] This finding suggests that acupuncture may also provide a nonspecific effect in patients with OA.

Furthermore, many researchers articulate that the general effect of acupuncture for patients with OA is due to increased blood flow to the peri and intra-articular tissues. For example, following acupuncture, Lazaro et al found a significant increase in vasodilation over the medial aspect of the knee.[225] Since the vasodilation disappeared upon application of L-NAME, a nitric oxide synthase inhibitor, the resulting change in vasodilation was likely due to an increase in nitric oxide. Whether CGRP also plays a role has yet to be

determined, but given the numerous studies that report an increase of CGRP post-acupuncture and the potential for CGRP to mediate nitric oxide release from endothelial cells,[295,298] it is also a likely player in the vasodilation. Importantly, the vasodilation was also inhibited by blocking neuromuscular junctions with succinylcholine, a nicotinic ACh receptor blocker, suggesting that muscle contraction via electroacupuncture may be required for CGRP and nitric oxide mediated vasodilation.[225]

The increased blood flow likely has three primary effects on joints with OA. First, while the role of microvascular restriction is unclear, a recent study by Hussain et al found that patients with retinal arteriole narrowing were twice as likely to develop knee OA and require a knee replacement.[339] This finding suggests that reduced microcirculation of the knee is likely a factor in the development of OA, to include the muscles that surround the joint.[339,340] Similarly, Biberthaler et al found reduced microcirculation in degenerative rotator cuff lesions.[341] That is, electroacupuncture/electrical dry needling may improve vascularity of the joint via CGRP and nitric oxide, thereby inhibiting and/or reversing symptoms associated with OA. Second, a number of studies have shown a significant reduction in inflammatory cytokines in the synovial fluid of osteoarthritic joints following acupuncture. The increased blood flow likely facilitates the recruitment of opioid producing immune cells required to reduce the level of inflammatory cytokines.

Ahsin et al reported a significant increase in plasma β-endorphin levels after electroacupuncture to local points at the knee that correlated with reductions in pain, stiffness and disability, which is likely due to vasodilation.[126] Electroacupuncture further blocks the local release of IL-1 β and TNF-α in the synovia of osteoarthritic joints[226] and the systemic release of IL-1 β and TNF-α by inhibiting melanocortin-4 in the periaqueductal gray of the brain stem.[227] Third, there is limited evidence suggesting

acupuncture may stimulate an increase in hyaluronic acid, allowing the synovial fluid to better lubricate the joint.[228] Therefore, acupuncture (i.e. dry needling without injectate, but not for the purpose of moving *qi* along one traditional Chinese acupuncture meridians) may be a viable and cost effective treatment for knee OA, especially when combined with traditional physical therapy interventions such as exercise and non-thrust joint mobilization.

The total effects of most interventions consist of non-specific and specific effects. Acupuncture and dry needling work to systemically reduce pain by activating opioid-based pain reduction,[227,320,321] mediated by endogenous cannabinoids[291,323,324] and the sympathetic nervous system,[325,326] and non-opioid pain relief via serotonin and norepinephrine from the brain stem.[227,228,288,327] Dry needling also triggers the HPA-axis centrally[328] and the CRH-POMC-corticosteroid axis locally[329] to inhibit COX-2, reducing inflammatory cytokines.

At a cellular level, electrical dry needling stimulates immune cells, fibroblasts and keratinocytes to release CGRP and substance-P,[295] altering CGRP stimulation of TTX receptors to reverse hyperalgesia.[294] It also encourages the supraoptic nucleus to release oxytocin to quiet ASIC receptors peripherally and stimulate opioid interneurons spinally.[301-303] Mechanotransduction of fibroblasts and peripheral nerves via TRPV1[304] and P2X/Y-mediated intercellular Ca^{2+} wave propagation and subsequent activation of the nucleus accumbens inhibits spinal pain transmission via glycinergic and opioidergic interneurons.[305,306] The increased ATP is metabolized to adenosine, which activates P1 purinergic receptors, events considered key to dry needling analgesia and rho kinase-based tissue remodeling.[307] Even trigger point dry needling has been shown to reduce some of biochemicals associated with pain and inflammation.[319,342,343] Specific to treatment for pain due to knee OA, Ahsin et al[126] found significant increases in plasma β endorphin levels

after electroacupuncture to local points at the knee that correlated with reductions in pain, stiffness and disability, which is likely due to vasodilation.

Strengths and Limitations

Major strengths of the current study include the inclusion of a large sample size with 18 treating physical therapists from 18 clinics in 10 different geographical states, and the use of the same standardized 9-point needling protocol and dosage parameters. However, we only assessed mid-term follow-up; thus, we do not know if the significant between-groups differences observed at 3 months would be sustained in the long-term. We also cannot be certain that the results are generalizable to other dry needling protocols, dosages, techniques or needle placements. Additionally, we did not include a dry needling placebo group; which should be included in future studies. Lastly, therapist and patient treatment preferences were not collected and could potentially affect the results.

Study 2 - Plantar Fasciitis

Findings

To our knowledge, this study is the first randomized clinical trial to investigate the combined effectiveness of electrical dry needling in addition to manual therapy, exercise and ultrasound in patients with PF. The results suggest that a mean of 6 sessions of manual therapy, exercise, and ultrasound plus electrical dry needling, using an 8-point standardized protocol targeting the foot locally at a frequency of 1-2 times per week over 4 weeks, resulted in greater improvements in first step morning pain, resting heel pain, pain during activity, function, medication intake, related-disability and foot health-related quality of life than manual therapy, exercise and ultrasound alone. For the primary outcome of first step morning pain, between-groups effect sizes were medium at 4 weeks and large at 3 months in favor of the dry needling group. The between-groups difference for change in first step pain, as measured by the NPRS (2.15 points, 95%CI 1.3, 3.0) exceeded the reported MCID (i.e. 1.74[265] for the 0-10 NPRS in a variety of chronic pain conditions and 19 mm[243] for the 0-100 VAS for first step pain in PF) at 3 months. In addition, for level of function (LEFS), pain (FFI Pain Subscale), related-disability (FFI Disability Subscale) and foot health-related quality of life (FFI Total), the point estimates for the between-groups change (LEFS (9.26 points, 95%CI 4.2, 14.3); FFI Pain (13.83%, 6.0, 21.8); FFI Disability (12.0%, 3.7, 20.3); FFI Total (9.85%, 3.8, 16.0) also exceeded the respective MCID (i.e., 9 points[276] for the LEFS; 12.3%[281] for FFI Pain; 6.7%[281] for FFI Disability; 6.5%[281] for FFI Total) for each of the measures at 3 months. Finally, the NNT suggests for every 2 patients treated with electrical dry needling, rather than manual therapy, exercise and ultrasound alone, one additional patient with plantar fasciitis achieves clinically important reductions in first step pain and related-disability at 3 months follow-up.

Similar to the findings of the current study, another randomized controlled trial of patients with chronic PF reported a 69% reduction in foot pain and an 80% success rate following 10 sessions of electroacupuncture over 5 weeks targeting the most tender points over the medial plantar aspect of the calcaneus with 2 to 6 needles left in place for 30 minutes.[235] Likewise, a recent randomized controlled trial of 84 patients with PF reported statistically significant differences in first-step pain and foot pain in favor of trigger point dry needling over sham dry needling;[45] nevetheless, neither the 14.4 mm improvement in first-step pain nor the 10.0 point improvement on the pain subscale of the Foot Health Status Questionnaire reported by Cochett et al[45] exceeded the 19 mm[243] (VAS 0-100 mm) and 13-point[243] minimum clinically important difference (MCID), respectively. In addition, the palpatory methods used by Cochett et al[45] to identify the location of target trigger points, and therefore the entry point, angulation, and depth of needle insertion, have not yet been found to possess accurate diagnostic validity[68,181,230] or acceptable inter-examiner reliability[68,130,158,231] for muscles in the foot or lower leg.

The underlying mechanisms as to why the electrical dry needling group in our study experienced greater improvements than the manual therapy, exercise and ultrasound alone group remains to be elucidated. However, mechanical and electric periosteal stimulation, peri-neural needling of the tibial and lateral plantar nerves, and the duration that the needles are left in situ may be important components to consider when using dry needling therapies in patients with PF.

Periosteal Pecking at the Medial Tubercle of the Calcaneus

Although the etiology of PF remains unclear, the proximal attachment of the plantar aponeurosis at the medial tubercle of the calcaneus is most often reported by patients as the origin of symptoms and the site of greatest discomfort.[60,232,233] Moreover, 3 of the 5 previous studies on dry needling in patients with PF have specifically targeted the insertion of the plantar fascia at or near the medial tubercle of the calcaneus.[234-236] Therefore, for 1 of the 8 mandatory needle placements, we used periosteal "pecking" or "peppering" to target the enthesis, i.e. the interface between the periosteum and plantar aponeurosis and/or the tendons of the flexor digitorum brevis and quadratus plantae,[44,55,56] by tapping the needle repeatedly onto or near the periosteum of the medial tubercle of the calcaneus bone as this technique has been previously used and appears to be an important component of the needling treatment in patients with PF.[244-247]

Periosteal "pecking" or "peppering", via mutliple penetrations with dry needles at or near the proximal attachment of the plantar fascia over the medial tubercle of the calcaneus, is intended to stimulate microtrauma and local inflammation,[344] augment the fibroblastic reparative process,[345] increase the concentration and reorganization of collagen fibers,[345-349] and mediate the proliferative and remodeling phase of healing at the interface between the periosteum and plantar aponeurosis (i.e. enthesis or teno-osseus junction).[349-351] Periosteal stimulation (i.e. pecking/peppering) has previously been performed in conjunction with injection therapies for PF.[244,245] In the case of corticosteroid injections, peppering resulted in significantly greater reductions in pain secondary to PF than corticosteroid injection alone.[246,247]

Similarly, another trial found that miniscalpel-needle release ("over the most painful tender point at the medial calcaneal tubercle") was superior to steroid injections in the short and long-term (1-, 6- and 12-months) for improving first step morning pain in patients with chronic recalcitrant PF.[47] Additionally, for the management of OA of the knee and/or hip, a number of studies demonstrated that periosteal needling leads to greater improvements in pain and disability than superficial needling approaches targeting muscle tissues.[251,315,316]

Peri-neural Needling

Importantly, a number of needle points that targeted peri-neural tissue associated with the posterior tibial nerve and lateral plantar nerve were used in our dry needling protocol, which provides the sensory innervation to the medial tubercle of the calcaneus.[352] A study found ultrasound-guided pulsed-radio frequency energy of the posterior tibial nerve to be a useful strategy for improving pain and tissue thickness secondary to PF.[353] In a separate study, Arslan et al also reported that pulsed-radio frequency ablation of the lateral plantar nerve is an effective technique for reducing pain associated with PF.[354] While peri-neural needling of the posterior tibial nerve and the proximal medial and lateral plantar nerve was not enough to achieve full pain relief in 18 patients with chronic PF, Tillu and Gupta noted that 61% of patients reported a reduction in pain after only 4 treatments.[355] Thus, a comprehensive dry needling approach for PF should likely consider peri-neural tissue associated with the condition.

Duration of Needle Placement

Aside from one cohort study that treated PF people with a single lidocaine injection in which the needle was immediately removed upon dispensing the injectate,[234] other studies have left the needles in place for 5 minutes,[45] 15 minutes,[112] 20 minutes,[236,237] and 30 minutes.[53] Notably, Cotchett et al[45] left the needles in place for a much shorter duration than the others (15-30 minutes[53,236,237]) and did not target the insertion of the plantar fascia at or near the medial tubercle of the calcaneus;[234-236,355] hence, this may be one reason why the between-groups difference in first-step pain intensity in the current study (i.e. 2.15 points on the 0-10 NPRS) exceeded the MCID, whereas the between-groups difference (i.e. 14.4 mm on the 0-100 VAS) in first-step pain (the primary outcome measure at the primary end point of 6-weeks) reported by Cotchett et al[45] did not exceed the minimum MCID for that measure.[238-240] It is perhaps worth noting that one of the most robust trials to date on the use of electroacupuncture for chronic PF inserted needles at the anteromedial aspect of the heel (i.e. at the location of greatest tenderness) and left the needles in situ for 30min. Following 5 weeks of convention treatment, including stretching exercises, orthotics and rescue meds plus 10 sessions of electroacupuncture, twice weekly, the authors reported an 80% success rate in treating chronic refractory PF vs a 13.3% success rate in a group only receiving convention treatment.[53]

Periosteal Needling and Tissue Repair

Periosteal needling may also help to augment a fibroblastic reparative response as it has been preiovusly discussed.[349,350,356-358] The plantar fascia is fibrous connective tissue consisting primarily of type I collagen fibers, a primary component of tendons and ligaments, and is a key player in wound healing and tissue repair.[357,359-363] Similar to the common extensor tendon in lateral epicondylalgia,[364] the plantar fascia has been shown to soften in patients with PF.[365,366] However, a recent study by Kim et al reported a significant hardening of the plantar fascia via sonoelastography following collagen injections in the vicinity of the medial calcaneal tubercle, which was associated with improvements in VAS in PF.[351] Notably, a number of studies have also demonstrated mechanotransduction of fibroblasts via needle manipulation[350,367-371], which leads to an increased concentration and reorganization of collagen fibers and mediates the proliferative and remodeling phase of healing.[349-351]

Rationale for Electrical Dry Needling

Electrical dry needling has been found to cause the release of substance-P and CGRG predominantly from non-neural structures, facilitating a negative feedback loop to neural and neuroactive components of the target tissue.[292,293] In the case of periosteal needling, this may lead to decreased inflammation of the densely innervated periosteum, i.e. at the proximal attachment of the plantar aponeurosis at the medial tubercle of the calcaneus which is most frequently reported by patients as the origin of symptoms and the site of greatest discomfort.

Notably, CGRP in high quantities causes inflammation, but the concurrent release of substance-P combined with electric stimulation in the vicinity of the periosteum may provide sustained, low levels of CGRP required for a anti-inflammatory and therefore anti-nociceptive effect.[294-297] CGRP also initiates a cascade of events mediated by protein kinase A (PKA) in vascular smooth muscle, leading to vasodilation.[298] Moreover, PKA stimulates nitric oxide synthase, increasing the production of nitric oxide, thereby exaggerating the vasodilation effect.[298] The improved vasodilation may improve the microcirculation in the plantar foot, resulting in increased opioid delivery and decreased inflammatory factors in the vicinity of the plantar aponeurosis.[126,226] Mechanical and electric needle stimulation close to the periosteum of bone may be particularly advantageous, as acupuncture has been shown to reduce IL-6 mRNA expression in bone marrow, thereby limiting inflammation, and inhibiting myelogenic osteoclast activity driving degeneration.[300]

Strengths and Limitations

Major strengths of the current study include the inclusion of a large sample size with 10 treating physical therapists from 10 clinics in 6 different geographical states, and the use of the same standardized 8-point needling protocol and dosage paramenters. However, we only assessed mid-term follow-up; thus, we do not know if the significant between-groups differences observed at 3 months would be sustained in the long-term. We also cannot be certain that the results are generalizable to other needling protocols, dosages, techniques or needle placements.

Conclusions

The results of the current PhD thesis include the following conclusions:

1. Patients with painful knee OA who received manual therapy, exercise and electrical dry needling experienced significantly greater improvements in pain intensity, related-disability, stiffness, physical function, and medication intake as compared to patients with painful knee OA receiving manual therapy and exercise alone.

2. Patients with plantar fasciitis who received manual therapy, exercise and ultrasound plus electrical dry needling experienced significantly greater improvements in first step morning pain intensity, resting heel pain, pain during activity, function, related-disability and foot health-related quality of life, and medication intake as compared to the group that received manual therapy, exercise and ultrasound alone.

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