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Effects of Transcutaneous Electrical Nerve Stimulation on Pain Control in Patients with Knee Osteoarthritis a Systematic Review

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Keywords
Knee osteoarthritis, Joint pains, TENS.

Introduction
Knee osteoarthritis (OA), which causes knee joint pain, stiffness, and functional disability [1], is common among elderly individuals [2]. A literature search suggested that 27.8% of individuals aged over 45 years old had a prevalence of radiographic knee OA grade of at least 2 in at least 1 knee and 43.3% had symptomatic knee pain, aching, or stiffness in at least 1 knee [3]. There is no perfect treatment or measures for knee OA patients up to date. Therefore, pain therapy is considered as a main treatment for those with knee OA.

Transcutaneous electrical nerve stimulation (TENS) is a commonly used conservative treatment method that is effective in reducing knee pain in patients with knee OA [4-6]. However, it is still controversial in effectiveness of TENS based on randomized controlled trials (RCTs) and systematic reviews compared with healthy control groups [7-9]. Therefore, it is effective in decreasing knee pain. In addition, the main outcome of the literature on TENS is level of knee pain, which was measured using instruments such as the visual analog scale (VAS) or Western Ontario and McMaster Universities Arthritis Index scale (WOMAC). Decrease in pain can lead improved normal physical function; however, limited studies have reported the effect of decrease in pain on physical function through factors such as muscle strength, speed, endurance, and balance. Further, it is been limited to confirm if TENS intervention is effective in reducing pain and developing physical tests [10,11].

In the previous studies, they have suggested that discrepancy between physical symptom and radiographic evaluation. The K/L grade is a common radiographic evaluation system for knee OA; it involves classification of knee OA according to the severity of bone deformity [12]. However, there was no statistically significant relationship between K/L grade and knee pain [13], leg extensor and flexor muscle strengths, and WOMAC [14,15]. In addition, people with K/L score 0 may have cartilage damage or bone marrow lesions, as demonstrated using magnetic resonance imaging [16]. There is possibility that even people with K/L grade 0 or 1 (preradiographic OA) have inadequate function and/or knee pain. Additionally, those with preradiographic OA, particularly with K/L grade 1, have been expected to develop to at least grade [2,17,18]. Moreover, another previous study reported that people with early-stage knee OA have higher possibility of having better response to treatment than those with late-stage knee OA [19].

Therefore, the purpose of this systematic review with meta-analysis was to determine whether TENS can alleviate joint pain in patients with knee OA. On the basis of the existing literature, we hypothesize that TENS treatment is effective in reducing joint pain for knee OA patients.

Methods
We searched PubMed, CINAHL, SPORT Discus, and Scopus databases from their earliest available date to March 2016 using the combination of key words, including 1) joint pain OR knee osteoarthritis OR TENS OR pain control OR 2) ACLR OR ACL injury; and 3) items 1 AND 2.

Inclusion and exclusion criteria
After the initial electronic search, duplicated articles were eliminated by comparing the results from each database. On the basis of title and abstracts, articles returned that were not relevant and English language, full text, or original articles were rejected [1-19].

The authors independently made the initial selection based on the

titles and abstracts of the papers. Any disagreement between the 2 authors was resolved by discussion. If there was still debate, a third reviewer (S.-Q.F.) was consulted and made a decision regarding its inclusion. Information including the authors, study design, mean age, sex, study population, stimulation frequency (of TENS), outcome measures, and follow-up periods were extracted from each included study.

Study	Study design	Inclusion/Exclusion criteria	Particiapants / Groups	Main Outcome measures for pain	Manufacturer TENS Unit	Treatment Duraiton (# of session)	Parameters	Progressive (Y/N)
Atamaz (2012)	RCT	Inclusion: (1) aged 50-80 (2) ACR criteria; (3) radiologically confirmed with a Kellgren-Lawrence grade of 2 or 3; (3) VAS for pain > 4 for at least 6 months Exclusion: (1) a history of any contraindication for electrotherapy, (2) corticosteroid therapy, (3) chondroprotective agents during the 30 days prior to the study, (4)viscosupplementation treatment within 6 months prior to the study, or (4) had undergone previous major surgery, such as joint replacement or arthroscopy, within 6 months prior to the study.	203 participants Groups: TENS sham (33) TENS (29), IFCs sham (34), IFCs (27) SWD (27)	VAS	Bio-stim SD-980,a Endomed CV-405,b and Sonopuls 492b Electrodes: 4 surface electrodes (5 x 5 cm)	5 times a week for 3 weeks (15 sessions)	Frequency (Hz): 80 Intensity (mA): 10-30 Duration (min): 20	Y: VAS N: WOMAC and ROM
Chen (2013)	RCT	Inclusion: (1) aged 50-80, (2) ACR criteria, (3) radiologically confirmed with a Kellgren-Lawrence grade of 2 or 3, and (4) VAS for pain > 4 for at least 6 months Exclusion: (1) a pacemaker, (2) previous knee operation (including replacement surgery), (3) rheumatoid arthritis, (4) severe medical or neurologic conditions, or (4) who had received intra-articular corticosteroid/HA injections over the previous 6 months	50 participants; HA injection (27) TENS (23)	VAS	Electrodes: SSR; 4 surface electrodes (5 x 3.5 cm)	3 times a week for 4 weeks (12 sessions)	Frequency (Hz): mixed-frequency constant mode of 3 - 20 Pulse width (µs): 200 Intensity (mA): vary Duration (min): 20	Y: VAS, Lequesne
Cherian (2016)	RCT	Inclusion: (1) aged 50-80, (2) ACR criteria, (3) radiologically confirmed with a Kellgren-Lawrence grade of 2 or 3, and (4) VAS for pain > 4 for at least 6 months Exclusion: (1) a pacemaker, (2) previous knee operation (including replacement surgery), (3) rheumatoid arthritis, (4) severe medical or neurologic conditions, or (4) who had received intra-articular corticosteroid/HA injections over the previous 6 months	70 participants: TENS Standard conservative therapy	VAS	N/A		Frequency (Hz): Intensity (mA): Duration (min):	Y: VAS
Govil (2020)		Inclusion: (1) aged 18-60, (2) ACR criteria, (3) able to ambulate to the mailbox and back (4) stable medication schedule over the prior 3 weeks, and (5) VAS for pain > 3 Exclusion: (1) knee surgery within the last 6 months, (2) knee injection within the last four weeks, (3) presence of any serious medical condition, and (4) uncontrolled diabetes mellitus or hypertension, dementia or cognitive impairment, (5) permanent lower extremity sensory loss and (6) prior TENS use.	74 participants; Groups: High-frequency Low-frequency Sham	VAS	Rehabilicare Maxima, Empi, Inc Electrodes: 4 (2 x 2 inch)		Frequency (Hz): 100 OR 4 Pulse width (µs): 100 Intensity (mA): vary Duration (min):	Y: VAS
Isik (2017)	RCT	Inclusion: (1) aged 18-60, (2) ACR criteria, (3) radiologically confirmed with a Kellgren-Lawrence grade of 2 or 3 Exclusion: (1) Diagnosis of rheumatoid arthritis and other systemic joint diseases, (2) Secondary osteoarthritis, (3) Arthroscopy or surgery of the knee, (4) Intra-articular injection in the past 3 months, (5) Physical therapy in the past 3months, (6) Skin disorders with or without exfoliation, scar or open wound on the knee, (7) Comorbidities, such as blood disorders, anemia, uncontrolled diabetes, severe depression or other psychological diseases, (8) Anticoagulation treatment, (9) Advanced joint deformity, (10) Pregnancy, (11) Intercurrent disease(s) thatmight interfere with the free use and evaluation of the affected knee.	105 participants: Groups: TENS: 53 Leech therapy: 52	VAS	N/A	5 times a week for 3 weeks (15 sessions)	Frequency (Hz): 40 - 150 Intensity (mA): vary Duration (min): 20	Y: VAS and Leech

Pietrosimone (2010)	RCT	Inclusion: (1) clinically diagnosed with OA, (2) K-L score between 1-4, (3) the greatest radiographic evidence of OA Exclusion: (1) ACLR, (2) a diagnosed heart condition limiting exercise, (3) altered sensation over the anterior knee, (3) and lower body surgery or knee trauma in the past 6 months.	33 participants Groups: TENS: 10 Placebo: 11 Contro: 12	VAS	TENS: EMPI, Inc., St. Paul, MN Electrodes: Four separate 2 × 2 inch self- adhesive electrodes (Re-ply reusable electrodes, Uni-Patch, Wabasha, MN)	3 times a week for 4 weeks (12 sessions)	Frequency (Hz): 150 Intensity (mA): 1-60 Pulse width (μs): 150 Duration (min): 20	Y: VAS at 2 and 4 weeks
Sajadi (2020)	RCT	Inclusion: (1) aged over 50, (2) ACR criteria, (3) radiologically confirmed with a Kellgren-Lawrence grade of 2 or 3, and (4) VAS for pain > 4 for at least 6 months Exclusion: (1) any neurologic and musculoskeletal disorders affecting lowerextremity function, (2) knee joint inflammatory disorders, (3) secondary OA, (4) development of other knee pathology during thestudy, (5)radicular back pain, diabetes mellitus (DM), (6) major depressive disorder (MDD), (7) history of knee surgery, (8) history of drug abuse, epilepsy, (9) acute or chronic infection, (10)pregnancy, (11) unstable conditions, (12)electrical implants such pacemakers, or (13) metal implants near electrode locations.	40 participants Groups: TENS: 20 tDCS: 20	VAS	N/A	3 times a week for 2 weeks (6 sessions)	Frequency (Hz): 100 Intensity (mA): vary Pulse width (μs): 100 Duration (min): 25	Y: VAS

Discussion

The systematic review is the first to pool data from individual studies on the effects of TENS on pain control in patients with knee OA. The results provide evidence that TENS treatments are effective in reducing self-reported pain level. More specifically, the TENS treatments, 12-15 sessions over 4-6 weeks, reduce VAS in pain right after the treatments and it lasts about 2 weeks. However, it did not show how long the effect lasted after 2 weeks. Different physical therapy approaches have been used to develop the clinical course of knee OA, but the evidence of effectiveness has not been sufficient based on randomized controlled studies and analyzed by a systematic review.

TENS is effective for nociceptive pain mechanisms based on the gait control theory of pain [20] and activation of endogenous opioids, and it may improve exercise tolerance in individuals who experience movement-evoked pain. Shimoura et al. [21] reported that TENS intervention was considered to reduce knee movement-evoked pain and increase walking distance without pain. Thus, participants in the TENS group may be able to walk longer distances in the post-assessment period. According to Isik's [22] study, they compared a three-session leech therapy applied on ambulatory patients with a routinely applied full term TENS therapy which involved 15 sessions of TENS therapy application on hospitalized patients in 3 weeks. In the evaluation of the main outcome scores on day 21st, pain score in VAS significantly decreased in both groups which were consistent with previous studies. In addition, Pietrosimone et al. [23] stated that although significant differences were not found between groups, moderate TENS effect sizes were found 4-weeks following the initiation of the intervention. In the most recent article in this systematic review, significant analgesic effect and functional improvement were observed in patients who received TENS.

Based on the RCTs in our systematic review, TENS decreases pain in patients with knee OA. Previous authors have concluded that the neural drive is immediately increased during the active administration of sensory TENS current, and that TENS immediately diminished the excitatory effect upon removal. Current theories suggest that TENS provides increased afferent stimuli interpreted by the CNS as excitatory resulting in the facilitation of inhibited motor neuron pools.

In conclusion, this systematic review indicated that: (1) patients who received TENS had significantly decreased pain compared with the control group; (2) there was no significant difference between the TENS and control groups in terms of the WOMAC index and all-cause discontinuation; (3) there was no significant difference between the TENS and control groups in the pain-limited ROM and/or total passive knee ROM; and (4) TENS might significantly improved the maximum knee ROM on day 10 and during follow-up compared with the control group.

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