PT Critically Appraised Topics   School of Physical Therapy

2010

Efficacy of transcutaneous electrical nerve stimulation (TENS) to relieve severe pain in patients with knee osteoarthritis (OA)

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Efficacy of transcutaneous electrical nerve stimulation (TENS) to relieve severe pain in patients with knee osteoarthritis (OA)

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Title: Efficacy of transcutaneous electrical nerve stimulation (TENS) to relieve severe pain in patients with knee osteoarthritis (OA).

Clinical scenario: The patient who led me to pursue this question is a 50 year old female with diagnoses including right knee OA, sepsis, deep vein thrombosis and gout. Her previous medical history includes hypertension, renal insufficiency, gastro esophageal reflux disease and heart transplant. Medical treatment to date for the OA has included medications and ice pack for pain relief. Problems identified include limited functional mobility and endurance secondary to knee pain, and general lower extremity weakness.

Brief introduction: For the purposes of my clinical question, I want to know what the research says about the use of TENS on patients with severe knee pain secondary to knee OA. The patients in the skilled nursing facility I am working in often have knee pain limiting functional mobility, although the knee pain is not always secondary to OA. The parameters such as frequency, pulse width and duration of treatment for TENS use in this population is also unclear.

My clinical question: Is TENS effective in reducing short term and/or long term knee pain as measured by the visual analogue scale (VAS) in patients with knee OA?

Clinical question PICO:
Population: Adults aged 50-75 years diagnosed by an orthopedic surgeon or physician with severe knee OA (grade III or IV), who are at least able to ambulate with an assistive device and have knee pain of 6/10 or greater on the VAS with activity
Intervention: TENS for pain relief
Comparison: No treatment or placebo TENS for pain relief
Outcome: Pain relief as measured by the VAS after each treatment session, after 10 treatment sessions and at a follow up session at least 2 weeks after treatment has ended

Overall clinical bottom line: Based on the results of the studies by Law *et. al* (2004) and Cheing *et. al* (2002), the use of TENS results in statistically significant improvements in pain across sessions, and based on the results by Law *et. al* (2004) the improvements achieve a clinically important difference in pain relief within treatment groups after 10 sessions and at the 2 week follow up. When comparing the pain outcomes to a placebo TENS intervention, the results from either study do not strongly suggest that TENS is more effective than placebo TENS treatment. If TENS treatment is used, however, it is more likely that the effects on pain relief are seen after 10 sessions and last up to 2-4 weeks after the end of TENS treatment. The most effective TENS parameters determined from both studies are 2 Hz and a pulse width of 576 µs or 100 Hz and a pulse width of 200 µs. The main threats to internal validity in both studies are the lack of blinding of therapists, a study loss of 6%, and small sample sizes. The first two threats are minor, but larger sample sizes would improve the generalizability of the outcomes. The main cost is time and financial cost of treatment, but the treatment is within reason to be covered by insurance. The recommendation from both studies is that as long as there are no contraindications to TENS and other pain relief methods have not worked for patients with knee OA, there is no harm in a TENS treatment trial with patient agreement to the TENS treatment as well as the time and financial cost associated with treatment using one of the 2 sets of TENS parameters mentioned above for 10 sessions with possible clinically important improvement in long term pain.

Search terms: Transcutaneous electric nerve stimulation, knee osteoarthritis, visual analogue scale/pain measurement

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Rationale for chosen articles: A systematic review by Rutjes *et al.* (2010) and meta-analysis by Bjordal *et al.* (2007) were found on the topic of TENS as a treatment option for patients with pain secondary to knee OA. After reviewing the list of articles, the following 3 articles were chosen because they were the best match to the clinical PICO in all aspects. The remaining articles were not chosen mainly because they did not have the VAS as one of the outcome measures, but used other pain measurement scales, and did not score any higher on the PEDro scale.

Article: Law PP and Cheing GL. Optimal stimulation frequency of transcutaneous electrical nerve stimulation on people with knee osteoarthritis. *Journal of Rehabilitation Medicine* 2004; 36(5):220-225.

PEDro score: 8/10
P: Patients with a mean age of 82.55 years with at least grade II OA in the knee, excluding those with prior knee surgery, intra-articular corticosteroid in the prior 4 weeks, TENS treatment in the last month, cardiac pacemaker, or presence of any chronic or uncontrolled comorbid diseases.
I: TENS at 2 Hz, 100 Hz, or alternating 2 Hz/100 Hz for 40 minutes 5 times a week for 2 weeks
C: Placebo TENS treatment for 40 minutes 5 times a week for 2 weeks
O: VAS measured at 0, 20, 40, 60, 80, 100 minutes during each session and at the 2 week follow up session, knee range of motion, timed up-and-go (TUG) test

Article: Cheing GL, Tsui AY, Lo SK, Hui-Chan CW. Optimal stimulation duration of TENS in the management of osteoarthritic knee pain. *Journal of Rehabilitation Medicine* 2003; 35(2):62-68.

PEDro score: 4/10
P: Patients aged 50 to 80 years with at least grade II OA in the knee with moderate knee pain who were independent ambulators in the community, and excluding those with prior knee surgery, corticosteroid injection or TENS in last 2 months, or cardiac pacemaker.
I: TENS at 100 Hz for 20, 40 or 60 minutes of treatment time, 5 times a week for 2 weeks
C: Placebo TENS treatment for 60 minutes, 5 times a week for 2 weeks
O: VAS before, immediately and 60 minutes after treatment

Article: Cheing GL, Hui-Chan CW, Chan KM. Does four weeks of TENS and/or isometric exercise produce cumulative reduction of osteoarthritic knee pain? *Clinical Rehabilitation* 2002; 16(7):749-760.

PEDro score: 7/10
P: Patients aged 50 to 75 years with at least grade II OA in the knee for 6 months or longer who were independent ambulators, and excluding those with prior knee surgery, corticosteroid injection or TENS in the prior 3 weeks.
I: Three groups: 1) 60 minutes of TENS, 2) 20 minutes of isometric exercise training, or 3) 60 minutes of TENS and 20 minutes of isometric exercise training 5 times a week for 4 weeks
C: Placebo TENS treatment for 60 minutes 5 times a week for 4 weeks
O: VAS measured at 0, 20, 40, 60, and 80 minutes during each session and at the 4 week follow up session

Table 1: Comparison of PEDro Scores

	Law PP *et al.* (2004)	Cheing GL *et al.* (2003)	Cheing GL *et al.* (2002)
Random	1	1	1
Concealed allocation	1	0	0
Baseline comparability	1	1	1
Blind subjects	1	0	1
Blind therapists	0	0	0
Blind assessors	1	0	1
Adequate follow-up	1	1	1
Intention to treat	0	0	0
Between group	1	1	1
Point estimates and variability	1	0	1
Total score	8/10	4/10	7/10

Table 1 shows a comparison of the PEDro scores. Of the 3 articles, the one by Law *et al.* (2004) had the highest PEDro score, with only a lack of blinding of therapists and no intention to treat analysis for the 6% study loss (2 out of 36 patients). However, none of the 3 articles had an intention to treat analysis. The population in the article by Law *et al.* (2004) was the least similar to the clinical population of interest, with a mean age of 82.55 years (actual age range not provided) which is higher than the age range of interest (50-75 years), and there was no mention of their ambulation status. The article by Cheing *et al.* (2002) had the next highest PEDro score, with a lack of blinding of therapists, and no mention of concealed allocation of groups to the assessors. There was also no intention to treat analysis for the 6% study loss (4 out of 66 patients). The article by Cheing *et al.* (2003) had the lowest PEDro score, with a lack of blinding of subjects, therapists and assessors and no concealed allocation of groups to the assessors. There was also no intention to treat analysis for the 5% study loss (2 out of 40 patients). Another shortfall of the article by Cheing *et al.* (2003) was that the main outcome measure of VAS score was only provided in a bar chart form and not actual numerical numbers for the mean and standard deviation. Based on the above comparisons, I have chosen to write this critically appraised paper on the articles by Law PP *et al.* (2004) and Cheing GL *et al.* (2002).

Article: Law PP and Cheing GL. Optimal stimulation frequency of transcutaneous electrical nerve stimulation on people with knee osteoarthritis. *Journal of Rehabilitation Medicine* 2004; 36(5):220-225.

Clinical bottom line: The results of this study suggest clinically important improvement in pain as measured by the VAS score with 40 minutes of TENS treatment at 2 Hz and a pulse width of 576 μs or at 100 Hz and a pulse width of 200 μs occurs after 10 sessions and at the 2 week follow up after the 2 week treatment period (10 sessions). Using TENS alternating between a frequency of 2 Hz and pulse width of 576 μs for 2 seconds and a frequency of 100 Hz and pulse width of 200 μs for 2.5 seconds may provide a clinically important improvement in pain after 10 sessions only. Both statistically significant differences and clinically important differences were found between each of the 3 TENS groups compared to the placebo TENS group, but not between the 3 TENS groups, suggesting that TENS treatment may be more effective than placebo TENS treatment for pain relief, but none of the 3 different TENS parameters were more effective than the other. It is unclear if the mean difference for VAS change scores between groups would still be clinically important with the 95% confidence interval taken into account since insufficient data was provided for these calculations. The primary threats to internal validity are lack of blinding of therapists, a 6% study loss and a small sample size. The first two threats are minor, but a larger sample size would improve the generalizability of the outcomes. Based on this study, as long as there are no contraindications to TENS, there is a potential benefit of improvement in pain relief in patients with knee OA after 10 sessions that could last up to 2 weeks after the last TENS treatment with no real harm to the patient. The TENS parameters used in the study that suggest possible improvement in long term pain are a frequency of 2 Hz and a pulse width of 576 μs, or a frequency of 100 Hz and a pulse width of 200 μs.

Article PICO:
Population: Patients with a mean age of 82.55 years with at least grade II OA in the knee, excluding those with prior knee surgery, intra-articular corticosteroid in the prior 4 weeks, TENS treatment in the last month, cardiac pacemaker, or presence of any chronic or uncontrolled comorbid diseases.
Intervention: TENS at 2 Hz, 100 Hz, or alternating 2 Hz/100 Hz for 40 minutes 5 times a week for 2 weeks
Comparison: Placebo TENS treatment for 40 minutes 5 times a week for 2 weeks
Outcome: VAS measured at 0, 20, 40, 60, 80, 100 minutes during each session and at the 2 week follow up session, knee range of motion, timed up-and-go (TUG) test

Blinding: This was a double blind study, with both assessors and subjects blinded to group allocation. Only the therapists who administered treatment to the subjects were not blinded to group allocation.

Controls: The group receiving placebo TENS treatment served as the control group (CG).

Randomization: Subjects were randomized into 4 equal groups of 9 subjects. Randomization was done by drawing lots from an envelope. There were three groups with active TENS at different frequency settings, and one CG. Randomization appears successful. At baseline there were no significant differences between groups for age, gender, body weight, height, body mass index, history of knee pain, x-ray grading of OA, baseline VAS score and Mini-mental state examination score.

Study: Thirty-six subjects were recruited from one local care home. Inclusion criteria were that subjects had at least grade II OA in the knee and that OA was the only cause of their present knee pain. Exclusion criteria were prior knee surgery, intra-articular corticosteroid in the prior 4 weeks, TENS treatment in the last month, cardiac pacemaker or the presence of any chronic or uncontrolled comorbid diseases. The subjects were randomized into 4 equal groups (n=9 each). The first treatment group (TG1) received TENS at a frequency of 2 Hz and a pulse width of 576 μs. The second treatment group (TG2) received TENS at a frequency of 100 Hz and a pulse width of 200 μs. The third treatment group (TG3) received TENS alternating between a frequency of 2 Hz with a pulse width of 576 μs for 2 seconds and a frequency of 100 Hz with a pulse width of 200 μs for 2.5 seconds. The CG received placebo TENS using a machine identical to the real treatment unit, but with the internal circuit disconnected. The indicator light still lit up when the machine was turned on and the digital display of intensity control functioned normally, but there was no electrical output. All 4 treatment groups received treatment for 40 minutes each session, 5 times a week for 2 weeks. Two pairs of rubber electrodes were placed over acupuncture points of the knee. The intensity of current for the 3 treatment groups was set at a comfortable level as determined by the subjects, and ranged from 25 mA to 35 mA. The current was turned up if the subjects accommodated to the current 5 minutes into the session. In an effort to keep subjects blinded, subjects in the CG were told that they may or may not feel the tingling sensation during the stimulation, and therapists also pretended to step up the intensity of stimulation 5 minutes into the session, similar to the 3 treatment groups. The battery in the TENS unit was replaced after each 10 hours of operation.

Outcome measures: The outcome measure of interest is the VAS score. The VAS scores were recorded at 0, 20, 40, 60, 80, 100 minutes during each session and at the 2 week follow up session. The VAS score was recorded as a measurement based on the mark subjects made on a 10 cm line. Each VAS score was recorded on a separate sheet so that subjects could not look at the previous VAS score. There was no mention of reliability or validity of the VAS in this study. The authors did not discuss the minimal clinically important difference (MCID) for the VAS score for this population. An MCID value of 1.99 on the VAS scale has been identified for the older population (mean age 67.9 ± 10.2 years) with knee OA (Tubach *et. al*, 2004).

Study losses: There was a study loss of 2 out of 36 subjects; one was for medical reasons and the other was because the subject had moved out of the elderly complex where the subject sample was taken from. This resulted in a total loss of 6%. There was no mention of intention to treat analysis to account for the study losses, or which groups the withdrawals were from and at what point they dropped out of the study.

Summary of internal validity: Randomization of the subjects, similarity of subjects at baseline, blinding of assessors and subjects to group allocation, similarity in treatment time and administration are strengths of internal validity for this study. The primary threats to internal validity include the lack of blinding of therapists, study losses and small sample size. The lack of blinding of therapists is a minor threat since they treated the CG similarly to the other 3 treatment groups by telling subjects that they may or may not feel a tingling sensation during treatment, and stepped up the intensity of stimulation 5 minutes into the treatment regardless of the group they were in. There was a study loss of 2 out of 36 subjects or 6% study loss. This is a minor threat since it was a small loss (< 15%). There was no mention of intention to treat analysis, and no mention of which groups the 2 withdrawals were from or at what point in the study they dropped out. The sample size is small, with only 9 subjects per group. The authors did not mention a power analysis to determine if there was enough power to detect differences with a sample size of 9 per group. This is a moderate threat because with a small sample size, there could have been a type II error, where a significant difference is not found when there is one. Overall, there are no major threats to internal validity.

Evidence: The authors reported statistically significant differences in VAS scores within the 3 treatment groups across sessions, but not within the placebo group. The authors also reported statistically significant differences between each of the 3 treatment groups to the placebo group at session 10 and the 2 week follow up. All the outcome measures between groups were analyzed using repeated measures ANOVA for statistical significance, and when there were interactions between sessions and groups, analysis was performed separately using one-way ANOVA. The outcome measure I am interested in is the VAS scores pre- and immediately post- treatment for session 1, after 10 sessions and at the 2 week follow up. Table 2 summarizes the data from the article, and the numbers are used to calculate the mean difference and effect size for VAS scores within groups in tables 3 and 4. Comparison of the calculated mean difference for VAS scores between groups is presented in table 5. The between groups 95% confidence interval (CI) for mean difference and between groups effect size could not be calculated because not enough data was provided in the article (either all individual data or the standard deviation (SD) for change scores). All calculations were calculated assuming n=9 for all groups.

Table 2: VAS scores with SD

	TG1	TG2	TG3	CG
Session 1 before treatment	6.6±2.0	5.2±1.8	5.4±2.2	5.8±3.0
Session 1 after treatment	4.6±2.9	2.6±2.2	2.3±2.3	4.6±3.3
Session 10 after treatment	1.4±1.5	0.7±0.7	1.1±1.7	4.1±2.6
2 week follow up	1.6±1.8	0.9±1.0	1.6±2.2	4.4±3.0

Table 3: Within group mean differences for VAS scores and 95% CI

	TG1	TG2	TG3	CG
Session 1 pre- to post- treatment difference (cm)	2.0$^{\#*}$ (-0.49 to 4.49)	2.6$^{\#*}$ (0.59 to 4.61)	3.1$^{\#*}$ (0.85 to 5.35)	1.2 (-1.95 to 4.35)
Session 1 pre- to session 10 post- treatment (cm)	5.2$^{\#+}$ (3.43 to 6.97)	4.5$^{\#+}$ (3.13 to 5.87)	4.3$^{\#+}$ (2.33 to 6.27)	1.7 (-1.11 to 4.51)
Session 1 pre- to 2 week follow up (cm)	5.0$^{\#+}$ (2.98 to 7.02)	4.3$^{\#+}$ (2.84 to 5.76)	3.8$^{\#*}$ (1.60 to 6.00)	1.4 (-1.60 to 4.40)

\# indicates a statistically significant difference was found
+ indicates the mean difference and 95% CI exceeded MCID
* indicates the mean difference (but not 95% CI) exceeded MCID

Table 4: Effect size for VAS scores within groups with 95% CI

	TG1	TG2	TG3	CG
Session 1 pre- to post- treatment difference	1.00 (large)	1.44 (large)	1.41 (large)	0.40 (medium)
Session 1 pre- to session 10 post- treatment	2.60 (large)	2.50 (large)	1.95 (large)	0.57 (medium)
Session 1 pre- to 2 week follow up	2.50 (large)	2.39 (large)	1.73 (large)	0.47 (medium)

Table 5: Between groups mean difference for VAS change scores

	Session 1 between groups for pre- to post- treatment difference	After 10 sessions between groups	2 week follow up between groups
TG1 and TG2	0.6	0.7	0.7
TG1 and TG3	1.1	0.9	1.2
TG2 and TG3	0.5	0.2	0.5
TG1 and CG	0.8	3.5*+	3.6*+
TG2 and CG	1.4	2.8*+	2.9*+
TG3 and CG	1.9	2.6*+	2.4*+

* indicates a statistically significant difference was found
+ indicates the mean difference exceeded the MCID

All calculations were made assuming n=9 for all groups. Since the authors did not specify what the final number of subjects in each group was based on the 2 study losses mentioned in the article, all combinations of number of subjects in each group based on 2 withdrawals were used in the calculations below, but did not change the interpretation. The number of subjects would have made a difference in the between groups 95% CI for mean difference and effect size, but those calculations were not done since insufficient data was provided in the article.

The mean difference for VAS scores within groups for TG1, TG2 and TG3 after 10 sessions and within groups for TG1 and TG2 at the 2 week follow up were all greater than the MCID of 1.99 (Table 3). Even the lower end of the 95% CIs exceeded the MCID in all but one of the comparisons. The effect sizes for VAS scores within treatment groups after 1 session, 10 sessions and at the 2 week follow up are all large (>0.8), and are medium (>0.2, <0.8) for the CG (Table 4).

The mean difference for VAS change scores between TG1, TG2 and TG3 to the CG after 10 sessions and at the 2 week follow up were all greater than the MCID of 1.99 (Table 5). Since there was insufficient data for calculation of the 95% CIs, it is unclear how generalizable the mean difference would be.

Overall, the results suggest a clinically important improvement in pain within all 3 treatment groups after 10 sessions with only TG1 and TG2 maintaining a clinically important improvement in pain at the 2 week follow up. The mean difference between groups (without taking the 95% CI into account) suggest a clinically important improvement in pain between each of the 3 treatment groups to the CG after 10 sessions and at the 2 week follow up. There were no significant differences between treatment groups. Thus, the results suggest that TENS treatment may be more effective than a placebo TENS treatment in pain reduction, but not one of the 3 different TENS settings were any more effective than the other.

Applicability of study results:
Similarity to my patients: The subjects in this study are similar to my patient population in terms of inclusion and exclusion criteria. The baseline VAS score in the study ranged from 5.2 cm to 6.6 cm on a 10 cm line, which is similar to my clinical PICO of 6/10 pain level at baseline. However, the mean age is higher than the age range in my patient population. The actual range of ages included in the study was not provided, but it is likely that there is some overlap with the age range in my clinical population. The slightly older population may have a different perception of pain and rating, which may affect the outcome.

Benefits vs. costs: The main cost is the time spent and the financial cost of TENS treatment for 40 minutes 5 times a week for 2 weeks (10 sessions). The main benefit is a clinically important improvement in pain as measured by the VAS score after the 10 TENS sessions and at the 2 week follow up in the TENS treatment groups.

Feasibility of treatment: TENS is a feasible treatment as most facilities have TENS units available and can be easily provided as a treatment to patients. The financial cost of 10 sessions of TENS treatment for 40 minutes each is also within reason to be covered by insurance.

Summary of external validity: The subject sample is similar to the clinical population of interest, except for the slightly older age range of subjects in the study. Also, they were sampled from only one local care home, and thus may be more difficult to generalize results to a wider and more diverse population range.

Article: Cheing GL, Hui-Chan CW, Chan KM. Does four weeks of TENS and/or isometric exercise produce cumulative reduction of osteoarthritic knee pain? *Clinical Rehabilitation* 2002; 16(7):749-760.

Clinical bottom line: The results of this study suggest TENS treatment at 80 Hz and a pulse width of 140 μs can result in statistically significant improvement in pain, as measured by the VAS score, after the first 60 minute session, after 10 sessions and at the 4 week follow up after the 4 week treatment period (20 sessions). The results are inconclusive as to whether the difference within the TENS treatment group is a clinically important change. There were no statistically significant differences in pain relief between the TENS and placebo TENS groups. The primary threats to internal validity are the lack of blinding of therapists, a 6% study loss and a small sample. The first two threats are minor, but a larger sample size would improve the generalizability of the outcomes. Based on this study, as long as there are no contraindications to TENS, there is no real harm to the patient to have a trial TENS treatment for 10 sessions if covered by insurance for potential pain relief for patients with knee OA.

Article PICO:
Population: Patients aged 50 to 75 years with at least grade II OA in the knee for 6 months or longer who were independent ambulators, and excluding those with prior knee surgery, corticosteroid injection or TENS in the prior 3 weeks.
Intervention: Three groups: 1) 60 minutes of TENS, 2) 20 minutes of isometric exercise training, or 3) 60 minutes of TENS and 20 minutes of isometric exercise training 5 times a week for 4 weeks
Comparison: Placebo TENS treatment for 60 minutes 5 times a week for 4 weeks
Outcome: VAS measured at 0, 20, 40, 60, and 80 minutes during each session and at the 4 week follow up session

Blinding: Subjects were blinded to whether they received the real or placebo TENS treatment, but therapists were not blinded to group allocation. Since the VAS scores were recorded by computer, we can consider the assessors blinded to group allocation.

Controls: The group receiving placebo TENS treatment served as the control group (CG).

Randomization: Subjects were randomized into 4 groups: the first treatment group (TG) receiving TENS (n=16), the second treatment group receiving exercise (n=15), the third treatment group receiving TENS and exercise (n=17), and the CG receiving placebo TENS (n=18). The method of randomization was not mentioned in the study, but randomization appears successful. At baseline, there were no significant differences in age, height, weight, body mass index (BMI) and gender, except for the exercise group with a significantly higher BMI than that of the TENS and exercise group. However, since only the TENs and placebo TENS groups are of interest in this appraisal, there were no significant differences in baseline characteristics for these 2 groups.

Study: Sixty-six subjects aged 50 to 75 years were recruited from the Prince of Wales Hospital in Hong Kong. Inclusion criteria were grade II or above knee OA for more than 6 months, were stable on medication for the 3 weeks prior to the study, received no paramedical treatment within the previous 2 weeks, and were able to walk on their own for 10 minutes. Exclusion criteria included prior knee surgery, corticosteroid injection or TENS in the prior 3 weeks. For those with bilateral knee OA, the more affected leg was considered the involved leg. All subjects were advised to keep their activity level and medication unchanged throughout the study period. The 66 subjects were randomized into 4 groups. The TG (n=16) received daily continuous TENS for 60 minutes at 80 Hz with a pulse width of 140 μs. Four surface electrodes were placed over acupuncture points of the knee. The intensity of TENS was adjusted to produce a tingling sensation approximately 3-4 times the subject's sensory threshold. Treatment was given at the same time each day to avoid fluctuation in pain intensity during the day. The CG (n=18) received placebo stimulation using the same parameters as the TG, except the TENS units were replaced

with placebo units that were identical, except that the internal circuit had been disconnected by the manufacturer. The indicator light was lit up when the placebo unit was switched on. All subjects were told that they might or might not feel the stimulation in order to keep subjects blinded to group allocation. The second treatment group (n=15) received isokinetic exercises for the involved leg for 20 minutes. The third treatment group (n=17) received 60 minutes of TENS and isokinetic exercises for 20 minutes, using the same parameters as the TG and second treatment group. All groups received treatment 5 times a week for 4 weeks. Details on the isokinetic exercises are not discussed here since the only groups of interest here are the TENS and placebo TENS groups.

Outcome measures: The outcome measure was the VAS score, which was recorded at 0, 20, 40, 60, 80 minutes during each 60 minute session and at the 4 week follow up session. The VAS score was recorded using a mechanical cursor on the scale which was connected to circuitry to produce a digital output, and subjects were told to return the mechanical cursor to the left end of the scale each time so they could not refer back to the previous VAS score. There was no mention of reliability or validity using this method of recording the VAS score in this study. The authors did not discuss the minimal clinically important difference (MCID) for the VAS score for this population. An MCID value of 1.99 on the VAS scale has been identified for the older population (mean age 67.9 ± 10.2 years) with knee OA (Tubach *et. al*, 2004).

Study losses: There was a study loss of 4 out of 66 subjects (6% study loss), 2 from the CG and 2 from the TENS and exercise group. Losses were due to time conflicts and medical reasons. Since only the TENS (n=16) and placebo TENS (n=18) groups were being considered, the actual study loss in consideration here is 2 out of 34 subjects, which is still a 6% study loss. There was no mention of intention to treat analysis, or at what point the subjects dropped out of the study. All data presented in this study did not include the 2 withdrawals from the CG, using the remaining 16 subjects in the CG for all data calculations.

Summary of internal validity: Taking just the TG and CG into account, randomization of the subjects, similarity of subjects at baseline, blinding of subjects and assessors to group allocation, similarity in treatment time and administration are strengths of internal validity for this study. The primary threats to internal validity include the lack of blinding of therapists, study losses and a small sample size. The lack of blinding of therapists is a minor threat since they treated the CG similarly to the other 3 treatment groups by telling subjects that they may or may not feel a tingling sensation during treatment. There was a study loss of 2 out of 34 subjects or 6% study loss. This is a minor threat since it is a small loss (< 15%). There was no mention of intention to treat analysis. Instead, all data presented did not take into account the 2 drop outs from the CG. The sample size is small (total n=66), with a range of 15 to 18 subjects per group. The study did not mention a power analysis to determine if there was enough power to detect differences with the sample size used in this study. This is a moderate threat because with a small sample size, there could have been a type II error, where a significant difference is not found when there is one. Overall, there are no major threats to internal validity.

Evidence: The authors reported statistically significant differences between pre- and post- treatment VAS scores within both the TG and the CG groups, but not between groups. All of the outcome measures between groups were analyzed using ANOVA for statistical significance, and then significant results were analyzed by post-hoc tests (least significant difference). The outcome measures I am interested in are the VAS scores pre- and post- treatment, after 10 sessions and at the 4 week follow up. Table 6 summarizes the data from the article, and the numbers are used to calculate the mean difference within groups in table 7. The effect size within groups cannot be calculated using normalized VAS scores. Normalized VAS scores are used for all calculations since raw VAS score data was not provided in the article. The VAS scores for each group were normalized to the values recorded before treatment in session 1 and presented as percentages.

Table 6: VAS scores (%) with standard deviation (SD); scores normalized to session 1 before treatment

	TG	CG
Session 1 before treatment	100.0±0	100.0±0
Session 1 after treatment	64.1±40.7	84.5±39.6
Session 10 after treatment	60.5±35.0	72.2±70.7
4 week follow up	51.5±32.9	67.9±78.6

Table 7: Mean difference for normalized VAS scores within groups with 95% confidence interval (CI)

	TG	CG
Session 1 pre- to post- treatment difference	35.9 (14.32 to 57.48)	15.5 (-5.50 to 36.50)
Session 1 pre- to session 10 post- treatment	39.5 (20.94 to 58.06)	27.8 (-9.69 to 65.29)
Session 1 pre- to 4 week follow up	48.5 (31.05 to 65.95)	32.1 (-9.58 to 73.78)

Since only normalized VAS scores are provided, comparisons using the mean difference to the MCID of 1.99 (on a 10cm scale) cannot be made. The mean difference within the TG after 1 session, 10 sessions and at the 4 week follow up are all positive, even with the 95% CI, which means there was some reduction in pain relief at each of those time points. However, without an MCID for normalized VAS scores for this population, it is unclear if these results are clinically important. The mean difference within the CG after 1 session, 10 sessions and at the 4 week follow up all have wide 95% CIs with negative lower limits, which means that the results could have been reversed with an increase in pain instead of pain relief if the study was repeated. No statistically significant differences were found between groups, so the mean differences and effect sizes between groups were not calculated. The results suggest that there could be a clinically important decrease in VAS score and hence pain relief after the first session, and after 10 sessions of TENS that is maintained up to 4 weeks after TENS treatment. However, there is no statistically significant difference in VAS scores between the TENS and placebo TENS groups, which suggest that TENS treatment may not be more effective than a placebo TENS treatment in pain reduction.

Applicability of study results:
Similarity to my patients: The subjects in this study are similar to my patient population in terms of age, inclusion and exclusion criteria. However, they were sampled from Hong Kong, and there could be a cultural difference between the Asian and Caucasian perception and rating of pain on the VAS. The baseline VAS score of subjects in the study was also not reported, so it is unknown if that criteria matches my clinical PICO.

Benefits vs. costs: The main cost is the time spent and the financial cost of TENS treatment for 60 minutes 5 times a week for 4 weeks (20 sessions). The benefit is immediate and long term pain relief up to 4 weeks after the end of 20 sessions of TENS treatment. With 10 sessions, the time and cost would be half as much, with a suggested clinically important improvement in pain as measured by the VAS score immediately after 10 TENS sessions. While the 10 sessions would be more cost effective and have similar immediate effects, it is not clear if similar long term pain relief 2-4 weeks after would occur.

Feasibility of treatment: TENS is a feasible treatment as most facilities have TENS units available and can be easily provided as a treatment to patients. The financial cost of 10 sessions of TENS treatment for 60 minutes each is also within reason to be covered by insurance. If the full 20 sessions were used as described in this study, it would still be within reason to be covered by insurance if the patient continues to show improvement in pain and function after each session. The protocol was described sufficiently in the article and can easily be reproduced in a clinical setting.

Summary of external validity: The subject sample is similar to the clinical population of interest, with the exception of culture differences that may affect pain perception and rating on the VAS scale. Also, they were sampled from only one hospital, and thus may be more difficult to generalize results to a wider population range including different ethnicities.

Synthesis/Discussion:

The purpose of this paper was to determine if TENS treatment was effective in pain relief in patients with severe knee OA. Both studies reviewed had blinded assessors and subjects, and a study loss of 6%. The PEDro score for the article by Law *et. al* (2004) was 8/10 and was 7/10 for the article by Cheing *et. al* (2002), with the difference being no mention of concealed allocation in the article by Cheing *et. al* (2002). Overall, both articles closely matched my clinical question. Both studies compared TENS treatment to placebo TENS treatment and used the VAS score as the pain measurement scale. I used the outcomes from both studies to answer my clinical question, with greater weight placed on the study by Law *et. al* (2004) because of the higher PEDro score and the fact that the population in the study by Cheing *et. al* (2002) had more differences from my clinical population.

Law *et. al* (2004) found a statistically significant improvement in pain in all 3 treatment groups across sessions but not in the placebo group. There was also a statistically significant improvement in pain between each of the 3 treatment groups and the placebo group. Only the 3 treatment groups had clinically important differences and large effect sizes within groups after 10 sessions and at the 2 week follow up for the first and second treatment groups. When comparing between the treatment groups and the placebo group, the mean differences between each of the 3 treatment groups to the placebo TENS group were greater than MCID after 10 sessions and at the 2 week follow up. Insufficient data was provided to calculate the 95% CI or effect sizes between groups. No clinically important differences were found between the 3 TENS groups. There is some suggestion of clinically important improvement in pain between TENS treatment to placebo TENS after 10 sessions and at the 2 week follow up, but no particular TENS parameters in the 3 groups was better than the other. Cheing *et. al* (2002) found statistically significant improvements in pain across sessions for both the TENS and placebo TENS groups, but not between groups. Only the TENS groups had a large improvement in VAS scores with wide 95% CI that stayed positive. Since only normalized VAS scores were provided, no comparisons could be made to the MCID.

In both studies, the comparison was TENS to placebo TENS, and did not include a comparison to no treatment. Clinically, one would decide between TENS and no treatment. The question of whether TENS treatment is effective in pain relief as compared to a true control group with no treatment remains unanswered, but if there is clinically important improvements in pain within a TENS treatment group and when compared to a placebo TENS group, I would be comfortable in making an assumption that TENS treatment is effective in pain relief.

The subject population in both studies were similar to my clinical population in terms of inclusion and exclusion criteria, with the exception that the study by Law *et. al* (2004) included some in an older age range and the study by Cheing *et. al* (2002) included subjects from Hong Kong. It is possible that in the Asian culture, they may have a different pain threshold affecting their perception and rating of pain on the VAS scale, which may have contributed to a lack of statistical significance between the TENS and placebo TENS groups. Overall, I would be comfortable generalizing the results of these 2 studies to a population including patients aged 50 - 85 years with at least grade II knee OA who are able to ambulate with or without an assistive device and who have a VAS score of 6/10 with activity.

The treatments were similar in frequency (5 times a week), but had slightly different parameters for the TENS treatment and duration. The TENS parameters are summarized in table 8. The placebo TENS was similar in both studies in that a real TENS unit was used, with the indicator light and all controls working, except the internal circuitry had been disconnected so there was no electrical output.

Table 8: Summary of TENS treatment parameters

TENS parameter	Law *et. al* (2004)			Cheing *et. al* (2002)
	Group 1	Group 2	Group 3	
Frequency	2 Hz	100 Hz	Alternating 2Hz for 2s and 100Hz for 2.5s	80 Hz
Pulse width	576 µs	200 µs	Alternating 576µs for 2s and 200µs for 2.5s	140 µs
Duration	40 minutes			60 minutes
Number of sessions	10 (5x/week for 2 weeks)			20 (5x/week for 4 weeks)

Both studies showed clinically important improvement in pain after 10 sessions and at a 2 or 4 week follow up within TENS groups, but only the TENS groups in the study by Law *et. al* (2004) showed a clinically important improvement in pain between the TENS groups to the placebo TENS group. Based on

the outcomes from both studies, I would recommend using 2 Hz and 576 μs or 100 Hz and 200 μs for 40 minutes 5 times a week for 2 weeks for pain relief in patients aged 50 – 85 years with knee OA. Since both studies used electrode placements on the knee acupuncture points, I would recommend following the protocol for placement of electrodes.

Recommendations for future research: Overall, both studies included a population similar to the clinical population of interest, had blinding of assessors and subjects, and described the TENS protocols well. However, insufficient raw data was provided for analysis, there was no mention of reliability or validity of the VAS score and small sample sizes were used. In future studies, I would recommend including a power analysis to determine the sample size, sampling from more than one facility, using a functional outcome such as the timed up-and-go test in addition to VAS scores and including reliability and validity for outcome measures used.

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