

Effect of Different Neuromuscular Electrical Stimulation Modalities on Clinical and Functional Outcomes in Older Adults with Knee Osteoarthritis: A Randomized Controlled Trial

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Introduction: Osteoarthritis (OA) is a chronic degenerative disease characterized by progressive cartilage degeneration, most commonly affecting the knee. Clinical symptoms such as pain, stiffness, and functional limitations significantly impact quality of life. Although neuromuscular electrical stimulation (NMES) is considered a complementary treatment, evidence comparing different waveforms in clinical management remains limited.

Objective: To compare the effects of three different NMES waveforms versus a placebo, applied for four weeks, on pain intensity, disability, and other functional outcomes in individuals with knee osteoarthritis (KOA).

Methods: A randomized clinical trial with 100 participants equally assigned to four groups: transcutaneous electric nerve stimulation (TENS) (n=25), interferential current (IFC) (n=25), Aussie current (n=25), and placebo (n=25). Primary outcomes were pain intensity, disability, and pressure pain threshold and secondary outcomes included aerobic capacity, gait speed, lower limb strength, functional mobility, superficial knee temperature, stability, and fall risk. Primary and secondary outcomes were assessed before and after four weeks.

Results: A significant group x time interaction, with a moderate effect size, was found for the WOMAC index ($P = 0.022$; $\eta^2 = 0.10$). Participants of the IFC, Aussie, and Placebo groups presented less disability after the treatment. No significant group x time interactions were observed for the other outcomes (all $P > 0.05$); however, a main effect of time was identified, with positive changes at week 4 in most variables, except for superficial knee temperature, stability, and risk of falls.

Conclusion: Different NMES protocols did not provide additional benefits over placebo for pain intensity, disability or functional outcomes in people with KOA. These findings highlight the need for further research to refine stimulation protocols and identify patient subgroups that may benefit most from NMES in the management of knee osteoarthritis.

Keywords: knee osteoarthritis, neuromuscular electrical stimulation, older adults

Introduction

Osteoarthritis (OA) is a chronic and degenerative disease characterized by the progressive degradation of cartilage and bone remodeling in synovial joints.^{1,2} Over time, it leads to changes in the physiological mechanisms of the joint, such as cartilage erosion, synovitis, and subchondral bone sclerosis.³⁻⁵ These structural changes result in clinical symptoms such as pain, stiffness, and functional limitations, significantly compromising quality of life, physical well-being, and the ability to perform daily activities.^{2,6}



It is estimated that approximately 240 million people worldwide live with symptomatic OA, making it one of the most prevalent conditions among older adults and women.⁷ The knee is one of the most commonly affected joints, with prevalence ranging from 7% to 35.1% in adults over 45 years of age.⁷ Major risk factors for the development of OA include advanced age, obesity, genetic predisposition, and metabolic alterations, all of which play a fundamental role in the pathogenesis of the disease.^{8,9}

Several studies have investigated the effects of different interventions to alleviate symptoms in these patients. Exercise is widely used due to its excellent cost-effectiveness.^{10–12} Both traditional exercise programs and those delivered online have been shown to improve pain, function, and quality of life.¹³ Neuromuscular electrical stimulation (NMES) has been considered as a complementary treatment for individuals with KOA, contributing to pain relief¹⁴ and increased muscle strength,¹⁵ especially when combined with exercise.¹⁶ This combination enhanced muscle strength of the quadriceps femoris, the primary dynamic stabilizer of the knee, compared to an active control group.¹⁷

Additional evidence reinforces its effectiveness in reducing pain, as measured by the Visual Analog Scale (VAS), when compared to a placebo group. Furthermore, the combination of NMES with other therapeutic approaches has proven to be superior to isolated interventions, not only in pain relief, but also in functional improvement, particularly in the medium and long term.¹⁸ An additional study revealed that a single NMES session was able to reduce pain inhibition and increase the distance covered in the 6-minute walk test in individuals with KOA.¹⁹

Different waveforms have been used to control pain in individuals with KOA, such as interferential current (IFC: 1–200 Hz burst frequency, 4000 Hz carrier frequency range), Aussie current (1–200 Hz burst frequency, 4000 Hz carrier frequency range), and transcutaneous electrical nerve stimulation (TENS: 1–200 Hz frequency range, 100–200 μ s),²⁰ have been used to manage chronic pain.^{21,22} TENS units have been widely used due to their low cost and ease of use and can serve as an independent treatment method.^{23,24} IFC and Aussie currents, however, deliver kilohertz-frequency alternating currents (KFAC), which pass through the tissues simultaneously and intersect with each other.²³ It has been claimed that KFAC in general decreases skin impedance, reducing the discomfort normally associated with low-frequency currents, although this assertion has been challenged.²⁵ However, an interesting systematic review with meta-analysis clearly demonstrated that both IFC (KFAC) and low-frequency current (TENS) are effective in reducing pain intensity and have similar effects on pain relief.²³

Despite the potential of different NMES waveforms in managing KOA, evidence remains limited.²⁶ Highlighted uncertainty regarding its effectiveness, citing inconclusive results due to small-scale RCTs with methodological flaws. Authors emphasize the need for rigorous, long-term RCTs to establish consistent clinical protocols,^{23,27,28} as methodological limitations hinder clinical applicability.²⁹ In addition, the effects of KFAC, such as Aussie and IFC currents, on pain management in KOA have only been demonstrated in an acute randomized clinical trial.³⁰ To address the need for RCTs evaluating the effects of NMES on KOA, the present study aimed to compare the effects of TENS, IFC, and Aussie currents on pain, disability, and pressure pain threshold in older adults with KOA, as well as their impact on gait, strength, mobility, knee temperature, postural stability and fall risk. We hypothesized that all NMES modalities would outperform placebo intervention in improving symptoms and function.

Methods

Trial Design

This is a randomized, double-blinded, parallel group, four-arm superiority clinical trial. The study was formed by four groups: (I) a group that received transcutaneous electrical nerve stimulation (TENS); (II) a group that received the interferential current (IFC); (III) a group that received the Aussie current; (IV) a group that received a Placebo intervention. Outcomes were assessed before (T0) and after 4-weeks of intervention (T1). Ethics approval was obtained by the Institutional Review Board of the Health Sciences Faculty, University of Brasilia (Approval number: 62256516.2.0000.0030), and all subjects signed a detailed consent form before entering the study. This research was prospectively registered at the Brazilian Registry of Clinical Trials (RBR-875zsw/ Date of registration: 11/24/2017) and reported in accordance with the CONSORT (Consolidated Standards of Reporting Trials).

Participants

Participants were recruited using advertisements within local clinics and hospitals located in the city of Brasília, Brazil. The trial was conducted at the Functional Performance Laboratory of the University of Brasília, Brasília, Brazil between March 2019 and August 2023. We included male and female participants aging 60 years or older with symptoms and radiographic evidence of knee osteoarthritis, confirmed by a minimum score of two on the Kellgren-Lawrence Scale. Additionally, to be included, participants had to experience pain with an intensity of 4 cm or higher on a 10-cm visual analog scale (VAS). Participants were excluded from the study if they had undergone physical therapy in the last three months, received knee injections in the last six months, had a history of hip, knee or ankle surgery in the last twelve months, had medical restrictions such as cardiorespiratory, neurological or rheumatological dysfunctions, or chronic conditions that caused knee pain.

Randomization and Allocation Concealment

Participants were randomized into experimental or placebo groups with an allocation ratio of 1:1:1:1 by means of block randomization (block size of 25) performed with the aid of a sequence of numbers generated on a computer using the website www.random.org. The allocation was hidden by means of opaque and sealed envelopes and numbered consecutively. One researcher generated the allocation sequence, hid the allocation, and allocated participants for interventions.

Blinding

One researcher collected data and performed all study assessments. A second researcher adjusted the parameters of the interventions for all groups. Finally, a third researcher applied and monitored the interventions in all groups. The equipment screen was covered by the second researcher; therefore, the researcher that applied the intervention, and the participants were blinded to group allocation.

Interventions

Protocol was conducted three times per week for four weeks across all groups. Participants were positioned supine with the upper and lower limbs extended. Group-specific parameters were: (I) TENS: 100 Hz pulse frequency, 200 μ s phase duration; (II) IFC: 100 Hz burst frequency, 4000 Hz carrier frequency (10 ms burst duration, 10 ms duty cycle interval), 125 μ s phase duration; (III) Aussie: 100 Hz burst frequency, 4000 Hz carrier frequency (4 ms burst duration, 16 ms duty cycle interval), 125 μ s phase duration; (IV) placebo: 100 Hz pulse frequency, 200 μ s phase duration. In the placebo group, the parameters were initially set to 100 Hz frequency and 200 μ s pulse duration, identical to the TENS group. However, to ensure proper blinding, the stimulation was delivered only for approximately 40 seconds, with a progressive decrease in intensity until it stopped completely. After that, no electrical current was delivered, but the device remained turned on and electrodes kept connected for the full session duration to mimic the experience of active treatment, as previous described.³¹ Self-adhesive electrodes (25 cm²) from two channels were placed around the patella: channel 1 near the medial femoral condyle and fibular head, and channel 2 on the lateral femoral condyle and medial tibial plateau. NMES was applied to the most affected knee for 20 minutes, with intensity gradually increased every 5 minutes to match the initial sensory threshold. Participants provided feedback to adjust intensity up to the maximum tolerable sensory threshold (Figure 1).

Outcomes

Initially, participants were screened to confirm eligibility. Participants' characteristics such as gender, age, body mass, height, body mass index, physical activity level, and personal history regarding surgery, prosthesis, and comorbidities were collected at the baseline assessment. Primary and secondary outcomes were measured at the baseline assessment and immediately after the four-week intervention period. Assessment was carried out for two days: day one included questionnaires, thermography, BIODEX and Pressure pain threshold and day two included physical measures.

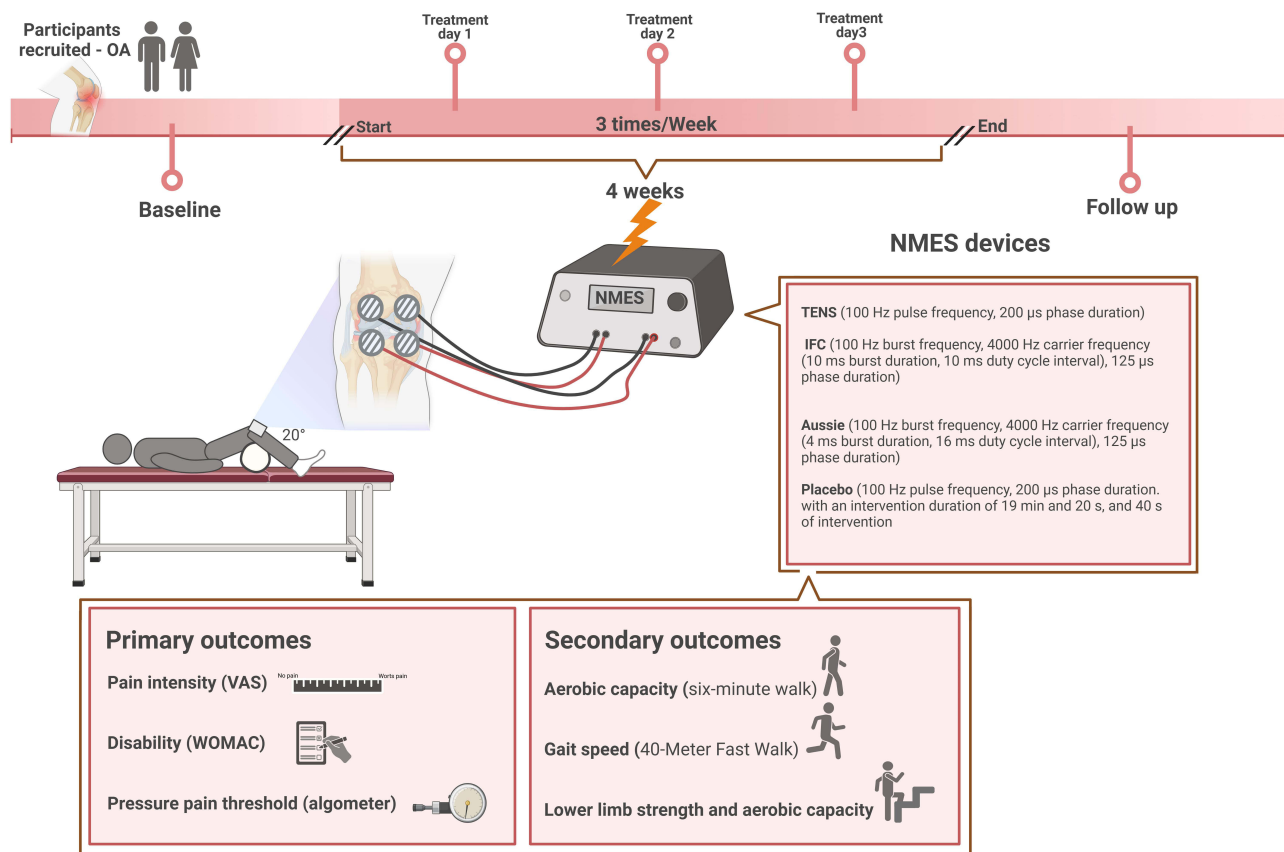


Figure 1 Study design.

Primary Outcomes

Pain Intensity

Pain intensity was assessed using a visual analogue scale (VAS), which consists of a numerical scale from 0 to 10 points, where 0 means no pain and 10 means the maximum pain ever experienced.³²

Pain, Stiffness and Physical Function

Disability was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire. This tool employs a 5-point Likert scale across three domains: pain, stiffness, and physical function. The pain domain (0–20) includes five questions on discomfort during activities such as walking on a flat surface, climbing stairs, nighttime pain in bed, sitting or lying down, and standing upright. The stiffness domain (0–8) consists of two questions, while the physical function domain (0–68) includes 17 questions. The total WOMAC index score (0–96) provides an overall measure of disability. Lower scores indicate less disability.³³

Pressure Pain Threshold

Pressure pain threshold was assessed using a pressure algometer (Kratos DDK, São Paulo, Brazil). Twelve points around the knee were assessed. (I) two cm below the medial epicondyle of the femur; (II) two cm below the lateral epicondyle of the femur; (III) two cm above the base of the patella; (IV) center of the patella; (V) one cm beyond the medial margin of the patella; (VI) one cm beyond the lateral margin of the patella; (VII) two cm below the medial margin of the patella; (VIII) two cm below the lateral margin of the patella; (IX) midpoint between the apex of the patella and the tibial tuberosity; (X) posterior region of the femoral epicondyle; (XI) five cm distal to the tuberosity of the lateral epicondyle; (XII) five cm distal to the tibial tuberosity. Three measurements at each point were performed, with a 1-minute rest between them, and the average of the 12 points was recorded for the analysis.³⁴

Secondary Outcomes

Aerobic Capacity

The six-minute walk test was also used to assess aerobic capacity. The test was conducted on a flat, straight, 20-meter corridor marked with cones at both ends. Participants were instructed to walk as fast as possible for six minutes at a self-selected pace, with the option to slow down or stop if necessary. Standardized verbal encouragement was provided at regular intervals. A single trial was performed, and the total distance walked in meters was used in the analysis. Higher distance indicates better aerobic capacity.³⁵

Gait Speed

The 40-Meter Fast Walk Test was used to assess gait speed. The test was conducted on a flat, straight, 40-meter corridor marked with cones at both ends. Participants were instructed to walk a total distance of 40 meters as fast as possible while maintaining a safe and controlled pace. Standardized verbal encouragement was provided at regular intervals. A single trial was performed, and the total time to complete the task was recorded in seconds for the analysis. Lower time to perform the test indicate higher gait speed.³⁶

Lower Limb Strength and Aerobic Capacity

The stair test was used to assess lower limb strength and aerobic capacity. Participants ascended and descended an 11-step stairway (17 cm per step) as quickly as possible. Use of the handrail for support was optional. A single trial was performed, and the total time to complete the task (from the bottom to the top and back down) was recorded in seconds for the analysis.¹⁹

Lower Limb Strength

The 30-Second Chair Stand Test (30CST) was used to assess lower limb strength. Participants began seated in a chair without armrests, with their arms crossed over their chest. They were instructed to stand up and sit down as many times as possible within 30 seconds. A repetition was counted only if the participant fully extended their hips and knees before returning to the seated position.³⁷ Three trials were performed, with a 1-minute rest between each. The total number of repetitions was recorded, and the average of the three trials was used in the analysis.

Functional Mobility

Timed Up and Go (TUG) test was used to assess functional mobility. Participants began seated in a chair without armrests and were instructed to stand up, walk 3 meters, turn around, return to the chair, and sit down. Three trials were performed, with a 1-minute rest between each. The time to complete the task was recorded in seconds, and the average of the three trials was used for the analysis.³⁵

Superficial Knee Temperature

Superficial knee temperature was measured using a real-time thermal thermometer with a 640 x 480-pixel resolution, sensitivity of 0.08°C and an accuracy of $\pm 2^\circ\text{C}$ for absolute temperature measurements (Flir C2™, Wilsonville, Oregon, USA). Superficial knee temperature was measured as a surrogate for knee surface inflammation.^{38,39} Three images were captured from the lateral, medial, and frontal regions of the knee using a specific software (FLIR Thermal Studio Suite™, Wilsonville, Oregon, USA). The average temperature from these three images was used in the analysis.³⁸

Postural Stability and Fall Risk

Biodex Balance System (Biodex Medical Systems, Inc., Shirley, NY, USA) was used to assess postural stability and fall risk. This system features a dynamic platform with adjustable stability levels, allowing for the evaluation of balance control under varying conditions. Participants performed standardized balance tests while standing on the platform, and postural sway was quantified using stability indices. Global Stability Index (GSI), which reflects overall postural stability, was calculated based on the anterior-posterior stability index (APSI) and medial-lateral stability index (MLSI). The Risk of Falls Index (RFI) was derived by comparing each participant's GSI to age-matched normative data from the Biodex database.⁴⁰ Higher GSI values indicate greater postural instability, while higher RFI values suggest an increased risk of falls.

Data Analysis and Sample Size

Data were analyzed using SPSS (Statistical Package for the Social Sciences) version 25.0. Descriptive statistics consisted in means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Data normality was tested using the Shapiro–Wilk test. One-way ANOVAs were used to compare the general characteristics across study groups. Between-group differences (treatment effects) and their 95% confidence intervals (CIs) were calculated using two-way ANOVAs (parametric data) or Generalized Estimated Equations (GEE) (non-parametric data). The groups (TENS × IFC × Aussie × Placebo) were used as the independent factor, time (T0 × T1) as the repeated factor, and the primary and secondary outcomes as dependent variables. Bonferroni's post hoc test was applied for pairwise comparisons. A significance level of $p < 0.05$ was used for all analyses. Effect sizes were determined using partial eta-squared (η^2). Values of $\eta^2 > 0.01$ were defined as small, $\eta^2 > 0.06$ as medium, and $\eta^2 > 0.14$ as large.⁴¹ Cohen's d (d) was used for the pairwise comparisons. Values of $d = 0.2$ were defined as small, $d = 0.5$ as medium, and $d = 0.8$ as large.⁴¹ An intention-to-treat analysis was performed for all randomized participants. Subgroup analyses were not performed. The sample size was calculated based on the mean score on the VAS for pain intensity, previously reported for a similar population of KOA patients (8.10 ± 1.23 cm).¹⁴ An assumption was made that a clinically significant change in VAS scores would have to correspond to 30% of the total value, and a significance level of 0.01 and 95% power were adopted. These criteria led to an estimated minimum sample size of 25 in each group.¹⁹

Results

Recruitment and Baseline Data

From a total of 166 participants assessed for eligibility, 100 were recruited and randomly assigned for one of the four study groups between March 2019 and August 2023. Four participants from TENS group, four from IFC group, five from Aussie group 3, and six from placebo group 4 did not complete the intervention and declined to attend the post-intervention assessments. The recruitment process and follow-up are described in the consort flow diagram (Figure 2).

Clinical characteristics of the participants can be seen in Table 1. In general, participants were women (88%) with a mean age of 68.02 ± 5.45 years, height of 1.55 ± 0.07 m, weight of 73.04 ± 10.92 kg, and a BMI of 30.20 ± 4.74 kg/m². Most participants had not undergone knee surgery (95%), did not have associated comorbidities (99%), and did not use prostheses (99%). It is important to note that knee surgeries performed more than 12 months prior to the start of the study, as well as prostheses in regions other than the knee joint, were permitted. Additionally, 31% of participants were classified as physically active at the beginning of the study. No significant between-group differences were found across the groups for the general characteristics ($P > 0.05$) (Table 1).

Regarding the baseline values of both primary and secondary outcomes, significant between-group differences, with a large effect size, were found only for the pressure pain threshold ($P = 0.006$, $\eta^2 = 0.13$), and for the 40-meter fast walk test ($P = 0.001$, $\eta^2 = 0.16$). No real differences were found for the pressure pain threshold ($P > 0.05$). Participants allocated to the TENS group demonstrated a significantly shorter distance, with a large effect size, in the 40-meter fast walk test compared to the AUSSIE group (mean difference = -9.74 , 95% CI -15.92 to -3.56 , $P < 0.001$, $d = 1.09$) (Table 2).

Primary Outcomes

No significant group × time interactions were found for pain intensity ($P = 0.398$; $\eta^2 = 0.05$), pain ($P = 0.562$; $\eta^2 = 0.03$), stiffness ($P = 0.547$; $\eta^2 = 0.03$), and physical function ($P = 0.799$; $\eta^2 = 0.01$) dimensions of the WOMAC questionnaire, and pressure pain threshold ($P = 0.858$; $\eta^2 = 0.21$). A time effect was found for all these outcomes ($P < 0.05$) with positive changes at week 4.

A significant group × time interaction, with a moderate effect size, was found for the WOMAC index ($P = 0.022$; $\eta^2 = 0.10$). Participants of the IFC (mean difference = 21.00 , 95% CI = 13.69 to 28.32 , $P < 0.001$, $d = 1.15$), Aussie (mean

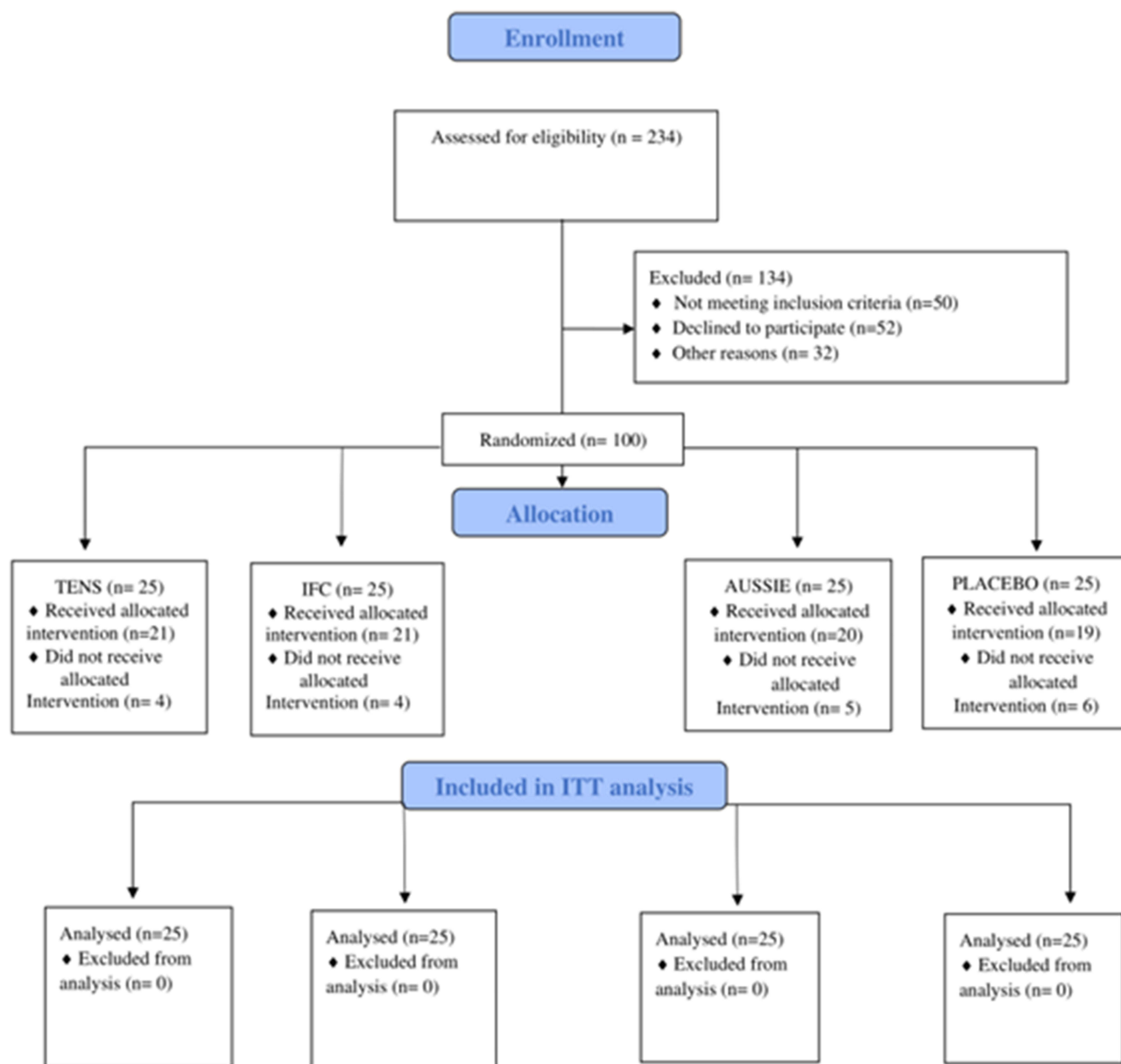


Figure 2 Flow diagram of the study.

difference = 8.37, 95% CI = 1.06 to 15.69, $P = 0.025$, $d = 0.42$), and Placebo (mean difference = 9.94, 95% CI = 2.62 to 17.25, $P = 0.08$, $d = 0.70$) groups presented less disability after the treatment (Table 3).

Secondary Outcomes

No significant group \times time interaction was found for the six-minute walk test ($P = 0.609$; $\eta^2 = 0.036$), forty-meter fast walk test ($P = 0.149$; $\eta^2 = 0.58$), stair test ($P = 0.679$; $\eta^2 = 0.17$), thirty second chair stand test ($P = 0.768$; $\eta^2 = 0.058$) and timed up and go test ($P = 0.864$; $\eta^2 = 0.029$). A time effect was found for all these outcomes ($P < 0.05$) with positive changes at week 4 (Table 4). Additionally, no significant group \times time interactions were found for the superficial knee temperature ($P = 0.920$; $\eta^2 = 0.007$), biodex balance global stability index ($P = 0.722$; $\eta^2 = 0.061$), and in the biodex balance risk of falls index ($P = 0.249$; $\eta^2 = 0.041$) (Table 4).

Table 1 Baseline Participants Characteristics (n=100)

	TENS (n=25)	IFC (n=25)	AUSSIE (n=25)	SHAM (n=25)	P*
Demographics					
Sex					
Male	3 (12%)	4 (16%)	4 (16%)	1 (4%)	0.518
Female	22 (88%)	21 (84%)	21 (84%)	24 (96%)	
Age, years	67.48 ± 5.35	67.68 ± 5.25	68.56 ± 5.06	68.36 ± 6.32	0.829
Weight, kg	74.50 ± 11.76	74.71 ± 12.69	71.42 ± 11.38	71.63 ± 7.41	0.584
Height, m	1.57 ± 0.07	1.55 ± 0.07	1.56 ± 0.08	1.55 ± 0.07	0.258
Body Mass Index, kg/m ²	29.91 ± 4.31	30.85 ± 5.08	29.59 ± 5.57	30.46 ± 4.08	0.634
Physical activity level – IPAQ					
Very active	6 (24%)	5 (20%)	6 (25%)	4 (16%)	0.140
Active	7 (28%)	11 (44%)	7 (29,2%)	6 (24%)	
Irregularly active	5 (20%)	6 (24%)	5 (20,8%)	9 (36%)	
Sedentary	7 (28%)	3 (12%)	6 (25%)	6 (24%)	
Personal History					
Surgery					
No	24 (96%)	23 (92%)	23 (92%)	25 (100%)	0.510
Yes	1 (4%)	2 (8%)	2 (8%)	0 (0%)	
Prosthesis					
No	25 (100%)	24 (96%)	25 (100%)	25 (100%)	0.387
Yes	0 (0%)	1 (4%)	0 (0%)	0 (0%)	
Comorbidities					
No	8 (32%)	13 (52%)	15 (60%)	9 (36%)	0.518
Yes	17 (68%)	12 (48%)	10 (40%)	16 (64%)	

Notes: Data presented as count and percentage or mean ± standard deviation. *Group effect – P < 0.05.

Abbreviation: IPAQ, International Physical Activity Questionnaire.

Table 2 Baseline Primary and Secondary Outcomes (n=100)

Outcomes	TENS (n=25)	IFC (n=25)	AUSSIE (n=25)	SHAM (n=25)	P*
Primary outcomes					
Pain intensity	8.28 ± 1.54	8.32 ± 1.43	7.95 ± 1.73	7.79 ± 1.79	0.660
WOMAC					
Pain, 0–20	11.78 ± 3.04	9.83 ± 3.35	10.00 ± 3.85	9.80 ± 3.47	0.140
Stiffness, 0–8	2.68 ± 2.83	2.52 ± 2.25	3.44 ± 2.55	3.08 ± 2.41	0.490
Physical function, 0-68	26.80 ± 12.50	30.88 ± 14.83	28.04 ± 14.40	28.28 ± 11.62	0.571
Index, 0-96	41.00 ± 18.39	47.16 ± 19.62	45.04 ± 17.93	44.24 ± 14.86	0.672
Pressure Pain threshold, Kgf	5.28 ± 1.96	5.29 ± 2.03	4.03 ± 1.14	4.05 ± 1.51	0.006*
Secondary outcomes					
Six-minute Walk test, m	393.28 ± 45.77	389.45 ± 47.28	390.29 ± 70.76	395.21 ± 48.72	0.977
Forty-meter fast walk test, s	33.63 ± 6.67 ^a	38.77 ± 6.98	43.38 ± 10.79 ^a	39.73 ± 6.89	0.001*
Stair test, s	80.29 ± 21.50	74.51 ± 23.41	77.76 ± 20.47	77.94 ± 16.46	0.813
Thirty seconds chair stand test, n	8.44 ± 2.97	8.28 ± 3.14	7.36 ± 2.70	7.24 ± 2.22	0.118
Timed up and go, s	14.27 ± 2.97	13.12 ± 2.97	13.98 ± 2.85	13.51 ± 2.98	0.278
Superficial knee temperature, °C	30.54 ± 1.72	30.62 ± 1.54	30.56 ± 1.54	30.64 ± 1.69	0.997
Global stability index, °	2.51 ± 1.31	2.47 ± 1.25	3.06 ± 1.47	2.20 ± 1.21	0.164
Risk of falls index, °	1.40 ± 0.70	1.26 ± 0.59	1.49 ± 0.67	1.42 ± 0.67	0.575
Pain-free range of motion, °	154.60 ± 12.41	153.11 ± 14.42	156.67 ± 9.43	156.91 ± 12.10	0.910

(Continued)

Table 2 (Continued).

Outcomes	TENS (n=25)	IFC (n=25)	AUSSIE (n=25)	SHAM (n=25)	P*
SF-36					
Functional Capacity, 0-100	43.96 ± 17.39	38.14 ± 19.64	36.08 ± 17.71	41.60 ± 18.18	0.439
Limitations, 0-100	34.00 ± 36.71	22.00 ± 34.09	25.00 ± 28.86	32.00 ± 37.16	0.514
Pain, 0-100	35.32 ± 19.98	32.61 ± 26.85	37.49 ± 32.31	37.19 ± 23.28	0.907
General health, 0-100	53.25 ± 25.47	41.71 ± 21.69	41.96 ± 25.22	46.47 ± 25.69	0.312
Vitality, 0-100	59.90 ± 28.11	60.13 ± 24.28	51.56 ± 33.34	48.60 ± 30.60	0.396
Social aspects, 0-100	77.12 ± 35.23	70.66 ± 29.40	88.04 ± 27.69	69.47 ± 38.84	0.229
Emotional Aspects, 0-100	61.42 ± 41.69	55.41 ± 45.95	57.61 ± 59.66	71.91 ± 45.92	0.666
Mental health, 0-100	69.74 ± 24.11	73.81 ± 21.64	74.44 ± 32.77	56.35 ± 37.97	0.393

Notes: Data presented as mean ± standard deviation. *Group effect – P < 0.05; ^aBetween-group differences – P < 0.05.

Abbreviations: WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; SF-36, Short Form Health Survey-36.

Table 3 Treatment Effects on the Primary Outcomes (n=100)

Outcomes	TENS (n=25)	IFC (n=25)	AUSSIE (n=25)	SHAM (n=25)	P*	η ²
Clinical aspects						
Pain intensity, 0-10						
T0	8.28 ± 1.54	8.32 ± 1.43	7.95 ± 1.73	7.79 ± 1.79	0.398	0.05
T1	4.02 ± 1.86	3.04 ± 2.29	3.57 ± 1.67	3.79 ± 2.83		
WOMAC						
Pain, 0-20						
T0	11.78 ± 3.04	9.83 ± 3.35	10.00 ± 3.85	9.80 ± 3.47	0.562	0.03
T1	5.96 ± 3.80	4.98 ± 3.08	4.54 ± 3.64	5.93 ± 3.77		
Stiffness, 0-8						
T0	2.68 ± 2.83	2.52 ± 2.25	3.44 ± 2.55	3.08 ± 2.41	0.547	0.03
T1	1.84 ± 2.06	1.66 ± 1.76	1.71 ± 2.24	1.30 ± 2.04		
Physical function, 0-68						
T0	26.80 ± 12.50	30.88 ± 14.83	28.04 ± 14.40	28.28 ± 11.62	0.799	0.01
T1	23.00 ± 11.71	24.50 ± 12.01	24.26 ± 14.99	19.46 ± 13.20		
Index, 0-96						
T0	41.00 ± 18.39	47.16 ± 19.62 ^a	45.04 ± 17.93 ^a	44.24 ± 14.8 ^a	0.022*	0.10
T1	35.84 ± 20.16	26.79 ± 15.69 ^a	37.31 ± 18.77 ^a	32.17 ± 19.5 ^a		
Pressure Pain threshold, Kgf						
T0	5.28 ± 1.96	5.29 ± 2.03	4.03 ± 1.14	4.05 ± 1.51	0.858	0.21
T1	5.85 ± 1.77	5.65 ± 2.15	4.92 ± 1.68	4.52 ± 2.20		

Notes: Data presented as mean ± standard deviation. *Group × time interaction – P < 0.05. ^aWithin-group differences – P < 0.05.

Abbreviations: T0, Baseline; T1, week 4; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 4 Treatment Effects on the Secondary Outcomes (n=100)

Outcomes	TENS (n=25)	IFC (n=25)	AUSSIE (n=25)	SHAM (n=25)	P*	η ²
Six-minute Walk test, m						
T0	393.28 ± 45.77	389.45 ± 47.28	390.29 ± 70.76	395.21 ± 48.72	0.609	0.03
T1	423.88 ± 40.76	417.025 ± 62.49	400.14 ± 67.17	402.98 ± 58.77		
Forty-meter fast walk test, s						
T0	33.63 ± 6.67	38.77 ± 6.98	43.38 ± 10.79	39.73 ± 6.89	0.149	0.58
T1	32.17 ± 6.42	35.21 ± 8.17	39.79 ± 9.82	37.86 ± 8.01		
Stair test, s						
T0	80.29 ± 21.50	74.51 ± 23.41	77.76 ± 20.47	77.94 ± 16.46	0.679	0.17
T1	64.20 ± 17.89	64.40 ± 23.94	67.28 ± 20.66	67.43 ± 19.13		

(Continued)

Table 4 (Continued).

Outcomes	TENS (n=25)	IFC (n=25)	AUSSIE (n=25)	SHAM (n=25)	P*	η^2
Thirty seconds chair stand test, n						
T0	8.44 ± 2.97	8.28 ± 3.14	7.36 ± 2.70	7.24 ± 2.22	0.768	0.05
T1	10.46 ± 3.11	9.99 ± 3.31	8.01 ± 4.39	8.83 ± 3.12		
Timed up and go, s						
T0	14.27 ± 2.97	13.12 ± 2.97	13.98 ± 2.85	13.51 ± 2.98	0.864	0.02
T1	12.70 ± 3.23	12.03 ± 4.13	11.89 ± 2.27	11.54 ± 2.62		
Superficial knee temperature, °C						
T0	30.54 ± 1.72	30.62 ± 1.54	30.56 ± 1.54	30.64 ± 1.69	0.920	0.007
T1	30.66 ± 1.32	30.64 ± 2.15	30.80 ± 1.83	31.01 ± 1.76		
Biodex global stability index, °						
T0	2.51 ± 1.31	2.47 ± 1.25	3.06 ± 1.47	2.20 ± 1.21	0.722	0,06
T1	2.29 ± 1.11	2.47 ± 1.60	2.46 ± 0.87	1.85 ± 0.74		
Biodex risk of falls index, °						
T0	1.40 ± 0.70	1.26 ± 0.59	1.49 ± 0.67	1.42 ± 0.67	0.249	0,04
T1	1.36 ± 0.85	1.43 ± 0.70	1.26 ± 0.92	1.04 ± 0.94		
Pain-free range of motion, °						
T0	154.60 ± 12.41	153.11 ± 14.42	156.67 ± 9.43	156.91 ± 12.10	0.678	0.06
T1	163.80 ± 12.01	161.00 ± 11.30	164.51 ± 12.44	160.91 ± 9.72		
Quality of life – SF 36						
Functional Capacity, 0-100						
T0	43.96 ± 17.39	38.14 ± 19.64	36.08 ± 17.71	41.60 ± 18.18	0.604	0.21
T1	49.61 ± 22.96	46.41 ± 26.33	45.25 ± 25.60	54.09 ± 20.64		
Limitation, 0-100						
T0	34.00 ± 36.71	22.00 ± 34.09	25.00 ± 28.86	32.00 ± 37.16	0.519	0.01
T1	47.99 ± 31.49	57.36 ± 41.96	47.81 ± 42.59	56.13 ± 41.80		
Pain, 0-100						
T0	35.32 ± 19.98	32.61 ± 26.85	37.49 ± 32.31	37.19 ± 23.28	0.091	0.07
T1	39.42 ± 23.71	50.54 ± 26.12	42.49 ± 29.98	34.99 ± 30.02		
General health, 0-100						
T0	53.25 ± 25.47	41.71 ± 21.69	41.96 ± 25.22	46.47 ± 25.69	0.949	0.004
T1	51.26 ± 18.42	41.51 ± 21.84	41.51 ± 27.90	44.74 ± 28.08		
Vitality, 0-100						
T0	59.90 ± 28.11	60.13 ± 24.28	51.56 ± 33.34	48.60 ± 30.60	0.909	0.006
T1	60.53 ± 21.34	64.30 ± 26.69	51.05 ± 30.25	57.51 ± 26.58		
Social aspects, 0-100						
T0	77.12 ± 35.23	70.66 ± 29.40	88.04 ± 27.69	69.47 ± 38.84	0.111	0.06
T1	77.96 ± 27.65	81.19 ± 29.61	80.01 ± 27.34	89.01 ± 23.54		
Emotional Aspects, 0-100						
T0	61.42 ± 41.69	55.41 ± 45.95	57.61 ± 59.66	71.91 ± 45.92	0.513	0.05
T1	57.53 ± 42.29	73.01 ± 53.36	66.34 ± 43.76	64.81 ± 40.97		
Mental health, 0-100						
T0	69.74 ± 24.11	73.81 ± 21.64	74.44 ± 32.77	56.35 ± 37.97	0.113	0.11
T1	67.89 ± 24.55	73.42 ± 24.12	54.46 ± 31.84	68.06 ± 33.65		

Notes: Data presented as mean ± standard deviation. T0, Baseline; T1, week 4; SF-36, Short Form Health Survey-36. *Group x time interaction – P < 0.05.

Discussion

To our knowledge, this is one of the few studies comparing the effects of different NMES modalities on pain intensity, disability, and pressure pain threshold in individuals with KOA over four weeks, as well as investigating their impacts on aerobic capacity, gait speed, lower limb strength, mobility, superficial knee temperature, stability and fall risk through different functional tests. Both IFC and Aussie groups showed significant improvements in the WOMAC index after treatment, suggesting that these interventions contributed to functional recovery. However, similar results were observed

in the placebo group, indicating that NMES, when applied alone, may not be superior to a placebo intervention. Given that 4-weeks of treatment using NMES did not outperform placebo treatment, this study does not suggest that it has an important short-term effect when compared with a placebo control, as a non-pharmacological treatment for people with KOA.

Extensive experimental research on the mechanisms of IFC and Aussie currents for pain management is lacking, with claims often extrapolated from TENS studies. Our findings, with a mean difference of approximately four to five-points in the VAS scale, indicate that the experimental conditions, met the minimum detectable change for knee pain (-1.99) on the VAS pain intensity.⁴² Pain is not merely a direct consequence of tissue injury, but rather the result of complex interactions between sensory, cognitive, emotional, and contextual inputs within the central nervous system. Pain is influenced by individual expectations, prior experiences, emotions, memories and environmental cues.⁴³ Therefore, we suggest that the improvement seen in the NMES, and placebo groups may be explained in part by the neuromatrix theory of pain presented above, especially for the expectations in the allocated treatment.⁴³⁻⁴⁵

Also, participants in our study reported significant levels of pain at the baseline assessment. It can be hypothesized that participants were experiencing a period of symptom exacerbation. Consequently, the improvements noted at the second assessment in four groups could, at least in part, reflect a regression to the mean phenomenon.⁴⁶ Lastly, pain levels are closely associated with arthrogenic muscle inhibition (AMI) of the quadriceps femoris in patients with KOA.⁴⁷ The NMES intensity was set at the sensory threshold, which might have been insufficient for meaningful analgesic effects, as higher intensities are often linked to better pain relief.^{22,48} Also, previous studies have shown that TENS applied for forty and sixty-minutes promoted higher improvements in pain intensity when compared to this same current delivered only for 20 minutes (our protocol) in patients with KOA.⁴⁹ It is therefore plausible that the intensity and duration of NMES applied in the intervention groups were insufficient to elicit meaningful motor-level contractions capable of overcoming AMI. As a result, the stimulation may not have produced a neuromuscular response robust enough to promote greater improvements in pain and functional performance when compared to the placebo condition.

Despite intensity and duration, another aspect that may have influenced the results was the lack of combination with proper exercise. Our study may not have demonstrated a significant difference compared to a Placebo group because NMES was not applied alongside exercise. No significant functional differences at the end of treatment regarding pain intensity, gait speed, and disability, with mean differences between groups below clinically relevant thresholds were found in a study that compared NMES alone to a placebo group for three weeks.⁵⁰ The combination of NMES with other interventions yielded significant improvements in pain intensity and disability in KOA patients, with positive effects observed in the short, medium, and long term.^{18,27} This suggests that the beneficial effects of NMES may surpass those of a placebo intervention when combined with another approach, such as exercise, highlighting the potential synergistic effects of multimodal strategies in KOA management.

No significant improvements were found in aerobic capacity, gait speed, lower limb strength, functional mobility, superficial knee temperature, postural stability and fall risk. These results are consistent with a recent systematic review and meta-analysis, which indicated that NMES applied alone did not improve functional outcome in the 6MWT in individuals with KOA undergoing surgical procedures.⁵¹ Also, our hypothesis is supported for a different study,⁵² which observed improvements in functional performance, as assessed by the ST, TUG, and 6MWT tests, in the group treated with NMES combined with functional activities versus a group that received isolated NMES. These results suggest that combining NMES with other interventions may enhance therapeutic effects not only in pain intensity, but also, in outcomes related to functional performance.

Our findings are particularly relevant given the high prevalence of KOA and its potential to trigger the development of other conditions, such as metabolic syndromes induced by immobilization, which are associated with cardiovascular diseases, recognized factors in determining population mortality.⁵³ Scientific and clinical implications can be formulated based on the results of this study. NMES programs applied in isolation do not show superior results compared to placebo. As evidenced by previous studies,^{14-16,18,27,52} NMES combined with other interventions has the potential to optimize functional performance and promote significant improvements in the quality of life of individuals with KOA, contributing to physical recovery and increased autonomy in daily activities.

Some limitations of this study must be highlighted. Individuals with comorbidities associated with KOA were included in the study, which may have influenced the results, especially regarding pain intensity and pressure pain threshold. The diversity of these conditions may have generated individual variabilities in the response to treatment, impacting the interpretation of the effects. Additionally, the 20-minute duration of NMES therapy may have been insufficient to detect potential chronic effects of the intervention, limiting the generalization of findings in the long term.²² The inclusion of movement-evoked pain (MEP) as a measurement could significantly enhance the understanding of NMES effects KOA.⁵⁰ Unlike pain at rest, MEP reflects the pain experienced during functional activities, such as walking or other movements, and is driven by distinct mechanisms.⁵⁴ Incorporating MEP into the study would allow for a more comprehensive assessment of NMES, particularly regarding pain during movement, which is often more disabling for patients with KOA than static pain. The use of painkillers and other prescribed treatments was not controlled. This may have introduced variability in pain and function outcomes, potentially confounding treatment effects. Future randomized controlled trials should improve the protocol used and investigate the long-term results with appropriate follow-up periods. Also, it is important to explore how individual variables influence treatment responses.

Conclusion

Neuromuscular electrical stimulation, using different modalities (TENS, IFC, and Aussie), did not demonstrate superiority over placebo for pain intensity, disability, pressure pain threshold, gait parameters, strength, mobility, knee temperature, postural stability, and fall risk over a four-week period in individuals with knee osteoarthritis (KOA). Although the IFC and Aussie modalities promoted improvements in the WOMAC index with moderate effect sizes, similar improvements were also observed in the placebo group, suggesting that these results are not superior to the placebo effect. Future research should investigate optimized NMES parameters, extended intervention durations, and combined therapies to enhance effectiveness.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of University of Brasília (protocol code CAAE 62256516.2.0000.0030). Written informed consent has been obtained from the patient(s) to publish this paper.

Data Sharing Statement

The data will be made available by the corresponding author upon reasonable request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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