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SYSTEMATIC REVIEW

The effects of neuromuscular electrical stimulation on strength, pain, and function in individuals with knee osteoarthritis: a systematic review with meta-analysis

Efeitos da estimulação elétrica neuromuscular na força, dor e função em indivíduos com osteoartrite de joelho: uma revisão sistemática com meta-análise

Efectos de la electroestimulación neuromuscular sobre la fuerza, el dolor y la función en personas con osteoartritis de la rodilla: una revisión sistemática con metaanálisis

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ABSTRACT | We aimed to investigate the effects of neuromuscular electrical stimulation on muscle strength, pain relief, and improvement in function in patients with knee osteoarthritis. Databases were searched from December 2017 to July 2020 and included PubMed, Embase, LILACS, and the Cochrane Central Register of Controlled Trials. A manual search was also performed by checking the reference lists of eligible articles. The PRISMA guidelines were followed. The studies selected compared NMES with an exercise program on isometric muscle strength as a primary outcome. The secondary outcomes were pain and function. The quality of the studies was assessed using the Risk of Bias assessment and PEDro scale, and the overall quality of the evidence was assessed using the GRADE approach. Eight studies were included in this systematic review. A total of 571 patients were analyzed. Neuromuscular electrical stimulation associated with exercise promoted an increase in isometric strength of the quadriceps muscle compared to the active control group, demonstrating heterogeneity and statistical difference (95% CI=1.16 to 5.10, I2=97%, p=0.002; very low-certainty evidence). NMES associated with exercise did not improve physical function (95% CI=−0.37 to 0.59, I2=0%, p=0.67; low-certainty evidence) and showed controversial results for pain compared to an active control group (qualitative assessment). In conclusion, NMES induces an increase in muscle strength in patients with osteoarthritis compared to an active control group. No differences were found for physical function and pain outcomes. Further research is needed due to the uncertain level of evidence.

Keywords | Electrical Stimulation; Isometric Contraction; Pain; Osteoarthritis; Physiotherapy.

RESUMO | O objetivo deste estudo foi investigar os efeitos da estimulação elétrica neuromuscular (EENM) na força muscular, alívio da dor e melhora da função em pacientes com osteoartrite de joelho. Realizou-se uma pesquisa em diferentes bases de dados, como PubMed, Embase, LILACS e o *Cochrane Central Register of Controlled Trials,* no período de dezembro de 2017 até julho de 2020. Procedeu-se a uma busca manual com o intuito de verificar as listas de referências dos artigos elegíveis. As diretrizes PRISMA foram seguidas. Os estudos selecionados comparavam a estimulação elétrica neuromuscular com um programa de exercícios de força muscular isométrica como desfecho primário. Os resultados secundários foram dor e função. A qualidade dos estudos foi avaliada usando avaliação de risco de viés e a escala PEDro e a qualidade geral das evidências foi avaliada usando a abordagem GRADE. Oito estudos foram incluídos nesta

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revisão sistemática com um total de 571 pacientes analisados. A EENM associada ao exercício promoveu o aumento da força isométrica do músculo quadríceps em relação ao grupo controle ativo, demonstrando heterogeneidade e diferença estatística (IC 95%=1,16 a 5,10, I2=97%, p=0,002; evidência de muito baixa certeza), mas não melhorou a função física (IC 95%=−0,37 a 0,59, I2=0%, p=0,67; evidência de baixa certeza) e mostrou resultados controversos para dor em comparação ao grupo de controle ativo (avaliação qualitativa). Conclui-se que a EENM induz o aumento da força muscular em pacientes com osteoartrite, porém não foram encontradas diferenças nos resultados de funcionalidade e dor em comparação com o grupo de controle ativo. Devido à incerteza das evidências, são necessárias mais pesquisas sobre o assunto.
Descritores | Estimulação Elétrica; Contração Isométrica; Dor; Osteoartrite; Fisioterapia.

RESUMEN | El objetivo de este estudio fue analizar los efectos de la electroestimulación neuromuscular (NMES) sobre la fuerza muscular, el alivio del dolor y la mejora de la función en pacientes con osteoartritis de la rodilla. Se realizó una búsqueda en las bases de datos PubMed, Embase, LILACS y *Cochrane Central Register of Controlled Trials*, en el periodo de diciembre de 2017 y julio de 2020. Se llevó a cabo una búsqueda manual para verificar las listas de referencias de los artículos elegibles. Se aplicó las pautas PRISMA. Los estudios seleccionados compararon la electroestimulación neuromuscular con un programa de ejercicio de fuerza muscular isométrica como resultado primario. Los resultados secundarios fueron el dolor y la función. La calidad de los estudios se evaluó mediante la evaluación del riesgo de sesgo y la escala PEDro, y la calidad general de la evidencia se estimó con el uso del sistema GRADE. Ocho estudios con un total de 571 pacientes compusieron esta revisión sistemática. La EENM asociada con el ejercicio aumentó la fuerza isométrica del músculo cuádriceps en comparación con el grupo control activo, demostrando una heterogeneidad y diferencia estadística (IC 95%=1,16 a 5,10, I2=97%, p=0,002; evidencia con muy baja seguridad), pero no mejoró la función física (IC 95%=−0,37 a 0,59, I2=0%, p=0,67; evidencia con baja seguridad) y mostró resultados controvertidos para el dolor en comparación con el grupo control activo (evaluación cualitativa). Se concluyó que la EENM indujo un aumento de la fuerza muscular en pacientes con osteoartritis, pero no se encontraron diferencias en los resultados de función y dolor en comparación con el grupo control activo. Debido a la incertidumbre de la evidencia, se necesitan más estudios sobre el tema.
Palabras clave | Estimulación Eléctrica; Contracción Isométrica; Dolor; Osteartritis; Fisioterapia.

INTRODUCTION

Knee osteoarthritis is currently the leading cause of lower-limb disability among older adults[1] and is mostly related to aging and the increased obesity in the global population[2]. Clinical symptoms and functional limitations found in knee osteoarthritis have been associated with muscle weakness, physical disabilities, stiffness, articulation deformities, crepitation, and decreased range of motion[3]. Exercise therapy has been widely recommended to control pain, increase quadriceps femoris strength, and improve the functional capacity of patients with knee osteoarthritis[4]. Neuromuscular electrical stimulation (NMES) is a therapeutic tool which is commonly used as an alternative to resistance exercise for this population[5-7]. The primary reason for using NMES in clinical practice is to provide an increase in muscle strength, improving performance in functional activities of individuals with osteoarthritis [8-10]. The use of NMES associated with an exercise program showed more significant gains in muscle strength when compared to exercise alone[11-12]. However, there is a lack of evidence demonstrating the effects of NMES alone on muscle strength gains, particularly related to improving functional capacity in situations when exercise is not indicated for these patients[12-14].

Previous systematic reviews have demonstrated conflicting results regarding the effectiveness of NMES in knee osteoarthritis [12,15,16]. Giggins, Fullen, and Coughlan[17] showed inconsistent evidence regarding the impact of NMES on measures of pain, function, and quadriceps femoris muscle strength in knee osteoarthritis. However, according to another review[18], this systematic review presents some bias, since non-randomized trials were included, and the risk of publication bias was not assessed, which downgraded the evidence level. Another systematic review[9] showed moderate evidence in favor of NMES alone or combined with exercise for isometric quadriceps strengthening in older adults with osteoarthritis. However, the authors also did not assess pain[9] and function[9,16]. Finally, new trials have updated the literature regarding the use of NMES for knee osteoarthritis, demonstrating improvement in muscle strength, reduction in pain, and increased physical function[14,15,19-21]. Among these studies, two showed no

difference in muscle strength and function after NMES treatment[15,20,21]. Due to these conflicting results regarding the clinical application of NMES, a systematic review and meta-analysis of randomized controlled trials was conducted to clarify the effects of NMES treatment versus an exercise program to promote an increase in muscle strength and function and a reduction in pain in subjects with knee osteoarthritis.

METHODOLOGY

Protocol and registration

Our systematic review and meta-analysis was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for systematic reviews of randomized controlled trials[22]. The study selection process included checking for duplicates, evaluating inclusion criteria, screening of titles, and reading of abstracts and full text (PROSPERO Registration Number: CRD42017082146, accessed at https://www.crd.york.ac.uk/PROSPERO/).

Eligibility criteria

We included randomized controlled trials that compared individuals with knee osteoarthritis submitted to isolated or exercise-associated NMES with active (any exercise program) control individuals for the outcomes of muscle strength, pain, and function. The primary outcome assessed was isometric muscle strength, evaluated by MVC (maximal voluntary contraction) at baseline and follow up treatments. The secondary outcomes were pain, evaluated by the Western Ontario and McMaster universities arthritis index (WOMAC), and function, evaluated by the timed up and go (TUG) test.

Search

The search was performed by two independent reviewers, and at the end of the search, a consensus was established. In case of disagreement, a third reviewer was consulted, and a consensus was reached through discussion. A bibliographic search was conducted, without restrictions on language, from December 2017 to July 2020, in the following electronic databases: PubMed, Embase, LILACS, PEDro, and Cochrane Central Register of Controlled Trials (CENTRAL). A manual search was also performed by checking the reference lists of eligible articles.

The search terms were selected according to the guidelines for Medical Subject Headings (MeSH) of the United States National Library of Medicine (NLM) as follows: "Osteoarthritis" OR "Arthritis" OR "Osteoarthritis of the knee" AND "Electrical Stimulation" OR "Neuromuscular Electrical Stimulation" OR "Electrical Stimulation Functional" OR "Electric Stimulation Therapy" OR "Electric Stimulation Therapy" OR "NMES" OR "FES" OR "EMS" AND "Muscle force" OR "Muscle-strengthening" AND "Pain" OR "Control Pain" AND "Physical Function" OR "Function". These terms were combined in each database.

Data collection process

Two authors were responsible for evaluating the studies for inclusion, assessing methodological quality with the PEDro scale[23], and extracting data. One author was responsible for the final review. Continuous variables were extracted as mean and standard deviation, when available. The authors were contacted to clarify any doubts regarding missing data; however, only one author answered the questions. The following data were analyzed: publication year, sample size, age and sex of the subjects, pulse duration, frequency, duty cycle, electrode size and intensity, volume, and duration of treatment with NMES. One study[15] presented values of muscle strength in kg/f normalized by body weight. We normalized the data in Nm using the following formula: Kg/f × bodyweight × 9.8. Considering these conversions, all studies that included the analysis of muscle strength were analyzed using the same unit of measure.

PEDro scale

The PEDro scale was used to evaluate the methodological quality of the selected studies[23]: (1) eligibility criteria; (2) subjects were randomly allocated to groups; (3) allocation was concealed; (4) the groups were similar at baseline regarding the most important prognostic indicators; (5) all subjects were blinded; (6) all therapists were blinded; (7) all assessors were blinded; (8) measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to the groups; (9) all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least

one key outcome were analyzed by "intention to treat"; (10) the results of between-group statistical comparisons are reported for at least one key outcome; (11) the study provides both point measures and measures of variability for at least one key outcome. Each item was checked as "yes (1)" or "no (0)", and only the final ten items were scored, providing a scale of 0 to 10, with higher scores reflecting higher quality studies.

Risk of bias

We assessed the risk of bias, including the following items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each item was classified as high, low, or unclear risk of bias. Different opinions between the reviewers were resolved through discussion, including a third independent reviewer when necessary.

Quality of evidence

The overall quality of the evidence was rated in accordance with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)[24], with five domains: (1) Study design and risk of bias; (2) Inconsistency; (3) Indirectness; (4) Imprecision; and (5) Other factors. The quality of the evidence was classified as High: when there were consistent results in at least 75% of the trials of good methodological quality, presenting consistent, direct, and precise data with no suspicious or known publication bias; Moderate: when at least one domain was not met; Low: when two of the domains were not met; Very low: when three domains were not met, the results are highly uncertain[25].

Statistical analysis

Data from each study were converted into mean differences (95%) between groups (NMES associated with exercise versus active control) using fixed and random effects models. The statistical heterogeneity of the data was determined by the I^2 test and interpreted according to the suggestion[25], which considers values above 25 and 50% as moderate and high heterogeneity, respectively. The results considered for analysis were isometric muscular strength of the quadriceps, knee pain, and physical function. A p-value <0.05 was considered significant. All analyses were performed using Review Manager Software, version 5.2.

RESULTS

Eight of 23,215 articles met all inclusion criteria and detailed data extraction was performed (Figure 1). The majority of the articles were excluded because they were not related to the research topic, and a few because they were duplicates. There was complete agreement between reviewers concerning inclusion. The characteristics of all studies and parameters of NMES are shown in Table 1. In total, 571 patients with a diagnosis of knee osteoarthritis were evaluated in the eight studies included in this review. Six included trials[6,7,14,15,19,21] that assessed isometric muscle strength. Pain was evaluated using the WOMAC questionnaire in three of the trials[5,6,14] and function was assessed using the TUG test in four of the trials[7,15,20,21].

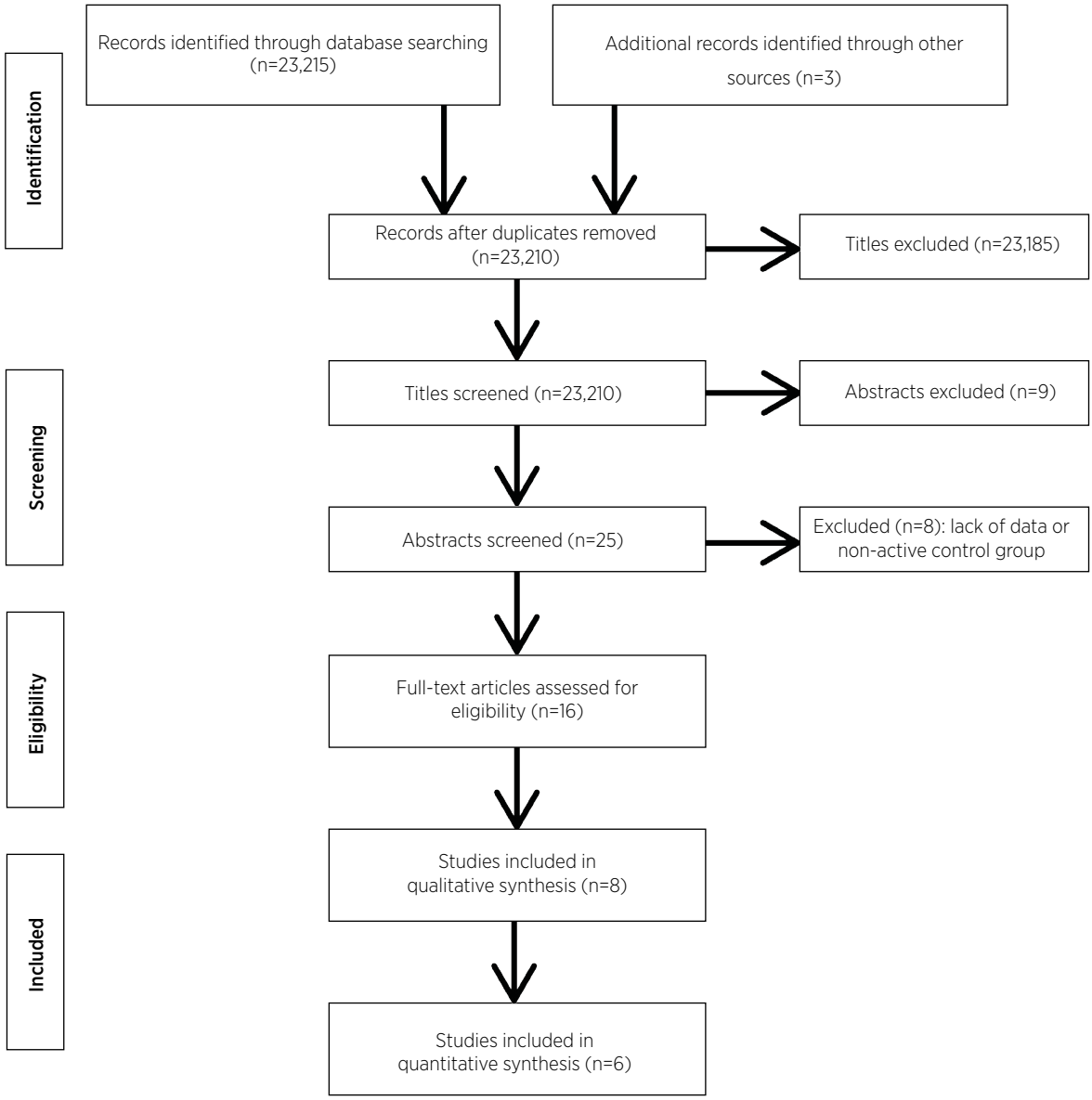

Figure 1. Flowchart of the literature review process

Table 1. Characteristics of the studies

Author (Year)	Sample (n)	Age (Mean)	Pulse (μs)	F (Hz)	Cycle duration	Electrode size (cm)	Intensity (mA)	Duration of TTO	Outcomes	Evaluation	Results
Park and Hawangbo[19] (2015)	NMES: 10; CON: 10	NMES: 68.2; CON: 68.4	400	80	25% (5 seconds/20 seconds)	Not mentioned	MIT	8 weeks	Muscle strength	MVC	Positive effect for NMES
Laufer et al.[15] (2014)	NMES: 25; CON: 25	NMES: 68.3; CON: 69.4	Not mentioned	Not mentioned	10 contractions	Not mentioned	MIT	12 sessions	Muscle strength/ Function	MVC/ WOMAC and TUG	There was no difference between groups

(continues)

Table 1. Continuation

Author (Year)	Sample (n)	Age (Mean)	Pulse (μs)	F (Hz)	Cycle duration	Electrode size (cm)	Intensity (mA)	Duration of TTO	Outcomes	Evaluation	Results
Imoto et al.[20] (2013)	NMES: 50; CON: 50	NMES: 60.6; CON: 58.7	250	50	20 minutes	7.5cm/13cm	MIT	8 weeks	Function	TUG	There was no difference between groups
Bruce-Brand et al.[14] (2012)	NMES: 10; CON: 6	NMES: 63.9;CON: 65.2	100-400	50	20 minutes	Not mentioned	MIT	6 weeks	Muscle strength/ Function/ Pain	MVC/ WOMAC/ WOMAC	Positive effect for NMES
Elboim Gabyzon et al.[21] (2013)	NMES: 25;CON: 25	NMES: 68.3;CON: 69.4	200	75	10 contractions	Not mentioned	100	6 weeks	Muscle strength/ Function/	MVC/ WOMAC and TUG	There was no difference between groups
Petterson et al.[7] (2009)	NMES: 100; CON: 100	NMES: 65.3; CON: 65.2	Not mentioned	50	10 contractions	7cm×12cm	30% MVC	6 weeks	Muscle strength / Function	MVC/ TUG	There was no difference between groups
Durmus et al.[5] (2007)	NMES: 25; CON: 25	NMES: 54.7; CON: 54.6	200	50	20 minutes	Not mentioned	70-120	4 weeks	Function/ Pain	WOMAC/ WOMAC	Positive effect for NMES
Rosemffet et al.[6] (2004)	NMES: 8; CON: 10	Total: 60	Not mentioned	25Hz	30 minutes	Not mentioned	60-80	8 weeks	Muscle strength/ Function	MVC/ WOMAC	Positive effect for NMES

F: frequency; Size: size; AVS: analog visual scale; WOMAC: Western Ontario and McMaster University Osteoarthritis index; CON: control group; NMES: neuromuscular electrostimulation; TUG: Time Up and Go; MIT: maximum intensity tolerated; TTO: treatment; MVC: maximum voluntary contraction; MR: magnetic resonance; Ma: milliamperes.

Neuromuscular electrical stimulation protocol

The studies demonstrated variations in the methods and physical parameters, especially in frequency, pulse duration, and training cycle. The frequency varied from 25 to 80Hz with a pulse width of 100 to 400μs, and the duty cycle ranged from 10 to 18 contractions for every 30 minutes of application. Of these parameters, the most frequently used randomized controlled trials were 50 Hz, 400μs, and ten elicited contractions (Table 1).

In most studies, the intensity of the stimulation elicited was established by the maximum intensity tolerated by the patients. The total duration of training ranged from 4 to 12 weeks. None of the studies mentioned any familiarity or current intensity adjustments due to sensory habituation.

Methodological quality assessment

The total scores of the articles on the PEDro scale (Table 2) ranged from 4 to 8 points, with a mean score of 5.5. Most of the studies used hidden allocation and presented similarity in baseline characteristics. Two studies reported blinding of the intervention for the therapist. Most of the studies used the monitoring and variability reports of the subjects. All studies used sample allocation and presented similarity in the initial characteristics. Some studies performed follow-up, and all presented variability reports. All studies reported differences between group.

Table 2. Methodological quality of included articles (PEDro scale)

Author (Year)	Sample allocation	Hidden allocation	Similarity at baseline	B.S.	B.T.	B.EV.	>85% of accompaniment	Analysis ITT	Difference between groups	Point of variability	T
Park and Hawangbo[19] (2015)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Laufer et al.[15] (2014)	Yes	Yes	Yes	No	Yes	No	No	No	Yes	Yes	6

(continues)

Table 2. Continuation

Author (Year)	Sample allocation	Hidden allocation	Similarity at baseline	B.S.	B.T.	B.EV.	>85% of accompaniment	Analysis ITT	Difference between groups	Point of variability	T
Imoto et al.[20] (2013)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Bruce-Brand et al.[14] (2012)	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes	5
Elboim-Babyzon et al.[21] (2012)	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5
Petterson et al.[7] (2009)	Yes	No	Yes	No	Yes	No	No	Yes	Yes	Yes	6
Durmus et al.[5] (2006)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Rosemffet et al.[6] (2004)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4

ITT: intent to treat; B.EV.: blindness of the evaluators; B.T.: blindness of the therapists; B.S.: blindness of the subjects; T: total points.

The risk of bias (Figure 2) evaluation revealed outcome assessment and participant and researcher blinding as the most prevalent biases, corresponding to approximately 75% of the selected studies for both criteria. The absence of a description of allocation concealment was also present in 75% of the studies. Random sequence generation was observed in 50% of the selected studies. All included studies presented a low risk of bias concerning selective reporting, and 70% concerning incomplete outcome data.

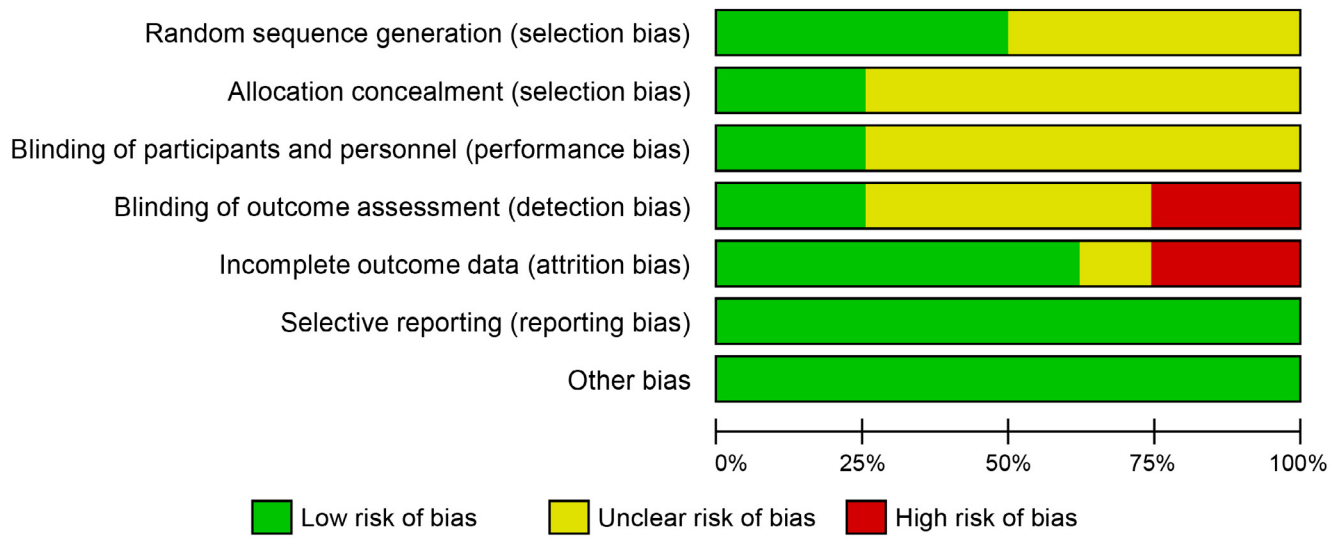

Figure 2. Risk of bias assessment

Isometric Muscle Strength – maximal voluntary contraction baseline and follow up

One study was excluded from the analysis because it presented only mean values[7]. Therefore, four studies were included[6,15,19,21]. Of these, two[15,21] found no differences between groups, and the other two[6,19] showed positive effects for NMES associated with exercise. The statistical analysis demonstrated heterogeneity and statistical difference, affirming that NMES associated with exercise is more effective than an active control group (3.13, CI 1.16 to 5.10, I^2=97%; with very low-certainty evidence) (Figure 3). One trial[14] was not included in the quantitative analysis because it compared NMES alone versus the active control group. In the qualitative analysis, there were no differences between groups for increasing isometric strength.

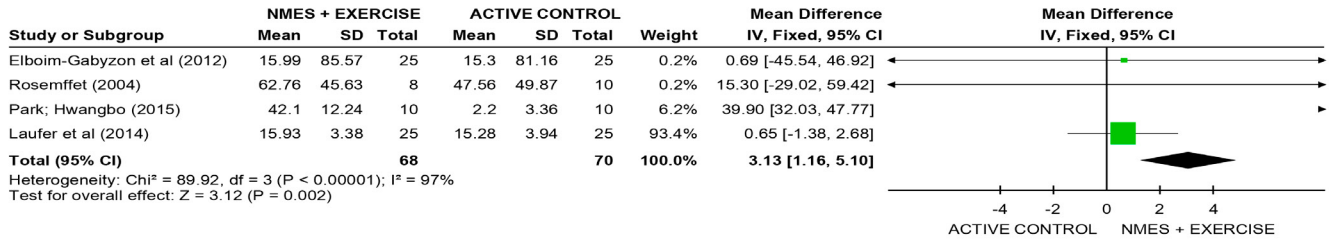

Figure 3. Comparison between NMES associated with exercise versus the active control group for isometric muscle strength

Pain – Western Ontario and McMaster universities arthritis index

The WOMAC pain quantitative analysis was not assessed since only two studies included[5,14] this questionnaire; therefore, herein, we describe the qualitative aspects. In total 66 patients were evaluated and compared NMES alone versus active control. One study[5] showed improvements in WOMAC pain scores in both groups, and the other trial[14], controversially, observed improvement in the score, between week one and week 8, only for the NMES group. One study[6] that compared NMES with exercise versus active control was excluded from this analysis because it did not present consistent values.

Physical function – timed up and go test

Four studies[5,15,20,21] were included in the analysis; qualitatively, they showed no differences between groups. The statistical analysis demonstrated homogeneity and no statistical difference between NMES with exercise or the active group (0.11, CI −0.37 to 0.59, I^2=0%; with low-certainty evidence) (Figure 4).

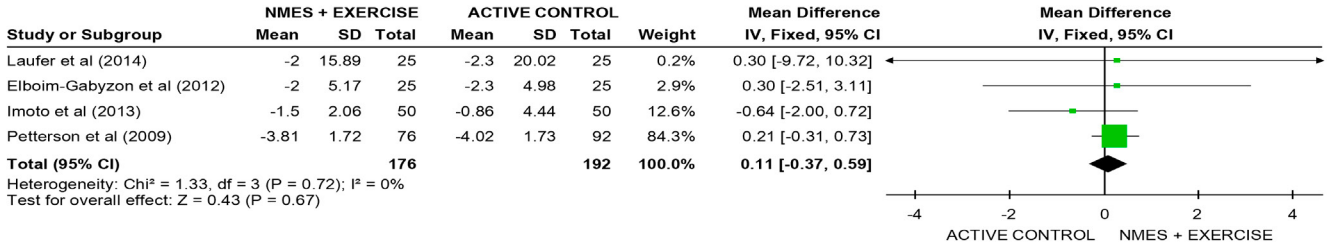

Figure 4. Comparison between NMES associated with exercise versus the active control group for Physical Function – TUG

DISCUSSION

This systematic review and meta-analysis present current evidence regarding the use of NMES alone and associated with exercise in the treatment of patients with knee osteoarthritis. Six of the included studies evaluated the effects of NMES on isometric muscular strength[6,7,14,15,19,21]. Of these, five compared NMES associated with exercise versus exercise alone and some studies did not show favorable effects in qualitative analyses[6,7,15,19,21]. However, the statistical analysis with four studies[6,15,19,21] demonstrated that NMES associated with exercise is more effective than an active control group. One trial that compared therapy with NMES alone versus non-active control, presented favorable benefits for increased muscular strength[26]. The positive results reported by these studies corroborate the data from this analysis since the positive effects of treatment with NMES for increasing strength can only be viewed when comparing NMES versus the control group. However, other studies showing favorable effects of NMES were not included in this review due to methodological criteria, such as a trial[27] that compared the use of NMES versus laser therapy and showed beneficial results in favor of the treatment with NMES. Although one systematic review[9] reported a moderate effect in favor of NMES, the diversity of methods of the studies, as described by the authors, was also an attenuating factor. Regarding joint angle of stimulation, even though optimal torque production occurs between 40° and 60°[28], only three studies positioned the knee at 60°[5,7,14], while two positioned the knee at 90°[19,20] and the remaining studies did not provide this information[6,15,21].

Secondary outcomes of pain and physical function demonstrated no precise results in this systematic review. The unfavorable results for outcomes of pain

and function differed from the findings of Giggins, Fullen, and Coughlan[17]. However, the authors present inconclusive evidence as to the use of NMES for these outcomes. The statistical analysis performed in the same review showed a significant difference in the reduction in pain and improvement in physical function. Since the majority of the studies in this review included male and female individuals in their sample, and since the self-report of chronic pain is more frequent in female patients[20], it is believed that these facts may add bias in the final interpretations.

The statistical analysis did not demonstrate improvement in physical function. A possible explanation for this result is that improvement in physical capacity may also be linked to improvement in pain, and this benefit was also not measured. Regarding the functional domain of the WOMAC, frequency of applications per week and total time of treatment seem to be important factors, considering that the only study that did not find a statistical difference in function performed the treatment three times a week for four weeks[12], whereas the other two carried out higher total[14] and per week frequencies of treatment[5]. Considering the TUG, even though individual improvements were found, these improvements were not maintained after statistical analysis. It is also important to emphasize that the TUG is not recommended for use as the only measurement for function evaluation and should be performed with other measurements[29].

Unfortunately, developing NMES protocols for this specific population based on the published literature is a challenge. There are differences in the parameters used in trials related to the choice of electrode size, evoked torque, and intensity of current using NMES. Most of the trials[5,7,14,20] used 50Hz as the frequency. A recent guideline proposed the performance of NMES in clinical settings using a frequency of more than 50Hz but no more than 75Hz and a pulse duration between 200 and 400μs for increasing quadriceps femoris strength and decreasing pain in adult patients with knee osteoarthritis [16]. In addition, electrode size and intensity parameters also showed large variability. Only four studies specified the electrode size[7,14,19,30]. Standardization of the electrode size is essential since small electrodes increase the density and lead to a more painful sensation, while larger electrodes stimulate antagonistic muscles and increase the response to the evoked torque[31].

The intensity of training with NMES has been increasingly considered as the key parameter for controlling the dosage of the intervention[17,29]. Four out of eleven trials performed therapy with the highest intensity tolerated[11,13,30,32]. Evidence indicates that the greater the intensity of treatment with NMES, the greater the effectiveness of therapy in impaired muscles[33,34]. In addition to using NMES at the maximum tolerated intensity, training performed at 30% to 40% of maximal voluntary isometric contraction (MVIC) may demonstrate an increase of 29% to 43% in the activation area of the quadriceps femoris muscle[35]. For strengthening with resistance exercises, previous meta-regressions indicate that increased knee extensor strength of 30% is necessary to achieve a significant beneficial effect on pain and physical function[36]. Likewise, only three trials[7,14,19] performed treatment based on this parameter. Some studies have reported that the force evoked by NMES is dependent on the increased intensity, where the deepest motor units are recruited[37].

Finally, a qualitative analysis of the PEDro and Risk of bias showed that none of the selected studies performed a double or triple-blind methodology. Since non-blind studies generally have more significant effect sizes, smaller values of p, and a greater frequency of significant results, none of the studies demonstrated the effect of the sample size and appropriate blinding. In five studies, the authors did not describe how the confidentiality of the allocation list was maintained[5-7,14,19] and did not describe the eligibility criteria correctly. Only two studies[14,20] included blinded evaluators for at least one outcome. According to the GRADE rating, the evidence was rated as very low-quality for muscle strength, downgraded by the risk of bias, inconsistency, and imprecision, since three studies did not report whether there was random allocation[6,15,19] and one of the included studies reported no blinded procedure[15]. The quality of evidence was low for physical function, downgraded by the risk of bias and imprecision, since two studies did not report whether there was random allocation[7,15], and three of the included studies did not report any blinding[7,15,20]. In addition, the inconsistency statistics showed heterogeneity of 97% for muscle strength (Figure 2) and homogeneity (0%) for physical function (Figure 3), and all the comparisons were below the optimal information size.

Some limitations arise due to the research strategy chosen to identify clinical studies. It is likely that some studies published in local databases might not have been included in this review. Moreover, the parameters used by studies to evaluate the effectiveness of NMES were heterogeneous, making it difficult to compare outcomes between studies, which may have influenced the results.

CONCLUSION

In conclusion, current evidence suggests that NMES associated with exercise, compared to an active control group, increased isometric muscle strength of quadriceps muscle in patients with knee osteoarthritis, with very low-certainty evidence. Additionally, NMES did not alter pain or physical function (low-certainty evidence) on the WOMAC questionnaire when associated with exercise. However, due to the limited number of high-quality studies, high heterogeneity between outcome measurements, and an insufficient description of the NMES parameters in most of the studies, the pertinence of this result is still limited. Clinicians should consider the benefits of NMES for patients with knee osteoarthritis for improvements in quadriceps isometric strength. This recommendation could be changed based on future and better-quality clinical trials.

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