

Effects of Noninvasive Electrostimulation on Symptoms of lower Limb Peripheral Arterial Disease: a Systematic Review

Ana Paula Ferreira,¹ Ana Flávia Ferreira,¹ Plínio dos Santos Ramos,^{2,3} Thiago Casali Rocha,² Djalma Rabelo Ricardo²

Universidade Federal de Minas Gerais,¹ Belo Horizonte, MG – Brazil

Faculdade de Ciências Médicas e da Saúde de Juiz de Fora,² Juiz de Fora, MG – Brazil

Faculdade de Ciências Médicas de Três Rios,³ Três Rios, RJ – Brazil

Abstract

Background: Peripheral arterial disease (PAD) is primarily characterized by intermittent claudication (IC), a symptom resulting from insufficient oxygen supply to skeletal muscles during physical activity. IC manifests as discomfort in the lower limbs during exertion due to muscle ischemia and is typically relieved by rest.

Objectives: To evaluate the effects of noninvasive electrostimulation on walking distance and claudication-related pain in individuals with lower limb PAD.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. Clinical trials published in English, Portuguese, or Spanish were selected from the MedLine, PEDro, and SciELO databases up to December 2024. The search strategy was guided by the PICO framework, using descriptors related to “peripheral artery disease,” “intermittent claudication,” and “noninvasive electrostimulation.” Studies were included if they involved human participants diagnosed with PAD and presenting with Fontaine stage II intermittent claudication.

Results: Seven clinical trials involving a total of 314 participants (mean age: 66.8 ± 3.6 years) were included. Four types of noninvasive electrostimulation were identified: neuromuscular electrical stimulation (NMES), transcutaneous electrical nerve stimulation (TENS), functional electrical stimulation (FES), and electroacupuncture. Most studies reported that electrostimulation improved both pain-free and maximum walking distances, as well as reduced claudication symptoms.

Conclusion: Noninvasive electrostimulation appears to be a promising adjunctive therapy for individuals with peripheral arterial disease, offering potential benefits in symptom relief and walking capacity. Given its safety, low cost, and ease of application, this intervention may serve as a practical strategy to complement traditional treatment approaches. However, further high-quality clinical trials are needed to establish standardized protocols and optimize clinical outcomes.

Keywords: Peripheral Arterial Disease; Intermittent Claudication; Electrostimulation; Transcutaneous Electrical Nerve Stimulation.

Introduction

The main symptom of peripheral arterial disease (PAD) is intermittent claudication (IC),¹ which results from an insufficient oxygen supply to skeletal muscles during activity.² IC is characterized by discomfort in the lower limbs during physical exertion due to muscle ischemia, which subsides with rest.²⁻⁶ It is associated with gait alterations, reduced functional capacity,⁷ and a decline in quality of life among individuals with PAD.⁸

Regular exercise, whether performed in supervised programs or at home, is recommended and has shown positive outcomes in enhancing functional capacity in people with

PAD.⁶ Clinical trials and meta-analyses^{3-6,9} have demonstrated that supervised exercise programs effectively improve IC symptoms and increase walking distance. Among the many benefits of exercise, the most notable are improved muscle adaptation, enhanced oxidative capacity, reduced reliance on anaerobic glycolysis, and decreased lactate accumulation.¹⁰

The most current physical exercise recommendation for the treatment of IC is walking at an intensity close to the point of symptom limitation, performed three times per week for at least thirty minutes. A duration of eight weeks is sufficient to observe improvements in the functional capacity of these individuals.¹⁰ While walking is the most recommended and effective modality for reducing claudication symptoms, other forms of exercise, such as modified aerobic training,¹¹ resistance training,¹² and warm-water exercise therapy,¹³ have also been employed and have shown positive results in individuals with PAD.

Although the benefits of exercise therapy are well established, many individuals with IC remain inactive and show low adherence to supervised training programs.¹⁴ In one study, after a three-month follow-up, only 16% of patients

Mailing Address: Ana Paula Ferreira •

Department of Physical Therapy, Universidade Federal de Minas Gerais (UFMG).

Postal Code: 31310-250, Av. Presidente Carlos Luz, 6627, Pampulha, Belo Horizonte, MG – Brazil

E-mail: anaferreira.ufmg@gmail.com

Manuscript received April 15, 2025; revised manuscript July 14, 2025; accepted September 8, 2025.

Editor responsible for the review: Gláucia Oliveira

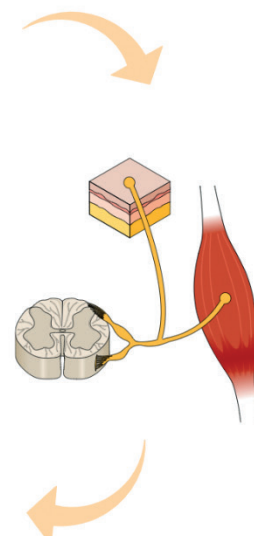
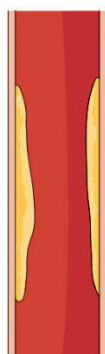
DOI: <https://doi.org/10.36660/ijcs.20250047>

Central Illustration: Effects of Noninvasive Electrostimulation on Symptoms of lower Limb Peripheral Arterial Disease: a Systematic Review

Mechanisms and clinical benefits of TENS in PAD: synthesis based on a systematic review of clinical trials

PAD is a condition caused by stenosis of peripheral arteries, mainly in the lower extremities, and is predominantly associated with atherosclerosis.

The mechanism of action is based on the gate theory of pain control, by the stimulation of neurotransmitters and their receptors and segmental and descending inhibition.



- ↑ Pain-free walking distance
- ↓ Claudication-related pain
- ↑ Functional walking capacity

Int J Cardiovasc Sci. 2025; 38:e20250047

with IC continued participating in an unsupervised walking program.¹⁵ One of the main reasons for this low adherence is the requirement to walk at an intensity close to moderate or maximum claudication symptoms.¹⁶ Given the challenge of implementing a treatment that induces discomfort in individuals with PAD, noninvasive electrostimulation has emerged as a safe and low-cost alternative for improving physical performance in this population (Central Illustration).¹⁴

Noninvasive electrostimulation therapies are typically delivered through transcutaneous nerve stimulation, in which electric currents are applied via electrodes placed on the skin. The resulting stimulus directly affects peripheral mechanoreceptors.¹⁷ Studies in experimental models^{18,19} have shown that low-frequency noninvasive electrostimulation promotes increased circulatory activation, enhances mitochondrial enzymatic activity, and improves the oxidative capacity of type I muscle fibers.²⁰

The technique may also contribute to the acute delay of claudication, as it is associated with the inhibition of muscle sympathetic activity. The effects produced by electrostimulation are similar to those of endogenous opioids²¹ and are closely linked to increased capillary density, enhanced resistance to fatigue, and improved oxygen uptake in ischemic muscles.^{20,22-24}

Given the strong external validity of this therapy as an adjunctive approach to reducing intermittent claudication in individuals with PAD, the aim of the present study was to evaluate, through a systematic review, the effects of noninvasive electrostimulation on walking distance and claudication-related pain in individuals with lower limb PAD.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology.²⁵

Literature search strategy

The literature search was independently performed by two researchers and completed in December 2024. No restrictions were applied regarding the publication period. The primary database used for identifying relevant studies was MedLine. Additionally, the SciELO and PEDro databases were consulted using the same keywords applied in the MedLine search. References from selected articles were also reviewed to identify studies not captured through the database search.

Descriptors and their synonyms, as defined by the Medical Subject Headings (MeSH), were used to

construct the search phrase. In accordance with Item 4 of the PRISMA methodology, which refers to PICO systematization, the following keywords were considered: P (Population): “peripheral artery diseases”; I (Intervention): “transcutaneous electrical stimulation”; C (Comparison): “electrostimulation” AND “functional electrical stimulation”; O (Outcome): “intermittent claudication”.

Inclusion, exclusion, and evaluated outcome criteria

We selected human clinical trials published in English that examined the effects of noninvasive electrostimulation in individuals with PAD and stage II IC according to the Fontaine classification. Stage II is defined by muscle pain during walking that is relieved by rest. The Fontaine classification categorizes PAD into four stages: Stage I (asymptomatic), Stage II (intermittent claudication), Stage III (rest pain), and Stage IV (ulceration or gangrene). Stage II is further subdivided into IIa (pain-free walking distance >200 meters) and IIb (<200 meters), which reflects functional limitation and helps guide treatment planning.

Studies involving individuals with critical lower limb ischemia who received invasive electrostimulation, as well as review articles—including systematic and integrative reviews—were excluded to ensure the analysis focused solely on primary clinical trial data. This approach was adopted to minimize the risk of data duplication and to enable a direct and critical evaluation of study design, intervention parameters, and outcomes. By concentrating exclusively on interventional trials, the review adheres to PRISMA and Cochrane guidelines for systematic reviews assessing the effectiveness of therapeutic interventions. Protocols, case series, and letters to the editor were also excluded.

Data extraction

The articles identified through the search strategy were analyzed by two independent researchers in the following stages: (1) title screening; (2) abstract screening; and (3) full-text reading when the abstract was relevant to the topic or insufficient to determine eligibility. Each step of the review process was conducted independently by two reviewers (APF and TCR), and the results were compared. In cases of disagreement, a third reviewer (DRR) was consulted to resolve discrepancies and make the final decision.

Risk of Bias Assessment in Included Studies

The risk of bias in the included studies was independently assessed by two authors. Following the recommendations of The Cochrane Collaboration’s “Risk of Bias” tool,²⁶ the following domains were evaluated: random sequence generation, allocation concealment, blinding of participants and personnel, outcome assessment blinding, incomplete outcome data, selective reporting, and other potential sources of bias (e.g., significant imbalance between participant groups or bias related to examiner or caregiver inexperience). Each criterion was classified as having a low risk of bias, high risk of bias, or an unclear risk of bias (due to insufficient information or uncertainty regarding potential bias). Any discrepancies between the reviewers were resolved by consensus.

Results

The search strategy identified 25 studies (Figure 1). After applying the predefined inclusion criteria, seven studies were selected, comprising a total of 314 participants with a mean age of 66.8 ± 3.6 years. All participants presented with intermittent claudication (Fontaine stage II), which was the focus of this review. Although inclusion criteria varied across studies, the presence of an ankle-brachial index (ABI) < 0.90, stable IC, and limited walking capacity (Fontaine stage II) was a consistent requirement.

A summary of the studies and their main findings regarding the use of noninvasive electrostimulation for the treatment of IC is presented in Table 1. Analysis of the data reveals that most studies reported a positive effect of noninvasive electrostimulation on walking performance, particularly in terms of increased pain-free and maximum walking distances. Low-frequency transcutaneous electrical nerve stimulation (TENS) and neuromuscular electrical stimulation (NMES) were the modalities most consistently associated with functional improvement. Studies with longer intervention durations or stimulation applied to multiple muscle groups tended to show more pronounced effects. Notably, few studies reported adverse events, indicating that these modalities are generally safe and well tolerated. Collectively, these findings support the potential clinical utility of noninvasive electrostimulation, particularly for patients with limited access to or tolerance for traditional exercise therapy.

Quality of evaluation

The Cochrane Collaboration tool was used to assess the risk of bias in the included studies. The reviewers’ judgments for each domain are presented in Figure 2 as percentages and detailed in Figure 3 for each individual study. Five of the seven studies were classified as having an “unclear risk” of selection bias due to inadequate random sequence generation and lack of allocation concealment.^{22,27–30} Performance bias in the five randomized studies was also rated as “unclear risk,” as none of them employed a double-blind design. Attrition bias was considered low, given the minimal dropout rate reported in one study.³¹ Publication bias was not formally assessed due to the limited number of studies and insufficient data to construct funnel plots.

Discussion

The results of this review indicate that noninvasive electrostimulation applied to the skeletal muscles of individuals with PAD can help reduce pain associated with intermittent claudication and improve functional capacity. These findings align with existing literature, such as the systematic review by Jéhannin et al.,³² which also examined the use of electrical stimulation in patients with PAD. However, our analysis differs by employing more stringent inclusion criteria, focusing exclusively on randomized controlled trials involving therapeutic interventions, and encompassing a range of noninvasive electrostimulation modalities. This approach enabled a more robust evaluation of the effects on pain and functional capacity, particularly in the context of intermittent claudication.

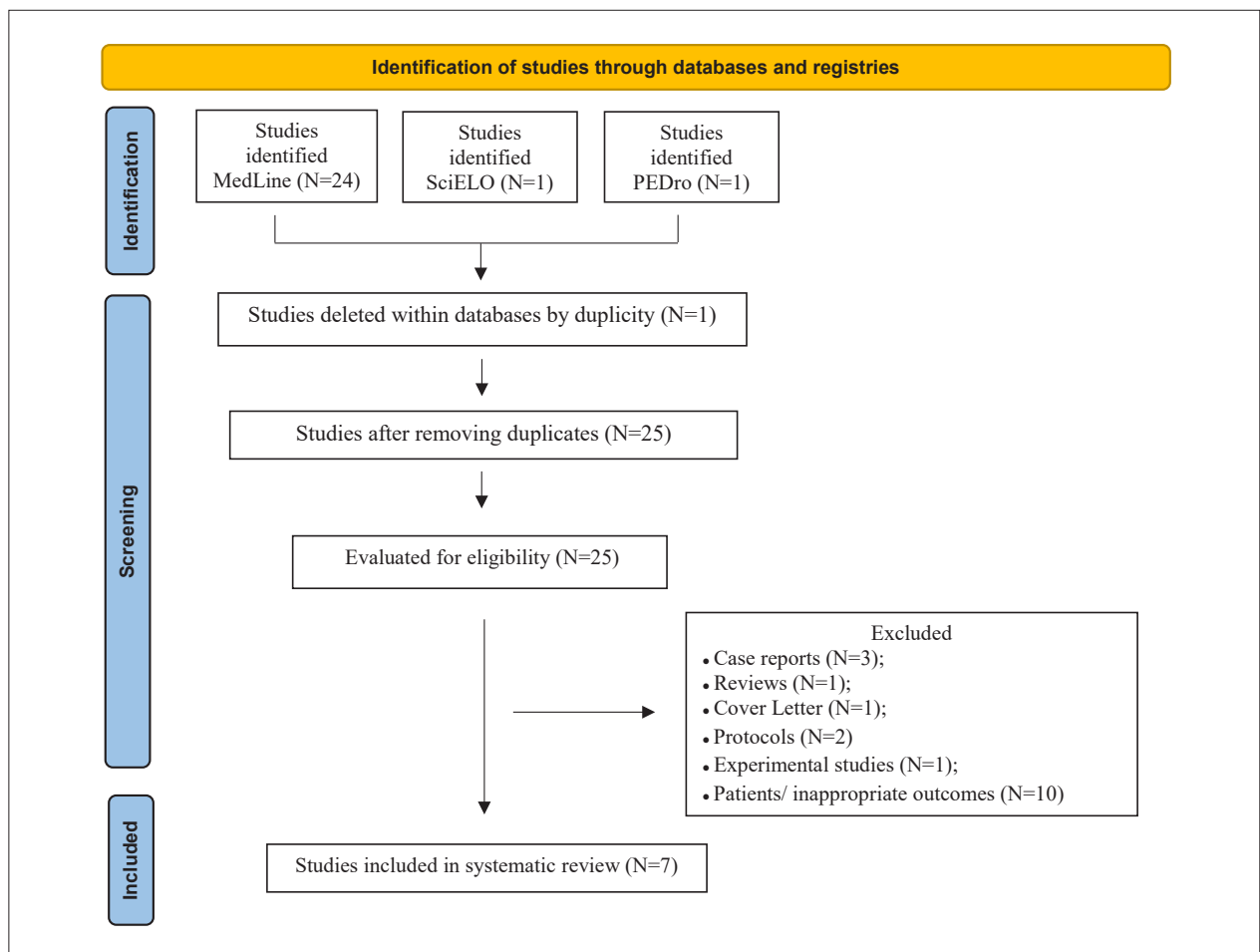


Figure 1 – Flowchart of the study selection process.

Most studies applied noninvasive electrostimulation to the plantar flexor muscles,²⁷⁻³¹ and low-frequency stimulation – regardless of the application site – proved to be an effective option for increasing the distance walked until the onset of maximum claudication. Both acute stimulation using TENS and chronic stimulation demonstrated significant improvements in pain-free walking distance.^{27,29}

Four types of noninvasive electrostimulation were identified: NMES,^{22,27} TENS,^{29,30} functional electrical stimulation (FES),^{28,31} and electroacupuncture.³³ Each modality operates with distinct electrical parameters and is believed to enhance walking ability by acting through vascular and/or non-vascular mechanisms. Proposed hypotheses for symptom improvement and pain relief in individuals with PAD include increased capillary density, transformation of muscle fibers to more oxidative types, analgesic effects, and reduced peripheral sympathetic activity.^{29,34}

Seenan et al.³⁰ demonstrated that low-frequency TENS applied to the gastrocnemius muscle significantly increased both initial and absolute claudication distances compared to placebo. These results suggest that even acute sessions of noninvasive electrostimulation may temporarily enhance

peripheral perfusion or reduce pain perception, potentially via activation of endogenous opioid pathways. These findings support the proposed analgesic mechanisms of TENS and highlight its potential role as a pre-exercise or rehabilitation support strategy. However, the lack of long-term follow-up limits conclusions regarding its sustained clinical benefits.

In contrast, using a similar protocol, Labrunée et al.²⁹ observed that TENS applied at 10 Hz to the gastrocnemius and quadriceps regions significantly delayed the onset of pain compared to placebo. This finding supports the hypothesis that low-frequency stimulation may preferentially modulate afferent nociceptive input and enhance ischemic muscle metabolism. The inclusion of the quadriceps as an additional stimulation site may have contributed to greater muscle recruitment, thereby improving walking tolerance. These results provide a rationale for exploring multi-site stimulation protocols in future clinical trials.^{24,35}

The study by Anderson et al.²⁷ offered valuable insights by demonstrating that short sessions of electrical muscle stimulation (EMS) can increase arterial blood flow in symptomatic limbs without inducing ischemia or muscle discomfort. This supports the vascular mechanism of benefit

Table 1 – Summary of studies and their main outcomes involving the use of noninvasive electrostimulation for the treatment of intermittent claudication

Study	Design	Country	Sample and inclusion criteria	Modality and Parameter	Intervention and methods	Outcomes		
						ICD	FCD	Pain
Del Río Solá et al. ²⁸ (2019)	Single-blinded, randomized	Spain	• 142 individuals	FES	• Intervention			
			• DMG = 71 (67.2 years) (59 male)	• DMG and NDMG FES + walking (symmetrical biphasic pulses at a rate of 25 PPS for dorsiflexors and 8–15 PPS for plantar flexors)	- FES during treadmill walking for 8 weeks (5 days per week)			
			ABI= 0.61 (0.12)		• Location: plantar flexors, mid portion in the stance phase (40% of gait cycle), and dorsiflexors, remaining 60% of the cycle	↑ DMG (74m) vs ↑ NDMG (41m) (p = 0.0001).	-	↓ pain DMG (24 points) vs 14 (points) NDMG (p = 0.0001)
Hackl et al. ³³ (2017)	double-blinded trial	Austria	ABI= 0.62 (0.12)	Three measurements were performed: baseline (T0), post-intervention (T1), and 3 months post-intervention (T2)	• Duration: 60 minutes daily			
			• IC (stage II of the Fontaine classification of PAD)					
Hackl et al. ³³ (2017)	double-blinded trial	Austria	• 40 individuals (26 male)	Electroacupuncture	• Intervention			
			• EG = 20 (65) ABI= 0.60 (0.37)	• EG Verum 1 Hz	- 8 weeks (6 days a week electroacupuncture + 2-day break)	initial claudication distance ↑ EG 182 m vs 345m (p <0.01) and CG 159m vs 268 m (p = 0.01)	-	
			• CG = 20 (66) ABI= 0.52 (0.35)	• CG (electroacupuncture device unattended)	• Location: nerve fibers (ear ramus) of the outer ear	12 (60%) individuals in EG and 5 (25%) in CG duplicate walking distance (p = 0.05)	-	
Hackl et al. ³³ (2017)	double-blinded trial	Austria	• ICD (stage IIb of the Fontaine classification of PAD)		• Duration: EG (40 minutes followed by a 20-minute break); CG (20 minutes every 12 hours)			

FES		Intervention:		Mean initial claudication distance
Embrey et al. ³¹ (2017)	Single-blind, randomized block study	United States of America	• 27 individuals • EG = 13 (67.2) - ABI=0.68 (0.11) • CG = 14 (68.7) - ABI= 0.60 (0.14) • Patients diagnosed with PAD and IC.	• EG - FES + walking (symmetrical biphasic pulses at a rate of 25 PPS for dorsiflexors and 8–15 PPS for plantar flexors) - CG • Walking
			- FES during walking for 8 weeks (6 days a week)	Walking distance measured by six-minute walking test). (p = 0.22)
			• Location: plantar flexors, midportion in the stance phase (40% of gait cycle), and dorsiflexors, remaining 60% of the cycle	↑ significantly in the EG, 43.8 m 95% CI, [8.2–79.3 m] (p = 0.0242.2) - between T0 and T1 and 42.2 m 95% CI [1.2–83, 8 m] (p = 0.04) - between T0 and T2
			• Duration: EG (60 minutes daily), CG (walked around for the same period without FES)	- Mean initial claudication distance ↓ between T0 and T1 (mean difference 26 points; 95% CI [12.5–39.5] (p = 0.001) - and continued to ↓ during follow-up, T0 and T2 (mean difference 30.2; 95% CI [13.0–47.3] (p = 0.001)

Seenan et al. ³⁰ (2015)	Block randomized, single-blind, placebo controlled stud	United Kingdom	• 36 individuals (29 male) • EG = 18 (70) • CG = 18 (70) - ABI= 0.63 (0.16) • IC (stage II of the Fontaine classification of PAD)	- TENS • EG - TENS (120 Hz) - TENS (2 Hz) • CG - TENS placebo (absence of electric current)
			• Intervention - 2 applications, 6 to 9 days apart • Location: gastrocnemius • Duration: variable, according to the time of performance of the test in running machine	- TENS (120 Hz) ↑ (p=0.004) - TENS (2 Hz) ↓ (p=0.96) - TENS (120 Hz) ↑ p=0.02 - TENS (2 Hz) ↑ p=0.04
				No group had changes in pain score (p < 0.05)

Original Article

Labrunée et al. ²⁶ (2015)	Single-blind control study	France	• 15 individuals (13 male) • EG = 15 (58.2) - ABI= 0.82 (0.09) • CI (stage II of the Fontaine classification of PAD)	TENS • EG -TENS 10 Hz (T10) -TENS 80 Hz (T80) -TENS sham - Control (without electrodes)	• Intervention - 5 applications (48 hours intervals for 2 weeks) • Location: gastrocnemius and quadriceps • Duration: 45 minutes	-	↑ of walking distance between T10, T80, sham, and control (p < 0.0003) 10-Hz TENS was shown to be more effective than 80-Hz TENS IC symptoms
Anderson et al. ²⁷ (2004)	Single-blind, randomized control study	United Kingdom	• 30 individuals (22 male) • EG = 15 (66) - ABI= 0.64 (0.10) • GC = 15 (71) - ABI= 0.63 (0.18) • Stable claudication for 3 months or longer.	LFCES and TENS • EG - LFCES 6Hz • CG - TENS 90 HZ	Intervention - EG: 3 applications/day, at least 2-h intervals, for 4 weeks - CG: 3 applications/day, 4 weeks • Location: sural triceps • Duration: 20 minutes	↑ significantly for maximum walking distance at 39 m (p < 0.05) with LFCES There was no effect with TENS for the same variable	-
Tsang et al. ²² (1994)	Single-blind, randomized control study	Spain	• 24 individuals (19 male) • EG = 12 (65) • CG = 12 (63) - ABI = Stable IC > 6 months with no change in ABI; walking distance < 500 m; ABI < 0.90; decrease of ABI in post-effort > 30 mmHg • Stable IC of greater than 6 months	CEMS and ENS • EG - CEMS 8 Hz • CG - sham	Intervention - EG: 3 applications/day at home (weekly reevaluations) for 4 weeks • Location: near the nerves popliteal and posterior tibia • Duration: 20 minutes	↑ significant in walking distance at 23m (p < 0.05) ↑ significantly in walking distance at 40 m (p < 0.05) after 4 weeks	-

EG (experimental group) = number of individuals (mean age in years) and CG (control group); DMG (diabetes mellitus group); NDMG (non-diabetes mellitus group); FCD (final claudication distance); ICD (distance walked until the first onset of pain); ACD (maximum distance walked until the pain prevents continuation). FES (functional electrical stimulation); LFCES (low-frequency chronic electrical stimulation); CEMS (chronic electromyostimulation); TENS (transcutaneous electrical nerve stimulation); SMWT (six-minute walking test); ABI (Ankle-Brachial Index). Values in parentheses represent mean and standard deviation, respectively. All studies adopted a statistical significance level of $p < 0.05$.

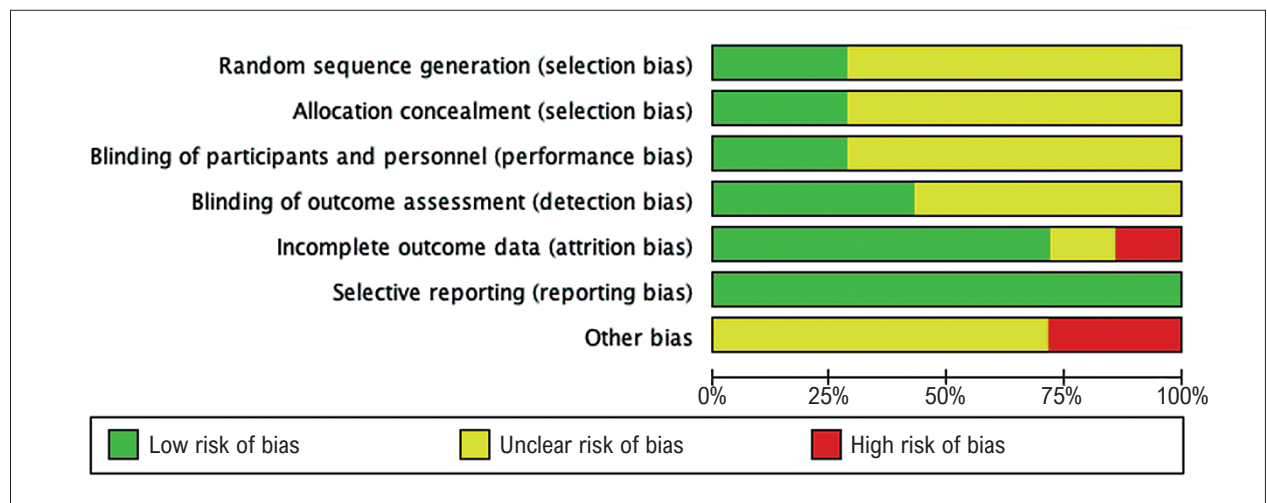


Figure 2 – Proportion of studies with each level ('low risk', 'high risk', and 'unclear risk') of bias for each bias item. Green: low risk; yellow: unclear risk; red: high risk of bias.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Andersohn et al. (2003)	?	?	?	?	+	+	?
del Rio Sola and Puerta (2019)	?	?	?	?	+	+	?
Embrey et al. (2017)	+	+	?	+	-	+	?
Hackl et al. (2017)	+	+	+	+	?	+	?
Labrune et al. (2015)	?	?	+	?	+	+	?
Seenan et al. (2015)	?	?	?	+	+	+	-
Tsang et al. (1994)	?	?	?	?	+	+	-

Figure 3 – Review of authors' judgements about each risk of bias item for each included study. Green and (+): low risk; yellow and (?): unclear risk; red and (-): high risk of bias.

associated with electrostimulation and suggests its potential use in early rehabilitation stages or in patients who are intolerant to exercise. However, the absence of claudication distance measurements and the short duration of the intervention limit the generalizability of these findings.

Another type of noninvasive electrostimulation identified was auricular nerve stimulation via electroacupuncture.³³ Although not widely used, it has shown promise as a conservative therapeutic alternative for improving the quality of life in individuals with PAD at Fontaine stage II, demonstrating benefits in walking speed and stair-climbing ability. In another study that applied this technique during the postoperative period following revascularization surgery, electroacupuncture also played a significant role in reducing postoperative pain and vascular reactivity.³⁶

Although noninvasive electrostimulation is generally considered safe and easy to administer, its application must account for the absence of specific contraindications. These include the presence of peripheral neuropathy – particularly reduced sensitivity in areas where electrodes are placed – pregnancy, cardiac pacemakers, epilepsy, and known allergies to electrode materials.³⁷

Finally, in studies involving noninvasive electrostimulation for PAD, there remains a shortage of research conducted in human models. It is important to note that each type of noninvasive electrostimulation may produce distinct effects through vascular and/or non-vascular mechanisms, depending on the type of stimulus and programming parameters used. Other forms of electrostimulation were identified but excluded from this review because they addressed outcomes outside its scope – specifically, studies involving patients at Fontaine stages III and IV or those using invasive spinal electrostimulation.

Although the included studies involved participants with clinically well-defined PAD and employed standardized diagnostic criteria, the small sample sizes and limited diversity in demographic and clinical profiles restrict the external validity of this review. Caution is warranted when generalizing

these findings, particularly to populations with comorbidities not addressed in the original studies, such as diabetes, obesity, or coronary artery disease. Further large-scale trials with broader inclusion criteria are needed to enhance the generalizability and clinical applicability of the results.

Limitations of the Study

One limitation of the present study is the variability in the types of electrical stimulation applied to the lower limbs of individuals with PAD, each of which may produce different physiological effects depending on the intended therapeutic goal. Additionally, the absence of appropriate control groups was a significant source of bias in most of the studies included in this review.

Strengths of the study

A notable strength of this study is its high external validity. Noninvasive electrostimulation – the focus of this investigation – was shown to be a safe, low-cost, and easy-to-administer technique, despite being applied with varying parameters and modalities. Its potential for broad clinical application makes it a valuable tool for reducing barriers and improving adherence to supervised exercise programs among patients with PAD.

The findings of this systematic review suggest that noninvasive electrical stimulation modalities may offer clinical benefits for patients with peripheral arterial disease (PAD), particularly in improving pain management and exercise tolerance. However, the variability in stimulation protocols, limited follow-up periods, and absence of long-term outcome data limit the generalizability of these results. Future studies should adopt standardized stimulation parameters, include larger and more diverse sample populations, and assess long-term efficacy. Two protocols already registered for ongoing or planned trials (Trial registration number: ACTRN12621001383853 and ClinicalTrials.gov ID: NCT02678403) underscore the importance of rigorous study design and reporting standards to strengthen the evidence base for neuromodulation strategies in PAD rehabilitation.

Conclusion

The results of this review indicate that noninvasive electrostimulation of the lower limbs may help reduce claudication-related pain when used alongside conventional therapeutic measures for treating IC, such as supervised exercise, pharmacological interventions, and lifestyle modifications. Additionally, its effects may contribute to increased walking distance in this patient population, positioning it as a low-cost adjuvant therapeutic option for individuals with symptomatic PAD.

However, further randomized clinical trials with lower risk of bias are needed to determine the most effective

modality, as variations in stimulation parameters—such as frequency, wavelength, and application site – can lead to differing outcomes. Moreover, the selection of noninvasive electrostimulation therapy should be tailored to the individual needs of each patient.

Acknowledgements

We extend our gratitude to the undergraduate research fellows at Faculdade de Ciências Médicas e da Saúde de Juiz de Fora (FCMS/JF-SUPREMA) who contributed to this study, as well as to Researcher Danielle Aparecida Gomes Pereira (UFMG) for her valuable guidance.

Author Contributions

Conception and design of the research: Ferreira AP, Ramos PS, Ricardo DR. Acquisition of data: Ferreira AP, Ferreira AF, Rocha TC, Ramos PS. Analysis and interpretation of the data: Ferreira AP, Ferreira AF, Rocha TC, Ramos PS. Writing of the manuscript: Ferreira AP, Ferreira AF, Rocha TC, Ramos PS, Ricardo DR. Critical revision of the manuscript for intellectual content: Ramos PS, Ricardo DR.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of Doctoral submitted by Ana Paula Ferreira, from Universidade Federal de Minas Gerais.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

References

1. Cooke JP, Chen Z. A Compendium on Peripheral Arterial Disease. *Circ Res*. 2015;116(9):1505-8. doi: 10.1161/CIRCRESAHA.115.306403.
2. Cimminiello C, Arpaia G, Friz HP, Boracchi P, Marano G, Spezzigu G, et al. A Prospective Multicentre Study on the Treatment of Cardiovascular Risk Factors and Claudication Symptoms in Patients with Peripheral Artery Disease (the IDOMENEO Study). *Vasa*. 2015;44(5):371-9. doi: 10.1024/0301-1526/a000456.
3. Vemulapalli S, Dolor RJ, Hasselblad V, Subherwal S, Schmit KM, Heidenfelder BL, et al. Comparative Effectiveness of Medical Therapy, Supervised Exercise, and Revascularization for Patients with Intermittent

- Claudication: A Network Meta-Analysis. *Clin Cardiol.* 2015;38(6):378-86. doi: 10.1002/clc.22406.
4. Gommans LN, Hageman D, Jansen I, de Gee R, van Lummel RC, Verhofstad N, et al. Minimal Correlation between Physical Exercise Capacity and Daily Activity in Patients with Intermittent Claudication. *J Vasc Surg.* 2016;63(4):983-9. doi: 10.1016/j.jvs.2015.10.060.
5. Bäck M, Jivegård L, Johansson A, Nordanstig J, Svanberg T, Adania UW, et al. Home-Based Supervised Exercise versus Hospital-Based Supervised Exercise or Unsupervised Walk Advice as Treatment for Intermittent Claudication: A Systematic Review. *J Rehabil Med.* 2015;47(9):801-8. doi: 10.2340/16501977-2012.
6. Parmenter BJ, Dieberg G, Smart NA. Exercise Training for Management of Peripheral Arterial Disease: A Systematic Review and Meta-Analysis. *Sports Med.* 2015;45(2):231-44. doi: 10.1007/s40279-014-0261-z.
7. Bapat GM, Bashir AZ, Malcolm P, Johanning JM, Pipinos II, Myers SA. A Biomechanical Perspective on Walking in Patients with Peripheral Artery Disease. *Vasc Med.* 2023;28(1):77-84. doi: 10.1177/1358863X221146207.
8. Kruidenier LM, Viechtbauer W, Nicolai SP, Büller H, Prins MH, Teijink JA. Treatment for Intermittent Claudication and the Effects on Walking Distance and Quality of Life. *Vascular.* 2012;20(1):20-35. doi: 10.1258/vasc.2011.ra0048.
9. Fakhry F, Spronk S, van der Laan L, Wever JJ, Teijink JA, Hoffmann WH, et al. Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial. *JAMA.* 2015;314(18):1936-44. doi: 10.1001/jama.2015.14851.
10. Gardner AW. Exercise Rehabilitation for Peripheral Artery Disease: An Exercise Physiology Perspective with Special Emphasis on the Emerging Trend of Home-Based Exercise. *Vasa.* 2015;44(6):405-17. doi: 10.1024/0301-1526/a000464.
11. Monteiro DP, Ribeiro-Samora GA, Britto RR, Pereira DAG. Effects of Modified Aerobic Training on Muscle Metabolism in Individuals with Peripheral Arterial Disease: A Randomized Clinical Trial. *Sci Rep.* 2019;9(1):15966. doi: 10.1038/s41598-019-52428-7.
12. Santos V, Massuca LM, Angarten V, Melo X, Pinto R, Fernhall B, et al. Arterial Stiffness following Endurance and Resistance Exercise Sessions in Older Patients with Coronary Artery Disease. *Int J Environ Res Public Health.* 2022;19(22):14697. doi: 10.3390/ijerph192214697.
13. Park SY, Wong A, Son WM, Pekas EJ. Effects of Heated Water-Based versus Land-Based Exercise Training on Vascular Function in Individuals with Peripheral Artery Disease. *J Appl Physiol.* 2020;128(3):565-75. doi: 10.1152/jappphysiol.00744.2019.
14. Wolosker N, Nakano L, Rosoky RA, Puech-Leao P. Evaluation of Walking Capacity Over Time in 500 Patients with Intermittent Claudication who Underwent Clinical Treatment. *Arch Intern Med.* 2003;163(19):2296-300. doi: 10.1001/archinte.163.19.2296.
15. Müller-Bühl U, Engeser P, Leutgeb R, Szecsenyi J. Low Attendance of Patients with Intermittent Claudication in a German Community-Based Walking Exercise Program. *Int Angiol.* 2012;31(3):271-5.
16. Abaraogu U, Ezenwankwo E, Dall P, Tew G, Stuart W, Brittenden J, et al. Barriers and Enablers to Walking in Individuals with Intermittent Claudication: A Systematic Review to Conceptualize a Relevant and Patient-Centered Program. *PLoS One.* 2018;13(7):e0201095. doi: 10.1371/journal.pone.0201095.
17. Rushton DN. Electrical Stimulation in the Treatment of Pain. *Disabil Rehabil.* 2002;24(8):407-15. doi: 10.1080/09638280110108832.
18. Skorjanc D, Jaschinski F, Heine G, Pette D. Sequential Increases in Capillarization and Mitochondrial Enzymes in Low-Frequency-Stimulated Rabbit Muscle. *Am J Physiol.* 1998;274(3):C810-8. doi: 10.1152/ajpcell.1998.274.3.C810.
19. Hicks A, Ohlendieck K, Göpel SO, Pette D. Early Functional and Biochemical Adaptations to Low-Frequency Stimulation of Rabbit Fast-Twitch Muscle. *Am J Physiol.* 1997;273(1 Pt 1):C297-305. doi: 10.1152/ajpcell.1997.273.1.C297.
20. Hudlicka O, Brown MD, Egginton S, Dawson JM. Effect of Long-Term Electrical Stimulation on Vascular Supply and Fatigue in Chronically Ischemic Muscles. *J Appl Physiol.* 1994;77(3):1317-24. doi: 10.1152/jappphysiol.1994.77.3.1317.
21. Schulz AP, Chao BC, Gazola F, Pereira GD, Nakanishi MK, Kunz RI, et al. Transcutaneous Electrical Nerve Stimulation Action on Pressure-Induced Pain Threshold. *Rev Dor.* 2011;12(3):231-4. doi: 10.1590/S1806-00132011000300007.
22. Tsang GM, Green MA, Crow AJ, Smith FC, Beck S, Hudlicka O, et al. Chronic Muscle Stimulation Improves Ischaemic Muscle Performance in Patients with Peripheral Vascular Disease. *Eur J Vasc Surg.* 1994;8(4):419-22. doi: 10.1016/s0950-821x(05)80960-0.
23. Hudlická O, Dodd L, Renkin EM, Gray SD. Early Changes in Fiber Profile and Capillary Density in Long-Term Stimulated Muscles. *Am J Physiol.* 1982;243(4):H528-35. doi: 10.1152/ajpheart.1982.243.4.H528.
24. Hudlicka O, Graciotti L, Fulgenzi G, Brown MD, Egginton S, Milkiewicz M, et al. The Effect of Chronic Skeletal Muscle Stimulation on Capillary Growth in the Rat: are Sensory Nerve Fibres Involved? *J Physiol.* 2003;546(Pt 3):813-22. doi: 10.1113/jphysiol.2002.030569.
25. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.* 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097.
26. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's Tool for Assessing Risk of Bias in Randomised Trials. *BMJ.* 2011;343:d5928. doi: 10.1136/bmj.d5928.
27. Anderson SI, Whatling P, Hudlicka O, Gosling P, Simms M, Brown MD. Chronic Transcutaneous Electrical Stimulation of Calf Muscles Improves Functional Capacity without Inducing Systemic Inflammation in Claudicants. *Eur J Vasc Endovasc Surg.* 2004;27(2):201-9. doi: 10.1016/j.ejvs.2003.10.003.
28. Del Río Solá ML, Puerta CV. Effectiveness of the Combined Treatment of Functional Electrical Stimulation and Deambulation in Diabetic Arterioopathy. *Ann Vasc Surg.* 2019;61:83-90. doi: 10.1016/j.avsg.2019.05.015.
29. Labrunée M, Boned A, Granger R, Bousquet M, Jordan C, Richard L, et al. Improved Walking Claudication Distance with Transcutaneous Electrical Nerve Stimulation: An Old Treatment with a New Indication in Patients with Peripheral Artery Disease. *Am J Phys Med Rehabil.* 2015;94(11):941-9. doi: 10.1097/PHM.0000000000000277.
30. Seenan C, McSwiggan S, Roche PA, Tan CW, Mercer T, Belch JJ. Transcutaneous Electrical Nerve Stimulation Improves Walking Performance in Patients with Intermittent Claudication. *J Cardiovasc Nurs.* 2016;31(4):323-30. doi: 10.1097/JCN.0000000000000258.
31. Embrey DG, Alon G, Brandsma BA, Vladimir F, Silva A, Pflugeisen BM, et al. Functional Electrical Stimulation Improves Quality of Life by Reducing Intermittent Claudication. *Int J Cardiol.* 2017;243:454-9. doi: 10.1016/j.ijcard.2017.05.097.
32. Jéhanin P, Craughwell M, Omarjee L, Donnelly A, Jaquinandi V, Mahé G, et al. A Systematic Review of Lower Extremity Electrical Stimulation for Treatment of Walking Impairment in Peripheral Artery Disease. *Vasc Med.* 2020;25(4):354-63. doi: 10.1177/1358863X20902272.
33. Hackl G, Prenner A, Jud P, Hafner F, Rief P, Seinost G, et al. Auricular Vagal Nerve Stimulation in Peripheral Arterial Disease Patients. *Vasa.* 2017;46(6):462-70. doi: 10.1024/0301-1526/a000660.
34. Medeiros AHO, Chalegre ST, Carvalho CC. Muscle Electrostimulation: Alternative Adjuvant Treatment to Patients with Peripheral Arterial Obstructive Disease. *J Vasc Bras.* 2007;6(2):156-62. doi: 10.1590/S1677-54492007000200010.

35. Egginton S, Hudlická O. Early Changes in Performance, Blood Flow and Capillary Fine Structure in Rat Fast Muscles Induced by Electrical Stimulation. *J Physiol.* 1999;515(Pt 1):265-75. doi: 10.1111/j.1469-7793.1999.265ad.x.
36. Sîntean ME, Deutsch PM, Lascu A, Focşa M, Ionac M. The Electroacupuncture in Patients Recently Operated for Peripheral Arterial Disease. A Comparative Study of the Two Electrostimulation Techniques. *Rev Med Chir Soc Med Nat Iasi.* 2009;113(3):788-94.
37. ELECTROPHYSICAL AGENTS - Contraindications And Precautions: An Evidence-Based Approach To Clinical Decision Making In Physical Therapy. *Physiother Can.* 2010;62(5):1-80. doi: 10.3138/ptc.62.5.



This is an open-access article distributed under the terms of the Creative Commons Attribution License