

Effects of Isometric Exercise on Cardiovascular and Metabolic Outcomes in Patients with Coronary Artery Disease: a Systematic Review

Efectos del ejercicio isométrico sobre los resultados cardiovasculares y metabólicos en pacientes con enfermedad coronaria: una revisión sistemática

Juan Carlos Sánchez-Delgado^{1,2,3}  , Andrés Mauricio Ariza Viviescas²  ,
 João Vitor Martins Bernal⁴  , Hugo Celso Dutra de Souza⁴  

¹ Facultad de Ciencias Médicas y de la Salud, Universidad de Santander, Bucaramanga, Colombia

² Universidad Santo Tomás, Bucaramanga, Colombia

³ Unidades Tecnológicas de Santander, Bucaramanga, Colombia

⁴ Laboratory of Physiology and Cardiovascular Physiotherapy, Department of Health Sciences, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, São Paulo, Brazil



Copyright

© 2026 María Cano University Foundation. The *Revista de Investigación e Innovación en Ciencias de la Salud* provides open access to all its content under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International \(CC BY-NC-ND 4.0\)](#) license.

Correspondence

Juan Carlos Sánchez-Delgado. Email: juancarlosanchezd@gmail.com

Editors

Fraidy-Alonso Alzate-Pamplona, MSc. 
 Efrén Murillo-Zamora, Ph.D. 

Declaration of interests

The authors declare no conflicts of interest.

Funding

This research received no external funding.

Abstract

Introduction. Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide. Although exercise-based interventions are a cornerstone of cardiac rehabilitation, existing evidence has predominantly focused on aerobic and dynamic resistance training. In contrast, the potential role of isometric exercise in patients with CAD remains insufficiently characterized, with limited and heterogeneous evidence regarding study designs, intervention protocols, and outcome measures, despite emerging findings suggesting favorable cardiovascular and metabolic adaptations when implemented through controlled protocols.

Objective. To synthesize and critically appraise the available evidence on the effects of isometric exercise training on cardiovascular and metabolic outcomes in individuals with CAD.

Method. A systematic search was conducted to identify randomized controlled trials (RCTs) published up to March 2026 in English, Portuguese, or Spanish. The databases searched included Scopus, Web of Science, PubMed, and Embase. Two independent reviewers performed the search, study selection, and data extraction. Methodological quality and risk of bias were assessed using the PEDro scale and the Cochrane Risk of Bias 2 (RoB 2) tool, respectively.

Ethics statement

Ethical approval was not required for this study because it did not involve human participants, animals, or identifiable personal data.

Data availability

All data supporting the findings of this study are available within the article. For additional details, please contact the corresponding author.

Author Contributions

Juan Carlos Sánchez-Delgado:

conceptualization, data curation, funding acquisition, investigation, methodology, project administration, resources, supervision, visualization, writing – original draft, writing – review & editing.

Andrés Mauricio Ariza Viviescas:

conceptualization, data curation, investigation, methodology, writing – original draft, writing – review & editing.

João Vitor Martins Bernal: formal analysis, methodology, validation, writing – original draft, writing – review & editing.

Hugo Celso Dutra de Souza: formal analysis, methodology, validation, writing – review & editing.

Generative AI declaration

The authors declare that no generative AI tools were used in the writing, editing, data analysis, or any other part of the preparation of this manuscript.

Cite this article

Sánchez-Delgado JC, Ariza Viviescas AM, Martins Bernal JV, Dutra de Souza HC. Effects of isometric exercise on cardiovascular and metabolic outcomes in patients with coronary artery disease: a systematic review. *Revista de Investigación e Innovación en Ciencias de la Salud*. 2026;8(1):1-24. e-v8n1a527. <https://doi.org/10.46634/riics.527>

Received: 10/19/2025

Revised: 12/02/2025

Accepted: 04/22/2026

Published: 05/25/2026

Disclaimer

The content of this article is the sole responsibility of the authors and does not necessarily represent the official views of their affiliated institutions or the *Revista de Investigación e Innovación en Ciencias de la Salud*.

Results. A total of 136 records were identified, of which thirteen met the eligibility criteria. The included studies reported both chronic and acute effects. Positive chronic adaptations were observed in cardiac structure, blood pressure, and coronary perfusion, whereas acute effects during isometric exercise included increased coronary collateral flow, reduced time and medication requirements for stress echocardiography, significant post-exercise hypotension, and metabolic responses characterized by a predominant reliance on carbohydrates as the primary energy substrate. The methodological quality of the included studies ranged from fair to good, while the RoB 2 assessment indicated risks of bias ranging from low to high.

Conclusion. Isometric exercise (IE) was well tolerated and demonstrated both chronic and acute benefits, supporting its potential to improve cardiovascular health and enhance the efficiency of diagnostic procedures in patients with CAD.

Keywords:

Cardiac rehabilitation, heart diseases, strength training.

Resumen

Introducción. La enfermedad arterial coronaria (EAC) sigue siendo una de las principales causas de morbilidad y mortalidad a nivel mundial. Aunque las intervenciones basadas en el ejercicio constituyen un pilar de la rehabilitación cardíaca, la evidencia disponible se ha centrado predominantemente en el entrenamiento aeróbico y de resistencia dinámica. En contraste, el papel potencial del ejercicio isométrico en pacientes con EAC permanece insuficientemente caracterizado, con evidencia limitada y heterogénea en términos de diseños de estudio, protocolos de intervención y variables de resultado, a pesar de hallazgos emergentes que sugieren adaptaciones cardiovasculares y metabólicas favorables cuando se implementa mediante protocolos controlados.

Objetivo. Sintetizar y evaluar críticamente la evidencia disponible sobre los efectos del entrenamiento con ejercicio isométrico en los desenlaces cardiovasculares y metabólicos en individuos con EAC.

Método. Se realizó una búsqueda sistemática para identificar ensayos clínicos aleatorizados publicados hasta marzo del 2026 en inglés, portugués o español. Las bases de datos consultadas fueron Scopus, Web of Science, PubMed y Embase. Dos revisores independientes realizaron la búsqueda, la selección de estudios y la extracción de datos. La calidad metodológica y el riesgo de sesgo se evaluaron mediante la escala PEDro y la herramienta Cochrane Risk of Bias 2 (RoB 2), respectivamente.

Resultados. Se identificaron un total de 136 registros, de los cuales trece cumplieron con los criterios de elegibilidad y fueron incluidos. Los estudios analizados informaron efectos tanto crónicos como agudos. Se observaron adaptaciones crónicas positivas en la estructura cardíaca, la presión arterial y la perfusión coronaria, mientras que los efectos agudos durante el ejercicio isométrico incluyeron un aumento del flujo colateral coronario, una reducción del tiempo y de los requerimientos de medicación para la ecocardiografía de estrés, hipotensión postejercicio significativa y respuestas metabólicas caracterizadas por una dependencia predominante de los

carbohidratos como sustrato energético principal. La calidad metodológica de los artículos fue calificada entre aceptable y buena, mientras que la evaluación del riesgo de sesgo (RoB2) indicó niveles de riesgo entre bajo y alto.

Conclusión. El ejercicio isométrico (EI) fue bien tolerado y demostró beneficios tanto crónicos como agudos, lo que respalda su potencial para mejorar la salud cardiovascular y la eficiencia de los procedimientos diagnósticos en pacientes con EAC.

Palabras clave:

Rehabilitación cardíaca, enfermedades del corazón, entrenamiento de fuerza.

Introduction

Cardiovascular diseases account for approximately 32% of all deaths worldwide, with ischemic heart disease representing the leading cause [1-4]. Robust evidence supports physical exercise as a cornerstone intervention for reducing morbidity and mortality in this population [5,6]. Accordingly, exercise-based cardiac rehabilitation (CR) programs are strongly recommended as part of secondary prevention strategies for patients with CAD [7-10].

Traditionally, CR programs have emphasized aerobic and dynamic resistance training because of their well-established benefits on cardiorespiratory fitness and muscular strength. In contrast, isometric exercise has been less frequently incorporated into clinical practice, mainly due to historical concerns regarding excessive blood pressure responses and the limited availability of standardized protocols and monitoring technologies [11-13].

Nevertheless, growing evidence indicates that well-controlled isometric exercise, particularly when implemented through structured protocols and, in some cases, real-time biofeedback systems, may induce favorable cardiovascular adaptations. Studies conducted in clinical populations have demonstrated improvements in functional capacity, enhanced coronary collateral recruitment, reductions in resting blood pressure, and beneficial vascular adaptations following acute or chronic isometric exercise protocols [10,14-17]. Importantly, isometric exercise is characterized by a relatively low metabolic demand and high feasibility, which may be advantageous for patients with functional limitations, orthopedic constraints, or intolerance to conventional aerobic or isotonic resistance exercise [18]. Furthermore, isometric muscle actions are intrinsic to many activities of daily living, reinforcing their potential relevance in functional rehabilitation.

Although several studies have explored the cardiovascular and metabolic effects of isometric exercise, evidence specifically focused on patients with CAD remains limited and heterogeneous. Considerable variability exists in study design, exercise protocols (e.g., intensity, duration, and muscle groups involved), outcome definitions, and methodological approaches, hindering a clear understanding of its clinical effects. This gap limits the integration of isometric exercise into evidence-based CR programs [19,20].

Therefore, the objective of this systematic review is to synthesize and critically appraise the available evidence on the effects of isometric exercise training on cardiovascular and metabolic outcomes in individuals with CAD, with particular attention to intervention characteristics, safety profiles, and clinical applicability within cardiac rehabilitation settings.

Method

This systematic review was conducted in accordance with the PRISMA guidelines and was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (Registration number: CRD420251028919), where the full review protocol is publicly available [21]. Primary studies (randomized controlled trials [RCTs] and crossover trials) published up to March 2026 in English were included to evaluate the acute and chronic effects of isometric training on cardiovascular and metabolic outcomes in patients with CAD. Studies with combined interventions were excluded for chronic outcomes. However, for acute responses, studies combining isometric exercise with pharmacological stress agents were considered if the effects of exercise could be clearly identified. Animal studies and studies involving patients undergoing chemotherapy were excluded.

Search strategy

The literature search was conducted in the following databases: Scopus, Web of Science, PubMed, and Embase. Keywords were derived from Medical Subject Headings (MeSH) or Emtree terms. Boolean operators “OR” were used to combine terms within the same group, while “AND” was used to connect descriptors related to population, intervention, comparator, outcomes, and study type descriptors. For the population, terms related to coronary artery disease and its clinical manifestations were included (e.g., “coronary artery disease”, “myocardial infarction”, “acute coronary syndrome”, and related synonyms). For the intervention, terms related to isometric exercise were used (e.g., “isometric exercise”, “isometric training”, “isometric contraction”, and “handgrip exercise”). Outcomes of interest included cardiovascular and metabolic parameters, such as blood pressure, heart rate, autonomic function, cardiac function, arterial stiffness, lipid profile, and major adverse cardiovascular events. The complete search strategies used for each database are available in [Appendix 1](#).

Study selection, methodological quality, and risk bias

After the initial search, duplicate records were removed by one author (AMA-V). Subsequently, titles and abstracts were screened according to the inclusion and exclusion criteria. Full texts of the eligible studies were then reviewed. Study selection was performed by two independent reviewers (AMA-V, MAG-D), and disagreements were resolved by a third reviewer (JCS-D).

The methodological quality of each included study was assessed using the PEDro scale (www.pedro.org.au) [22]. This tool consists of 11 items that evaluate eligibility criteria, randomization, blinding, allocation concealment, baseline comparability, blinding of participants and assessors, intention-to-treat (ITT) analysis, and follow-up procedures. Each item (except eligibility criteria) was scored as 1 when rated as “Yes” and 0 when rated as “No”, and the total PEDro score was calculated as the sum of all scored items. The total PEDro score ranges from 1 to 10, with higher scores indicating better methodological quality. Articles scoring 9-10 were classified as excellent, 6-8 as good, 4-5 as fair, and below 4 as poor quality [23].

Risk of bias in the included RCTs was assessed using the Cochrane Risk of Bias tool, version 2 (RoB 2), which evaluates bias at the outcome level across five domains: the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result. Each domain and the overall risk of bias were judged as low risk, some concerns, or high risk according to Cochrane guidance, and these judgments were used to inform the interpretation of the results.

Data extraction and analysis

Data synthesis was conducted using a narrative approach, with qualitative summaries of sample size, participant age, type of intervention, and outcomes related to cardiometabolic health.

Results

Initially, a total of 136 records were identified. After the removal of duplicates, 90 records were screened based on title and abstract. Of these, 22 full-text articles were assessed for eligibility. Nine studies were excluded for the following reasons: incorrect study design ($n = 2$), inappropriate intervention ($n = 3$), ineligible population ($n = 3$), and conference abstract ($n = 1$). Ultimately, thirteen studies met the inclusion criteria and were included in the qualitative synthesis of this systematic review [10,14-17,24-31] (Figure 1).

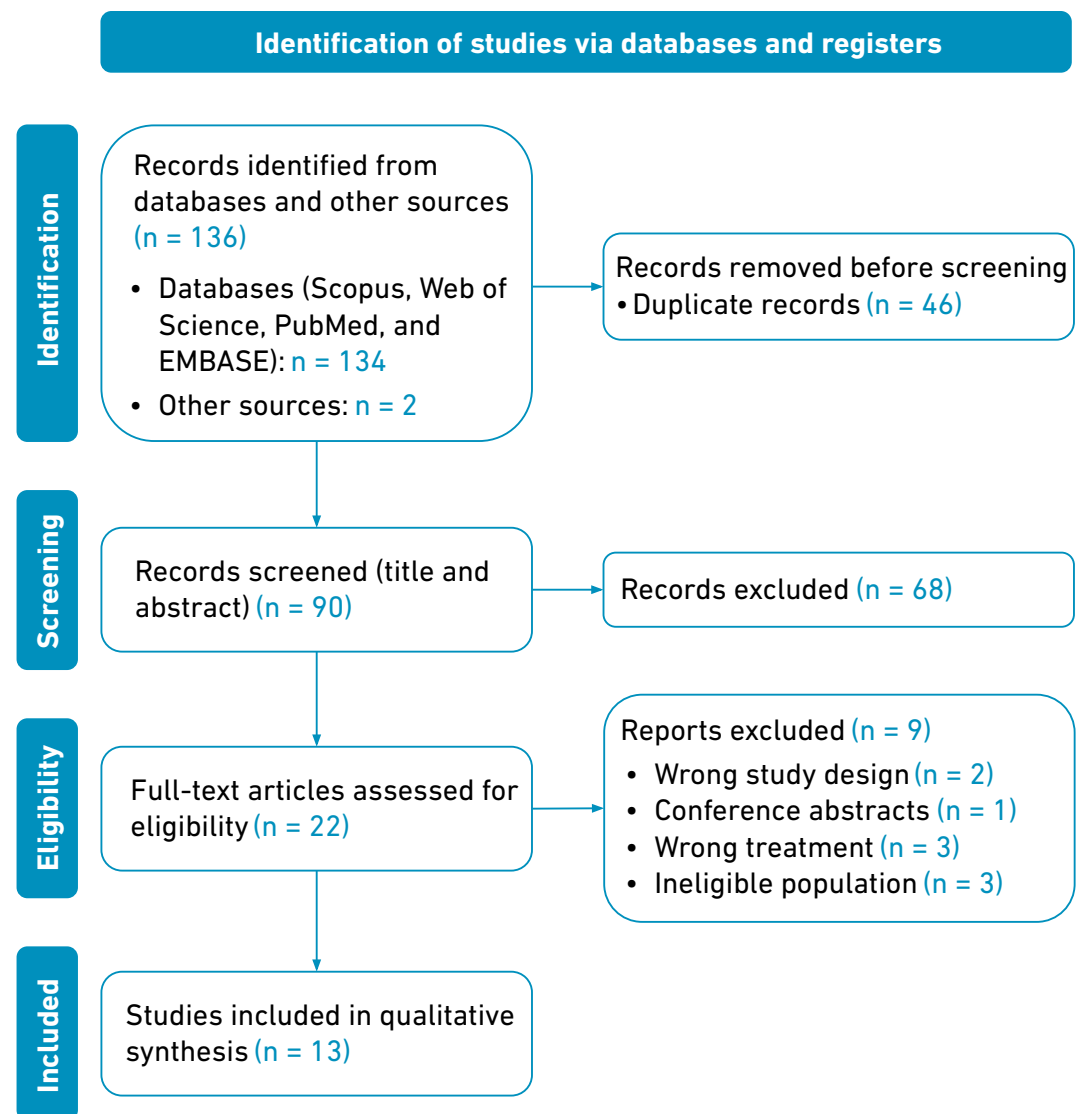


Figure 1. PRISMA flow diagram of study selection.

All included studies met the core PEDro criteria, including randomization, baseline comparability, between-group comparisons, and reporting of variability for at least one key outcome. However, none of the studies applied an ITT analysis, and blinding of participants and personnel was not feasible due to the nature of exercise interventions. Blinding of outcome assessors was limited and inconsistently reported across studies. Overall, methodological quality scores on the PEDro scale ranged from 4 to 6, indicating fair-to-good methodological quality (Table 1).

Table 1. Methodological Quality Assessment of Included Trials (n = 13) Based on the PEDro Scale.

First author	Eligibility criteria	Random Assignment	Allocation concealment	Initial comparability	Participant Blinding	Provider Blinding	Blinding of Outcome Assessors	Retention	Analysis by intention to treat	Comparison between groups	Variability of key outcome provided	Total Score	Quality of study
Chen et al. (2019) [17]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5	FAIR
Goessler et al. (2016) [28]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5	FAIR
Gordon et al. (2019) [31]	N	Y	N	N	N	N	N	Y	N	Y	Y	4	FAIR
Guiraud et al. (2017) [10]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5	FAIR
Kollet et al. (2021) [29]	Y	Y	Y	Y	N	N	Y	Y	N	Y	N	6	GOOD
Lin et al. (2012) [14]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5	FAIR
Lin et al. (2014) [15]	Y	Y	N	Y	N	N	Y	Y	N	Y	Y	6	GOOD
Yao et al. (2003) [16]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5	FAIR
Guiraud et al. (2015) [24]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5	FAIR
Eibel B et al (2022) [30]	Y	Y	N	Y	N	N	N	N	N	Y	Y	4	FAIR
Caminiti et al. (2025) [25]	Y	Y	N	Y	N	N	Y	Y	N	Y	Y	6	GOOD
Caminiti et al. (2025b) [26]	Y	Y	N	Y	N	N	Y	Y	N	Y	Y	6	GOOD
Vitarelli et al (2025) [27]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5	FAIR

Note. Abbreviations: Y = yes; N = no. Each PEDro item was scored as 1 (Yes) or 0 (No). Total score represents the sum of all scored PEDro items.

Figures 2 and 3 present the risk-of-bias assessment of the included trials. Overall, risk of bias ranged from low to high, with most studies judged as having some concerns, mainly due to insufficient reporting of the randomization process and unclear allocation concealment. In crossover trials, additional concerns were related to potential carryover effects. Studies evaluating chronic effects showed similar limitations, including baseline imbalances, absence of ITT analysis, and incomplete outcome data.

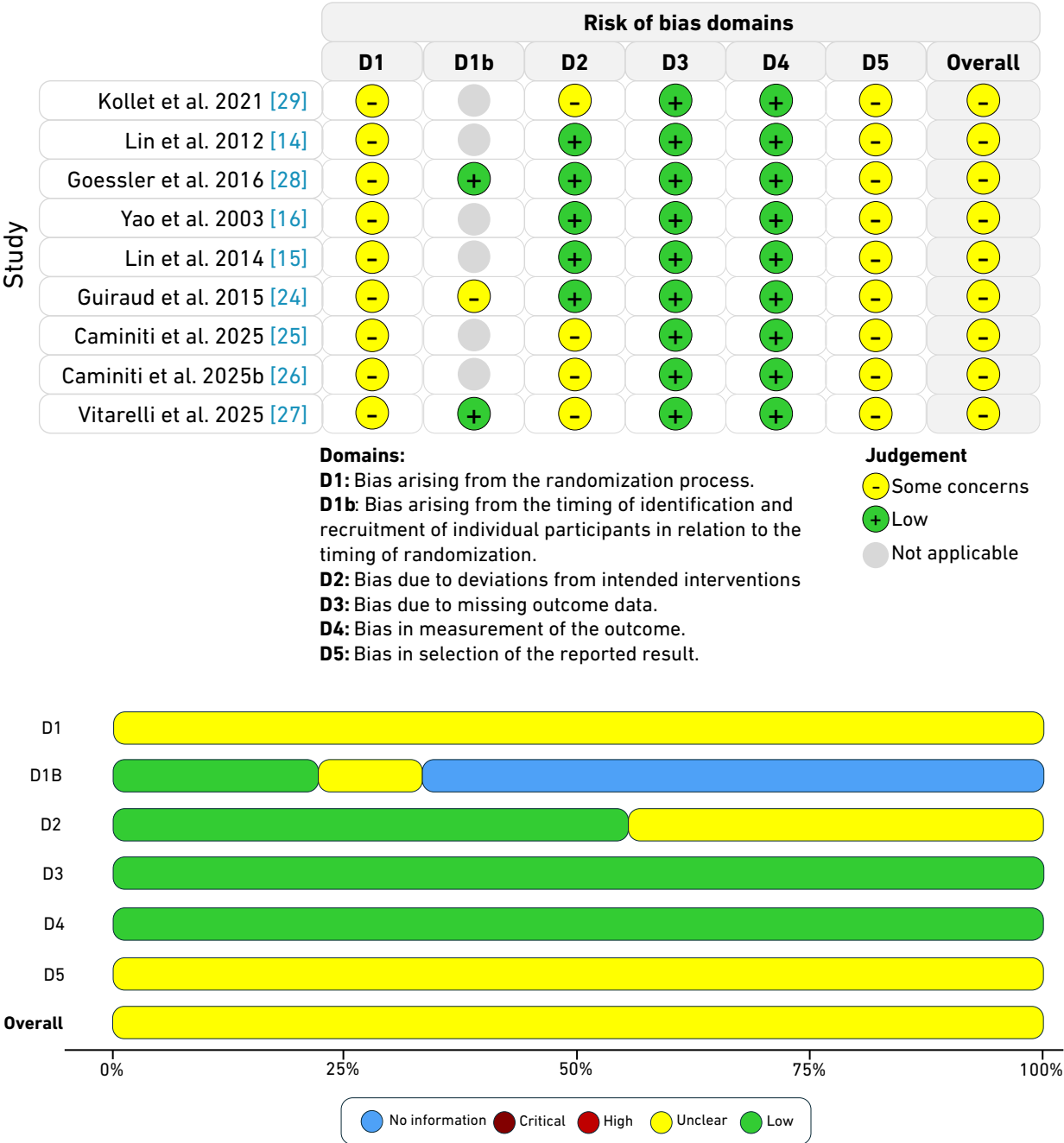


Figure 2. Risk of bias assessment of studies investigating acute effects.

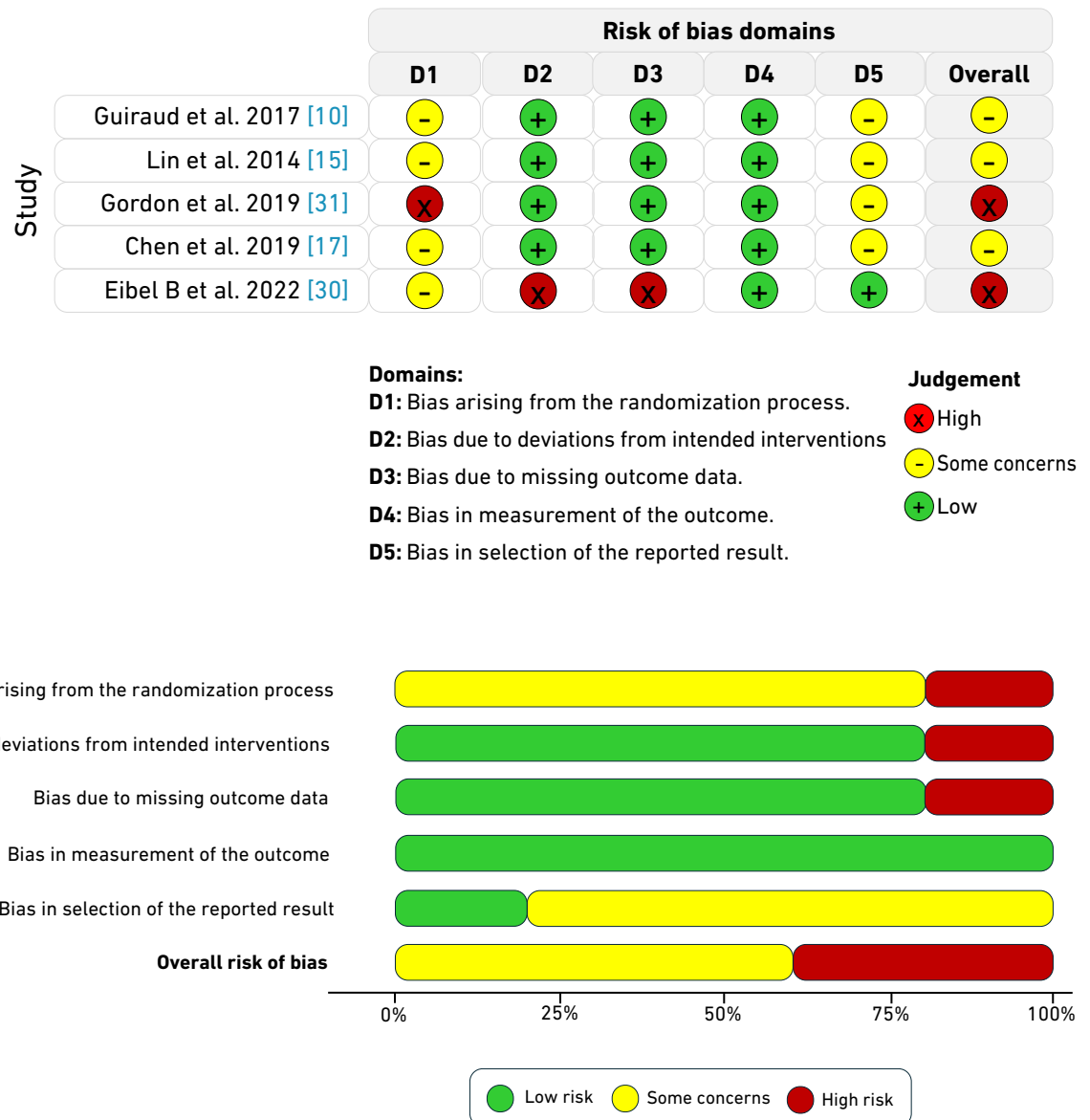


Figure 3. Risk of bias assessment of studies investigating chronic effects.

The included studies comprised a total of 559 participants, with a mean age of 63 ± 12.5 years, all diagnosed with acute coronary syndrome, with or without revascularization procedures. Participants had 50–100% stenosis in the affected coronary arteries and a left ventricular ejection fraction (LVEF) above 40%. Of the thirteen studies analyzed, ten were randomized controlled trials and three were crossover studies; eight investigated acute effects, four examined chronic effects, and one addressed both acute and chronic effects.

Acute effects

Overall, acute isometric exercise elicits heterogeneous cardiovascular, hemodynamic, and metabolic responses depending on intensity, muscle mass involvement, and exercise modality.

Evidence from coronary intervention settings suggests beneficial acute vascular effects. Lin et al. reported that isometric handgrip contractions at 50% of maximal voluntary contraction (MVC) for one minute during controlled coronary occlusion improved the contralateral coronary flow index and coronary occlusion pressure [14,15]. Similarly, Yao et al. demonstrated that isometric handgrip exercise at 33% MVC performed during peak dobutamine and atropine stress increased the heart rate response ($\Delta = 50.9 \pm 14.4$ bpm vs. 38.1 ± 17.7 bpm; $p < 0.0001$), reduced test duration ($p = 0.004$), and decreased cumulative pharmacological dose ($p = 0.025$), indicating an interaction between isometric effort and pharmacological stress responses [16].

Beyond hemodynamic responses, Guiraud et al. reported a metabolic shift during acute isometric exercise (40–70% MVC), with carbohydrate oxidation increasing from 71% to 91%, suggesting an acute exercise-induced change in substrate utilization [24].

Regarding post-exercise blood pressure responses, Caminiti et al. found that isometric handgrip exercise induces intensity-dependent post-exercise hypotension, with greater reductions at 50% MVC compared with 30% MVC at 30 and 45 minutes of recovery in patients with ischemic heart disease [25].

When different isometric modalities are compared, clearer distinctions emerge. Caminiti et al. (2025) showed that bilateral isometric knee extension (IKE; 30% MVC, 3 min) induces substantially greater acute increases in systolic blood pressure (130 ± 10 to 160 ± 15 mmHg; $p < 0.001$) and myocardial workload (global work index and global constructive work, $p < 0.001$), accompanied by reduced myocardial efficiency (global work efficiency decreased by 2–3%). In contrast, isometric handgrip at the same relative intensity (30% MVC, 3 min) produced lower systolic blood pressure responses (140–145 mmHg) and a more favorable myocardial work profile, suggesting lower cardiovascular strain compared with lower-limb isometric exercise [26].

Similarly, when comparing isometric and combined modalities, Vitarelli et al. (2025) reported modality-dependent blood pressure responses. IKE (20% MVC) and combined exercise (CE; aerobic exercise at RPE 13–14 plus resistance exercise at 60% 1RM) both reduced systolic blood pressure versus control, with a greater reduction observed after combined exercise (-8.4 ± 2.1 mmHg; $p < 0.001$) compared with isometric exercise (-3.7 ± 1.6 mmHg; $p = 0.036$, indicating superior acute hypotensive effects of multimodal training strategies [27].

In contrast, the studies by Kollet et al. and Goessler et al. did not show significant acute changes in vascular function or blood pressure following the application of low-intensity isometric handgrip training (IHT) (Table 2) [28,29].

Chronic effects

Overall, chronic isometric training appears to induce heterogeneous cardiovascular, vascular, and functional adaptations, with responses influenced by training modality, intensity, and duration.

Evidence from exercise tolerance outcomes suggests functional benefits of isometric training. Guiraud et al. demonstrated that isometric training using the Huber Motion Lab (HML) device, performed four times per week for four weeks at 70% MVC, resulted in greater improvements in exercise tolerance assessed by cycle ergometry compared with traditional dynamic resistance training at 60% of one-repetition maximum, performed with the same frequency and duration [10].

Table 2. Acute effects of isometric exercise on cardiovascular and metabolic parameters in patients with coronary artery disease.

Study (year)	Study Design	Participants <i>n</i> at Baseline		Age (years)	Intervention (Intensity)	Evaluated Outcomes	Significant differences between Groups
Kollet et al. 2021 (Brazil) [29]	RCTs	AE	<i>n</i> =10	58.6 ± 9.0	AE on cycle ergometer; 30 min at 12–14 on the Borg scale.	FMD; PWV; PVR; cSBP; cDBP.	IE showed no significant improvements in vascular function parameters.
		IE	<i>n</i> =10	56.0 ± 9.8	IE using analog dynamometer; 4 bilateral sets at 30% MVC; 2 min per hand with 1 min rest between sets.		
Lin et al. 2012 (China) [14]	RCTs	IE	<i>n</i> =33	59.2 ± 11.3	IE at 50% MVC for 1 min, performed simultaneously with 1-min coronary artery occlusion (as part of percutaneous coronary intervention).	HR, SBP, DBP, PCWP, CFI, poccl, Pao, CVP.	CFI increased significantly in the IE group compared to controls ($\Delta = 0.04$; $p < 0.01$).
		NG	<i>n</i> =32	59.2 ± 11.3	1-min coronary artery occlusion at the stenotic site (part of the revascularization procedure), without exercise.		
Goessler et al. 2016 (Belgium) [28]	Crossover	BPG	<i>n</i> =21	68.4 ± 7.0	Experimental session: 2 sets per hand (2 min each) at 30% MVC. Blood pressure measured every 15 min for 1 hour post-exercise in supine position. Control session: 15 min seated rest with same post-evaluation. 3-day interval between sessions.	Ambulatory: HR, SBP, DBP, MBP. ABPM: 24-hour monitoring with BP readings every 20 min (day, night, and 24-h averages).	Low-intensity handgrip exercise did not lead to significant changes in BP after 24 hours.
Yao et al. 2003 (EUA) [16]	RCTs	IHG	<i>n</i> =58	69 ± 14	Dobutamine stress echocardiography: infusion at increasing doses (10, 20, 30, 40 µg/kg/min, 3 min each). Handgrip exercise at 33% MVC from min 6 to 10 (during 30–40 µg/kg/min infusion).	HR increase; duration of stress test; dose of dobutamine/atropine.	HR increase greater in handgrip group ($\Delta = 50.9 \pm 14.4$ bpm) vs. no handgrip ($\Delta = 38.1 \pm 17.7$ bpm; $p < 0.0001$). Stress test duration was shorter (16.4 ± 6.9 vs. 20.7 ± 8.4 min; $p = 0.004$), and dobutamine dose was lower (25.8 ± 13.5 vs. 32.4 ± 16.4 mg; $p = 0.025$) in the handgrip group.
		NEG	<i>n</i> =55	68 ± 16	Same dobutamine protocol without isometric exercise.		

Lin et al. 2014 (China) [15]	RCTs	IHG	n=37	58.81 ± 10.75	1 min of handgrip IE at 50% MVC using a hydraulic dynamometer in a fixed position.	LVEF, PCWP, CVP, poccl, Pao, BP, CFI	poccl and CFI increased significantly in the IHG group but not in the NEG group (p < 0.01), suggesting that isometric handgrip favors recruitment of collateral circulation during occlusion.
		NEG	n=37	61.50 ± 9.07	1 min of balloon occlusion at rest		
Guiraud et al. 2015 (France) [24]	Crossover	CAD	n=20	53.1 ± 9.9	Two acute HML sessions were performed in random order at 40% and 70% of MVC (one per week over two weeks). Each 45-min session comprised six exercise blocks in different postures with 6-s isometric contractions and 10-s passive recovery.	VO ₂ , HR, BP, ventilation, energy expenditure.	Compared with W40, W70 elicited higher ventilation and heart rate, greater active energy expenditure, similar oxygen uptake, and a shift toward higher carbohydrate and lower lipid oxidation; both sessions were safe and well tolerated..
Caminiti et al., 2025 (Italy) [25]	RCTs	IHG	n=14	66.4 ± 11.2	Isometric handgrip: high (70% MVC)	Hemodynamic responses and postexercise BP changes (systolic and diastolic BP), heart rate, echocardiographic indices	Highintensity IHG (70% MVC) produced a significant reduction in postexercise systolic BP at 30 and 45 min vs control; no significant differences between high vs low intensity or low vs control for most measures
		IHG	n=14	65.9 ± 12.7	Isometric handgrip: low intensity (30% MVC)		
		Control	n=14	66.1 ± 12	No exercise		
Caminiti et al. 2025b (Italy) [26]	RCTs	IKE:	n=16	64.9 ± 14.2	Bilateral knee extension; 30% MVC; 3 min; constant force; seated at 120° trunk angle.	SBP; HR; myocardial work parameters (GWI, GCW, GWE).	IKE significantly increased SBP (rest: ~130 ± 10 vs exercise: ~160 ± 15 mmHg, p < 0.001) and myocardial workload (GWI and GCW increased significantly, p < 0.001), while myocardial work efficiency decreased (GWE reduced by ~2–3%, p < 0.05); IHG induced smaller increases in SBP (~140–145 mmHg during exercise) and myocardial workload, showing a more tolerable hemodynamic response (p < 0.05).
		IHG	n=16	63.4 ± 16.1	Handgrip; 30% MVC; 3 min; constant force; supine at 120° trunk angle.		
		Control	n=16	64.2 ± 13.5	No exercise (rest condition).		

Vitarelli et al. 2025 (Italy) [27]	Crossover	CAD	n=25	63.4 ± 16.1	IKE: bilateral knee extension; 20% MVC; 20 min (5 × 2 min, 2 min rest). CE: aerobic (RPE 13–14) + resistance (60% 1RM); 60 min. Control: rest. Interventions were performed in a randomized order	SBP; DBP; HR.	CE reduced SBP more than control (−8.4 ± 2.1 mmHg; p < 0.001) and IES (p = 0.004); IES also reduced SBP vs control (−3.7 ± 1.6 mmHg; p = 0.036).
------------------------------------	-----------	-----	------	-------------	---	---------------	--

Legend: RCTs: Randomized Controlled Trial; AE: Aerobic Exercise; IE: Isometric Exercise; MVC: Maximum Voluntary Contraction; FMD: Flow-Mediated Dilation; PWV: Pulse Wave Velocity; PVR: Peripheral Vascular Resistance; cSBP: Central Systolic Blood Pressure; cDBP: Central Diastolic Blood Pressure; HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; PCWP: Pulmonary Capillary Wedge Pressure; CFI: Coronary Flow Index; poccl: Coronary Perfusion Pressure During Vessel Occlusion; Pao: Aortic Perfusion Pressure; CVP: Central Venous Pressure; BP: Blood Pressure; MBP: Mean Blood Pressure; ABPM: Ambulatory Blood Pressure Monitoring; GWI: Global Work Index; GCW: Global Constructive Work; GWE: Global Work Efficiency; IHG: Isometric Handgrip Group; IKE: Isometric Knee Extension; CE: Combined Exercise; NEG: No Exercise Group; BPG: Blood Pressure Group; LVEF: Left Ventricular Ejection Fraction; CAD: Coronary Arterial Disease; VO₂: Oxygen uptake.

With respect to cardiac and vascular adaptations, several studies indicate potential improvements in cardiac function and angiogenic signaling. Lin et al. reported that isometric handgrip training (IHT) at 50% MVC, performed five times per week over three months, significantly improved left ventricular ejection fraction (LVEF) and increased vascular endothelial growth factor (VEGF) levels compared with a non-exercising control group (p < 0.01) [15]. Similarly, Chen et al. observed that a three-month isometric training program at 40–50% MVC, performed five times per week, improved myocardial perfusion and LVEF compared with physiological ischemic training. Notably, both interventions reduced systolic and diastolic blood pressure and increased VEGF levels, suggesting shared cardiovascular benefits across isometric-based interventions [17].

Beyond functional and hemodynamic outcomes, short-term isometric training may also influence oxidative stress markers. Eibel et al. (2022) reported that one week of daily isometric handgrip training (20 min, submaximal contractions) reduced sulphydryl levels (from 46 to 30 μmol TNB/mg protein) without significant changes in other oxidative stress biomarkers, indicating early biochemical adaptations [30].

In contrast, not all studies have demonstrated favorable chronic hemodynamic adaptations. Gordon et al. reported no significant changes in blood pressure following a six-week low-intensity isometric handgrip training program, with no differences between intervention and control groups, highlighting variability in training responsiveness, particularly at lower intensities (Table 3) [31].

Table 3. Chronic effects of isometric exercise on cardiovascular and metabolic parameters in patients with coronary artery disease.

Study (Year)	Study Design	Participants <i>n</i> at Baseline		Age (years)	Intervention (Intensity)	Evaluated Outcomes	Significant differences between Groups
Guiraud et al. 2017 (France) [10]	RCTs	HML	<i>n</i> = 25	51.2 ± 9.4	Isometric training using the Huber Motion Lab (HML) device; 8 contractions of 6 s at 70% MVC with 10 s recovery; frequency: 4 sessions/week; duration: 4 weeks.	Weight, BMI, Waist circumference, Fat mass, Fat-free mass, Peak power output, Max HR, MVC, SF-36 QoL.	HML training improved peak power (<i>p</i> =0.035) compared to isotonic machine-based training. Both training types enhanced lower-limb strength and quality of life without significant changes in endothelial function or body composition.
		TST	<i>n</i> = 25	58.4 ± 9.5	Circuit-based isotonic training (leg press, chest press, shoulder press, low row, butterfly, leg extension); 3 sets of 12 reps per machine.		
Lin et al. 2014 (China) [15]	RCTs	IHT	<i>n</i> = 10	66.5 ± 5.1	Handgrip IE at 50% MVC; 3-month program, 5 sessions/week, 2 sessions/day; each session: 10 contractions per hand, 1 min each, 1 min rest.	EDV, ESV, SV, LVEF, VEGF.	LVEF increased significantly in the IHT group (37.80 ± 9.15 to 47.50 ± 3.83; <i>p</i> < 0.01). Changes in LVEF (Δ = 9.70 ± 9.53 vs 2.10 ± 3.57; <i>p</i> < 0.05) and VEGF (65.3 ± 15.1 to 98.5 ± 17 pg/mL; <i>p</i> < 0.01) were also greater in the IHT group compared to controls.
		NTG	<i>n</i> = 10	67.2 ± 13.8	No exercise intervention		
Gordon et al. 2019 (EUA) [31]	RCTs	IHG	<i>n</i> = 6	68.5 ± 2.8	6-week program; 3 sessions/week; 4 contractions at 30% MVC for 2 min each, 1 min rest between; performed with dominant hand only.	SBP, DBP	No significant changes in BP were observed; no between-group differences detected.
		CON	<i>n</i> = 5	72.6 ± 3.6	No exercise intervention		
Eibel B et al. 2022 (Brazil) [30]	RCTs	IHT	<i>n</i> = 5	66.4 ± 4.3	Daily IHG at 30 % MVC (20 min/session; bilateral 2-min contractions with 1-min rest), combined with 20 min of conventional physiotherapy, performed daily for 1 week until hospital discharge.	BP, 6-MWT, FMD; Oxidative stress.	Isometric exercise did not induce significant hemodynamic changes and was associated with indications of increased oxidative stress.
		VMT	<i>n</i> = 4	63.7 ± 5.7	Daily 20-min inspiratory muscle training at 30% MIP plus conventional physiotherapy until discharge.		
		CG	<i>n</i> = 6	58.8 ± 7.7	Twice-daily physiotherapy with respiratory, motor, and mobility exercises until discharge.		

Chen et al. 2019 (China) [17]	RCTs	EIT	$n=19$	62.8 ± 5.5	10 contractions per hand at 40–50% MVC, 1 min each with 1 min rest; alternated between hands; 2 sessions/day, 5 days/week for 3 months.	SBP, DBP, LVEF, LVEDD, VEGF, Anaerobic Threshold (AT), VO_2 max	Both intervention groups showed significant reductions in SBP and DBP ($p<0.01$) and improvements in VEGF, cardiac function, and structure ($p<0.01$). At the end of training, EIT group showed superior cardiac function and structure compared to CIT ($p<0.01$).
		CIT	$n=18$	64.4 ± 8.3	Vascular occlusion: 3 min ischemia followed by 5 min reperfusion (upper limbs alternately); 3 sessions/day, 5 days/week for 12 weeks.		
		NE	$n=18$	65.9 ± 5.5	Conventional pharmacological treatment only		

Legend: RCTs: Randomized Controlled Trial; HML: Huber Motion Lab; TST: Traditional Strength Training; MVC: Maximum Voluntary Contraction; 1RM: One-Repetition Maximum; IHT: Isometric Handgrip Training; NTG: No Training Group; EDV: End-Diastolic Volume; ESV: End-Systolic Volume; SV: Stroke Volume; LVEF: Left Ventricular Ejection Fraction; VEGF: Vascular Endothelial Growth Factor; IHG: Isometric Handgrip Group; CON: Control Group; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; VMT: ventilatory muscle training; CG: Conventional Group; EIT: Isometric Exercise Training Group; CIT: Vascular Occlusion Training Group; NE: No Exercise Group; LVEDD: Left Ventricular End-Diastolic Diameter; QoL: Quality of Life; 6 MWT: Six-minute walk test; FMD: Flow Mediated Dilatation; MIP: Maximal static inspiratory pressure.

Discussion

The present study demonstrated that IHT is the most commonly used modality of isometric exercise in patients with CAD. Its acute effects include improved collateral coronary blood flow during transient occlusion and enhanced efficiency of stress echocardiography through reduced test duration and pharmacological dosage. Comparative evidence suggests that lower-limb isometric exercise induces greater increases in systolic blood pressure and myocardial workload than handgrip exercise, while combined exercise produces greater acute reductions in systolic blood pressure than isometric exercise alone. Regarding chronic effects, improvements in functional capacity, cardiac function, and proangiogenic parameters were observed, whereas evidence on metabolic effects remains limited.

The results of the studies by Lin et al. indicate that isometric exercise can acutely modulate coronary hemodynamics when applied under controlled clinical conditions, with potential relevance for collateral perfusion [14]. Although the exact mechanisms underlying this effect, particularly those involving remote muscle ischemia and collateral vessel formation are not fully understood, current evidence suggests that this modality may serve as a therapeutic target in patients with CAD by improving perfusion in ischemic regions, potentially enhancing myocardial survival and reducing clinical symptoms [15]. In this regard, isometric contractions performed by healthy limbs may represent a safe, non-invasive, and practical adjunct to cardiac rehabilitation programs, with potential cardiovascular benefits in this population.

Another acute effect was reported by Yao et al., who found that incorporating IHT during dobutamine stress echocardiography helped patients reach target heart rates more rapidly, reducing both test duration and the required doses of dobutamine (by 23%) and atropine (by 41%) [16]. These findings suggest that including isometric exercise in diagnostic testing may

improve cost-effectiveness by minimizing adverse effects related to pharmacological agents, such as uncontrolled tachycardia and arrhythmic events, while eliciting a more physiological hemodynamic response that may enhance the sensitivity and specificity of the test [32-38]. Although other studies involving IHT were not randomized, their results align with those of Yao et al. Collectively, these findings suggest that incorporating this exercise modality not only improves diagnostic sensitivity but also appears safe and well tolerated, with no reported adverse events and high protocol adherence among patients [39-41].

The primary acute metabolic response observed in this study was a predominant reliance on carbohydrates as a fuel source. This finding could be particularly relevant for individuals with coronary heart disease, who often exhibit insulin resistance and reduced muscular glucose uptake, factors associated with impaired functional capacity [42,43]. While these results reflect acute effects, longer-term isometric training interventions warrant further investigation to determine their potential metabolic implications over time.

The findings of Caminiti et al. [25] suggest that high-intensity isometric handgrip exercise more consistently reduces post-exercise blood pressure compared with lower intensities (-15.5 mmHg at 50% MVC vs -5 mmHg at 30% MVC), without compromising myocardial efficiency during exercise. Proposed mechanisms include stimulation of mechano and metaboreceptors, reduced sympathetic activity, and reactive hyperemia [44]. Overall, these results are promising and consistent with previous studies in healthy or hypertensive individuals, highlighting the need for further investigation of this intervention in cardiac populations to confirm its safety and efficacy as a non-pharmacological strategy for hypertension management [45-47].

Caminiti et al. (2025) demonstrated that IKE induces substantially greater increases in systolic blood pressure (SBP) and myocardial workload, along with reduced myocardial efficiency, compared with IHT at the same relative intensity [26]. These findings are consistent with previous physiological evidence indicating that greater active muscle mass during isometric contractions elicits stronger pressor responses due to increased peripheral resistance and enhanced sympathetic activation [48,49]. In contrast, isometric handgrip exercise appears to induce a more moderate hemodynamic response, which may be more suitable for populations with coronary artery disease, in whom excessive increases in afterload may be undesirable.

Comparative evidence between isometric exercise and multimodal training modalities suggests modality-dependent blood pressure regulation. Vitarelli et al. (2025) reported that both lower-limb isometric exercise and combined exercise reduce SBP; however, greater reductions were observed following combined aerobic and resistance training compared with isolated isometric exercise [27]. These findings are consistent with previous meta-analytic evidence demonstrating that the combination of aerobic and resistance training produces more robust and sustained reductions in resting blood pressure than isolated exercise modalities, likely due to complementary adaptations in vascular function, autonomic regulation, and arterial compliance [50]. Overall, these results suggest that although isometric exercise provides favorable acute hypotensive effects, multimodal training may induce superior systemic cardiovascular adaptations.

Regarding chronic effects, the reviewed studies highlighted improvements in exercise tolerance, as well as cardiac and endothelial function. Guiraud et al. reported greater exercise tolerance, assessed via cycle ergometry, following four weeks of training using the HML device compared with traditional strength training [10]. This may be attributed to several advantages of HML over conventional resistance training. For example, the HML device recalculates MVC in each session, enabling automatic, progressive intensity adjustments. In

contrast, conventional training in that study employed manual load progression only once a week. Moreover, the HML features a rotating surface that enhances the activation of stabilizing muscles, thereby promoting greater movement efficiency. This likely facilitates more effective muscular synergies and optimized effort distribution, outcomes that are less achievable with segmented training methods targeting isolated muscle groups [24,51]. Given these advantages, along with its low risk profile and neuromuscular potential, the HML platform warrants further investigation, especially in early rehabilitation phases or among patients with low tolerance to dynamic exercise.

In terms of improvements in cardiac and endothelial function, studies by Lin et al. and Chen et al. found an increase in LVEF among patients performing IHT at 40%-50% MVC [15,17]. This effect may be linked to improved collateral perfusion induced by remote muscle ischemia [14]. One plausible mechanism involves increased expression of VEGF, whose levels were elevated in the handgrip training group [52-54]. While this is not the only mechanism capable of promoting angiogenesis or arteriogenesis, studies involving dynamic exercise have shown the release of endothelial progenitor cells, supporting the inclusion of such biomarkers in future research involving CAD patients [55,56]. Taken together, these findings suggest that IHT may activate angiogenic pathways that enhance myocardial contractility, which is particularly relevant for patients with ventricular dysfunction.

Regarding the reduction in blood pressure observed by Chen et al. after a three-week training program at 40%-50% MVC, it is worth noting that the underlying physiological mechanisms remain incompletely understood [57]. However, the previously mentioned increase in VEGF expression may play a role, as it not only promotes angiogenesis but also stimulates nitric oxide release. This is further facilitated by shear stress on the endothelium during exercise, contributing to vasodilation, improved vascular tone, and reduced peripheral vascular resistance [58-60].

International hypertension guidelines (American College of Cardiology/American Heart Association and European Society of Cardiology/European Society of Hypertension) recommend aerobic and dynamic resistance exercise as first-line non-pharmacological strategies for blood pressure control, while cautiously acknowledging emerging evidence on isometric exercise. Meta-analyses and randomized trials suggest that isometric training is associated with moderate-to-strong reductions in blood pressure, supporting its potential complementary role, although some studies show methodological limitations [61-65]. Furthermore, some studies suggest that, under specific conditions mainly in adults with prehypertension or hypertension and using low to moderate intensity handgrip exercises this isometric modality may be more effective for blood pressure control compared to traditional resistance training. [50]. However, sustained reductions in blood pressure have not been clearly demonstrated in CAD populations, limiting the extrapolation of findings from general hypertensive cohorts and emphasizing the need for further research specifically in patients with CAD.

The chronic metabolic response observed in this study was characterized by a reduction in sulfhydryl levels after one week of daily IHT. This finding may reflect an increased utilization of antioxidant reserves to counterbalance exercise-induced reactive oxygen species [66]. Such a response suggests a necessary and transient increase in oxidative stress that primes the organism for subsequent metabolic and vascular adaptations rather than indicating a deleterious effect, particularly considering the short duration of the training protocol.

Considering the current evidence, the integration of isometric training appears to be a promising complementary strategy within modern cardiac rehabilitation programs. This approach is particularly relevant for individuals unable to tolerate high-intensity dynamic

exercise. Its implementation is further supported by its minimal space and equipment requirements, and its demonstrated safety, affordability, and adaptability across clinical and home settings.

Limitations and Recommendations

Among the limitations of this review are the small number of available studies, limited sample sizes, substantial methodological heterogeneity, and short or absent long-term follow-up across trials. Importantly, several methodological limitations were consistent across included studies, including the absence of ITT analyses and the inability to blind participants and personnel due to the nature of exercise interventions. In addition, blinding of outcome assessors was inconsistently reported, contributing to potential detection bias.

This methodological variability and risk-of-bias profile limited the comparability of findings and precluded the performance of a meta-analysis, as well as sensitivity analyses and a formal assessment of the certainty of evidence. Future research should address these limitations by adopting more rigorous reporting standards, including explicit ITT analyses where appropriate, improved allocation concealment procedures, and clearer reporting of outcome assessor blinding. Additionally, larger and longer-term randomized controlled trials are needed, incorporating isometric protocols targeting a broader range of muscle groups and clinically relevant outcomes such as rehospitalization rates and mortality.

Conclusions

IHT is the most widely studied isometric modality in patients with CAD and appears to be safe and well tolerated across studies.

Acute effects include improvements in collateral coronary blood flow during transient occlusion and enhanced efficiency of stress echocardiography, reflected in shorter test duration and reduced pharmacological agent doses. Emerging evidence indicates that acute physiological responses are modality-dependent, with lower-limb isometric exercise eliciting greater increases in blood pressure and myocardial workload compared with IHT, while combined aerobic and resistance training may produce more pronounced reductions in blood pressure than isometric exercise alone.

Chronic training is associated with improved functional capacity, left ventricular function, and proangiogenic parameters, potentially mediated by enhanced myocardial perfusion and angiogenic pathways.

Evidence regarding metabolic outcomes remains very limited. Acute responses suggest predominant carbohydrate utilization, and short-term training may transiently increase oxidative stress. However, long-term metabolic effects are largely unexplored, and future studies should investigate additional metabolic markers such as lipid profiles, insulin sensitivity, and oxidative or inflammatory biomarkers relevant to cardiovascular risk in patients with CAD.

The small number of studies, limited sample sizes, heterogeneity of protocols, and lack of long-term follow-up restrict the certainty of the conclusions. Future research should include larger, methodologically rigorous trials assessing both cardiovascular and metabolic outcomes across a broader range of isometric exercises.

References

1. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, et al. Heart disease and stroke statistics—2023 update: A report from the American Heart Association. *Circulation* [Internet]. 2023;147(8):e93-e621. doi: <https://www.ahajournals.org/doi/10.1161/CIR.0000000000001123>
2. Liu Z, Gu H, Dai Q, Wang H, Yao J, Zhou L. Exercise exerts its beneficial effects on acute coronary syndrome: Clinical evidence. In Xiao J, editor. *Exercise for Cardiovascular Disease Prevention and Treatment. From Molecular to Clinical, Part 2* [Internet]. Singapore: Springer; 2017. p. 9-29. doi: https://doi.org/10.1007/978-981-10-4304-8_2
3. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). *Eur Heart J* [Internet]. 2020;41(3):407-77. doi: <https://doi.org/10.1093/eurheartj/ehz425>
4. Fernández-Rubio H, Becerro-de-Bengoa-Vallejo R, Rodríguez-Sanz D, Calvo-Lobo C, Vicente-Campos D, Lopez Chicharro J. Exercise training and interventions for coronary artery disease. *J Cardiovasc Dev Dis* [Internet]. 2022;9(5):131. doi: <https://doi.org/10.3390/jcdd9050131>
5. Anderson L, Oldridge N, Thompson DR, Zwisler AD, Rees K, Martin N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: Cochrane systematic review and meta-analysis. *J Am Coll Cardiol* [Internet]. 2016;67(1):1-12. doi: <https://doi.org/10.1016/j.jacc.2015.10.044>
6. Prabhu NV, Maiya AG, Prabhu NS. Impact of cardiac rehabilitation on functional capacity and physical activity after coronary revascularization: A scientific review. *Cardiol Res Pract* [Internet]. 2020;2020:1236968. doi: <https://doi.org/10.1155/2020/1236968>
7. El-Sobkey SB. Resistance training is an effective exercise therapy in cardiac rehabilitation program for patients with coronary artery disease: a systematic review. *Beni-Suef Univ J Basic Appl Sci* [Internet]. 2022;11(1):22. doi: <https://doi.org/10.1186/s43088-022-00206-2>
8. Yamamoto S, Hotta K, Ota E, Mori R, Matsunaga A. Effects of resistance training on muscle strength, exercise capacity, and mobility in middle-aged and elderly patients with coronary artery disease: a meta-analysis. *J Cardiol* [Internet]. 2016;68(2):125-34. doi: <https://doi.org/10.1016/j.jjcc.2015.09.005>
9. Dibben GO, Faulkner J, Oldridge N, Rees K, Thompson DR, Zwisler AD, et al. Exercise based cardiac rehabilitation for coronary heart disease: a meta analysis. *Eur Heart J* [Internet]. 2023;44(6):452-69. doi: <https://doi.org/10.1093/eurheartj/ehac747>
10. Guiraud T, Labrunee M, Besnier F, Senar JM, Pillard F, Riviere D, et al. Whole-body strength training with Huber Motion Lab and traditional strength training in cardiac rehabilitation: A randomized controlled study. *Ann Phys Rehabil Med* [Internet]. 2017;60(1):20-6. doi: <https://doi.org/10.1016/j.rehab.2016.07.385>

11. De Oliveira Gois M, Simões RP, Porta A, Kunz VC, Pastre CM, Catai AM. Cardiovascular responses to low-intensity isometric handgrip exercise in coronary artery disease: effects of posture. *Braz J Phys Ther* [Internet]. 2020;24(5):449-57. doi: <https://doi.org/10.1016/j.bjpt.2019.07.010>
12. Brown TM, Pack QR, Aberegg E, Brewer LP, Ford YR, Forman DE, et al. Core components of cardiac rehabilitation programs: 2024 update: a scientific statement from the American Heart Association and the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* [Internet]. 2024;150(18):e328-47. doi: <https://doi.org/10.1161/CIR.0000000000001289>
13. Edwards JJ, Coleman DA, Ritti-Dias RM, Farah BQ, Stensel DJ, Lucas SJE, et al. Isometric exercise training and arterial hypertension: an updated review. *Sports Med* [Internet]. 2024;54(6):1459-97. doi: <https://doi.org/10.1007/s40279-024-02036-x>
14. Lin S, Lu X, Chen S, Ye F, Zhang J, Ma Y, et al. Human coronary collateral recruitment is facilitated by isometric exercise during acute coronary occlusion. *JRM* [Internet]. 2012;44(8):691-5. doi: <https://doi.org/10.2340/16501977-0989>
15. Lin S, Chen Y, Li Y, Li J, Lu X. Physical ischaemia induced by isometric exercise facilitated collateral development in the remote ischaemic myocardium of humans. *Clin Sci (Lond)* [Internet]. 2014;127(10):581-8. doi: <https://doi.org/10.1042/CS20130618>
16. Yao SS, Moldenhauer S, Sherrid MV. Isometric handgrip exercise during dobutamine-atropine stress echocardiography increases heart rate acceleration and decreases study duration and dobutamine and atropine dosage. *Clin Cardiol* [Internet]. 2003;26(5):238-42. doi: <https://doi.org/10.1002/clc.4960260509>
17. Chen W, Ni J, Qiao Z, Wu Y, Zheng J, Chen R, et al. Comparison of the clinical outcomes of two physiological ischemic training methods in patients with coronary heart disease. *Open Med (Wars)* [Internet]. 2019;14(1):224-33. doi: <https://doi.org/10.1515/med-2019-0016>
18. Edwards JJ, Jalaludeen N, Shanmugam N, Ray R, Jouhra F, Cheriyan J, et al. Isometric exercise training in patients with heart failure with preserved ejection fraction: a randomised controlled study. *Eur J Prev Cardiol* [Internet]. 2026;33(2):229-37. doi: <https://doi.org/10.1093/eurjpc/zwaf541>
19. Kwak M, Benitez B, Mitchinson CJ, Snell ER, Bergstrom HC. Effects of different isometric exercise modalities on microvascular and metabolic function. *Microcirculation* [Internet]. 2025;32(7):e70031. doi: <https://doi.org/10.1111/micc.70031>
20. Reddy HK, Weber KT, Janicki JS, McElroy PA. Hemodynamic, ventilatory and metabolic effects of light isometric exercise in patients with chronic heart failure. *J Am Coll Cardiol* [Internet]. 1988;12(2):353-8. doi: [https://doi.org/10.1016/0735-1097\(88\)90405-6](https://doi.org/10.1016/0735-1097(88)90405-6)
21. Sanchez Delgado JC, Silva JVMB, Ariza Viviescas AM, Dutra HC. Effects of isometric exercise on cardiovascular and metabolic health in patients with coronary artery disease: a systematic review protocol. *PROSPERO* 2025:CRD420251028919 [Internet]. 2025. Available from: <https://www.crd.york.ac.uk/PROSPERO/view/CRD420251028919>

22. Moseley AM, Elkins MR, Van der Wees PJ, Pinheiro MB. Using research to guide practice: the physiotherapy evidence database (PEDro). *Braz J Phys Ther* [Internet]. 2020;24(5):384-91. doi: <https://doi.org/10.1016/j.bjpt.2019.11.002>
23. Cashin AG, McAuley JH. Clinimetrics: physiotherapy evidence database (PEDro) scale. *J Physiother* [Internet]. 2020;66(1):59. doi: <https://doi.org/10.1016/j.jphys.2019.08.005>
24. Guiraud T, Labrunee M, Pillard F, Granger R, Bousquet M, Richard L, et al. Whole-body strength training using a Huber Motion Lab in coronary heart disease patients. Safety, tolerance, fuel selection, and energy expenditure aspects and optimization. *Am J Phys Med Rehabil* [Internet]. 2015;94(5):385-94. doi: <https://doi.org/10.1097/PHM.0000000000000181>
25. Caminiti G, Vitarelli M, Volterrani M, Marazzi G, Manzi V, Antoni V, et al. Pilot Study Assessing the Hemodynamic Impact and Post-Exercise Hypotension Induced by High-Versus Low-Intensity Isometric Handgrip in Patients with Ischemic Heart Disease. *J Cardiovasc Dev Dis* [Internet]. 2025;12(10):405. doi: <https://doi.org/10.3390/jcdd12100405>
26. Caminiti G, Marazzi G, Volterrani M, Antoni V, Fecondo S, Vadala S, et al. Effect of Different Isometric Exercise Modalities on Myocardial Work in Trained Hypertensive Patients with Ischemic Heart Disease: A Randomized Pilot Study. *J Funct Morphol Kinesiol* [Internet]. 2025;10(2):108. doi: <https://doi.org/10.3390/jfmk10020108>
27. Vitarelli M, Laterza F, Peñin-Grandes S, Perrone MA, Santos-Lozano A, Volterrani M, et al. Post-Exercise Hypotension Induced by a Short Isometric Exercise Session Versus Combined Exercise in Hypertensive Patients with Ischemic Heart Disease: A Pilot Study. *J Funct Morphol Kinesiol* [Internet]. 2025;10(2):189. Published 2025 May 25. doi: <https://doi.org/10.3390/jfmk10020189>
28. Goessler K, Buys R, Cornelissen VA. Low-intensity isometric handgrip exercise has no transient effect on blood pressure in patients with coronary artery disease. *J Am Soc Hypertens* [Internet]. 2016;10(8):633-9. doi: <https://doi.org/10.1016/j.jash.2016.04.006>
29. Kollet DP, Marengo AB, Belle NL, Barbosa E, Boll L, Eibel B, et al. Aerobic exercise, but not isometric handgrip exercise, improves endothelial function and arterial stiffness in patients with myocardial infarction undergoing coronary intervention: a randomized pilot study. *BMC Cardiovasc Disord* [Internet]. 2021;21(1):101. doi: <https://doi.org/10.1186/s12872-021-01849-2>
30. Eibel B, Marques JR, Dipp T, Waclawovsky G, Marschner RA, Boll LC, et al. Ventilatory Muscle Training for Early Cardiac Rehabilitation Improved Functional Capacity and Modulated Vascular Function of Individuals Undergoing Coronary Artery Bypass Grafting: Pilot Randomized Clinical Trial. *Int J Environ Res Public Health* [Internet]. 2022;19(15):9340. doi: <https://doi.org/10.3390/ijerph19159340>
31. Gordon BDH, Whitmire S, Zacherle EW, Doyle S, Gulati S, Leamy L, et al. “Get a Grip on Hypertension”. Exploring The Use Of Isometric Handgrip Training In Cardiopulmonary Rehabilitation Patients. *J Cardiopulm Rehabil Prev* [Internet]. 2019;39(6):E31-4. doi: <https://doi.org/10.1097/HCR.0000000000000468>

32. Stefadouros MA, Grossman W, Shahawy M, Witham AC. The effect of isometric exercise on the left ventricular volume in normal man. *Circulation* [Internet]. 1974;49(6):1185-9. doi: <https://doi.org/10.1161/01.CIR.49.6.1185>
33. Camarozano AC, Siqueira-Filho AG, Weitzel LH, Resende P, Noe RA. The effects of early administration of atropine during dobutamine stress echocardiography: advantages and disadvantages of early dobutamine-atropine protocol. *Cardiovasc Ultrasound* [Internet]. 2006;4:17. doi: <https://doi.org/10.1186/1476-7120-4-17>
34. Minardi G, Manzara C, Pulignano G, Pino PG, Pavaci H, Sordi M. Feasibility, safety and tolerability of accelerated dobutamine stress echocardiography. *Cardiovasc Ultrasound* [Internet]. 2007;5:40. doi: <https://doi.org/10.1186/1476-7120-5-40>
35. Lee C, Dow S, Shah K, Henkin S, Taub C. Complications of exercise and pharmacologic stress echocardiography. *Front Cardiovasc Med* [Internet]. 2023;10:1228613. doi: <https://doi.org/10.3389/fcvm.2023.1228613>
36. Tsutsui JM, Osorio AFF, Lario FC, Fernandes DRA, Sodre G, Andrade JL, et al. Comparison of safety and efficacy of the early injection of atropine during dobutamine stress echocardiography with the conventional protocol. *Am J Cardiol* [Internet]. 2004;94(11):1367-72. doi: <https://doi.org/10.1016/j.amjcard.2004.07.141>
37. Huang Q, Wang J, Li D, Zhao J, Feng X, Zhou N. Exercise electrocardiography combined with stress echocardiography for predicting myocardial ischemia in adults. *Exp Ther Med* [Internet]. 2021;21(2):130. doi: <https://doi.org/10.3892/etm.2020.9562>
38. Wierzbowska-Drabik K, Picano E, Cortigiani L, Kasprzak JD. Comparison of coronary flow reserve feasibility in different stress echocardiography protocols: dobutamine, dipyridamole, exercise, and rapid pacing. *Pol Arch Intern Med* [Internet]. 2021;131(9):830-9. doi: <https://doi.org/10.20452/pamw.16035>
39. Chauvel C, Bogino E, Reynaud P, Fischer B, Montserrat P, Sourdille N, et al. Usefulness of isometric exercise during dobutamine administration for stress echocardiography. *Am J Cardiol* [Internet]. 1998;81(2):255-8. doi: [https://doi.org/10.1016/S0002-9149\(97\)00875-8](https://doi.org/10.1016/S0002-9149(97)00875-8)
40. Afridi I, Main ML, Parrish DL, Kizilbash A, Levine BD, Grayburn PA. Usefulness of isometric hand grip exercise in detecting coronary artery disease during dobutamine atropine stress echocardiography in patients with either stable angina pectoris or another type of positive stress test. *Am J Cardiol* [Internet]. 1998;82(5):564-8. doi: [https://doi.org/10.1016/S0002-9149\(98\)00398-1](https://doi.org/10.1016/S0002-9149(98)00398-1)
41. Dattilo G, Patane S, Zito C, Lamari A, Tulino D, Marte F, et al. Handgrip exercise associated with dobutamine stress echocardiography. *Int J Cardiol* [Internet]. 2010;143(3):298-301. doi: <https://doi.org/10.1016/j.ijcard.2009.03.016>
42. Nishitani M, Shimada K, Sunayama S, Masaki Y, Kume A, Fukao K, et al. Impact of diabetes on muscle mass, muscle strength, and exercise tolerance in patients after coronary artery bypass grafting. *J Cardiol* [Internet]. 2011;58(2):173-80. doi: <https://doi.org/10.1016/j.jjcc.2011.05.001>

43. Cho YR, Ann SH, Won KB, Park GM, Kim YG, Yang DH, et al. Association between insulin resistance, hyperglycemia, and coronary artery disease according to the presence of diabetes. *Sci Rep* [Internet]. 2019;9(1):6129. Published 2019 Sep 2. doi: <https://doi.org/10.1038/s41598-019-42700-1>
44. McGowan CL, Levy AS, Millar PJ, Guzman JC, Morillo CA, McCartney N, et al. Acute vascular responses to isometric handgrip exercise and effects of training in persons medicated for hypertension. *Am J Physiol Heart Circ Physiol* [Internet]. 2006;291(4):H1797–H1802. doi: <https://doi.org/10.1152/ajpheart.01113.2005>
45. Javidi M, Ahmadi S, Argani H, Najafi A, Ebrahim K, Salehi N, et al. Effect of Lower-versus Higher-Intensity Isometric Handgrip Training in Adults with Hypertension: A Randomized Controlled Trial. *J Cardiovasc Dev Dis* [Internet]. 2022;9(9):287. doi: <https://doi.org/10.3390/jcdd9090287>
46. Gill KF, Arthur ST, Swaine I, Devereux GR, Huet YM, Wikstrom E, et al. Intensity-dependent reductions in resting blood pressure following short-term isometric exercise training. *J Sports Sci* [Internet]. 2015;33(6):616-21. doi: <https://doi.org/10.1080/02640414.2014.953979>
47. Wiles JD, Coleman DA, Swaine IL. The effects of performing isometric training at two exercise intensities in healthy young males. *Eur J Appl Physiol* [Internet]. 2010;108:419-28. doi: <https://doi.org/10.1007/s00421-009-1025-6>
48. MacDougall JD, Tuxen D, Sale DG, Moroz JR, Sutton JR. Arterial blood pressure response to heavy resistance exercise. *J Appl Physiol* [Internet]. 1985;58(3):785-90. doi: <https://doi.org/10.1152/jappl.1985.58.3.785>
49. Fisher JP, Seifert T, Hartwich D, Young CN, Secher NH, Fadel PJ. Autonomic control of heart rate by metabolically sensitive skeletal muscle afferents in humans. *J Physiol* [Internet]. 2010;588(7):1117-27. doi: <https://doi.org/10.1113/jphysiol.2009.185470>
50. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. *J Am Heart Assoc* [Internet]. 2013;2(1):e004473. doi: <https://doi.org/10.1161/JAHA.112.004473>
51. Seo G, Park JH, Park HS, Roh J. Developing new intermuscular coordination patterns through an electromyographic signal-guided training in the upper extremity. *J NeuroEngineering Rehabil* [Internet]. 2023;20(1):112. doi: <https://doi.org/10.1186/s12984-023-01236-2>
52. Heil M, Eitenmuller I, Schmitz-Rixen T, Schaper W. Arteriogenesis versus angiogenesis: similarities and differences. *J Cell Mol Med* [Internet]. 2006;10(1):45-55. doi: <https://doi.org/10.1111/j.1582-4934.2006.tb00290.x>
53. Toyota E, Warltier DC, Brock T, Ritman E, Kolz C, O'Malley P, et al. Vascular endothelial growth factor is required for coronary collateral growth in the rat. *Circulation* [Internet]. 2005;112(14):2108-13. doi: <https://doi.org/10.1161/CIRCULATIONAHA.104.526954>
54. Pichiule P, Agani F, Chavez JC, Xu K, LaManna JC. HIF-1 alpha and VEGF expression after transient global cerebral ischemia. In Dunn JF, Swartz HM, editors. *Oxygen Transport to Tissue XXIV* [Internet]. New York: Springer; 2003. p. 611-7. doi: https://doi.org/10.1007/978-1-4615-0075-9_60

55. Wan CX, Li J, Yi L. Enhancement of homing capability of endothelial progenitor cells to ischaemic myocardium through physiological ischaemia training. *JRM* [Internet]. 2011;43(6):550-5. doi: <https://doi.org/10.2340/16501977-0815>
56. Xiao M, Lu X, Li J, Ling L, Li Y. Physiologic ischaemic training induces endothelial progenitor cell mobilization and myocardial angiogenesis via endothelial nitric oxide synthase related pathway in rabbits. *J Cardiovasc Med (Hagerstown)* [Internet]. 2014;15(4):280-7. doi: <https://doi.org/10.2459/JCM.0b013e32836009fe>
57. Millar PJ, McGowan CL, Cornelissen VA, Araujo CG, Swaine IL. Evidence for the role of isometric exercise training in reducing blood pressure: Potential mechanisms and future directions. *Sports Med* [Internet]. 2014;44(3):345-56. doi: <https://doi.org/10.1007/s40279-013-0118-x>
58. Smart NA, Way D, Carlson D, Millar P, McGowan C, Swaine I, et al. Effects of isometric resistance training on resting blood pressure. Individual participant data meta-analysis. *J Hypertens* [Internet]. 2019;37(10):1927-38. doi: <https://doi.org/10.1097/HJH.0000000000002105>
59. Cahu Rodrigues SL, Farah BQ, Silva G, Correia M, Pedrosa R, Vianna L, et al. Vascular effects of isometric handgrip training in hypertensives. *Clin Exp Hypertens* [Internet]. 2020;42(1):24-30. doi: <https://doi.org/10.1080/10641963.2018.1557683>
60. Sanchez-Delgado JC, Cohen DD, Camacho-Lopez PA, Carreño-Robayo J, Castañeda-Hernandez A, Garcia-Gonzalez D, et al. Handgrip strength is associated with specific aspects of vascular function in individuals with metabolic syndrome. *Biomedicines* [Internet]. 2023;11(9):2435. doi: <https://doi.org/10.3390/biomedicines11092435>
61. Bakris G, Ali W, Parati G. ACC/AHA versus ESC/ESH on hypertension guidelines: JACC guideline comparison. *JACC* [Internet]. 2019;73(23):3018-26. doi: <https://doi.org/10.1016/j.jacc.2019.03.507>
62. Carlson DJ, Dieberg G, Hess NC, Millar PJ, Smart NA. Isometric exercise training for blood pressure management: a systematic review and meta-analysis. *Mayo Clinic Proceedings* [Internet]. 2014;89(3):327-34 doi: <https://doi.org/10.1016/j.mayocp.2013.10.030>
63. Inder JD, Carlson DJ, Dieberg G, McFarlane JR, Hess NCL, Smart NA. Isometric exercise training for blood pressure management: a systematic review and meta-analysis to optimize benefit. *Hypertens Res* [Internet]. 2016;39:89-94. doi: <https://doi.org/10.1038/hr.2015.111>
64. Baffour-Awuah B, Pearson MJ, Dieberg G, Wiles JD, Smart NA. An evidence-based guide to the efficacy and safety of isometric resistance training in hypertension and clinical implications. *Clin Hypertens* [Internet]. 2023;29(1):9. doi: <https://doi.org/10.1186/s40885-022-00232-3>
65. Edwards JJ, Coleman DA, Ritti-Dias RM, Farah BQ, Stensel DJ, Lucas SJE, et al. Isometric Exercise Training and Arterial Hypertension: An Updated Review. *Sports Med* [Internet]. 2024;54(6):1459-97. doi: <https://doi.org/10.1007/s40279-024-02036-x>
66. Powers SK, Jackson MJ. Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. *Physiol Rev* [Internet]. 2008;88(4):1243-76. doi: <https://doi.org/10.1152/physrev.00031.2007>

Appendix 1. Search strategy

Database	Search strategy
PUBMED	("Coronary Artery Disease"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "coronary artery disease"[tiab] OR "acute coronary syndrome"[tiab] OR "myocardial infarction"[tiab] OR "ischemic heart disease"[tiab]) AND ("Isometric Exercise"[Mesh] OR "isometric exercise"[tiab] OR "isometric training"[tiab] OR "isometric handgrip"[tiab] OR "handgrip exercise"[tiab]) AND ("Blood Pressure"[Mesh] OR "blood pressure"[tiab] OR "Heart Rate"[Mesh] OR "heart rate"[tiab] OR "Vascular Stiffness"[tiab] OR "Endothelium, Vascular"[Mesh] OR "endothelial function"[tiab] OR "Cardiovascular Diseases/outcomes"[Mesh] OR "cardiovascular outcome"[tiab] OR "Metabolic Diseases/outcomes"[Mesh] OR "metabolic outcome"[tiab] OR "Major Adverse Cardiovascular Events"[tiab]) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR random*[tiab] OR trial[tiab])
EMBASE	('coronary artery disease'/exp OR 'acute coronary syndrome'/exp OR 'myocardial infarction'/exp OR 'coronary artery disease' OR 'acute coronary syndrome' OR 'myocardial infarction' OR cad) AND ('isometric exercise'/exp OR 'isometric training' OR 'isometric handgrip' OR 'handgrip exercise') AND ('blood pressure'/exp OR 'heart rate'/exp OR 'vascular stiffness'/exp OR 'endothelial function' OR 'cardiovascular outcome' OR 'metabolic outcome' OR 'major adverse cardiovascular event') AND ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'random*' OR 'crossover') AND ([english]/lim OR [portuguese]/lim OR [spanish]/lim)
WEB OF SCIENCE	(TS=("coronary artery disease" OR "acute coronary syndrome" OR "myocardial ischemia" OR "myocardial infarction" OR "ischemic heart disease")) AND (TS=("isometric exercise" OR "isometric training" OR "isometric contraction" OR "isometric handgrip" OR "handgrip exercise")) AND (TS=("blood pressure" OR "heart rate" OR "arterial stiffness" OR "vascular stiffness" OR "endothelial function" OR "cardiac function" OR "functional capacity" OR "cardiovascular outcome*" OR "metabolic outcome*" OR "major adverse cardiovascular events")) AND (TS=("randomized controlled trial" OR "controlled clinical trial" OR random* OR trial) NOT TS=(animal* OR mice OR rat OR "animal model"))
SCOPUS	(TITLE-ABS-KEY ("coronary artery disease" OR "acute coronary syndrome" OR "myocardial ischemia" OR "myocardial infarction" OR "ischemic heart disease" OR "coronary artery bypass" OR "CABG")) AND (TITLE-ABS-KEY ("isometric exercise" OR "isometric training" OR "isometric handgrip" OR "handgrip exercise" OR "handgrip training")) AND (TITLE-ABS-KEY ("blood pressure" OR "heart rate" OR "functional capacity" OR "vascular stiffness" OR "endothelial function" OR "cardiovascular outcome" OR "metabolic outcome" OR "major adverse cardiovascular event")) AND (TITLE-ABS-KEY ("randomized controlled trial" OR "controlled clinical trial" OR "random*" OR "trial")) AND NOT (TITLE-ABS-KEY ("animal" OR "animals")) AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (EXACTKEYWORD , "Human"))