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Review Article

Could Cardiac Shockwave Therapy Be the Breakthrough Solution for Refractory Angina? A Systematic Review and Meta-analysis

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Abstract

Refractory Angina (RA) is a chronic condition unresponsive to standard treatments like Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG), leaving limited options for many patients. Cardiac Shockwave Therapy (CSWT) is a novel, non-invasive modality that improves myocardial perfusion of stimulating microvascular regeneration. The present systematic review and meta-analysis were designed to assess the therapeutic efficacy of CSWT in patients with RA. Relevant studies were identified through a structured search of major electronic databases, including Cochrane, PubMed, and ScienceDirect, including comparative studies with controls that evaluated CSWT in RA patients between 2010 and 2024. Studies not in English, with irrelevant outcomes, or lacking full-text access, were excluded. Data were extracted and analyzed using a random-effects model to address heterogeneity. Seven studies with a total of 417 patients were analyzed. CSWT demonstrated significant improvements in multiple clinical outcomes. CSWT reduces angina severity in CSWT reduces angina severity in CCS grade (MD -0.76, 95% CI -0.97, -0.55, $P < 0.00001$) and in NYHA class (MD -0.62, 95% CI -0.95, -0.30, $P = 0.0002$), increased the 6-Minute Walk Test (6MWT) distance by 57.63 meters (MD 57.63, 95% CI 16.71, 98.54, $P = 0.006$), increased SAQ scores by 10.96 points (MD 10.96, 95% CI 1.66, 20.26, $P = 0.02$), improved Left Ventricular Ejection Fraction (LVEF) by 4.43% (MD 4.43, 95% CI: 2.66 to 6.21, $P< 0.01$), and decreased nitroglycerin usage by 1.62 intake per week (MD -1.62, 95% CI -2.61, -0.62, $P = 0.001$). However, there was no significant difference in LVEDD between the two groups. CSWT appears to be a promising therapeutic option for patients with RA, demonstrating improvement in Canadian Cardiovascular Society (CCS) angina class, New York Heart Association (NYHA) class, 6-minute walk test distances, SAQ score, LVEF, and reducing nitroglycerin usage.

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Keywords: Cardiac Shockwave Therapy, Refractory Angina, Non-invasive Cardiac Therapy, Chronic Angina Treatment, Innovative Angina Therapies

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Introduction

Atherosclerotic plaque buildup in the arterial lumen is a hallmark of Coronary Artery Disease (CAD), which impairs myocardial oxygenation and blood flow. It remains the primary global cause of mortality and a significant contributor to disability.[1] Standard management options for angina typically encompass pharmacological therapy with anti-anginal agents, Percutaneous Coronary Intervention (PCI), and surgical revascularization through Coronary Artery Bypass Grafting (CABG). While PCI and CABG restore blood flow of the main blood vessels, they fail to address microvascular occlusion, dysfunction, or loss. Furthermore, advanced CAD frequently leads to cardiac dysfunction due to chronic multivessel disease, resulting in extensive myocardial necrosis, fibrosis, and reduced ventricular compliance.

Refractory Angina (RA) is defined as a chronic syndrome, persisting for more than three months, in which patients experience ongoing anginal symptoms secondary to coronary insufficiency in the setting of CAD, despite optimal medical therapy, percutaneous angioplasty, or coronary bypass surgery.[2-3] Many RA patients have undergone multiple CABG or PCI procedures, often rendering them unsuitable for additional revascularization due to high procedural risks or diminished vascular integrity.[3] Patients with prior CABG, particularly those with graft degeneration or progressive atherosclerosis, frequently present with refractory angina or ischemic cardiomyopathy, yet are no longer viable candidates for PCI or repeat CABG due to vascular limitations or poor clinical prognosis. Consequently, alternative therapeutic approaches, such as gene therapy, transmyocardial revascularization, and spinal cord stimulation, have been explored, though they remain in clinical trials and are more invasive.[4] Another alternative is Cardiac Shock Wave Therapy (CSWT), which has emerged as a less invasive and novel strategy for managing RA, showing potential for improving heart disease treatment outcomes.[5]

CSWT has gained recognition as an emerging non-invasive therapy, utilizing focused shock waves to augment myocardial perfusion and relieve anginal symptoms in patients with RA. The technique applies controlled acoustic energy, delivered via a commercially available shockwave generator, directly to ischemic myocardial segments.[4] This biomechanical stimulation generates cavitation effects and shear stress within the myocardium, leading to the upregulation of angiogenic mediators such as Vascular Endothelial Growth Factor (VEGF) and Nitric Oxide (NO). Notably, VEGF is a central driver of microvascular neovascularization, thereby improving myocardial perfusion and reducing ischemic burden.[6-7]

Although its mechanistic rationale is increasingly understood, the role of CSWT in patients with refractory angina who have previously undergone revascularization remains insufficiently investigated. To our knowledge, no prior meta-analysis has systematically quantified its therapeutic impact and clinical applicability within this subgroup. Accordingly, we conducted a systematic review and meta-analysis to rigorously evaluate the efficacy and clinical outcomes of CSWT in the treatment of refractory angina.

Methods

The protocol for this study was prospectively documented in the International Prospective Register of Systematic Reviews (PROSPERO; Registration ID: CRD42024604283), with full details available at https://www.crd.york.ac.uk/prospero/. The conduct and reporting of the review adhered rigorously to the standards outlined in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement, available at http://www.prisma-statement.org/.[8]

Literature Search

The systematic review followed the PRISMA framework, incorporating a structured literature search across three primary databases: Cochrane, PubMed, and ScienceDirect. The search strategy utilized the terms ("cardiac shockwave therapy" OR "extracorporeal shockwave therapy") AND ("refractory angina" OR "severe angina pectoris") to maximize the identification of relevant studies. Additional Medical Subject Headings (MeSH) and supplementary keywords were integrated to refine retrieval. Eligible studies were limited to full-text, English-language publications between 2010 and 2025. Titles and abstracts of potentially relevant studies were screened, followed by qualitative analysis and full-text review.

Eligibility Criteria

Inclusion criteria required studies to: (1) involve participants diagnosed with refractory angina; (2) use cardiac shockwave therapy (low or high-intensity) as the intervention; (3) include a control group rather than a pre- and post-treatment comparison within the same participants; and (4) report outcomes related to refractory angina symptoms. Exclusion

criteria comprised: (1) non-English studies; (2) studies lacking relevant data or results; (3) inaccessible full texts; and (4) non-original research formats such as editorials, letters, or reviews. All primary comparative studies, including randomized controlled trials (RCTs), quasi-experiments, and prospective and retrospective observational studies, were included if they met the criteria and statistically compared outcomes.

Comparators

Because inclusion required a concurrent control arm, we extracted the exact intervention received by the control groups in all included studies. Controls comprised either Optimal Medical Therapy (OMT) alone or sham procedures (device inoperative) superimposed on OMT.

Study Selection

Two reviewers (FDP and MRA) independently evaluated all retrieved records according to predefined inclusion and exclusion criteria. Each reviewer conducted a comprehensive assessment, and any discrepancies were resolved through collegial discussion. Studies deemed ambiguous underwent further deliberation before final decisions were made. Subsequently, all included articles were validated by consensus among the investigators. A structured data extraction form was then developed to consolidate and organize findings from the eligible studies systematically.

Data Extraction

Data extraction was conducted independently by two investigators (FDP and MRA) under the guidance and consultation of the senior author (MM). A standardized data extraction form was used to collect information, including the author's name, year of publication, study design, sample size, treatment details for cardiac shockwave therapy, and study outcomes. Titles and abstracts of retrieved studies were independently screened by the investigators, with discrepancies resolved through discussion and arbitration by the senior author following the removal of duplicates. Eligible studies were catalogued using a shared spreadsheet and subsequently assessed for inclusion until consensus was achieved. Priority was given to publications with the largest sample size and the most recent publication date when multiple sources discussed the same study. In cases of missing data, corresponding authors were contacted to obtain additional information.

Quality Assessment

The evaluation of study quality and potential bias was performed independently by FDP and MRA, with oversight from MM, utilizing established tools specific to the type of study. Randomized controlled trials were assessed using the Modified Jadad Scale, which examines key elements such as randomization methods, blinding procedures, and

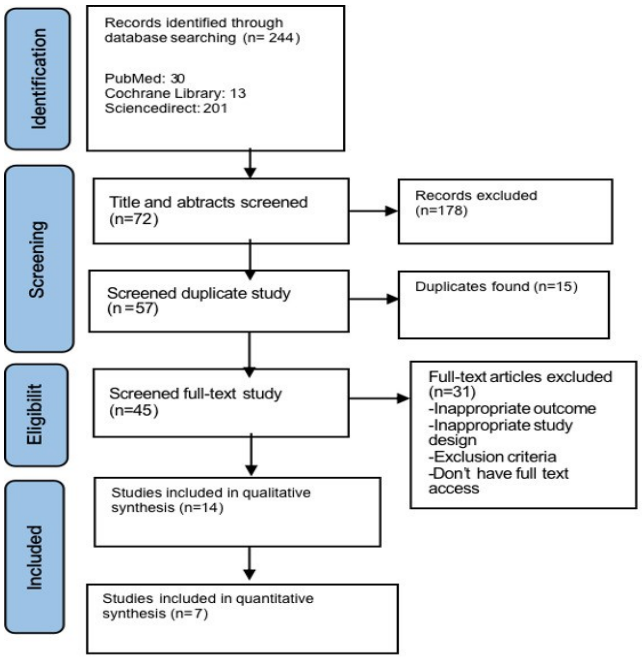

Figure 1. Diagram of study selection using PRISMA flowchart.

the management of participant withdrawals. Trials receiving scores of four or higher (out of eight) were deemed high quality, while those scoring below four were considered low quality. For observational studies, the Newcastle-Ottawa Scale (NOS) was employed, focusing on participant selection, group comparability, and the reliability of outcome or exposure measurements. Studies scoring above seven were categorized as high-quality. Any disagreements in the quality evaluation process were resolved through discussion, ensuring a consistent and thorough assessment under the guidance of the senior author.

Statistical Analysis

Meta-analyses were performed using Review Manager (RevMan) version 5.4. Continuous outcomes were synthesized as mean differences (MD) with corresponding 95% Confidence Intervals (CI). Statistical heterogeneity was examined using chi-square tests and quantified by the I^2 statistic, classified as low (below twenty-five percent), moderate (twenty-five to fifty percent), or high (more than fifty percent). In the presence of significant heterogeneity, a random-effects model was employed, and findings were illustrated using forest plots.

In addition to random-effects modeling when heterogeneity was present, we prespecified subgroup analyses by study design (Randomized Controlled Trials [RCTs] vs observational studies) and tested between-subgroup differences using χ^2 statistics. We further conducted sensitivity analyses by (i) excluding studies rated at high risk of bias, (ii) excluding studies rated high risk plus those with some concerns, and (iii) performing leave-one-out analyses for primary outcomes. We interpreted pooled effects cautiously when substantial heterogeneity ($I^2 > 50\%$) or significant subgroup differences were observed, and we withheld a single pooled estimate when subgroup effects differed.

Results

Search Results

The database search yielded 244 records (PubMed: 30; Cochrane Library: 13; ScienceDirect: 201). After title/abstract screening (n = 72) and duplicate removal (n = 15), 45 full texts were assessed for eligibility. Fourteen (14) studies met the inclusion criteria and were retained for the qualitative synthesis. Of these, seven studies provided comparable, adequately reported, two-arm data and were therefore included in the quantitative meta-analysis. The remaining seven studies were excluded from quantitative synthesis due to at least one of the following: non-eligible outcomes, non-comparative design (e.g., single-arm/pre–post), failure to meet exclusion criteria upon full-text assessment, or lack of full-text access. Figure 1 displays the PRISMA diagram for the study flow.

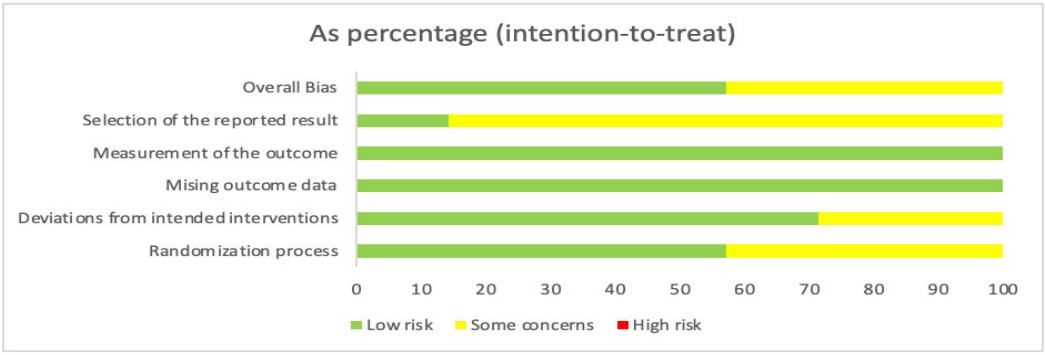

Figure 2-1. Risk of bias graph.

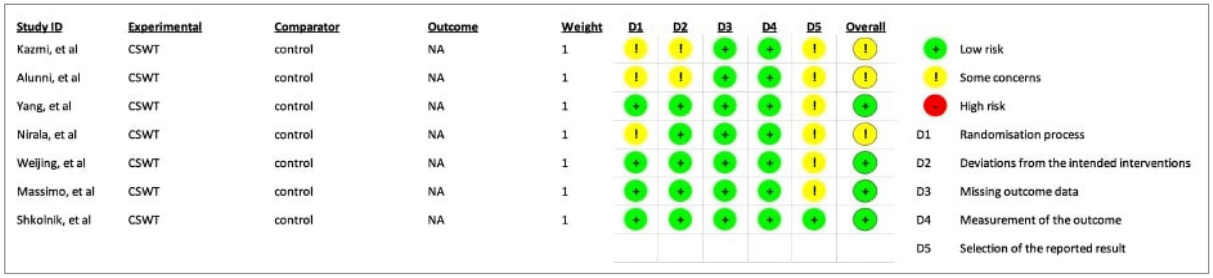

Figure 2-2. Risk of bias summary.

Risk of Bias Assessment

The appraisal of methodological quality, performed with the Cochrane Risk of Bias instrument, is illustrated in Figure 2.[9] Of the included trials, four demonstrated a low likelihood of bias, while three were judged to harbor moderate concerns regarding validity.

Summary of Included Studies

The sample sizes of the eligible studies ranged from 23 to 87 participants. An overview of the characteristics of selected studies is summarized in Table 1. The control group comprised either Optimal Medical Therapy (OMT) alone or sham procedures superimposed on OMT. Specifically: Liu Weijing 2021—OMT only (control); Shkolnik 2018—triple-blind sham procedure plus OMT; Ping Yang 2012—sham (device without energy) plus routine therapy; Alunni 2015, Slavich 2017, Kazmi 2012, and Nirala 2016—usual care/OMT without CSWT. Individuals presenting with acute myocardial infarction within the preceding three months, advanced chronic obstructive pulmonary disease, valvular pathology beyond grade II, intraventricular thrombus, pregnancy, or active malignancy were excluded.

The review identified seven eligible articles published between 2010 and 2025, comprising both qualitative and quantitative studies. Single-arm studies lacking control groups or using only pre- and post-treatment comparisons were excluded from the meta-analysis. Shockwaves were administered to ischemic myocardial regions identified through stress imaging tests. The principal clinical endpoints encompassed: (1) grading of angina according to the Canadian Cardiovascular Society (CCS) classification; (2) functional status based on the New York Heart Association (NYHA) class; (3) Left Ventricular Ejection Fraction (LVEF); (4) Left Ventricular End-Diastolic Diameter (LVEDD); (5) performance on the 6-Minute Walk Test (6MWT); (6) health-related quality of life assessed with the Seattle Angina Questionnaire (SAQ); and (7) frequency of weekly nitrate use.

Sensitivity Analysis

Risk-of-bias–informed sensitivity analyses supported the robustness of the CCS and NYHA findings: excluding the high-risk study did not change the direction or significance of the results. In contrast, 6MWT and SAQ proved less stable: effects remained significant within the RCT-only subset but attenuated or lost significance when "some concerns" studies were removed, reflecting the dispersion seen in Figure 2. These results justify interpreting 6MWT by study design rather than as a single pooled metric.

Table 1. Characteristics of selected studies.

Author (year)	Patients, CSWT/ control	Study design	Age (years)	Sex, male, n (%)	Follow up, months	BMI, kg/m^2	Hyper-tension	Diabetes	Control (Comparator)
Weijing, et al, 2021	46/41	RCT	68.1 ± 6.7/ 68.9 ± 6.6	70/71	6 months	24.7 ± 3.8/ 24.9 ± 3.7	27/23	52/56	Optimal medical therapy (OMT) only (no CSWT)
Gianluca, 2015	43/29	Cohort study, observational	70±5.3/ 71±5.3	83.7/79	6 months	Not stated	100/100	32.5/27	Usual care/ OMT without CSWT
S. Nirala, 2016	41/11	Cohort study, observational	63.4±10.8/ 71±6.52	35/8	6 months	23.9±2.7/ 23.21±2.35	Not stated	30.77	Usual care/ OMT without CSWT
Evgeny S., 2018	37/35	RCT, triple-blind	67.6±8.3/ 68.8±8.3	62.3/82.3	6 months	29.7±4.1/ 30.1±3.8	96.3/97.1	21.6/28.8	Sham procedure (device inoperative) + OMT
Massimo S., 2018	19/4	Cohort study, retrospective	69.79±10.22/ 65.25±5.74	79/75	6 months	Not stated	79%/100%	42%/75%	Usual care/ OMT without CSWT
Ping Y, 2012	14/11	RCT	63.7±8.60/ 66.45± 8.51	71.4/72.7	6 months	Not stated	57.1/45.5	42.9/45.5	Sham (device inoperative) + routine therapy
Waqar H, 2012	43/43	Cohort study	58.7±9.5/ 56.6±11.6	87/84	6 months	Not stated	56/44	77/74	Usual care/ OMT without CSWT

Canadian Cardiovascular Society (CCS) Grade

The analysis included six studies (n=345),[6,10–14] comprising two RCTs and four observational studies (Figure 3-1). Marked heterogeneity was detected across the trials (P = 0.009, I^2 = 67%), warranting the adoption of a random-effects analytical model. The pooled estimates demonstrated a statistically significant benefit of CSWT over control (MD = –0.76; 95% CI = –0.97 to –0.55; P < 0.00001). In practice, patients undergoing CSWT showed an average reduction of 0.76 points on the CCS angina severity scale compared with those receiving standard therapy.

Subgroup analysis by design showed consistent direction of benefit in both RCTs and observational studies; heterogeneity was primarily driven by smaller observational cohorts.

NYHA Class

Four studies (n = 235)[10,12–14] assessed changes in NYHA class between CSWT and control groups, comprising two randomized controlled trials (RCTs) and two observational studies (Figure 3-2). Substantial heterogeneity was detected (P < 0.0001, I^2 = 87%), necessitating a random-effects model. Pooled analysis demonstrated a significant improvement in NYHA class among CSWT-treated patients (MD –0.62; 95% CI –0.95 to –0.30; P < 0.0002), corresponding to an average improvement of 0.62 points compared with controls. No statistically significant difference between RCT and observational subgroups was detected; however, because of the high heterogeneity, we should assess the result carefully.

6-minute Walk Test

Three studies[11-12,14] (n = 188), including two RCTs and one observational trial, investigated the effect of CSWT on the 6MWT (Figure 3-3). Substantial inter-study heterogeneity was present (P = 0.03, I^2 = 73%), necessitating the use of a random-effects model. There were significant between-subgroup differences (forest-plot test for subgroup differences, P = 0.01). RCTs demonstrated a significant improvement (approximately MD ≈ 76 m), whereas the single observational study showed a small adverse effect (≈ −5 m). In view of this statistically substantial subgroup effect, we

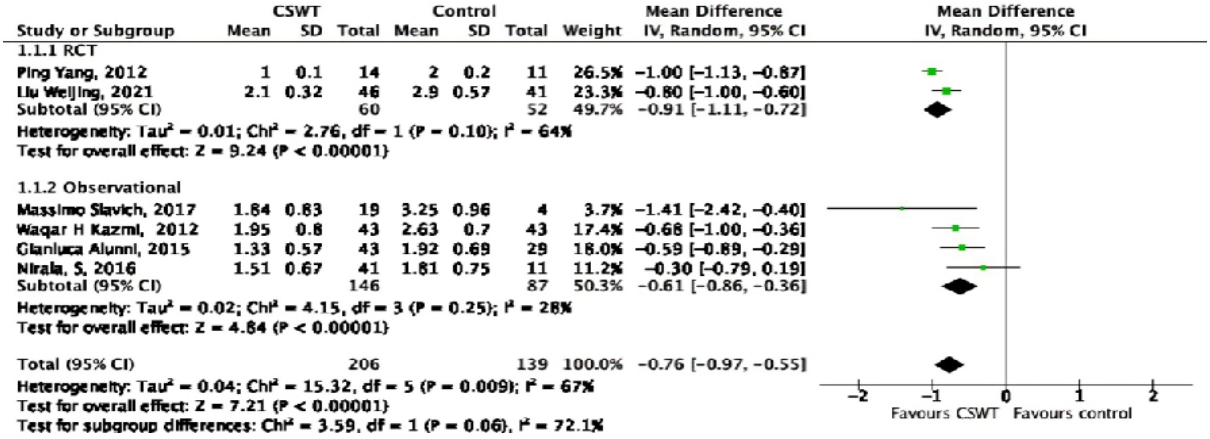

Figure 3-1. Forest plot of the CSWT group vs the control group-CCS score.

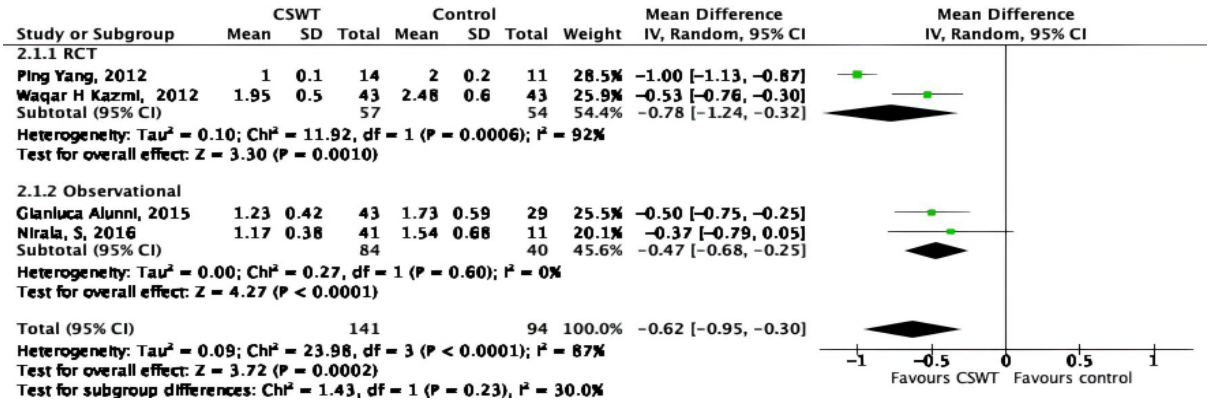

Figure 3-2. Forest plot of the CSWT group vs the control group-NYHA class.

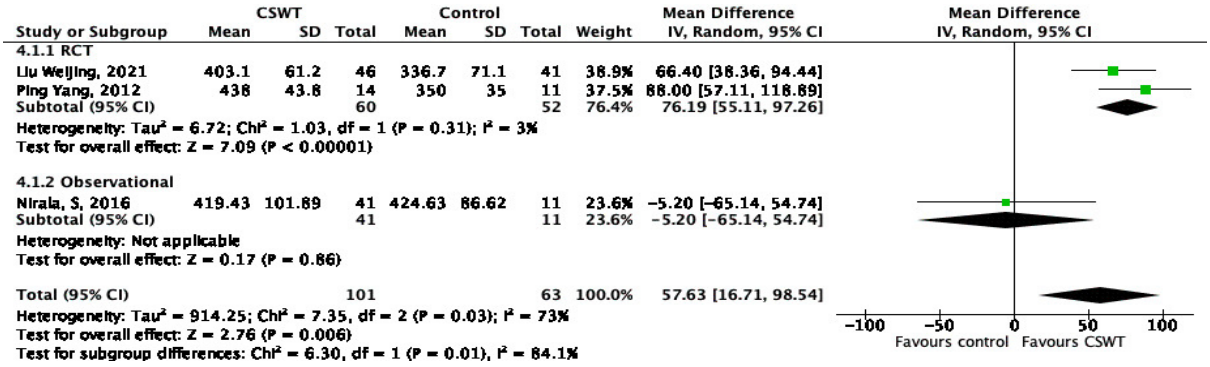

Figure 3-3. Forest plot of the CSWT group vs the control group-6 min walk test.

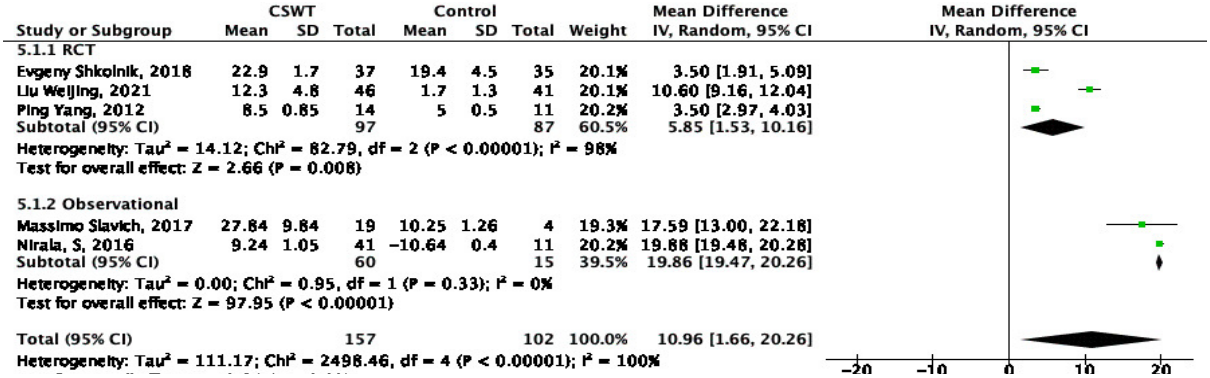

Figure 3-4. Forest plot of the CSWT group vs the control group-SAQ score.

refrain from presenting a single pooled estimate and interpret RCT and observational results separately.

SAQ Score

Five studies[6,11-12,14-15] (n = 259), including three RCTs and two observational studies, evaluated SAQ total scores following intervention (Figure 3-4). The result indicated a benefit with CSWT (pooled MD 10.96; 95% CI 1.66 to 20.26), but heterogeneity was extreme ($I^2 \approx 100\%$). Study design-based subgrouping did not resolve the dispersion/heterogeneity; effects were larger and more stable in RCTs and markedly variable in observational studies. These features lower certainty and warrant cautious interpretation.

Left Ventricular end Diastolic (LVEDD)

Three studies[6,11-12] (n = 135), including two randomized controlled trials (RCTs) and one observational study, assessed changes in Left Ventricular End-Diastolic Diameter (LVEDD) between CSWT and control groups (Figure 4-1). Meta-analysis revealed significant heterogeneity (P< 0.00001, I^2=96%), necessitating the use of a random-effects model. The pooled estimate showed no statistically significant difference between groups (MD = –1.50 mm; 95% CI: –5.18 to 2.18; P = 0.42). No meaningful RCT–observational difference was detected.

Left Ventricular Ejection Fraction (LVEF)

Four studies[6,10–12] (n = 221), comprising two RCTs and two observational trials, investigated the impact of CSWT on Left Ventricular Ejection Fraction (LVEF) **(Figure 4-2)**. High heterogeneity was evident across the studies (P < 0.00001, I^2 = 98%), warranting the application of a random-effects framework. Meta-analytic results demonstrated a significant elevation in LVEF favoring CSWT (MD=4.43%; 95%CI 2.66 to 6.21; P<0.00001). Subgroup analysis by study type demonstrated no statistically significant differences. The result should be interpreted carefully.

Weekly Nitroglycerin Used

Weekly nitroglycerin consumption was reported in four studies[11–14] (n = 236), including two RCTs and two observational studies **(Figure 4-3)**. High heterogeneity was identified (P<0.00001, I^2= 98%), for which a random-effects model was utilized. The synthesis of available data indicated a significant reduction in nitrate use in the CSWT group compared with controls (MD –1.62 doses/week; 95%CI –2.61 to –0.62; P=0.001). Subgroup analyses by study design showed no significant between-group differences. Because of the high heterogeneity, the result should be interpreted carefully.

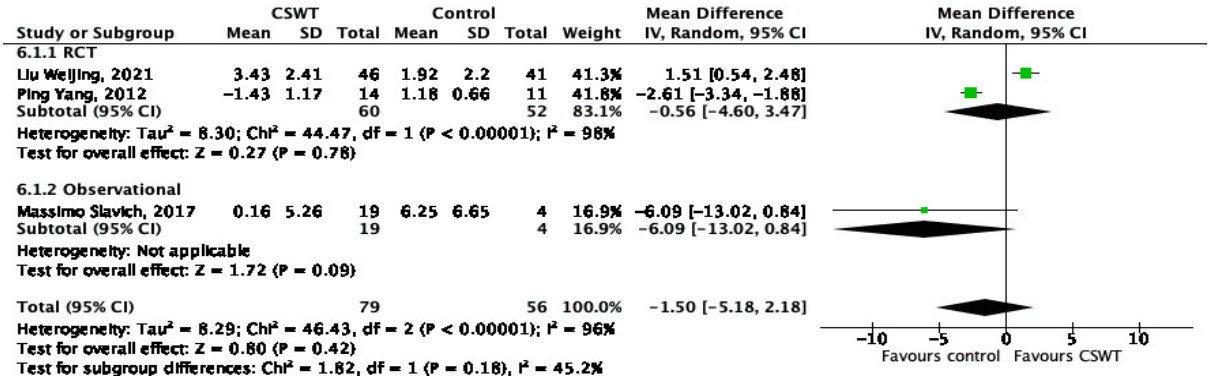

Figure 4-1. Forest plot of the CSWT group vs the control group-LVEDD.

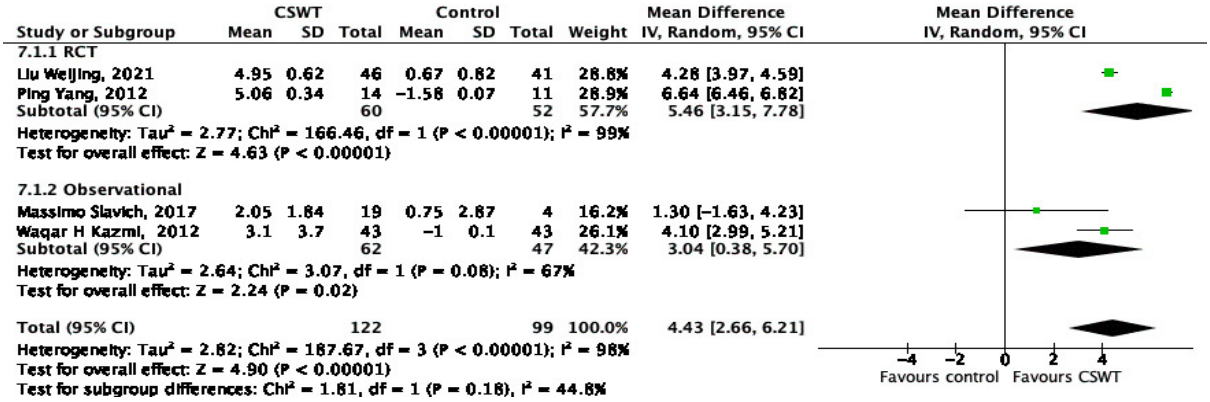

Figure 4-2. Forest plot of the CSWT group vs the control group-LVEF.

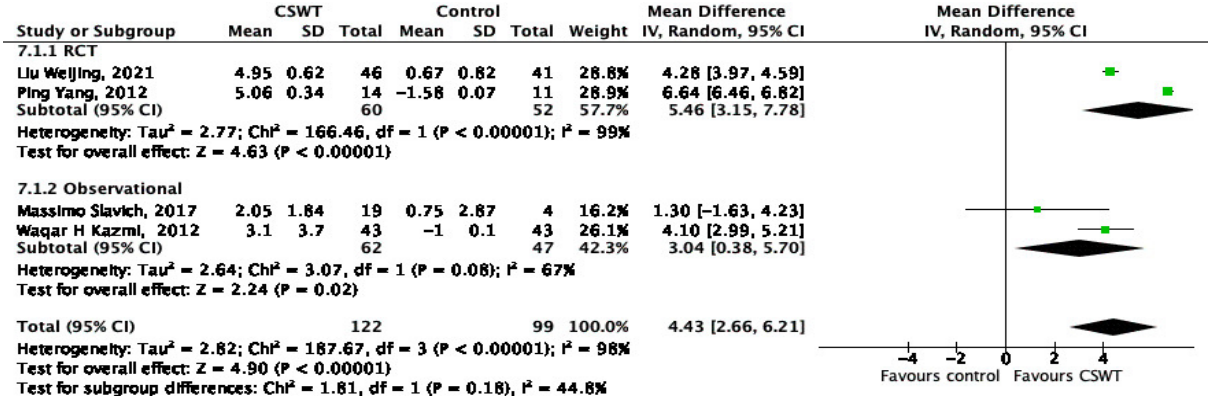

Figure 4-3. Forest plot of the CSWT group vs the control group-Nitroglycerin used.

Discussion

Mechanistically, CSWT is a non-invasive modality that enhances myocardial perfusion and mitigates anginal symptoms by delivering focused shockwave pulses to ischemic myocardial regions, typically localized via imaging.[4] Its therapeutic effect is mediated by shockwave-induced mechanotransduction, which stimulates angiogenesis through vasodilation, neocapillarization, and upregulation of multiple angiogenic signaling pathways.[16-17]

The magnitude of effect observed here is clinically relevant. A mean CCS reduction of 0.76 classes approximates a one-category improvement, often translating into fewer anginal episodes and less rescue nitrate use in daily life. The 6MWT gain in RCTs (~70–80 m) clearly exceeds the typical minimal clinically important difference reported for cardiopulmonary populations (~25–45 m), indicating a tangible improvement in functional capacity. A ~11-point increase in SAQ corresponds

to a noticeable improvement in health-related quality of life for stable angina. However, the pronounced heterogeneity and instability observed in the sensitivity analyses, especially for the 6MWT and SAQ, indicate that the most reliable evidence comes from randomized controlled trials, whereas findings from observational studies should be interpreted with caution.

Clinically plausible explanations for the 6MWT discrepancy include: (i) rigorous stabilization of background therapy and mitigation of expectation effects in sham-controlled RCTs versus usual-care controls in observational designs; (ii) residual confounding and selection in non-randomized cohorts; and (iii) small-study effects. Therefore, we prioritize subgroup-specific interpretation for 6MWT and integrate risk-of-bias–guided sensitivity analyses, as recommended by contemporary evidence-synthesis standards.

Angiogenesis and vasculogenesis are the predominant mechanisms underlying CSWT, culminating in myocardial repair and functional recovery. The underlying biological effects are predominantly mediated through the upregulation of Vascular Endothelial Growth Factor (VEGF) and Placental Growth Factor (PlGF), both of which serve as pivotal regulators of angiogenic remodeling and tissue repair.[18] Moreover, CSWT induces a phenomenon often referred to as the "cavitation effect," wherein microscopic bubbles form within myocardial tissue. Their subsequent oscillation and collapse generate mechanical forces, specifically shear stress, that act directly upon cellular membranes. Notably, Fluid Shear Stress (FSS) has been identified as an important trigger of arteriogenesis, particularly after arterial occlusion or severe stenosis, thereby enhancing blood flow and vessel formation in the affected regions.[19]

CSWT is delivered via a generator integrated with cardiac ultrasound for precise targeting of ischemic regions, and is synchronized with the Electrocardiogram (ECG) to avoid electrical impulses during myocardial repolarization, thereby reducing arrhythmogenic risk. Each session typically delivers 1,000 shocks across targeted areas, with a standard protocol of 9 sessions. The procedure is well tolerated and associated with minimal side effects, although poor acoustic windows and left ventricular thrombus are relative contraindications.[16]

By combining the most recent research and examining a range of clinical outcomes, to our knowledge, this is the updated meta-analysis specifically addressing the impact of CSWT in patients with RA. The principal observations can be summarized as follows: (1) CSWT attenuates the frequency of anginal episodes, reflected in reduced nitrate utilization, lower CCS grading, and enhanced SAQ scores; (2) CSWT augments left ventricular performance, demonstrated by improvements in LVEF; (3) CSWT ameliorates overall cardiac function, evidenced by favorable shifts in NYHA classification, thereby translating into tangible gains in daily activity and functional status; and (4) CSWT enhances exercise tolerance, as indicated by an increased distance covered during the 6-minute walk test. However, LVEDD was not statistically significant.

Our results are broadly consistent with earlier evidence syntheses. Xinze Wu et al.[20] in a meta-analysis encompassing 19 trials with 1,254 subjects, reported substantial benefits in functional capacity, angina classification, nitrate requirement, and LVEF, although no significant differences were observed for SAQ scores or exercise duration. Another meta-analysis by Hai Tao Yang in 2020, including 26 studies and involving 781 patients, concluded that CSWT offers pronounced improvements in anginal symptomatology, exercise endurance, quality of life, nitrate consumption, and myocardial perfusion. Together, these findings highlight the multifaceted benefits of CSWT, particularly in enhancing myocardial perfusion and functional recovery.[5]

The first clinical trial of the application of CSWT in refractory angina was conducted by Yoshihiro et al. in protocols employing low-intensity shockwave delivery (4,000–8,000 shocks over 20–40 spots) thrice during the initial week. Remarkably, without anesthesia or analgesic requirements, investigators observed symptomatic relief, reduced nitroglycerin dependence, and enhanced myocardial perfusion in ischemic regions, all without procedure-related complications or adverse sequelae.[6] Subsequent studies confirmed that CSWT significantly enhances left ventricular function in patients with Ischemic Heart Disease (IHD).[21] Another use of shockwave therapy is in the perioperative context, where prophylactic low-energy SWT facilitates wound healing following saphenous vein harvesting for CABG. The proposed mechanisms include upregulation of VEGF and Flt-1, stimulation of angiogenesis, and enhanced production of nitric oxide via nonenzymatic pathways.[23]

CSWT may be especially valuable for patients with Multiple-Vessel Coronary Artery Disease (MVD) who are candidates for PCI or CABG. In such patients, extensive myocardial necrosis,

fibrosis, or impaired ventricular compliance limits the efficacy of conventional revascularization strategies. The therapeutic principle of CSWT relies on the delivery of low-energy, high-frequency shockwaves to ischemic myocardial tissue. These pulses induce mechanical shear stress, cavitation, and microstreaming, thereby stimulating angiogenesis and microvascular remodeling. The precision of this intervention is enhanced by echocardiography-guided localization, with shockwave delivery synchronized to the R wave of the electrocardiogram during the absolute refractory period, thereby ensuring procedural safety.[5]

Despite its promising outcomes, several limitations exist regarding the clinical application of CSWT. First, a restricted acoustic window limits treatment to accessible myocardial regions, most often the anterior wall. Second, concerns have been raised regarding potential pulmonary injury due to adjacent tissue exposure. As an alternative, an epicardial approach during surgical procedures has been proposed to optimize energy delivery. Recent intraoperative studies combining CSWT with CABG have demonstrated encouraging results, including significant improvements in LVEF and exercise capacity among patients with ischemic cardiomyopathy.[22-23] These findings suggest that hybrid strategies may broaden the therapeutic scope of CSWT and improve its clinical utility.

Most trials included in this analysis are relatively small, single-center, single-arm studies, and some lack sufficient methodological transparency and result reporting. The predominance of high heterogeneity across outcomes necessitates a cautious interpretation of the pooled findings. This meta-analysis specifically focused on RA patients and double-arm (controlled) studies to provide more robust evidence. CSWT has not yet been widely adopted in clinical practice, despite its excellent tolerability, minimal side effects, significant symptomatic benefits, and non-invasive nature. This limited adoption may be attributed to the need for specialized, high-cost equipment, advanced expertise in ultrasound scanning and CSWT application, and the considerable time commitment required for the full course of treatment.[24] Nevertheless, CSWT represents a promising adjunctive treatment for managing RA, offering an effective and innovative treatment option.[25]

Conclusion

Patients with RA may benefit from the new, non-invasive treatment known as CSWT. It appears to enhance exercise tolerance through multiple pathways: by diminishing the frequency of anginal episodes, as evidenced by reductions in CCS grading and nitrate use; by yielding higher SAQ scores; and by augmenting left ventricular performance, reflected in measurable gains in LVEF, improves cardiac performance, as shown by the decrease in NYHA classification, and can increase the distance of a 6-minute walk. LVEDs were not statistically significant, nevertheless. CSWT may be a promising, safe, and effective cardioprotective strategy that should be further explored in patients with refractory angina. It is hoped that this procedure will lessen the need for re-revascularization following PCI/CABG. However, substantial heterogeneity and a statistically significant RCT-versus-observational divergence for 6MWT warrant cautious interpretation and emphasis on sham- or OMT-controlled randomized evidence. Furthermore, information on its long-term effectiveness in relieving symptoms, improving cardiac function, and reducing mortality rates remains insufficient. Therefore, future multicentre RCTs with standardized comparators and transparent reporting of control interventions are needed to consolidate indications and optimize CSWT protocols in refractory angina.

List of Abbreviations

6MWT	6 Minute Walking Test
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CCS	Canadian Cardiology Society
CI	Confidence Interval
CSWT	Cardiac Shock Wave Therapy
ECG	Electrocardiogram
FSS	Fluid Shear Stress
IHD	Ischemic Heart Disease
LVEDD	Left Ventricular End Diastolic Dimension
LVEF	Left Ventricular Ejection Fraction
MD	Mean Differences
MVD	Multiple-Vessel Coronary Artery Disease
NO	Nitric Oxide
NYHA	New York Heart Association
PCI	Pecutaneous Coronary Intervention
PlGF	Placental Growth Factor
PRISMA	Preffered Reportinf Items for Systematics Review and Meta-Analysis

PROSPERO	Prospective Register for Systematic Reviews
RA	Refractory Angina
RCT	Randomized Controlled Trial
SAQ	Seattle Angina Quetionnaire Score
SD	Standard Deviation
VEGF	Vascular Endothelial Growth Factor

Ethical Clearance

Not applicable.

Publication Approval

All authors have read, critically revised, and approved the final version of the manuscript for submission and publication.

Authors Contributions

FDP and MRA developed the concept for the project and formulated the methodology. FDP managed the study protocol. Both FDP and MRA conducted the literature review, study selection, data collection, and bias risk assessment. FDP carried out the formal data analysis. FDP created visual representations of the results. FDP and MRA analyzed and interpreted the findings. FDP, MRA, and MM prepared the initial draft of the manuscript. They also collaboratively reviewed, validated, and finalized the manuscript, with MRA editing it for submission. MM was responsible for overarching project supervision. All contributors critically evaluated and endorsed the final version of the manuscript for submission.

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None.

Conflict of Interest

All authors (FDP, MRA, MM) of the study declare no conflict of interest.

Availability of Data and Materials

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