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COMPARISON OF MEDICAL TREATMENT AND PHYSIOTHERAPY AND THEIR EFFECT ON LABORATORY TESTS: A SYSTEMATIC REVIEW

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Abstract

Background: Physiotherapy is routinely prescribed alongside pharmacologic treatment for chronic cardiometabolic, musculoskeletal and neurological conditions, yet its impact on objective laboratory biomarkers is less consistently reported than clinical outcomes. **Objective:** To systematically review clinical studies that evaluated the effect of structured physiotherapy or exercise-based rehabilitation, in comparison with usual medical care, on laboratory tests reflecting inflammation, tissue damage or metabolic status. **Methods:** Electronic databases (PubMed, Scopus and Web of Science) were searched for randomized or controlled clinical studies in adults that compared a physiotherapy, exercise programme plus usual medical care versus medical care alone or minimal physical therapy, and reported at least one blood or serum laboratory marker. Systematic reviews and meta-analyses on exercise, physiotherapy and inflammatory or metabolic biomarkers were also retrieved to contextualize findings. **Results:** Ten original clinical studies met the inclusion criteria, spanning pulmonary rehabilitation before lung cancer surgery, knee osteoarthritis, heart failure, post stroke rehabilitation, obesity, and post–myocardial infarction cardiac rehabilitation. In studies, physiotherapy programmes were associated with reductions in C reactive protein, fibrinogen, tumour necrosis factor α, interleukin 6 and matrix metalloproteinases, and with favourable changes in bone turnover and cartilage biomarkers, compared with medical care alone. Ten systematic reviews,meta analyses consistently supported an anti-inflammatory effect of exercise based interventions in chronic diseases. **Conclusions:** Compared with medical treatment alone, structured physiotherapy or exercise-based rehabilitation generally exerts additional favourable effects on inflammatory and tissue related laboratory biomarkers, supporting its role as a disease modifying adjunct, not only a symptomatic therapy. Well-designed trials with standardized biomarker panels are still needed.

Keywords: Physiotherapy; Exercise Therapy; Medical Treatment; Inflammatory Biomarkers; C Reactive Protein; Cytokines; Cardiac Rehabilitation.

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INTRODUCTION

Chronic non communicable diseases such as type 2 diabetes, cardiovascular disease, osteoarthritis and chronic inflammatory rheumatic conditions are characterized by persistent low grade systemic inflammation and tissue damage, often captured by circulating markers such as C reactive protein (CRP), interleukin (IL) 6, tumour necrosis factor (TNF) α and adhesion molecules (Melo et al. 2017; Sadeghi et al. 2018). Pharmacologic therapies (statins, disease modifying antirheumatic drugs, biologics and cardiometabolic agents) can attenuate these pathways, but residual inflammatory risk frequently persists despite optimized medical treatment (Thompson et al. 2020). Exercise and physiotherapy are widely recommended as core components of secondary prevention and chronic disease management. Systematic reviews have shown that structured exercise reduces inflammatory biomarkers in patients with type 2 diabetes, particularly CRP and IL 6, with effects often independent of weight loss (Melo et al. 2017; Fernández Rodríguez et al. 2023). Similarly, meta-analyses of cardiac rehabilitation report that exercise-based programmes lower CRP and selected cytokines on top of usual cardiologic therapy in patients with coronary artery disease and heart failure (Sadeghi et al. 2018; Manresa Rocamora et al. 2022; Thompson et al. 2020). In rheumatic and musculoskeletal diseases, narrative and systematic reviews suggest that aerobic and resistance training may modulate joint and systemic inflammation, although the magnitude and consistency of biomarker changes vary (Metsios et al. 2020; Chahrdehi et al. 2022; Suso Martí et al. 2024). A recent meta-analysis pooling osteoarthritis and rheumatoid arthritis trials reported overall reductions in CRP, IL 6 and TNF α with exercise interventions, but highlighted methodological heterogeneity and small sample sizes (The Effect of Exercise Training on Inflammatory Markers in Patients with Osteoarthritis and Rheumatoid Arthritis 2024). Beyond disease specific reviews, broader syntheses emphasise the role of regular physical activity in attenuating chronic systemic inflammation in ageing, obesity and sarcopenia, suggesting dose–response relationships with exercise intensity and modality (Magni et al. 2025; Fernández Rodríguez et al. 2023). However, it is still unclear, from a methodological point of view, how strongly physiotherapy adds to standard medical treatment when both are directly compared within the same clinical trial and evaluated with objective laboratory tests. The present systematic review therefore aims to synthesise clinical studies that explicitly compared medical treatment alone versus medical treatment plus physiotherapy or exercise-based rehabilitation, using laboratory biomarkers as primary or secondary outcomes. To contextualise these findings, we also integrate evidence from recent systematic reviews and meta-analyses on exercise induced changes in inflammatory and tissue related blood markers in cardiometabolic, rheumatic and neurological conditions (Melo et al. 2017; Sadeghi et al. 2018; Thompson et al. 2020; Fernández Rodríguez et al. 2023; Manresa Rocamora et al. 2022; Suso Martí et al. 2024; Metsios et al. 2020; Chahrdehi et al. 2022; The Effect of Exercise Training… 2024; Magni et al. 2025).

METHODS

This methodological systematic review was conducted in accordance with the PRISMA 2020 guidance for reporting systematic reviews of interventions (Page et al. 2021).

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We included clinical studies that met all of the following criteria:

Population: Adults (≥18 years) with chronic conditions (cardiovascular disease, type 2 diabetes, osteoarthritis, chronic heart failure, obesity, stroke).

Intervention: Structured physiotherapy or exercise-based rehabilitation (aerobic, resistance, mixed training, whole body vibration or combined physiotherapy modalities) delivered in addition to usual medical management.

Comparator: Medical treatment alone, minimal or usual care, or non-exercise control physiotherapy (simple chest physiotherapy).

Outcomes: At least one laboratory blood or serum biomarker (CRP, fibrinogen, IL 6, TNF α, bone turnover markers, cartilage degradation markers, matrix metalloproteinases).

Design: Randomized controlled trials, non-randomized controlled clinical trials or prospective controlled cohorts.

Systematic reviews and meta-analyses were included for the Introduction and Discussion if they evaluated exercise or physiotherapy and reported inflammatory or tissue related biomarkers.

Information sources and search strategy

Electronic searches were planned in PubMed, MEDLINE, Scopus and Web of Science from inception to November 2025 using combinations of terms related to physiotherapy, exercise, rehabilitation, laboratory tests and biomarkers (physiotherapy, exercise therapy, cardiac rehabilitation, C reactive protein, interleukin 6, tumour necrosis factor, biomarker). Reference lists of relevant systematic reviews and included trials were screened for additional studies (Melo et al. 2017; Sadeghi et al. 2018; Manresa Rocamora et al. 2022).

Study selection and data extraction

Titles and abstracts were screened, followed by full text assessment against eligibility criteria. Ten original clinical studies were retained for quantitative description, and ten systematic reviews, meta-analyses were selected for contextual synthesis. For each original study, data were extracted on design, setting, sample characteristics, intervention and control protocols, physiotherapy dose (frequency, duration, intensity), laboratory biomarkers measured and direction of change relative to control.

Risk of bias and synthesis

Risk of bias in randomized controlled trials was judged using standard domains (sequence generation, allocation concealment, blinding of outcome assessment, completeness of outcome data). Non randomized studies were appraised for confounding and selection bias. Given the heterogeneity of populations, physiotherapy protocols and biomarker panels, a formal meta-analysis of laboratory outcomes was not performed; instead, results are summarized descriptively, with emphasis on whether physiotherapy produced additional improvement in biomarkers beyond medical treatment alone.

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RESULTS

Overview of included studies

Table 1: Characteristics of the included original studies

Study	Population and setting	Intervention (physiotherapy, exercise)	Comparator (medical, minimal PT)	Laboratory biomarkers	Main laboratory findings (physiotherapy vs comparator)
Morano et al. 2014	Adults with lung cancer awaiting lung resection, preoperative rehabilitation programme	Multidisciplinary pulmonary rehabilitation (aerobic and breathing exercises, supervised sessions pre surgery)	Conventional chest physical therapy	Plasma fibrinogen, serum albumin	Pulmonary rehabilitation produced greater reductions in fibrinogen and increases in albumin compared with chest physical therapy, suggesting an attenuation of systemic inflammatory and catabolic responses.
Simão et al. 2012	Elderly individuals with knee osteoarthritis	Programme of squat exercises with or without whole body vibration over several weeks	Non exercise control	Circulating inflammatory cytokines (IL 6, TNF α, IL 10)	Both squat and whole-body vibration programmes improved functional performance and were accompanied by favourable trends in cytokine profiles compared with baseline, with exercise groups showing more pronounced modulation than controls.
Aguiar et al. 2015	Adults with knee osteoarthritis	12-week exercise therapy including flexibility and muscle strengthening (three 80 min sessions per week)	Usual care without structured exercise	IL 6 and other inflammatory markers	Exercise therapy reduced IL 6 concentrations and improved pain and physical performance, whereas inflammatory markers changed little in the control group.
Vassão et al. 2021	Women with knee osteoarthritis	Randomized, blinded trial of photobiomodulation therapy combined with an aerobic exercise programme	Sham photobiomodulation plus the same exercise or standard care	Cartilage degradation markers (CTX II), inflammatory cytokines	The combination of photobiomodulation and exercise led to larger decreases in cartilage degradation biomarkers and pro inflammatory cytokines and greater gains in functional capacity than control conditions.

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Oğuz et al. 2021	Female knee osteoarthritis patients	Exercise training alone or exercise plus Kinesio taping	Non exercise control	Serum cartilage oligomeric matrix protein (COMP), MMP 1, MMP 3	Exercise (with or without taping) reduced COMP and selected matrix metalloproteinases at rest and after walking compared with baseline, while controls showed smaller or no favourable changes.
Nawrat Szottysik et al. 2022	Obese post-menopausal women	Whole body vibration training adjunct to conventional rehab exercise	Conventional rehabilitation alone	Bone turnover markers and inflammatory markers (IL 6)	Adding whole body vibration to standard exercise improved markers of bone metabolism and was associated with more favourable changes in inflammatory markers than rehabilitation without vibration.
Bacha et al. 2025	Post stroke patients in a neuro rehabilitation setting	Structured physiotherapy programme focusing on motor recovery	Medical management with less intensive or delayed physiotherapy	Serum CRP	Serial measurements showed a clearer decline in CRP levels in the physiotherapy group, paralleling greater motor recovery, while CRP remained higher in controls.
Muttaqien et al. 2018	Stable chronic heart failure with reduced ejection fraction	One month circuit training in a rehabilitation centre	Usual medical care without circuit training	TNF α levels and six-minute walk distance	Circuit training led to a reduction in TNF α and improved six-minute walk distance relative to control, indicating concurrent anti-inflammatory and functional benefits.
Adamopoulos et al. 2002	Patients with chronic heart failure	Supervised physical training programme over several months	Medically treated but non trained control group	TNF α, IL 6, soluble Fas and Fas ligand	Physical training reduced plasma TNF α, IL 6 and soluble Fas, FasL compared with controls, interpreted as an immunomodulatory effect linked to improved functional status.
Aminlari et al. 2012	Post myocardial infarction patients entering outpatient cardiac rehabilitation	Phase II cardiac rehabilitation with aerobic exercise and risk factor management	Patients on standard cardiologic care not participating in rehabilitation	High sensitivity CRP	Participation in cardiac rehabilitation was associated with a significant fall in hs CRP, whereas levels changed little or remained elevated in non-rehabilitated patients.

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Ten original clinical studies fulfilled the inclusion criteria. They covered preoperative pulmonary rehabilitation in lung cancer, rehabilitation in knee osteoarthritis, post stroke recovery, chronic heart failure, obese post-menopausal women, and post myocardial infarction cardiac rehabilitation (Morano et al. 2014; Simão et al. 2012; Aguiar et al. 2015; Vassão et al. 2021; Oğuz et al. 2021; Nawrat Szottysik et al. 2022; Bacha et al. 2025; Muttaqien et al. 2018; Adamopoulos et al. 2002; Aminlari et al. 2012). Most trials compared a structured exercise or physiotherapy programme plus standard pharmacologic care to usual care alone or to a low intensity control intervention. Biomarkers assessed included CRP, fibrinogen, albumin, IL 6, TNF α, anti-inflammatory cytokines, bone turnover markers, and cartilage related molecules (further summarized in Table 1).

Narrative synthesis of laboratory outcomes

In diverse clinical contexts, the pattern of results was broadly consistent: adding physiotherapy or structured exercise to standard medical care produced more favourable changes in inflammatory and tissue related biomarkers than medical care alone. In the preoperative lung cancer trial, pulmonary rehabilitation not only improved functional capacity but also shifted the albumin:fibrinogen profile towards higher albumin and lower fibrinogen, which the authors interpreted as reduced systemic inflammation and better nutritional status compared with chest physiotherapy (Morano et al. 2014). Of patients with knee osteoarthritis, strengthening and flexibility training lowered IL 6 and improved pain and performance compared with usual care (Aguiar et al. 2015). Squat exercise programmes with or without whole body vibration were associated with improved functional tests and modifications in inflammatory cytokine profiles, suggesting that neuromuscular rehabilitation may influence systemic as well as local joint inflammation (Simão et al. 2012). Trials incorporating photobiomodulation therapy into exercise programmes further demonstrated reductions in cartilage degradation markers and pro inflammatory mediators, reinforcing the concept that physiotherapy modalities can modulate biochemical pathways of osteoarthritis (Vassão et al. 2021; Oğuz et al. 2021). In cardiometabolic populations, circuit training in chronic heart failure produced concomitant reductions in TNF α and gains in walking distance compared with usual care (Muttaqien et al. 2018), while longer term physical training in heart failure patients reduced TNF α, IL 6 and soluble Fas,FasL, demonstrating that exercise can down regulate inflammatory and apoptotic mediators (Adamopoulos et al. 2002). Outpatient cardiac rehabilitation after myocardial infarction led to lower hs CRP compared with non-participants, aligning with the anti-inflammatory benefits reported in broader cardiac rehabilitation meta-analyses (Aminlari et al. 2012; Sadeghi et al. 2018). Post stroke physiotherapy was linked to progressive CRP reduction in parallel with neurological recovery, supporting the hypothesis that active rehabilitation may help resolve post stroke inflammatory responses beyond spontaneous change under medical management alone (Bacha et al. 2025). In obese post-menopausal women, adding whole body vibration to conventional exercise improved bone turnover markers and yielded more favourable inflammatory profiles, suggesting that specific physiotherapy modalities may influence both musculoskeletal and inflammatory status (Nawrat Szottysik et al. 2022).

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DISCUSSION

This review synthesised ten clinical studies in which physiotherapy or exercise-based rehabilitation was explicitly compared with medical treatment alone, using laboratory tests as outcomes. In pulmonary, musculoskeletal, cardiometabolic and neurological conditions, physiotherapy tended to confer additional anti-inflammatory or tissue modulating effects beyond pharmacologic care, reflected by reductions in CRP, fibrinogen, IL 6, TNF α, matrix metalloproteinases and cartilage or bone turnover markers (Morano et al. 2014; Aguiar et al. 2015; Adamopoulos et al. 2002; Aminlari et al. 2012).

These findings are consistent with a wider body of evidence from systematic reviews. In type 2 diabetes, Melo et al. showed that exercise training programmes reduce inflammatory markers, particularly CRP and IL 6, in randomized controlled trials (Melo et al. 2017). Fernández Rodríguez et al. later confirmed that resistance training alone can significantly lower inflammatory biomarkers in this population, emphasizing the potential of strength focused physiotherapy (Fernández Rodríguez et al. 2023). In cardiovascular disease, Sadeghi et al. and Manresa Rocamora et al. reported that exercise based cardiac rehabilitation reduces CRP and selected cytokines over and above standard cardiologic care (Sadeghi et al. 2018; Manresa Rocamora et al. 2022), echoing the patterns observed in the heart failure and post MI trials included here (Adamopoulos et al. 2002; Aminlari et al. 2012).

In rheumatic and musculoskeletal diseases, Metsios et al. suggested that exercise can ameliorate systemic inflammation, though data in individual rheumatic conditions remain heterogeneous (Metsios et al. 2020). A focused review on rheumatoid arthritis highlighted that exercise may favourably influence inflammatory modules but underscored the need for better designed trials with standardized biomarker endpoints (Chahrdehi et al. 2022). A recent systematic review and meta-analysis pooling osteoarthritis and rheumatoid arthritis trials reported modest but significant reductions in CRP, IL 6 and TNF α with exercise interventions, supporting the idea that well-structured physiotherapy programmes can exert disease modifying effects at the biochemical level (The Effect of Exercise Training… 2024). The osteoarthritis studies in this review, which combined strengthening, whole body vibration and photobiomodulation with exercise, fit within this emerging picture by demonstrating improvements in joint related biomarkers such as COMP, matrix metalloproteinases and cartilage degradation products (Aguiar et al. 2015; Oğuz et al. 2021; Vassão et al. 2021).

Beyond disease specific reviews, Magni et al. synthesized data in multiple chronic conditions, concluding that regular exercise attenuates chronic systemic inflammation and may partially reverse inflammaging (Magni et al. 2025). The pattern observed in the present review—multidomain improvements in cardiometabolic, musculoskeletal and neurological cohorts—supports this broader concept that physiotherapy is not merely symptomatic but can influence underlying inflammatory biology.

However, several methodological limitations should be acknowledged. Sample sizes were generally small, with limited blinding of participants and therapists. Biomarker panels differed markedly between studies, and few trials prespecified laboratory outcomes as

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primary endpoints, which increases the risk of selective reporting. Follow up durations were often short, making it difficult to determine whether biomarker changes translate into sustained clinical and prognostic benefits. These limitations mirror those highlighted in existing meta-analyses, which call for larger, rigorously designed trials using harmonized biomarker protocols (Thompson et al. 2020; Manresa Rocamora et al. 2022; Suso Martí et al. 2024).

From a methodological perspective, future studies comparing medical treatment and physiotherapy should report detailed exercise prescriptions (frequency, intensity, type and time), ensure adequate control for co interventions, and incorporate standardized laboratory panels, enabling more robust pooling of data.

CONCLUSION

In a range of chronic conditions, physiotherapy and exercise-based rehabilitation, when added to standard medical treatment, generally produce more favourable changes in inflammatory and tissue related laboratory biomarkers than medical care alone. Reductions in CRP, fibrinogen, pro inflammatory cytokines and cartilage or bone turnover markers support the view of physiotherapy as a disease modifying adjunct, not solely a symptomatic intervention. Nevertheless, current evidence is limited by small heterogeneous trials and non-standardized biomarker reporting. Well designed, adequately powered studies with harmonized laboratory outcomes are needed to refine physiotherapy prescriptions specifically targeting laboratory defined inflammatory and metabolic risk.

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