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The effects of physical exercise on quality of life and physical fitness among lipedema patients

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202530124

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 March 2025 and was last updated on 28 March 2025.

INTRODUCTION

Review question / Objective The aim of this review is to evaluate the effects of physical exercise on the incidence of health-related quality of life, physical fitness and psychological outcomes in lipedema patients.

Rationale Lipedema is a chronic, progressive disorder of subcutaneous adipose tissue (SAT) that primarily affects females, with an estimated global prevalence of 11% among adult women. It is characterized by disproportionate adipocyte hypertrophy, interstitial fluid accumulation, and a distinct, non-pitting "fatty" swelling, predominantly in the lower extremities. The condition leads to pain, tenderness, easy bruising, and reduced mobility. While its progression is unpredictable, comorbidities such as obesity, depression, lymphedema, and peripheral artery disease can accelerate its severity. Despite its distinct clinical features, lipedema is often misdiagnosed as obesity or lymphedema due to the lack of definitive histopathologic or molecular markers. The etiology of lipedema remains poorly understood. However, its rapid progression has been linked to hormonal fluctuations (e.g., puberty, pregnancy, menopause), vascular or lymphatic dysfunction, and stressors such as surgery or trauma. A genetic predisposition is also suspected, as the condition is frequently observed in individuals with a family history of lipedema. Frequent misdiagnosis results in inappropriate treatment recommendations, often centered around weight loss through diet and exercise, despite evidence suggesting that lipedema fat is resistant to such interventions. In some cases, these stressors may even exacerbate fat accumulation, leading to frustration, disordered eating, and a significant psychological burden. Many patients report body dissatisfaction, self-stigmatization, anxiety, depression, and suicidal ideation. Additionally, mobility impairments due to

joint hypermobility, enlarged lower extremities, and comorbid obesity can further reduce physical activity levels, exacerbating symptoms such as muscle weakness, fatigue, and weight gain due to non-lipedema fat accumulation. As the disease progresses, secondary complications like lymphedema, venous disease, orthopedic issues, and obstructive sleep apnea may develop, further reducing quality of life.

Currently, no cure exists for lipedema, and treatment focuses on symptom management and disease progression prevention. Physical exercise, particularly low-intensity aerobic or aquatic exercise, is often recommended as part of conservative management. While exercise is well-established as beneficial for numerous clinical conditions such as obesity, cardiovascular disease, and cancer, its effects on lipedema remain largely unexplored. Current recommendations are primarily based on expert opinions rather than lipedema-derived exercise studies and thus may not be tailored to individual patient needs. For instance, emerging evidence suggests that lipedema patients exhibit greater muscle weakness compared to obese individuals, which may affect their exercise capacity and response to training. Given the increasing number of studies on this topic, a comprehensive review of the literature is essential to better understand the potential benefits of exercise in lipedema management.

Condition being studied The effects of physical exercise on quality of life and physical fitness among lipedema patients.

METHODS

Search strategy This systematic review will be conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The Boolean search method (AND/OR) will be used as strategic to find relevant literature. Search lines selected: (lipedema OR lipoedema [All Fields]) AND ("physical activity" OR "physical exercise" OR "functional exercise" OR "physical endurance" OR "muscle power" OR exercise OR fitness OR "aerobic exercise" OR "strength exercise" OR "endurance exercise" OR "resistance exercise" OR "combined exercise" OR "strength training" OR "endurance training" OR "resistance training" OR "combined training"[All Fields]) AND NOT (lymphedema OR lymphoedema [All Fields]). In each database we will use a similar strategy to find relevant articles.

Searches will be conducted without publication date restrictions and without filters.

Participant or population Female patients aged 18 or older with a clinical diagnosis of lipedema at any stage of the disease.

Intervention Studies reporting the effects of prescription of physical exercise (PE) combined with pharmacological and/or non-pharmacological treatment.

Comparator Comparator groups should include individuals who do not engage in physical exercise or comparison with pre-intervention values as in the case of pre-post studies.

Study designs to be included We will include any type of study designs, except case studies. Letters, editorials, meeting abstracts, commentaries and reviews will be excluded.

Eligibility criteria Only studies published in English, Spanish, and Portuguese will be considered for inclusion in the review The studies must comply with following inclusion criteria: (1) Population: female patients, over 18 years of age, diagnosed with lipedema (all stages of the disease), without any restrictions regarding race / ethnicity or sociodemographic characteristics; (2) Intervention: prescription of physical activity or physical exercise (aerobic training and strength/ aerobic training) combined with pharmacological and/or non-pharmacological treatment; (3) Comparison: with a reference group or with pre-intervention values as in the case of pre-post studies; (4) Outcomes: changes in anthropometrics (e.g. limb circumference), physical fitness (e.g. aerobic capacity and/or strength), health-related quality of life and/or psychological status by a validated instrument (e.g. WHOQOL-BREF, RAND-36, EQ-5D-3L); (5) Type of study: all types of studies will be considered.

Information sources The databases that will be used are: PubMed, Scopus, EBSCOhost, EMBASE and Web of Science.

Main outcome(s) The main outcomes are those related to health-related quality of life (QoL) and/or psychological status, physical fitness (aerobic capacity and/or strength) and anthropometry/body composition.

Additional outcome(s) No.

Data management The data will be screened through at Endnote software to eliminate duplicates though manual verification and Rayyan software for a critical evaluation and analysis.

Article selection in both platforms will be conducted by expert reviewers.

Quality assessment / Risk of bias analysis The risk of bias will be evaluated using the RoB 2 tool for randomized trials or the ROBINS-I tool for non-randomized studies. Each study will be evaluated in six bias domains: selection of participants, confounding variables, measurement of exposure, blinding of outcome assessments, incomplete outcome data and selective outcome reporting. Risk of bias will be judged at study-level by two authors. In case of discrepancies, disagreements will be resolved through consensus or consultation with a third reviewer if necessary. To ensure the rigor of the findings, all included studies will undergo a thorough risk of bias assessment, which will be considered in the interpretation of results.

Strategy of data synthesis Two independent authors will collect data for all outcomes, with any disagreements resolved by consensus. All extracted data will be systematically organized using Excel.

Subgroup analysis We do not expect that there will be enough studies to conduct subgroup analyses; but if available, subgroup analyses could be done for age groups, stage of disease and features of exercise prescription (e.g. mode, type, frequency, intensity, duration), level of supervision and delivery mode (home versus clinical-based).

Sensitivity analysis In case of need, sensitivity analysis will be performed by re-running analyses after removing studies with a high risk of bias (e.g., based on RoB 2 or ROBINS-I) to evaluate whether weaker methodological quality influences the overall findings, by investigating the impact of heterogeneity by excluding specific subgroups (e.g., studies with extreme effect sizes), and by systematically removing one study at a time to determine whether any single study disproportionately influences the pooled estimate.

Language restriction Just international peer-reviewed studies written in English, Spanish and Portuguese will be selected.

Country(ies) involved Portugal.

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Keywords Lipedema; physical activity; aerobic exercise; strength exercise; combined exercise; fitness capacity; quality of life.

Dissemination plans This systematic review will be disseminated in conferences and published in international peer-reviewed journals with impact factor.

Contributions of each author
Author 1 - Daniela Gomes - DG participated in the planning and will be involved in data extraction and analysis, manuscript draft, review and final approval.
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Author 4 - Daniel Moreira-Gonçalves - DMG contributed to study planning and will participate as third reviewer when consensus is needed, manuscript draft, review and final approval.