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Systematic Reviews and Meta-Analysis

Cultivating Vitality: Unveiling the Transformative Effects of Exercise on Menopausal Women's Well-being and Physiological Markers: A Meta-Analysis of Randomized Control Trial

Alfredo Wijaya, Alifian Singgih Fachrani, Gloria Claudia Kastanja, Indy Zahrotul Firdaus¹, Muhammad Rifky Alif Syahputra

Faculty of Medicine, Universitas Brawijaya/dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia

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CORRESPONDING AUTHOR*

Indy Zahrotul Firdaus ind1211@student.ub.ac.id Faculty of Medicine Universitas Brawijaya/ dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia

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ABSTRACT

Introduction: Menopause frequently coincides with age-related hormonal decline, elevated blood pressure, and unfavorable body composition changes, collectively heightening the risk of cardiovascular disease. Addressing the adverse effects of menopause is crucial through the integration of suitable lifestyle interventions, such as exercise. Nonetheless, there remains controversy within studies regarding the significance of exercise in improving Quality of Life (QoL), reducing Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Total Cholesterol (TC), and Low-Density Lipoprotein (LDL), as well as maintaining Bone Mineral Density (BMD). Thus, this review aims to determine and clarify the influence of exercise on patient outcomes.

Materials/Methods: This meta-analysis followed the PRISMA statement guidelines, utilizing databases such as PubMed, ScienceDirect, and Google Scholar over the past ten years. Inclusion criteria adhered to the PICOS framework, and the literature quality assessment was based on the Risk of Bias 2.0 Tool.

Results: Out of 14 included studies, the majority indicated no significant improvements in menopause women undergoing exercise regarding QoL [MD: -6.62 (95% CI: -16.90 – -3.66, I²=91%)], SBP [MD: -4.74 (95% CI: -10.54 – 1.05, I²=100%)], DBP [MD: -4.52 (95% CI: -8.59 – -0.46, I²=99%)], TC [MD: -4.06 (95% CI: -8.75 – 0.64, I²=57%)], LDL [MD: -2.26 (95% CI: -7.37 – 2.86, I²=65%)], and BMD [MD: 0.06 (95% CI: -0.01 – 0.13, I²=86%)]. Significant improvements were seen only in DBP outcomes

Conclusion: Menopause exercise women may effectively raise QoL, reduce SBP, DBP, TC, and LDL, also maintain BMD.

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INTRODUCTION

Menopause, defined as the cessation of menstrual periods, is a gradual and natural process for women, typically occurring between the ages of 42 and 55. This transitional phase holds significant importance, impacting various aspects of a woman's life, including physical, emotional, and social dimensions [1]. The onset of menopause can influence the quality of life and the ability to manage work responsibilities, as a large majority of middle-aged women (up to 80%) report experiencing menopausal symptoms [2,3]. These symptoms commonly include hot flashes, sleep disturbances, and mood swings [4]. Specific symptoms, such as difficulties in concentration and feelings of depression, often disrupt work performance during the menopausal period [5,6].

Recently, issues related to menopause have increased public and researcher attention. Furthermore, around 80% of women experience symptoms associated with estrogen and testosterone depletion, which can be debilitating and last for an average of four years but up to 12 years [7]. These symptoms include hot flashes, night sweats, sleep disturbances, fatigue, difficulty concentrating, depression, anxiety, mood swings, irritability, and loss of confidence. Women experiencing troublesome menopausal symptoms often have lower levels of health-related quality of life and require more healthcare than those without symptoms. Prolonged estrogen deficiency can impact the cardiovascular system and increase the risk of long-term conditions such as osteoporosis [7].

While many women experience problematic menopausal symptoms, fewer opt for Hormone Replacement Treatment (HRT). Besides, the risks of HRT administration may outweigh the benefits. Thus, alternative treatments are needed. Emerging evidence suggests that physical activity may be beneficial in alleviating some menopausal symptoms and reducing the risk of diseases associated with menopause. Physical activity encompasses activities such as occupational, sports, conditioning, household chores, and others. At the same time, exercise refers to planned, structured, and repetitive physical activity aimed at improving or maintaining physical fitness [7]. There is strong evidence that physical activity throughout life protects against chronic conditions, including coronary heart disease, obesity, type 2 diabetes, and mental health issues. Despite clear UK recommendations regarding the benefits of physical activity, strength training, and the recommended weekly activity, many women tend to decrease physical activity during the menopausal transition. Many women need to meet the recommended activity levels, particularly in moderate activity and strength training [7].

Research suggests that although physical activity levels among menopausal women are low, there is a high desire to be more active, especially when recommended by a healthcare professional. Many women experiencing menopausal symptoms seek medical advice from their general practitioners, but not all opt for or have access to HRT. Strengthening the evidence base for all intervention options could enhance women's agency in managing menopause [7]. This overview evaluates the effectiveness of physical activity and exercise interventions targeted at menopausal women. While numerous recent and ongoing systematic reviews exist in this area, there currently needs to be a comprehensive overview.

MATERIALS/METHODS

This review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (<u>http://prisma-statement.org/</u>).

Eligibility Criteria

Prior to commencing the literature search, specific inclusion and exclusion criteria were established to enhance the precision of the review process. Inclusion criteria encompassed experimental (clinical) studies published within the previous decade up to March 2024. The inclusion criteria were structured following the Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework, incorporating: 1) Population: Pre-, peri-, and post-menopausal women; 2) Intervention: Exercise (aerobic, anaerobic, or combination); 3) Outcome: One or more of the following: Quality of Life (QoL), Blood Pressure (SBP and DBP), Lipid Profile (Total Cholesterol and LDL), and Bone Mineral Density (BMD). QoL was evaluated utilizing the MENQOL questionnaire, comprising four dimensions: vasomotor, psychosocial, physical, and sexual. Exclusion criteria were defined as 1) Full-text articles inaccessible; 2) Studies conducted in languages other than English; 3) Retracted studies.

Search Strategy

Five autonomous researchers undertook a literature search spanning from January to March 2024. Multiple databases, such as PubMed, ScienceDirect, and Google Scholar, were queried. The search employed keywords including ("Menopause") AND ("Exercise") AND ("Quality of Life" OR "Blood Pressure" OR "Lipid profile" OR "Bone Mineral Density") AND ("RCT"). The identification and screening process were documented using the PRISMA Flowchart (Fig.1).

Data Extraction and Analysis

Five authors independently extracted selected studies into a Google Sheet and then collectively evaluated the studies' accuracy and suitability authors. Oversight of this process was provided by SS, who subsequently reviewed and documented the findings. Discrepancies encountered during the compilation were resolved through discussions among the authors.

Risk of Bias Assessment

SS employed the Cochrane Risk of Bias Tool 2 for Randomized Controlled Trials to evaluate the risk of bias in the selected studies. The other authors provided insight into this procedure. This instrument considers five domains: Random sequence generation (selection bias), Allocation concealment (selection bias), Blinding of participants and personnel (performance bias), Blinding of outcome assessment (detection bias), Incomplete outcome data (attrition bias), and Selective reporting (reporting bias). These domains were categorized into three levels of bias risk: low, moderate, and high.

Quantitative Analysis

This meta-analysis utilized Review Manager 5.4.1 (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen) (https://revman.cochrane.org/myReviews). Data were assessed based on the mean change from baseline and standard deviation for QoL, SBP, DBP, TC, LDL, and BMD. These were treated as continuous variables with a 95% confidence interval (CI). The statistical method employed was the inverse variance model, and the random effects model with a mean difference was utilized for outcome analysis due to homogeneity in units and measurements.

Heterogeneity analysis was performed using Review Manager, where an I² score of $\geq 0\%$, $\geq 25\%$, $\geq 50\%$, and $\geq 75\%$ indicated no significant, low, moderate, or high heterogeneity among the included studies, respectively. A p-value of < 0.05 signified the significance of heterogeneity. Furthermore, a test for significance among subgroups was conducted to evaluate the significance of the subgroup analysis results, where p < 0.05 was considered significant.

Intervention of Interest

Menopause signifies a natural transition in the female life cycle, characterized by decreased estrogen levels. This hormonal alteration manifests in symptoms such as sleep disturbances, mood fluctuations, fatigue, and musculoskeletal discomfort. These symptoms have a considerable impact on women's quality of life and elevate their susceptibility to conditions like cardiovascular disease, hypertension, and osteoporosis. Exercise emerges as a promising non-pharmacological intervention to alleviate these menopausal symptoms and associated risks. Therefore, this review aims to determine and clarify the influence of exercise on patient outcomes.

Outcome of Interest

This review primarily examined the average changes in BMD from before to after intervention across the included studies. The study's primary outcomes of interest include QoL, SBP, DBP, TC, LDL, and BMD, which collectively assess the clinical status of patients and facilitate deeper exploration into the advantages of exercise for menopausal women.

RESULTS

Study Selection and Identification

Following the literature search, a total of 4,232 articles published within the last decade were identified across three databases. Of these, eight articles were excluded due to duplication of studies. Additionally,

4,197 articles were excluded as they contained ineligible data, such as review articles and books, or were inaccessible due to subscription requirements. The PRISMA flowchart depicted in Fig.1 illustrates this process. Consequently, 14 articles met the inclusion criteria and were included in the meta-analysis.

Risk of Bias Assessment

Overall, there were 12 studies with a low risk of bias, three studies with a moderate risk of bias, and 1 study with a high risk of bias (Fig.2). All studies showed a moderate risk of bias in domain 2 (allocation concealment) due to unblinded research samples. However, studies with blood pressure, lipid profile, and bone mineral density outcomes were objectively measured, and participants' knowledge of group allocation did not directly influence the study results. Meanwhile, for the OoL outcome, the majority of studies utilized the MENQOL questionnaire, which emphasizes self-reporting assessment, thereby posing a high risk of bias due to participants' knowledge of group allocation affecting assessment and causing bias. Studies with moderate risk of bias occurred because articles did not mention the blinding process of participants and personnel, rendering them ineligible to fulfill domain 3. Studies with a high risk of bias occurred due to suspected reporting bias assessment in the fifth domain. In this study, the control group had the same unexplainable values pre- and post-intervention for all outcomes. Most of the data examined have been covered in detail despite the varied levels of bias included in the studies. Reviewers concluded that the data were appropriate enough for this analysis.

Summaries of the Included Studies

This review included 14 studies. The exercise interventions are used in various forms, including aerobic (brisk walking, football, and aquatic), anaerobic (yoga exercise, resistance training, and Rusie Dutton exercise), and a combination of aerobic and anaerobic. A total of 1,092 patients with pre-, peri-, and post-menopausal women were diagnosed with the following conditions: (1) hypertension, (2) osteoporosis, and (3) healthy population were included as participants. The duration of the intervention ranges from 12 weeks to 9 years. Table 1 displays the studies that were included.

QoL Analysis

There were four studies reporting exercise vs. control in improving QoL. Overall, exercise was associated with a six-fold improvement in QoL [MD: -6.62 (95% CI: -16.90 - -3.66, I²=91%)]. However, these findings were not statistically significant with p=0.21 and exhibited high heterogeneity (I² > 75%) (Fig. 3).

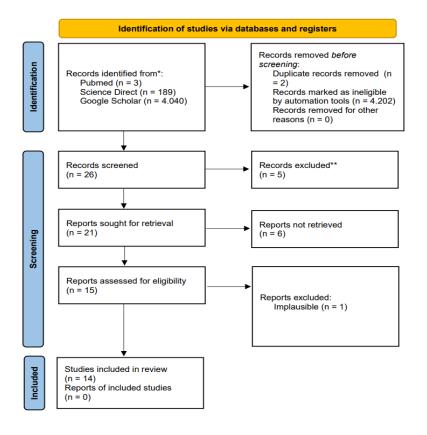


Fig.1. PRISMA Flowchart

SBP Analysis

There were eight studies reporting exercise vs. control in declining SBP. Overall, exercise was associated with a four-fold reduction in SBP [MD: -4.74 (95% CI: -10.54 – 1.05, I²=100%)] (p=0.11). However, these findings were not statistically significant and exhibited high heterogeneity (I² > 75%) (Fig.4).

DBP Analysis

There were eight studies reporting exercise vs. control in declining DBP. Overall, exercise was associated with a significant four-fold reduction in DBP [MD: -4.52 (95% CI: -8.59 – -0.46, I²=99%)] (p=0,03). However, these findings exhibited high heterogeneity (I² > 75%). Based on the analysis, exercise was superior and could improve DBP compared to the control group (Fig.5).

TC Analysis

There were four studies reporting exercise vs. control in TC reduction. Overall, exercise was associated with a four-fold decrease in TC [MD: -4.06 (95% CI: -8.75 – 0.64, I²=57%)] (p=0,09). However, these findings were not statistically significant and exhibited moderate heterogeneity (I² > 50%) (Fig.6).

LDL Analysis

There were four studies reporting exercise vs. control in LDL reduction. Overall, exercise was associated with a two-fold decrease in LDL [MD: -2.26 (95% CI: -7.37 – 2.86, I²=65%)] (p=0,39). However, these findings were not statistically significant and exhibited moderate heterogeneity (I² > 50%) (Fig.7).

BMD Analysis

There were two studies reporting exercise vs. control in BMD at total hip. Overall, exercise was associated with a 0.06-fold reduction in LDL [MD: 0.06 (95% CI: -0.01-0.13, I²=86%)] (p=0,09). However, these findings were not statistically significant and exhibited high heterogeneity (I² > 75%) (Fig.8).

DISCUSSION

Menopause, a natural occurrence in women's lives, brings a range of physical and psychological symptoms that impact their quality of life. Exercise shows potential in alleviating these symptoms and improving the overall well-being of menopausal women. Research conducted by Aliabadi et al. (2021), Vélez-Toral et al. (2017), Reed et al. (2014), and Waller et al. (2017) demonstrates the positive effects of exercise on quality of life (8-11). For instance, Vélez-Toral et al. (2017) observed significant enhancements in physical and mental health outcomes among sedentary post-menopausal women following a 20-week exercise program (9). While not directly addressing hot flashes, exercise correlates with an overall improvement in health-related quality of life, indicating its potential in managing menopausal symptoms. Additionally, exercise offers psychological benefits by reducing anxiety, depression, and stress while also enhancing mood and promoting social support and community engagement. The release of endorphins during exercise contributes to a sense of well-being and aids in mitigating mood disturbances commonly experienced during menopause [10]. Moreover, participating in group exercises or sports fosters a sense of community and provides valuable support, further enhancing mental well-being.

On the other hand, maintaining cardiovascular health is crucial for post-menopausal women, as they are at an increased risk of developing cardiovascular diseases. Regular physical activity has been shown to impact the cardiovascular health of menopausal women positively. Studies have demonstrated that exercise can lead to reductions in SBP, DBP, TC, and LDL, which are important indicators of cardiovascular health [9,12–16].

Prior research indicates that both aerobic and resistance exercise training programs result in notable decreases in SBP and DBP among post-menopausal women. The BP reduction observed in our study might be attributed to several factors. Firstly, the notable decrease in fat mass and potential reduction in adipose tissue-derived inflammatory adipokines could play a role [17]. Secondly, a significant increase in lean body mass, which has been linked to protection against hypertension, may contribute to this [18]. Additionally, there may be an improvement in nitric oxide (NO) bioavailability, as increased estradiol levels have been associated with increased NO production and vasodilatory function [19]. Previous findings have shown that markers of NO bioavailability notably increase following resistance exercise training, which could also be a contributing factor. However, further research is needed to understand these potential mechanisms fully. Clinically, even modest reductions in systolic BP by 2 mm Hg have been linked to decreased mortality from stroke and coronary heart disease. Therefore, the observed reduction in systolic BP by approximately 3 mm Hg in our study may have significant implications for reducing cardiovascular events and disease prevalence in this population [14].

Additionally, menopausal women often experience elevated levels of low-density lipoprotein (LDL) and total cholesterol (TC), which are common risk factors for cardiovascular disease (CVD). Dyslipidemia is closely linked to the development of atherosclerotic plaque formation and inflammatory processes that contribute to plaque destabilization and subsequent CVD events. The increased risk of CVD after menopause is believed to be associated with estrogen deficiency and dysregulated lipid metabolism [20]. Estrogen plays a protective role in the cardiovascular system and is primarily synthesized in the ovaries using LDL-C as a substrate. However, during menopause, circulating LDL cannot be utilized for estrogen synthesis, leading to decreased estrogen production. Consequently, menopause is associated with elevated systemic LDL-C levels and heightened CVD risk [20].

Regular exercise has significantly reduced levels of low-density lipoprotein (LDL) and total cholesterol in menopausal women [21]. This improvement in LDL-C levels attributable to exercise may be linked to enhanced activity of the low-density lipoprotein receptor (LDL-R) in hepatocyte membranes, which facilitates the uptake and metabolism of LDL-C in the body. Dysregulation of LDL-R is associated with hypercholesterolemia, and exercise enhances LDL-R activity and expression on cell membranes, leading to improved LDL-C levels [22]. Additionally, exercise may enhance the expression of LDL receptor messenger ribonucleic acid (LDL-R mRNA) by increasing insulin sensitivity, thereby accelerating LDL-C metabolism. While the precise mechanism by which resistance training (RT) impacts this pathway is not fully elucidated, studies have highlighted its favorable effects on LDL-C levels. For instance, Cunha et al. reported that RT improved LDL-C levels in middle-aged and older adults. However, it did not affect levels of triglycerides (TG) or high-density lipoprotein cholesterol (HDL-C) [23].

The decline in estrogen levels postmenopause contributes to decreased bone mineral density, elevating the risk of osteoporosis and fractures. Meta-analysis has indicated a significant positive correlation between exercise and bone mineral density, particularly in the hip area, among menopausal women. Various weightbearing exercises like walking, jogging, or resistance training have enhanced bone mineral density in this population. However, the findings of this study yielded insignificant results, possibly due to the study's duration. The length of the training period and ground reaction force appear to be crucial factors in maximizing the benefits of exercise on post-menopausal women's bone mineral density. Studies with training periods exceeding six months consistently reported increases in bone mineral density [4,24,25]. The human bone-remodeling cycle typically lasts about 4-6 months, with unevenly distributed resorption and formation phase durations. Osteoclastic resorption activity lasts approximately 3-6 weeks, followed by osteoblast-mediated bone formation lasting 5-9 weeks. Consequently, a 10-week exercise program may be more suitable for investigating bone turnover markers rather than bone mineral accumulation compared to longer-term programs (e.g., 20–30 weeks).

CONCLUSION

Exercise has shown promising benefits for pre-, peri, and post-menopausal women, including improved QoL and reductions in SBP, DBP, TC, LDL, and maintenance of bone mineral density. However, only a significant improvement in diastolic blood pressure was observed compared to the control group. This study underscores the potential of exercise as a nonpharmacological treatment option for menopausal patients, particularly those experiencing declines in quality of life, hypertension, dyslipidemia, and osteoporosis. Further research is warranted to explore more consistent exercise interventions, including standardized preparations, dosages, administration intervals, and serum analysis of bone markers.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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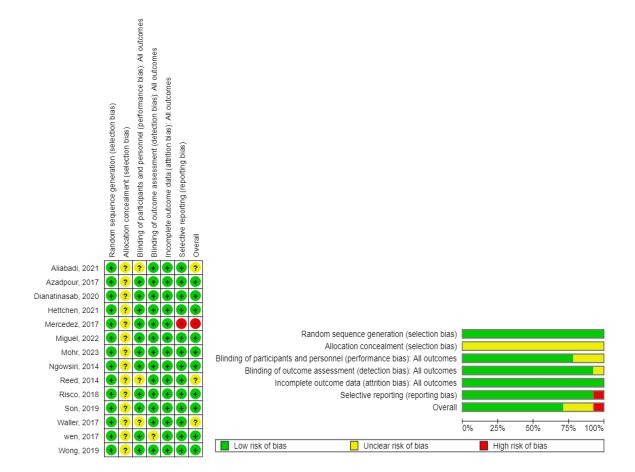
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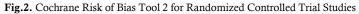
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	Exp	periment	al	(Control			Mean difference	Mean difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	IV, Random, 95% CI
Aliabadi, 2021	-26.2	20	24	5.23	18.09	26	22.0%	-31.43 [-42.03 , -20.8	33]
Mercedez, 2017	-1.46	20.64	80	0	27.11	86	25.1%	-1.46 [-8.76 , 5.8	34]
Reed, 2014	-0.9	1.16	95	-0.6	0.82	129	28.7%	-0.30 [-0.57 , -0.0	03]
Waller, 2017	6.6	17.81	43	3.5	21.76	44	24.2%	3.10 [-5.25 , 11.4	15]
Total (95% CI)			242			285	100.0%	-6.62 [-16.90 , 3.6	6]
Heterogeneity: Tau ² =	95.75; Chi ²	2 = 33.84,	df = 3 (P	< 0.00001); I ² = 919	%			•
Test for overall effect:	Z = 1.26 (P	= 0.21)							-50 -25 0 25 50
Test for subgroup diffe	erences: No	t applicat	ole					Fav	ours [experimental] Favours [control]

Fig.3. Mean Differences of Exercise vs Control Group for QoL Improvement in Menopause Women

	Exp	perimental		(Control			Mean difference	Mean difference
Study or Subgroup	Mean [mmHg]	SD [mmHg]	Total	Mean [mmHg]	SD [mmHg]	Total	Weight	IV, Random, 95% CI [mmHg]	IV, Random, 95% CI [mmHg]
Aliabadi, 2021	3	10.8	80	0.38	1.58	86	13.4%	2.62 [0.23 , 5.01]	
Azadpour, 2017	-5.84	4.28	12	0.09	3.81	12	13.1%	-5.93 [-9.17 , -2.69]	
Cheng, 2022	0.5	1.13	15	2.04	11.11	15	12.1%	-1.54 [-7.19 , 4.11]	
Mohr, 2023	-9.9	14.56	120	0.2	14.89	13	10.6%	-10.10 [-18.60 , -1.60]	
Ngowsiri, 2014	-10.4	10.2	24	3.2	18.4	26	10.7%	-13.60 [-21.77 , -5.43]	
Risco, 2018	-6.93	12.1	75	-7.63	12.7	75	12.8%	0.70 [-3.27 , 4.67]	_ _
Son, 2019	-0.1	0.4	10	0.3	0.5	10	13.7%	-0.40 [-0.80 , -0.00]	-
Wong, 2019	-11	1	52	1	1	48	13.7%	-12.00 [-12.39 , -11.61]	•
Total (95% CI)			388			285	100.0%	-4.74 [-10.54 , 1.05]	
Heterogeneity: Tau ² =	64.05; Chi ² = 17	30.29, df = 7 (F	o < 0.000	01); I² = 100%					•
Test for overall effect:	Z = 1.60 (P = 0.1	1)							-20 -10 0 10 20
Test for subgroup diffe	erences: Not appl	licable						Favour	rs [experimental] Favours [cont



	Exp	Experimental			Control			Mean difference	Mean difference
Study or Subgroup	Mean [mmHg]	SD [mmHg]	Total	Mean [mmHg]	SD [mmHg]	Total	Weight	IV, Random, 95% CI [mmHg]	IV, Random, 95% CI [mmHg]
Azadpour, 2017	-2	1.38	12	. 0.5	1.13	12	13.9%	-2.50 [-3.51 , -1.49]	•
Dianatinasab, 2020	-2.52	8.87	15	0.75	8.29	15	10.6%	-3.27 [-9.41 , 2.87]	
Mercedez, 2017	0.17	1.05	80) 0	1.23	86	14.0%	0.17 [-0.18 , 0.52]	L
Mohr, 2023	-2.4	6.8	12	5.4	7.53	13	11.1%	-7.80 [-13.42 , -2.18]	
Ngowsiri, 2014	-10.4	10.2	24	3.2	18.4	26	9.0%	-13.60 [-21.77 , -5.43]	
Risco, 2018	-5.66	5.58	75	-3.44	7.5	75	13.5%	-2.22 [-4.34 , -0.10]	
Son, 2019	-2.9	1.5	10) -1.4	1	10	13.9%	-1.50 [-2.62 , -0.38]	-
Wong, 2019	-9	1	52	2 0	1	48	14.0%	-9.00 [-9.39 , -8.61]	•
Total (95% CI)			280)		285	100.0%	-4.52 [-8.59 , -0.46]	•
Heterogeneity: Tau ² =	30.68; Chi ² = 12	08.32, df = 7 (F	o < 0.000	01); I² = 99%					•
Test for overall effect:	Z = 2.18 (P = 0.0	03)							-20 -10 0 10 20
Test for subgroup diffe	erences: Not appl	icable						Favou	Irs [experimental] Favours [control]

Fig.5. Mean Differences of Exercise vs Control Group for DBP Reduction in Menopause Women

	Exp	perimental		(Control			Mean difference	Mean difference
Study or Subgroup	Mean [mg/dl]	SD [mg/dl]	Total	Mean [mg/dl]	SD [mg/dl]	Total	Weight	IV, Random, 95% CI [mg/dl]	IV, Random, 95% CI [mg/dl]
Dianatinasab, 2020	-4.25	9.66	15	-1.12	9.24	15	24.1%	-3.13 [-9.89 , 3.63]	
Mohr, 2023	-0.5	0.71	12	0.7	0.74	13	47.9%	-1.20 [-1.77 , -0.63]	•
Risco, 2018	-21.8	25.2	75	-11.5	18	75	23.2%	-10.30 [-17.31 , -3.29]	
wen, 2017	-9	42.32	24	-2	27.22	22	4.8%	-7.00 [-27.40 , 13.40]	
Total (95% CI)			126	i		125	100.0%	-4.06 [-8.75 , 0.64]	•
Heterogeneity: Tau ² = Test for overall effect:			= 0.07); l	2 = 57%					-20 -10 0 10 20
Test for subgroup diffe	erences: Not app	olicable						Favours	[experimental] Favours [contro

Fig.6. Mean Differences of Exercise vs Control Group for TC Reduction in Menopause Women

	Exp	perimental		(Control			Mean difference	Mean difference
Study or Subgroup	Mean [mg/dl]	SD [mg/dl]	Total	Mean [mg/dl]	SD [mg/dl]	Total	Weight	IV, Random, 95% CI [mg/dl]	IV, Random, 95% Ci [mg/di]
Dianatinasab, 2020	0.69	12.07	15	-2.08	12.37	15	19.1%	2.77 [-5.98 , 11.52]	
Mohr, 2023	-0.4	0.55	12	0.4	0.58	13	43.3%	-0.80 [-1.24 , -0.36]	-
Risco, 2018	-23.9	19	75	-14.5	18.7	75	27.1%	-9.40 [-15.43 , -3.37]	_
wen, 2017	-3	27.51	24	-4	19.67	22	10.5%	1.00 [-12.74 , 14.74]	
Total (95% CI)			126			125	100.0%	-2.26 [-7.37 , 2.86]	
Heterogeneity: Tau ² =	15.68; Chi ² = 8.	49, df = 3 (P =	= 0.04); l	² = 65%					
Test for overall effect:	Z = 0.86 (P = 0.	39)							-20 -10 0 10 20
Test for subgroup diffe	erences: Not app	olicable						Favou	rs [experimental] Favours [contr



Study or Subgroup	Exp Mean [g/cm^2]	perimental SD [g/cm^2]	Total	(Mean [g/cm^2]	Control SD [g/cm^2]	Total	Weight	Mean difference IV, Random, 95% CI [g/cm^2]	Mean difference IV, Random, 95% CI [g/cm^2]
Hettchen, 2021	-0.001	0.016	27	-0.09	0.02	27	56.4%	0.09 [0.08 , 0.10]	
wen, 2017	0.02	0.08	24	0	0.09	22	43.6%	0.02 [-0.03 , 0.07]	i -
Total (95% CI)			51			49	100.0%	0.06 [-0.01 , 0.13]	
Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diffe	Z = 1.72 (P = 0.0	9))7); ² = 8	6%					-0.2 -0.1 0 0.1 0.2 Favours [control] Favours [experim

Fig.8. Mean Differences of Exercise vs Control Group for BMD Reduction in Menopause Women

Table 1. Summaries Included Studies

Study,	Duration	Grou	p	Sample of Intervention	Mean Age	Outcome	Summary of Results
Year	Duration	Intervention	Comparison	vs Control (n)	(SD)	Observed	Summary of Results
Aliabadi, 2021 [8]	20 weeks	Yoga exercise (8 sessions x 2h/week)	Control group (no specific intervention)	33 vs 33	Intervention: 52.93 ± 3.29 Control: 53.20 ± 2.84	QoL (vasomotor, psychosocial, physical, and sexual dimension)	 After 20 weeks of study, the Menopause-Specific Quality of Life (MENQOL) assessment revealed a substantial improvement in the mean change from baseline of QoL for the intervention group (-26.2 ± 20.0) compared to the control group (5.23 ± 18.09) (p < 0.001). Vasomotor symptoms significantly decreased in the intervention group compared to the control group (P = 0.02). The intervention group experienced significant enhancements in psychosocial, physical, and sexual dimensions, whereas these aspects were notably poorer in the control group.
Miguel, 2022 [16]	48 weeks	Brisk walking (3 sessions x 1h/week)	Control group (counseling)	30 vs 30	Intervention: 49.7 ± 3.7 Control: 50.1 ± 2.9	BMD	 After 48 weeks of body weight intervention, participants in the body weight group experienced a notable 8.23% increase in femoral neck BMD. However, no significant changes were observed in the BMD of the lumbar spine, greater trochanter, and Ward's triangle.
Hettchen, 2021 [26]	12 weeks	Resistance training (3 sessions x 2h/ week)	Control group (low- intensity physical activity)	27 vs 27	Intervention: 53.6 ± 2.0 Control: 54.5 ± 1.6	BMD	 There are no significant effects on total hip BMD. However, the mean change from baseline in the experimental group indicated less deterioration in bone density compared to the control group (experimental group: -0.01±0.016 vs control group: -0.009±0.020 mg/cm2, p=0.129).
Ngowsiri, 2014 [27]	13 weeks	Rusie Dutton exercise (20 - 30 min/day)	Control group (no specific intervention)	24 vs 26	Intervention: 52.9 ± 4.3 Control: 50.7 ± 3.6	SBP, DBP, QoL (vasomotor, psychosocial, physical, and sexual)	 After 13 weeks, the experimental group showed a notable decrease in both SBP and DBP, while the control group did not exhibit significant changes. The experimental group also displayed significant improvements across all MENQOL domains (vasomotor, physical, psychosocial, and sexual), whereas the control group did not show significant improvements. Overall, there was a significant difference between the two groups, with the experimental group showing greater reductions in SBP, DBP, and MENQOL domain scores compared to the control group.
Mercedez, 2017 [9]	12 months	Aerobic + anaerobic exercise (3 sessions x 1h/ week)	Control group (no specific intervention)	80 vs 86	Intervention: 56.16 ± 4.09 Control: 55.70 ± 3.98	QoL (overall, vasomotor, psychosocial, physical and sexual)	 After 12 months of follow-up, the intervention group consistently demonstrated superior HRQoL across all domains compared to the control group. The intervention group experienced a significant 5.5% decrease in SBP (p=0.002) and a non-significant 4.3% decrease in DBP from baseline to post-intervention. However, from post-intervention to the 12-month follow-up, there was a non-significant increase of 3.2% in SBP (p=0.186) and 2.3% in DBP (p=0.226) in the intervention group.
Mohr, 2023 [28]	9 years	Football exercise (1 - 3 sessions x 1h/ week)	Control group (no specific intervention)	12 vs 13	(not informed)	SBP, DBP, Lipid profile (TC, LDL, HDL, TG)	 A reduced SBP in experimental group by - 9.9 [- 19.0;-0.5] mmHg (P =0.04), and no change in control group (+0.2 [- 8.8;9.2] mmHg (P interaction = 0.12). while DBP favor the experimental group and the control group showed an unaltered increase of f 5.4 [0.8;9.9] mmHg (P interaction = 0.02). Respectively, TC and LDL are lowered in the experimental group - 0.5 [- 1.0;-0.1], - 0.4 [- 0.8;-0.1] mmol/1 compared to control group 0.7 [0.2;1.1], 0.4 [0.1;0.8] mmol/1 (P<0.05)
Azadpour, 2017 [13]	10 weeks	Moderate-intensity aerobic exercise	Control group (no	12 vs 12	Intervention: 57.58 ± 4.29	SBP, DBP	- SBP and DBP decreased by 4.6% and 2.4% (P < 0.001), respectively, in the exercise group compared with the control group

		(3 sessions x 25-40 min/week)	specific intervention)		Control: 56.58 ± 4.17		 It occurred so due to training-induced changes in BP inversely associated with the changes in Fibromuscular dysplasia (FMD) and beta-2-adrenoreceptor (ADRB2) (r values range -0.55 to -0.78), and positively associated with Angiotensin II and ACE (r values range 0.68-0.86) (P < 0.001).
Dianatinas ab, 2020 [29]	8 weeks	Running (aerobic) exercise (3 sessions x 30 - 60 min/week)	Control group (no specific intervention)	15 vs 15	Overall: 53.47 ± 6.53	SBP, DBP, TG, LDL, HDL, and TC	 Aerobic exercise leads to a gradual reduction in SBP (-5.18 ± 13.45) and TG (-13.66 ± 12.39) compared to anaerobic exercise, combination exercise, and the control group. Anaerobic exercise results in a gradual decrease in DBP (-3.51 ± 9.59) compared to aerobic exercise, combination exercise, and the control group. A combination of aerobic and anaerobic exercise leads to a gradual decrease in LDL (-5.16 ± 11.16), an increase in HDL (2.83 ± 8.43), and a reduction in TC (-5.58 ± 13.13) compared to anaerobic exercise, combination exercise, and the control group.
Reed, 2014 [10]	12 weeks	Yoga (anaerobic) exercise (90 min weekly)	Control group (no specific intervention)	95 vs 129	Intervention: 54.3 ± 3.9 Control: 54.2 ± 3.5	QoL	 In the yoga (anaerobic) group compared to the control group, significant improvements were observed from baseline to 12 weeks for MENQOL total score (-0.3; 95% CI, -0.6 to 0; P=0.02), the vasomotor symptom domain (P=0.02), and the sexuality domain (P=0.03) scores. Exercise demonstrated a positive effect on the MENQOL physical domain score at 12 weeks (P=0.02).
Risco, 2018 [12]	4 months	Aerobic + anaerobic exercise (3 sessions x 1h/ week)	Control group (counseling)	75 vs 75	Intervention: 52.8 ± 4.48 Control: 52.7 ± 4.51	SBP, DBP, TG, LDL, HDL, and TC	 After further adjusting for baseline values and diet, the exercise group exhibited lower LDL-C concentrations compared to the counseling group (10.2mg/dl; 95% confidence interval: 19.4-0.96; p=0.031). Both groups showed borderline significant reductions in total cholesterol and diastolic blood pressure, with slightly more favorable outcomes observed in the exercise group (p= 0.068 and p= 0.090, respectively).
Son, 2020 [14]	12 weeks	Aerobic + anaerobic exercise (3 sessions x 70 min/week)	Control group (no specific intervention)	10 vs 10	Intervention: 67.7 ± 1.0 Control: 67.4 ± 1.1	SBP, DBP	- There were significant group-by-time interactions ($P < 0.05$) for systolic BP, which significantly decreased ($P < 0.05$) after exercise compared to no changes in the control group. There were no significant differences ($P > 0.05$) in diastolic BP after 12 weeks.
Waller, 2017 [11]	16 weeks	Aquatic (aerobic) exercise (3 sessions x 1h/ week)	Control group (no specific intervention)	43 vs 44	Intervention: 63.8 ± 2.4 Control: 63.9 ± 2.4	QoL	 No significant result between-group differences could be seen in any domain of the QoL. However, the intervention group exhibited higher mean change from baseline compared to the control group (6.6 vs 3.5)
Wen, 2017 [30]	10 weeks	Aerobic exercise (3 sessions x 1.5 h/ week)	Control group (no specific intervention)	24 vs 22	Intervention: 58.8 ± 3.2 Control: 57.5 ± 3.5	BMD, TG, LDL, HDL, and TC	 There was no significant change and improvement of BMD in both groups - No significant result between-group differences could be seen in any domain of lipid profile. However, intervention group exhibited a reduction in mean change from the baseline of TC compared to the control group (-3.9 ± 15.9 vs -0.2 ± 9.0) (in percentage), while control group showed reduction in mean change from the baseline of TG, HDL, and LDL compared to the intervention group
Wong, 2019 [31]	20 weeks	Aquatic (aerobic) exercise (3 - 4 sessions x 45 min / week)	Control group (no specific intervention)	52 vs 48	Intervention: 74 ± 4 Control: 75 ± 3	SBP and DBP	 There was a significant improvement for SBP (- 11 mm Hg) and DBP (- 9 mm Hg), which significantly decreased (P < 0.05), while no incremental improvement could be observed in the control group.