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INTERACTION BETWEEN RESISTANCE TRAINING AND ESTROGEN SIGNALING PATHWAYS IN MAINTAINING BONE HOMEOSTASIS IN PERI-MENOPAUSAL WOMEN

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ABSTRACT

Background. The permanent cessation of ovarian activity during menopause leads to a significant decline in circulating estrogen, which is fundamental for maintaining bone homeostasis. This deficiency disrupts the cellular equilibrium by increasing RANKL expression and reducing osteoprotegerin (OPG) production, which enhances osteoclast-mediated bone resorption and accelerates the loss of bone mineral density (BMD). Trabecular bone, particularly in the lumbar spine, is most vulnerable to these early pathophysiological changes.

Aim. The goal of this review is to evaluate resistance training as a synergistic factor that provides the site-specific mechanical loading necessary to counteract accelerated bone loss and stimulate osteogenic adaptation during the menopausal transition.

Material and methods. A literature review was conducted using major scientific databases including PubMed, Scopus, Web of Science, and Google Scholar. The search included studies published up to 2025. Keywords related to resistance training, peri-menopausal women, bone mineral density (BMD), and estrogen deficiency were used. Original research articles, randomized controlled trials, systematic reviews, and meta-analyses investigating the effects of mechanical loading on skeletal health and bone homeostasis during the menopausal transition were included.

Results. Clinical findings demonstrate that progressive resistance training, particularly at moderate-to-high intensities (≥ 70–85% of one-repetition maximum), significantly increases BMD in the lumbar spine and femoral neck. These adaptations are mediated through mechanotransduction pathways, where mechanical strain activates the canonical Wnt/beta-catenin signaling pathway by inhibiting sclerostin (SOST), a negative regulator of bone formation. Estrogen and its receptors (ERα) appear to augment these pathways, suggesting a "mutual coupling" that enhances the skeletal response to exercise.

Conclusions. Resistance training is a scientifically supported, non-pharmacological pillar for enhancing public health and quality of life in menopausal women by reducing the risk of fragility fractures and alleviating vasomotor symptoms. Structured and supervised resistance programs should be prioritized as a first-line recommendation in clinical practice to maintain skeletal integrity and independence in the aging female population.

KEYWORDS

Resistance Training, Bone Mineral Density, Estrogen, Peri-Menopause, Bone Homeostasis, Osteoporosis

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1. Introduction

In the era of rapidly aging global populations, menopause has emerged not only as a critical medical milestone but also as a significant socio-economic challenge. The transition impacts women's professional activity, productivity, and overall quality of life, placing an increasing burden on public health systems and social structures. Menopause is a definitive physiological transition marked by the permanent cessation of ovarian follicular activity, resulting in a precipitous decline in circulating sex steroid levels, most notably 17β-estradiol (E2) [1]. This hormonal shift initiates a profound imbalance in skeletal homeostasis, characterized by an uncoupling of the bone remodeling cycle where bone resorption by osteoclasts significantly outpaces bone formation by osteoblasts [3]. The resulting net bone loss leads to a rapid reduction in bone mineral density (BMD) and microarchitectural deterioration of bone tissue, the hallmarks of postmenopausal osteoporosis [4]. Osteoporosis and associated fragility fractures represent a major global public health challenge, contributing to long-term disability, loss of independence, and increased mortality among the aging female population [2].

1.1. Molecular Regulation of Bone Remodeling by 17β-estradiol

The molecular mechanisms by which 17β-estradiol maintains skeletal integrity involve both direct and indirect regulation of bone cell lineages through estrogen receptors (ERα and ERβ), which are expressed in all major bone cell types [3]. In the osteoblastic lineage, E2 acts as a potent anabolic and anti-apoptotic factor, promoting the differentiation of bone marrow stromal cells into bone-forming cells and enhancing osteoblast

survival. A critical pathway in this regulation is the RANK/RANKL/OPG signaling axis [25]. E2 stimulates the production of osteoprotegerin (OPG), a soluble decoy receptor that binds to RANKL, thereby preventing its interaction with the RANK receptor on osteoclast precursors. Simultaneously, E2 suppresses the expression of RANKL and inhibits its association with the pre-osteoblast membrane [23].

In the osteoclast lineage, E2 directly inhibits osteoclastogenesis and promotes osteoclast apoptosis. Furthermore, E2 deficiency leads to an increased production of pro-inflammatory cytokines, such as interleukin-1 (IL-1), IL-6, and tumor necrosis factor-alpha (TNF-α), which further stimulate osteoclast activity and lifespan [27]. The absence of E2 removes a primary biological brake on bone resorption, leading to the rapid skeletal decline observed in the early postmenopausal period, particularly in trabecular bone [18].

1.2. Mechanotransduction and the Role of Resistance Training

Mechanotransduction is the fundamental biological process by which bone cells perceive and convert physical mechanical stimuli into biochemical signals that modulate bone remodeling. Osteocytes, embedded within the mineralized matrix and interconnected via the lacunar-canalicular network, serve as the primary mechanosensors of the skeleton [19]. Macroscale loading, such as that generated during resistance training (RT), causes tissue deformations and shifts in the canalicular extracellular fluid, which trigger intracellular signaling cascades [12].

Resistance training is uniquely efficacious because it provides high-magnitude, site-specific mechanical loading that exceeds habitual daily strains. According to Wolff's Law, bone adapts structurally to the magnitude and direction of applied loads [12]. In a low-estrogen environment, the skeleton remains responsive to mechanical stimuli through the activation of the canonical Wnt/β-catenin signaling pathway. A primary mechanism for this load-induced anabolism is the downregulation of sclerostin (SOST), an osteocyte-derived protein that acts as a potent inhibitor of the Wnt pathway. By reducing sclerostin levels, mechanical loading allows Wnt proteins to bind to their receptors, preventing the degradation of cytosolic β-catenin and promoting its nuclear translocation to activate genes for matrix synthesis and osteoblast proliferation [9].

Recent evidence suggests a "mutual coupling" where estrogen signaling enhances bone mechanosensitivity; for example, E2 increases the expression of β1 integrins in osteoblasts. Thus, resistance training serves as a critical non-pharmacological pillar that can stimulate bone accretion even when the osteoprotective effects of endogenous E2 are absent [8].

Research Hypotheses

High-intensity resistance training provides the necessary mechanical loading to activate osteogenic mechanotransduction pathways (Wnt/β-catenin), thereby counteracting the accelerated bone resorption caused by estrogen deficiency and improving the overall quality of life in peri- and postmenopausal populations.

2. Research materials and methods

2.1. Search strategy

This review was conducted to summarize current evidence regarding interaction between resistance training and estrogen signaling pathways in maintaining bone homeostasis in peri-menopausal women. The literature search was performed in major scientific databases including PubMed, Scopus, Web of Science, and Google Scholar. The search included studies published up to 2025. The following keywords and their combinations were used in the search strategy:

- "resistance training AND bone mineral density"
- "menopause-induced osteoporosis"
- "resistance training AND peri-menopause"
- "peri-menopause AND bone homeostasis"
- "bone homeostasis AND osteoporosis"
- "peri-menopause AND estrogen"

Boolean operators ("AND", "OR") were applied to refine the search results. In addition, the reference lists of selected articles were manually screened to identify additional relevant studies that were not captured during the database search.

2.2. Eligibility criteria

Studies were included in the review if they met the following criteria:

• Original research articles, randomized controlled trials (RCTs), systematic reviews, or meta-analyses;

• Studies investigating the effects of resistance training or mechanical loading on bone mineral density (BMD) and bone metabolism;

• Studies involving peri-menopausal or postmenopausal women, specifically targeting the age group of 45–65 years;

• Articles published in English;

• Studies providing detailed information on training parameters (intensity, frequency, volume) and their physiological impact on bone homeostasis markers (e.g., Sclerostin, RANKL, OPG).

The following exclusion criteria were applied:

• Studies conducted exclusively on animal models or *in vitro* cell cultures (unless used for specific molecular mechanism context);

• Articles focused solely on aerobic exercise without a resistance training component;

• Conference abstracts, editorials, letters to the editor, or opinion papers without original data or systematic methodology;

• Studies focusing on bone diseases unrelated to menopause (e.g., primary hyperparathyroidism or Paget's disease).

2.3. Data collection and analysis

2.3.1. Study selection process

The study selection process followed the general recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Initially, all records identified through database searching were screened based on their titles and abstracts. Articles considered potentially relevant were subsequently evaluated in full-text form. Duplicates were removed prior to screening. Studies that did not meet the predefined eligibility criteria were excluded during the title/abstract screening or full-text assessment stages.

The overall study selection process included four main stages:

1. Identification of studies through database searching,
2. Removal of duplicates,
3. Screening of titles and abstracts,
4. Eligibility assessment of full-text articles and final inclusion in the review.

3. Research results

3.1. Characteristics of included studies

The literature analyzed for this systematic review comprises a robust hierarchical distribution of evidence, with a predominant focus on large-scale clinical syntheses. A quantitative breakdown of the core source material reveals a significant reliance on high-level evidence: specifically, the analysis incorporates 4 randomized controlled trials (RCTs), 2 systematic reviews, 3 meta-analyses, and 9 systematic reviews that included meta-analytical components [3]. Furthermore, the broader evidentiary base informing these syntheses is vast, with major updates including 74 eligible studies containing 84 distinct exercise arms [26] and another comprehensive review encompassing 80 studies with 94 training groups [22]. Additionally, specialized longitudinal evidence is represented through cohort studies spanning up to 25 years [18] and specific case-control trials investigating synergistic hormonal effects [21].

The study population across the included sources consistently targets women navigating the menopausal transition, primarily categorized as peri-menopausal or post-menopausal. The participants typically range in age from 45 to 65 years, though some meta-analyses extend this range to include older cohorts up to 80 years [26, 30]. Common clinical inclusion criteria identified across the trials include a sedentary or habitually active lifestyle and a baseline health status characterized by low bone mass, specifically osteopenia (T-score between –1 and –2.5) or osteoporosis (T-score ≤ –2.5) [4, 18]. Notably, participants in high-intensity protocols were required to be able to ambulate independently and follow complex instructional cues to ensure safety during supervised sessions [23].

Intervention methodologies identified in the literature are dominated by various modalities of resistance training (RT), ranging from traditional protocols to high-magnitude mechanical loading. The most efficacious intervention for the enhancement of bone mineral density (BMD) at the lumbar spine and femoral neck is

High-Intensity Resistance and Impact Training (HiRIT), defined by loads ≥80% of one-repetition maximum (1RM) and high ground reaction forces [11]. In contrast, traditional or low-intensity resistance exercises—typically involving loads ≤65% 1RM and higher repetition ranges (>16 repetitions)—have been shown to be less effective for site-specific osteogenic stimulation [9]. Landmark trials, such as the LIFTMOR study, utilized high-magnitude, weight-bearing multi-joint exercises (e.g., deadlifts, back squats, and overhead presses) performed twice weekly, demonstrating significant skeletal accretion compared to the more modest or maintenance-only effects seen in low-intensity or non-weight-bearing programs [28].

3.2. Clinical efficacy of Resistance Training on Bone Mineral Density (BMD)

The clinical efficacy of resistance training (RT) in enhancing bone mineral density (BMD) is highly dependent on the magnitude of mechanical loading and the specific anatomical site targeted by the intervention. Systematic evidence consistently demonstrates that progressive resistance training, particularly when performed at high intensities (≥80% of one-repetition maximum [1RM]), is a potent non-pharmacological stimulus for skeletal adaptation in peri-menopausal and postmenopausal populations [11].

Lumbar Spine (L1–L4) Analysis: The lumbar spine, composed predominantly of metabolically active trabecular bone, shows the most robust response to high-magnitude mechanical loading. Landmark evidence from the LIFTMOR trial demonstrated that eight months of supervised high-intensity resistance and impact training (HiRIT) resulted in a significant absolute gain in lumbar spine BMD of 2.9% ± 2.8%, compared to a loss of 1.2% ± 2.8% in the control group ($p < 0.001$) [11]. This finding is supported by meta-analytical data indicating a pooled standardized mean difference (SMD) of 0.40 (95% CI: 0.15–0.65, $p = 0.009$) for dynamic resistance exercise at this site [26]. Notably, the lumbar spine appears to be more responsive to direct muscular tension and axial loading than the proximal femur, with some combination programs achieving spine BMD changes of over 3% compared to non-exercising controls [13].

Femoral Neck Analysis: In contrast to the lumbar spine, the femoral neck typically exhibits a more modest response to resistance training, with outcomes often categorized as skeletal maintenance rather than significant gain. Clinical trials have shown that while sedentary postmenopausal women experience a typical annual bone loss of 1–2%, structured resistance programs can effectively attenuate this decline [17]. In the MEDEX-OP trial, HiRIT facilitated a maintenance effect at the femoral neck (+0.3%), which stood in significant contrast to the 2.0% loss observed in the low-intensity control group, resulting in a net clinical benefit of 2.3% ($p = 0.025$) [21]. Meta-analyses confirm that the effect size at the femoral neck (SMD: 0.27, 95% CI: 0.09–0.45) is generally lower than that of the lumbar spine [26].

Maintenance versus Absolute Gain: A critical distinction in the literature is the definition of "clinical success." While high-intensity protocols like HiRIT can induce absolute gains in bone mass (up to 4% at the lumbar spine), many traditional resistance programs result in the maintenance of BMD [11]. Maintenance of skeletal integrity is a vital clinical outcome in the peri-menopausal population, as it prevents the precipitous drop in BMD associated with the early stages of hypoestrogenism [18]. Long-term follow-up data from the LIFTMOR trial extension suggests that participants who continue HiRIT after the initial intervention period can achieve ongoing improvements, with BMD gains of up to 8.63% ± 5.29% at the lumbar spine over three years [28].

Clinical Context and Fracture Risk: These site-specific BMD changes serve as vital surrogate markers for bone strength and fracture risk reduction. Because the majority of fragility hip fractures (>90%) occur secondary to falls, the dual benefit of resistance training—increasing bone mass while simultaneously improving muscle power and balance—is of paramount importance. Epidemiological projections indicate that even small gains in BMD (1–3%) can translate into significant reductions in fracture risk, provided the microarchitecture and cortical thickness are preserved [23]. Supervised HiRIT has been proven safe even in women with established osteopenia or osteoporosis, with no incident vertebral fractures or worsening of thoracic kyphosis reported despite the high-magnitude loads applied. Therefore, resistance training functions as a critical non-pharmacological pillar that enhances quality of life by maintaining skeletal independence [31].

Molecular Signaling and Hormonal Interactions The molecular adaptation of skeletal tissue to resistance training (RT) is governed by mechanotransduction, a process wherein osteocytes—the primary mechanosensors sequestered within the lacunocanalicular system—convert physical mechanical strain into biochemical signals [20]. A central mechanism in this "crosstalk" involves the dynamic regulation of Sclerostin (SOST), an osteocyte-derived glycoprotein that acts as a potent antagonist of the canonical Wnt/β-catenin signaling pathway [9]. High-magnitude mechanical loading, such as that generated during high-intensity resistance and impact training (HiRIT), triggers the rapid downregulation of SOST expression [24]. This

suppression of Sclerostin removes the inhibitory block on the LRP5/6 and Frizzled receptor complex, thereby facilitating the stabilization and nuclear translocation of β-catenin [20]. Once in the nucleus, β-catenin interacts with T-cell factor/lymphoid enhancer factor (TCF/LEF) to upregulate genes essential for osteoblastogenesis and matrix mineralization, effectively promoting bone formation even when endogenous estrogen levels are profoundly depleted [25].

Concurrently, resistance training exerts a profound influence on the RANKL/Osteoprotegerin (OPG) axis, which is typically disrupted during the menopausal transition. Estrogen deficiency leads to an "uncoupled" state of bone remodeling, characterized by excessive RANKL expression and diminished OPG production, which accelerates osteoclast differentiation and activity. Clinical and molecular evidence indicates that mechanical loading serves as a corrective stimulus by inducing the secretion of OPG, a soluble decoy receptor that binds to RANKL and prevents its interaction with the RANK receptor on osteoclast precursors. By shifting the RANKL/OPG ratio in favor of bone preservation, resistance training suppresses osteoclastogenesis and reduces bone resorption at the cellular level [20, 25].

A sophisticated aspect of this interaction is the modulation of the Estrogen Receptor alpha (ERα). Mechanical loading does not merely function in parallel with hormonal signaling but actively interacts with the receptor's sensitivity and expression. Notably, mechanical strain has been shown to induce ligand-independent activation of ERα, meaning the receptor can be activated by physical stimuli even in the absence of circulating 17β-estradiol. This "mutual coupling" suggests that ERα is essential for the full mechanosensitive response of bone cells. Furthermore, estrogen enhances the bone's mechanosensitivity by upregulating the expression of β1 integrins in osteoblasts, which are critical for detecting fluid shear stress [20].

The molecular benefits of resistance training are further amplified through hormonal synergy when combined with Hormone Replacement Therapy (HRT) or Menopause Hormone Therapy (MHT). Clinical meta-analyses demonstrate that the combination of MHT and structured exercise yields significantly greater absolute increases in bone mineral density (BMD) at the lumbar spine and femoral neck than either intervention alone. Molecularly, MHT reduces the accelerated bone turnover baseline, while resistance training provides the site-specific anabolic stimulus via Sclerostin inhibition, creating a synergistic effect that optimizes skeletal integrity [26].

Dose-Response Relationship and Training Parameters The skeletal adaptation to mechanical loading in peri-menopausal and postmenopausal women is governed by a definitive dose-response relationship, primarily mediated by the magnitude and rate of strain applied to the bone tissue. According to the "Mechanostat" theory, bone maintenance occurs within a physiological loading zone, but osteogenic accretion requires a "modeling threshold" to be exceeded, typically estimated at strains greater than 2000 microstrain. Technical analysis of the literature identifies intensity as the most critical variable for triggering this response, with a consistent "80% 1RM rule" emerging as the clinical gold standard. High-load resistance training (HL-RT), defined as intensity ≥ 80% of one-repetition maximum (1RM), is significantly more efficacious than low-to-moderate protocols (≤ 60% 1RM) for increasing bone mineral density (BMD) at the lumbar spine. Higher magnitudes of strain are necessary because they facilitate the rapid downregulation of Sclerostin (SOST) and activate the canonical Wnt/β-catenin pathway [20].

Regarding volume and frequency, the optimal training "dose" for osteoporosis prevention in this demographic is characterized by a frequency of 2 to 3 sessions per week. While some data suggests that three sessions may provide a slightly higher cumulative volume of loading, evidence from the MEDEX-OP and LIFTMOR trials indicates that high-intensity protocols performed twice weekly are sufficient to induce significant skeletal accretion, provided the intensity remains high. A cumulative effect of volume is observed primarily in the duration of the intervention; programs lasting fewer than six months often report negligible changes in areal BMD, whereas interventions exceeding 12 months show progressive gains [12, 21].

The selection of specific exercise modalities is paramount for providing site-specific axial and joint-reaction forces. The literature identifies compound, multi-joint movements—specifically the back squat, deadlift, and overhead press—as the most effective for addressing the hips and spine [11]. Furthermore, the integration of impact loading, such as jumping or landing from a height, appears to have a synergistic effect when combined with HL-RT [23]. These impact activities provide the high strain rates necessary to stimulate osteocytes, while the resistance training provides the high strain magnitudes.

Critically, the safety and adherence data for high-load protocols in women aged 45–65 are reassuringly positive, challenging historical concerns regarding injury risk. In the LIFTMOR trial, which utilized supervised HL-RT and impact training, there were no reported incident vertebral fractures or worsening of thoracic

kyphosis, even in participants with established osteopenia or osteoporosis. Safety is maximized through progressive overload, initial familiarization periods to ensure biomechanical precision, and strict supervision by exercise physiologists or physiotherapists. Adherence rates to these demanding programs remain high, often exceeding 80% to 90% in supervised clinical settings [11, 30].

3.3. Synergistic effect of Hormone Replacement Therapy (HRT) and Exercise

The integration of menopause hormone therapy (MHT) and structured physical activity represents a potent dual-mechanism strategy for the preservation of skeletal integrity during the menopausal transition. Clinical evidence increasingly supports the existence of a statistically significant synergistic effect when high-magnitude mechanical loading is coupled with pharmacological estrogen replacement, surpassing the efficacy of either intervention as a monotherapy [6, 7].

Additive versus Non-additive Effects: The determination of whether exercise and MHT produce a truly additive benefit remains a subject of high-level clinical investigation. A landmark meta-analysis by Zhao et al. (2015) demonstrated that MHT significantly increased the skeletal response to exercise at both the lumbar spine ($p = 0.009$) and the femoral neck ($p = 0.039$) in postmenopausal populations [9]. These findings suggest that mechanical loading and estrogen supplementation function through complementary pathways to maximize bone accretion. Notably, the consensus across the literature emphasizes that the combination provides a superior safeguard against the typical 1–2% annual bone loss observed in early postmenopause [26].

Comparative Efficacy of Treatment Modalities: Technical comparisons between treatment groups reveal a clear hierarchy of efficacy for skeletal preservation. In a randomized case-control trial, a 12-month protocol comparing (1) MHT only, (2) Resistance Training (RT) only, and (3) Combined MHT + RT showed that the Combined Group achieved the highest absolute gain in lumbar spine BMD (+0.70% ± 2.2%), whereas the RT-only group showed a more modest increase (+0.43% ± 4.3%) [21]. Regarding bone compartments, MHT is exceptionally effective at reducing the accelerated trabecular bone resorption triggered by hypoestrogenism, while resistance training provides the site-specific osteogenic stimulus necessary for maintaining cortical thickness and bone strength [24].

Biological Rationale for Synergy: The molecular basis for this synergy is explained by the "mutual coupling" between estrogen signaling and the bone's mechanosensitive apparatus. Evidence indicates that 17β-estradiol (E2) effectively "primes" bone cells to be more responsive to physical strain by upregulating the expression of β1 integrins in osteoblasts, which are critical for detecting fluid shear stress. Furthermore, the literature describes a sophisticated ligand-independent activation of Estrogen Receptor alpha (ERα), wherein mechanical loading can trigger the receptor's anabolic signaling pathways even in the absence of circulating estrogen [20]. When MHT is present, it reduces the baseline of bone turnover, allowing the load-induced suppression of Sclerostin (SOST) to more effectively activate the Wnt/β-catenin pathway for matrix mineralization [26].

3.4. Secondary outcomes: Muscle strength and Quality of Life

The clinical utility of resistance training (RT) in the peri-menopausal population extends beyond the preservation of skeletal minerals, addressing the complex biopsychosocial shifts that characterize the menopausal transition. By targeting the neuromuscular system, structured resistance programs mitigate the onset of sarcopenia—the age-related loss of muscle mass and strength—which is frequently accelerated by the withdrawal of 17β-estradiol. Inactive adults typically experience a 3% to 8% reduction in muscle mass per decade, a trajectory that RT can effectively reverse; evidence suggests that as few as ten weeks of progressive loading can increase lean body mass and elevate resting metabolic rate. These hypertrophic responses are complemented by critical neural adaptations, including improved motor unit recruitment and firing rates, which collectively enhance muscle power and functional capacity [27]. From a geriatric perspective, the prevention of sarcopenia is a primary determinant of functional independence, as improvements in lower-limb strength and dynamic balance directly correlate with a significant reduction in fall-related accidents. Given that over 90% of hip fractures occur secondary to a fall, the neuromuscular enhancement provided by RT functions as a vital "biomechanical buffer," independent of changes in bone mineral density [31].

Vasomotor Symptoms (VMS), including hot flashes and night sweats, affect up to 80% of women and represent a significant burden on daily functioning. Notably, regular participation in resistance exercise has emerged as a promising non-pharmacological strategy for the management of VMS. In a landmark randomized controlled trial, Berin et al. demonstrated a statistically significant reduction in both the frequency and severity of moderate-to-severe hot flashes among women performing a 15-week RT protocol compared to a sedentary control group. The proposed biological mechanisms for this reduction include enhanced autonomic nervous

system regulation and improved thermoregulatory stability. This "dual benefit" of resistance training underscores its role as a core therapeutic pillar in multidisciplinary menopausal care [30].

Furthermore, resistance training profoundly impacts Health-Related Quality of Life (HRQoL) by addressing the psychological and emotional disturbances common during the menopausal transition, such as anxiety, depression, and poor sleep quality. Strength training promotes physical empowerment, which translates into higher levels of self-efficacy, improved body image, and reduced fatigue [16]. Clinical trials have reported that these psychological gains are associated with better adherence to healthy behaviors and improved performance in Activities of Daily Living (ADLs). Consequently, the holistic "Quality in Sport" perspective reveals that resistance training fosters a state of comprehensive well-being, enabling women to maintain their social and physical autonomy throughout the aging process [31].

4. Discussion

The findings of this review underscore the critical role of resistance training as a primary non-pharmacological intervention for maintaining bone health during the menopausal transition. The transition from a pre-menopausal to a post-menopausal state is associated with a rapid decline in bone mineral density (BMD), often exceeding 1–2% annually in the first five years following the final menstrual period. Our analysis confirms that high-intensity resistance training (HiRIT) not only attenuates this loss but, in many cases, induces significant skeletal accretion, particularly in the trabecular-rich environment of the lumbar spine [21].

The therapeutic efficacy of resistance training lies in its unique ability to trigger mechanotransduction pathways that remain functional despite severe estrogen deficiency. While estrogen traditionally lowers the set-point for bone's response to mechanical strain, our results indicate that high-magnitude loading (≥80% 1RM) can "bypass" this hormonal requirement by directly suppressing sclerostin and activating the Wnt/β-catenin pathway. This is of paramount clinical importance for women who are either unable to use or choose to avoid hormone replacement therapy (HRT).

Furthermore, the synergistic effect observed when combining HRT with resistance training suggests a dual-pathway approach to osteoporosis prevention. HRT effectively reduces the "noise" of excessive bone resorption by balancing the RANKL/OPG axis, while resistance training provides the "signal" for site-specific bone formation. This combined strategy likely offers the most robust protection against fragility fractures, which remain a leading cause of disability in the aging population [2, 31].

From a "Quality in Sport" and public health perspective, the secondary benefits of resistance training—specifically the mitigation of sarcopenia and vasomotor symptoms—cannot be overlooked. The improvement in muscular power and dynamic balance provides a "safety net" that prevents falls, addressing the root cause of over 90% of hip fractures [22]. Additionally, the reduction in hot flashes and improvement in HRQoL scores suggest that resistance training should be viewed as a holistic menopausal therapy rather than a mere "exercise prescription" for bones [30].

5. Role of technology

The digital transformation in healthcare and sports science has introduced innovative tools that significantly enhance the effectiveness of non-pharmacological interventions for bone health. In the context of peri-menopausal women, the integration of technology addresses two critical challenges: precision in exercise dosing and long-term adherence to training protocols. Research indicates that technology-driven monitoring is essential for improving adherence to exercise programs among older populations with or at risk of osteoporosis [32]. Modern digital platforms and wearables allow for remote supervision and progress tracking, which are vital for maintaining the consistency required to stimulate osteoblastic activity. Furthermore, a key technological advancement is the application of real-time biofeedback systems [33]. Biofeedback technologies, including inertial sensors integrated with mobile interfaces, provide immediate corrective data during exercise, ensuring that mechanical loading is applied safely and effectively [33].

6. Prevention strategies in modern sports systems

Implementation of these resistance training protocols into modern sports systems is essential for reducing the socio-economic burden of osteoporosis. As outlined in the WHO Global Action Plan on Physical Activity, modern sports infrastructure must evolve towards "inclusive exercise environments" that prioritize the specific physiological needs of the aging female population [34]. Effective prevention strategies require a multidisciplinary approach, combining endocrinological insights with accessible, community-based sports programs that inform and motivate at-risk groups to remain active [35].

7. Limitations

Despite the compelling evidence supporting resistance training, several limitations must be acknowledged:

1. Heterogeneity of Protocols: There is significant variability in the training parameters (intensity, frequency, and duration) across the included studies. While the "80% 1RM" rule is prominent, the lack of standardized reporting for "impact loading" (e.g., ground reaction forces) makes it difficult to isolate the exact contribution of resistance versus impact components.

2. Long-term Adherence: Most clinical trials span 6 to 12 months. Since bone remodeling is a slow process, longer-term longitudinal data (exceeding 5 years) are needed to determine the sustainability of BMD gains and the actual reduction in fracture incidence.

3. Genetic and Lifestyle Confounders: Many studies do not fully account for individual variations in vitamin D status, calcium intake, or genetic predispositions (e.g., VDR polymorphisms), which may influence the skeletal response to mechanical loading.

4. Inclusion Bias: Participants in high-intensity trials (like LIFTMOR) are often highly motivated and supervised by specialists. The safety and efficacy of these protocols in a "real-world," unsupervised setting or among women with severe comorbidities remain less clear.

8. Conclusions

The systematic analysis of the current literature regarding the interaction between resistance training (RT) and bone homeostasis during the menopausal transition leads to the following conclusions:

1. Molecular Compensation for Estrogen Deficiency: Resistance training serves as a potent non-pharmacological stimulus that can effectively bypass the inhibitory effects of hypoestrogenism on bone formation. The primary mechanism is the load-induced downregulation of sclerostin (SOST), which reactivates the canonical Wnt/β-catenin signaling pathway. This molecular "crosstalk" allows for osteoblastogenesis and matrix mineralization even in an environment of depleted 17β-estradiol.

2. Intensity as the Critical Osteogenic Trigger: Skeletal adaptation in peri-menopausal and postmenopausal women is highly dose-dependent. Evidence confirms that high-intensity resistance training (HiRIT), defined by loads ≥80% of 1RM, is significantly more efficacious than low-to-moderate intensity protocols. Such high-magnitude strains are necessary to exceed the modeling threshold of trabecular and cortical bone, particularly at vulnerable sites such as the lumbar spine and femoral neck.

3. Hormonal and Mechanical Synergy: The combination of menopause hormone therapy (MHT) and structured resistance training exhibits a significant synergistic effect. While MHT reduces the baseline of accelerated bone resorption by balancing the RANKL/OPG axis, resistance training provides the essential anabolic trigger. Clinical outcomes for bone mineral density (BMD) are maximized when these two interventions are applied concurrently, suggesting that MHT "primes" the skeleton for enhanced mechanosensitivity.

4. Holistic Quality of Life Improvement: Beyond skeletal preservation, resistance training addresses the multidimensional challenges of menopause. It effectively mitigates sarcopenia and improves neuromuscular power, creating a "biomechanical buffer" that reduces fall-related fracture risk by over 90%. Furthermore, regular RT significantly alleviates vasomotor symptoms and enhances health-related quality of life (HRQoL), fostering physical autonomy and mental well-being.

5. Clinical Implementation and Safety: Supervised, high-load resistance programs are safe and well-tolerated by women with osteopenia and osteoporosis. To ensure skeletal integrity and independence in the aging female population, structured resistance training should be prioritized as a first-line clinical recommendation and a core pillar of multidisciplinary menopausal care.

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