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POSTMENOPAUSAL ESTROGEN DEFICIENCY AND TENDON DEGENERATION: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Postmenopause is characterized by a significant decline in estrogen levels, which has important implications for tendon biology, biomechanics, and clinical outcomes. While bone and muscle have been extensively studied, tendons remain comparatively underexamined despite evidence of direct hormonal regulation.

Methods: A systematic literature search of PubMed (MEDLINE), Scopus, and Embase was conducted in July 2025 to identify studies published from January 2015 onward examining the effects of estrogen deficiency, menopause, or hormone therapy on tendon structure, mechanics, and cellular function. Human, animal, and *in vitro* studies were eligible. Nineteen articles met inclusion criteria.

Results: Included articles demonstrated that estrogen deficiency is associated with reduced tendon elasticity, altered load transfer, impaired healing capacity, and changes in collagen turnover. Tenocytes express estrogen receptors, particularly estrogen receptor beta (ERβ), which appear to modulate repair processes and limit fatty infiltration. Hormone replacement therapy and selective estrogen receptor modulators showed potential benefits for tendon elasticity, especially when combined with mechanical loading, though effects on tensile strength were inconsistent.

Conclusions: Current evidence supports estrogen deficiency as a modifier of tendon degeneration and repair following menopause. Estrogen signaling influences tendon structure and function across molecular, biomechanical, and clinical domains. Further translational and clinical studies are needed to optimize tendon-focused interventions in postmenopausal women.

KEYWORDS

Estrogen deficiency, hormone therapy, menopause, postmenopause, tendon degeneration, tendon healing

INTRODUCTION

Menopause involves a significant decline in estrogen levels, which affects a wide range of body systems—including the musculoskeletal system[1,2]. Among these, tendons are recognized as sensitive to hormonal changes, yet they remain understudied compared to bone and muscle. Tendon injuries represent a substantial clinical and economic burden, with global incidence estimated at

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80–90 cases per 100,000 individuals per year, translating to approximately 6–7 million tendon ruptures annually[3]. The direct healthcare costs and societal impact of these injuries are considerable, highlighting the importance of understanding tendon health across populations[3]. For instance, full-thickness rotator cuff tears are approximately three times more common in postmenopausal women than in those who are premenopausal[4]. Gluteal tendinopathy (greater trochanteric pain syndrome) is another tendon issue found to be more prevalent in postmenopausal women[5]. Tendon health represents a significant musculoskeletal burden in the postmenopausal population.

Beyond hormonal changes, tendinopathies have increasingly been linked to metabolic and chronic diseases[6]. A recent systematic review demonstrated moderate evidence linking lower extremity tendinopathies with obesity and inflammatory rheumatologic conditions—including ankylosing spondylitis, psoriatic arthritis, and reactive arthritis—as well as limited evidence for associations with familial hypercholesterolemia and systemic lupus erythematosus[6]. These findings suggest that tendon pathology may reflect broader systemic metabolic dysregulation rather than isolated mechanical overload alone.

Hormonal fluctuations during both menopause and the menstrual cycle—particularly in estrogen—have been shown to affect tendon stiffness, with important implications for physical performance and injury risk. For example, chronic low estrogen exposure in monophasic oral contraceptive pill users reduced Achilles tendon strain, whereas normal cyclical fluctuations had minimal effect[7]. Preclinical models also demonstrate that estrogen deficiency impairs tendon repair quality and cellular proliferation, while estrogen presence supports healing processes[8,9]. Surgical menopause caused tissue-specific alterations in gene expression, suggesting metabolic reprogramming that may increase risk of tendon injury or degeneration post-menopause[10]. Biomechanical studies of postmenopausal women show significantly higher tendon stiffness and natural frequency, but reduced damping capacity, suggesting compromised shock absorption and greater susceptibility to injury[11].

From an orthopedic standpoint, reduced estrogen is not only a systemic event but a direct modifier of tendon degeneration and clinical outcomes. Estrogen appears to influence collagen turnover, fibroblast function, extracellular matrix remodeling, and overall tendon elasticity[12-17]. While hormone replacement or estrogen-like compounds can enhance collagen synthesis and improve matrix organization, their effects on tensile strength are variable and may depend on dose, timing, or concurrent mechanical loading[12,14,15]. Estrogen receptors alpha and beta (ERα and ERβ) are expressed in both healthy and diseased tendons, supporting the idea that tenocytes are direct targets of hormonal signaling, though functional effects remain incompletely understood[13,18].

Although interest in this topic has grown, the research remains dispersed across human, animal, and *in vitro* studies. This updated review incorporates findings from the past decade, including evidence of tendon-specific gene expression changes post-surgical menopause[10], detailed biomechanical characterization in postmenopausal women[11], and preclinical studies elucidating the role of estrogen in tendon repair and extracellular matrix remodeling[8,9]. By combining these new insights with human clinical observations and emerging therapeutic strategies, this review aims to provide a more comprehensive and mechanistically informed understanding of how estrogen deficiency affects tendon health, highlighting implications for injury risk, rehabilitation, and postmenopausal musculoskeletal care.

METHODS

In July 2025, a comprehensive literature search was conducted in PubMed (MEDLINE), Scopus, and Embase to identify studies published from January 2015 onward examining the relationship between menopausal hormonal changes and tendon biology, including tenocyte activity, extracellular matrix remodeling, collagen turnover, mechanical properties, and hormone receptor signaling. Human, animal, and *in vitro* studies were eligible.

Methods for this systematic review were informed by PRISMA guidelines[19]. This review was not prospectively registered in PROSPERO; however, the protocol was developed a priori and followed predefined eligibility and synthesis methods. Search queries comprised a combination of menopause- or hormone-related terms and tendon pathology terms, and are detailed in *Table 1*. Two independent reviewers screened articles in sequential stages (title, abstract, and full-text review). Disagreements were resolved by consensus. Only English-language articles directly addressing tendon-related outcomes in the

PubMed (MEDLINE), Scopus, Embase	(menopause OR menopausal OR postmenopause OR post-menopause OR postmenopausal OR post-menopausal OR perimenopause OR peri-menopause OR perimenopausal OR peri-menopausal) OR (“estrogen deficiency” OR estrogen OR estradiol OR “hormone replacement therapy” OR “hormonal therapy” OR “sex hormones”) AND (tendon OR tendinopathy OR “tendon degeneration” OR “tendon remodeling” OR “tendon healing” OR “tendon injury” OR “connective tissue” OR tenocyte OR enthesopathy)

Table 1. *Search strategy.*

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context of estrogen levels or menopause were included. Full eligibility criteria are detailed in *Table 2*. Ultimately, nineteen articles met inclusion criteria.

Risk of bias was assessed according to study design. Human observational studies were evaluated using the Newcastle–Ottawa Scale (NOS), randomized controlled trials using the Cochrane Risk of Bias 2 (RoB2) tool, and animal experiments using the SYRCLE Risk of Bias tool. Studies that included both *in vivo* animal and *in vitro* components were assessed using SYRCLE for the animal experiment, while purely *in vitro* studies were evaluated narratively due to the absence of a standardized risk-of-bias tool for cell-based experiments. NOS scores were reported as total scores out of nine possible stars, while RoB2 and SYRCLE were summarized using domain-level judgments and overall qualitative assessments. Risk-of-bias assessments were performed by a single reviewer.

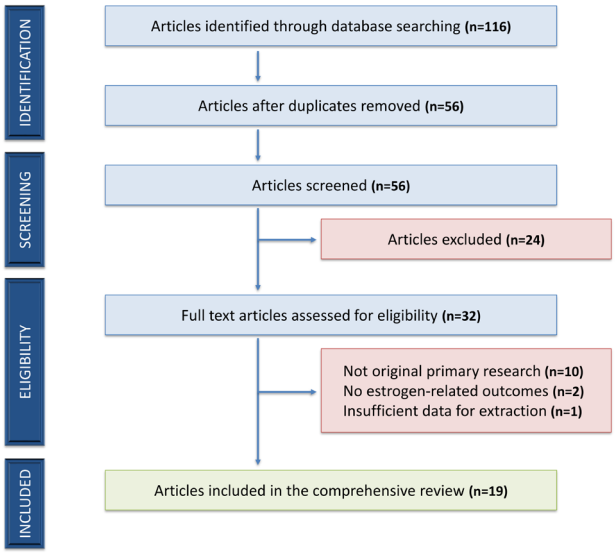


Figure 1. *Article screening flow diagram.*

RESULTS

As shown in *Figure 1*, the search identified 116 records and after duplicates were removed, 56 remained. After initial screening, 32 articles remained, and after eligibility analysis on full text, 19 articles were included. The 19 included articles encompassed human, animal, and *in vitro* models. Findings from these studies were synthesized into two major categories: estrogen deficiency on tendons and therapeutic implications.

The first category examines structural and biomechanical vulnerabilities that arise after menopause, the mechanistic roles of estrogen deficiency in tendon healing, and the functional significance of estrogen receptors in tendon tissue. The second category explores hormonal therapies, estrogen-like interventions, and other emerging therapeutic approaches aimed at mitigating tendon degeneration and improving repair outcomes.

Estrogen deficiency and tendons

Structural and biomechanical tendon vulnerabilities postmenopause (human clinical studies)

Human studies consistently report that postmenopausal women exhibit structural and mechanical changes in tendons. In a cohort of 1,443 women, age, hypertension, osteoporosis, and sarcopenia were identified as significant predictors of supraspinatus tendon tears[20]. Lower-limb studies in 73 women found that Achilles and gastrocnemius medialis stiffness was lowest in osteosarcopenic participants, with reduced stiffness associated with poorer balance[21]. Genetic analyses further indicated that a single nucleotide polymorphism (SNP), rs4986938, in the Erβ gene was significantly associated with risk of posterior tibial tendon (PTT) dysfunction, particularly in postmenopausal women, whereas no association was found for rs1256049[22]. Similarly, the ERα XbaI A/A genotype was

Domain	Inclusion criteria	Exclusion criteria
Language	Articles published in English	Articles published in languages other than English
Publication date	From January 2015 to July 2025	Before 2015
Study design	Original research including randomized controlled trials, cohort studies, case–control studies, cross-sectional studies, animal studies, and *in vitro* laboratory studies	Reviews, editorials, commentaries, conference abstracts, letters
Population/model	Human participants, animal models, or *in vitro* tendon/tenocyte models	Studies not involving tendon tissue or tenocytes
Intervention/exposure	Studies examining estrogen deficiency, menopausal hormonal changes, or hormone replacement therapy effects on tendon tissue	Studies focused exclusively on estrogen effects in bone, osteoporosis, or non-tendon tissues
Outcomes	Tendon-related outcomes including tendinopathy, tendon healing, degeneration, remodeling, injury, biomechanics, or cellular behavior	Outcomes unrelated to tendon health (e.g., bone density, fracture risk)
Diagnosis	Tendinopathy, tendon pathology, tenocyte biology, tendon-related disorders	Studies unrelated to the tendon pathology

Table 2. *Inclusion and exclusion criteria.*

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linked to higher prevalence of PTT tendinopathy, while PvuII polymorphisms showed no association[23]. Together, these studies describe a combination of systemic, mechanical, and genetic factors affecting tendon structure in postmenopausal populations.

Mechanistic role of estrogen deficiency in tendon healing (animal model studies)

Preclinical models demonstrate that estrogen deficiency impairs tendon healing processes at the cellular and molecular level. In 48-week-old rats, rotator cuff tendons exhibited significantly lower expression of collagen type I alpha 1 *(Col1a1)*, collagen type III alpha 1 *(Col3a1)*, and elastin compared with 12-week-old rats, with no significant differences at intermediate ages[24]. In mice, estrogen and testosterone improved the structural organization of tendon entheses and reduced inflammation, though no significant change in biomechanical strength was observed; testosterone also restored activity levels[25]. Additional work in mice revealed sex differences in extracellular matrix (ECM) remodeling even in the absence of hormones, with estrogen and progesterone exerting complementary but independent effects on turnover[26]. These data indicate alterations in collagen, elastin, and ECM remodeling associated with hormonal status and age.

Estrogen receptors and their functional role in tendons (animal model studies)

Both ERα and ERβ are expressed in healthy and diseased tendons[18]. In rat models of tendinopathy, ERβ expression increased with disease severity, and mechanical stress combined with estrogen deficiency further exacerbated tendon degradation[27]. Mice lacking ERβ showed impaired Achilles tendon healing, decreased collagen I deposition, weakened mechanical properties, and disrupted interferon regulatory factor 5 (IRF5)–C–C motif chemokine ligand 3 (CCL3) signaling during ECM remodeling[28]. Additionally, ERβ deletion led to worse histological outcomes and increased adipocyte accumulation via peroxisome proliferator-activated receptor gamma (PPARγ) activation[29].

Therapeutic implications

Hormonal therapies and tendon health (human clinical studies and animal model studies)

Multiple studies examined the effects of hormone supplementation on tendon healing. In rats, 17β-estradiol improved tendon matrix composition, reduced inflammation and apoptosis, and activated ERα and phosphoinositide 3-kinase / protein kinase B (PI3K/Akt) signaling in a dose-dependent manner[30]. In a cohort of 132 humans with body mass index (BMI) <25, menopausal hormone therapy combined with exercise and education led to higher Victorian Institute of Sport Assessment–Gluteal (VISA-G) scores compared with placebo at baseline, 12 weeks, and 52 weeks[31].

Estrogen-like compounds as therapeutics (animal model studies)

Animal studies have explored estrogen analogs and selective receptor modulators. Diethylstilbestrol improved rotator cuff tendon repair in mice by increasing osteogenic, angiogenic, and tendon maturation markers, restoring fibrocartilage closer to intact tendon structure[32]. Genistein administration in estrogen-deficient rats enhanced tendon mechanical properties and increased expression of proliferation-related genes such as tenomodulin, proliferating cell nuclear antigen, and tissue inhibitor of metalloproteinases 1[33]. Ginsenoside Rg1 promoted tendon healing by reducing apoptosis and inflammation, enhancing cell proliferation and migration, and upregulating matrix-related genes through insulin-like growth factor 1 receptor (IGF1R) and mitogen-activated protein kinase (MAPK) pathways in an estrogen receptor–dependent manner[34]. Other estrogen-like compounds, including estradiol, vitamin D, and certain isoflavones, increased tenocyte proliferation via ERα and vitamin D receptor pathways but did not significantly affect collagen I or scleraxis expression[35].

Other interventions for postmenopausal tendon health (human clinical studies and animal model studies)

Non-hormonal interventions also influenced tendon outcomes. Adipose-derived mesenchymal stromal cells enhanced tenocyte proliferation and matrix expression in estrogen-deficient rats, with allogenic cells showing superior effects compared to autologous ovariectomized-derived cells[36]. In 52 human participants, connective tissue massage improved menopausal symptoms, including hot flashes and emotional status, in the short term[37]. In rats, swimming training increased myotendinous junction evagination length and promoted tendon tissue reorganization, partially mitigating menopause-related reductions in sarcomere length and muscle-tendon interface size[38].

Quality assessment

Risk-of-bias assessment revealed variable methodological quality across study types. Among human cohort studies, NOS scores ranged from 3 to 9, with two studies achieving the maximum score and demonstrating strong methodological rigor, while others showed moderate limitations primarily related to confounding control and follow-up.

The two randomized controlled trials were judged to have “some concerns” using RoB2, largely due to unavoidable limitations in intervention blinding and incomplete reporting of allocation procedures. In contrast, the majority of animal studies were rated as having an overall unclear risk of bias using the SYRCLE tool, primarily because key methodological safeguards—including randomization methods, allocation concealment, and blinding—were not

reported. Studies consisting solely of *in vitro* experiments demonstrated several methodological limitations related to simplified experimental systems, supraphysiologic hormone exposure, and the absence of functional or biomechanical outcome measures.

DISCUSSION

Understanding the interplay between hormonal changes and tendon health is increasingly important for improving musculoskeletal outcomes in postmenopausal women. However, the current evidence base is uneven, with substantial variation in study design, population characteristics, and outcome measures. This discussion synthesizes current findings, with emphasis on the relative strength of evidence across human, animal, and *in vitro* studies, and on the limitations that constrain clinical translation. *Table 3* summarizes the principal findings and implications of the included studies.

Estrogen deficiency and tendons

Structural and biomechanical tendon vulnerabilities postmenopause

Evidence from human studies suggests an association between menopause and adverse tendon structural and mechanical features, but this evidence is largely observational and therefore limited in its ability to establish causality. Human studies demonstrating increased tendon tear prevalence in postmenopausal women suggest that systemic estrogen deficiency may contribute to compromised tendon resilience[20]. The coexistence of sarcopenia, osteoporosis, and vascular alterations likely amplifies this vulnerability, indicating that tendon health cannot be fully separated from the broader musculoskeletal and metabolic context of menopause[20,21]. This clustering of comorbidities introduces heterogeneity that complicates attribution of tendon changes specifically to estrogen deficiency. Biomechanical data showing altered stiffness and damping properties reinforce the view that estrogen is associated with maintaining the viscoelastic balance of tendon tissue[11]. Genetic associations with ERα and ERβ polymorphisms further suggest that inherent variability in estrogen receptor sensitivity may predispose certain women to tendon degeneration, offering a potential explanation for the heterogeneity in clinical outcomes observed across populations[22,23].

Given that menopause is also accompanied by significant shifts in body composition, including increased adiposity and redistribution of lean mass, mechanical loading patterns across the muscle–tendon unit may be altered. Cross-sectional data in postmenopausal women demonstrate a positive association between appendicular skeletal muscle mass and body fat percentage[39]. Excess adiposity may modify functional loading capacity and tendon strain exposure, potentially compounding estrogen-related matrix vulnerability.

Mechanistic role of estrogen deficiency in tendon healing

Mechanistic insight is derived predominantly from preclinical models, which consistently demonstrate that estrogen deficiency alters tendon matrix homeostasis. Mechanistic models converge on the idea that estrogen deficiency disrupts the balance between anabolic and catabolic processes in tendon healing. Reduced collagen synthesis, elevated matrix metalloproteinase activity, and disorganized ECM architecture collectively point to a shift toward tissue degradation[8,9,24]. The strength of this evidence is high at the cellular and molecular level, but its external validity to human tendon healing remains uncertain.

These alterations may explain the slower and mechanically weaker repair responses observed in postmenopausal populations following injury. However, direct human evidence linking hormonal status to impaired post-injury tendon healing is sparse. The finding that estrogen reintroduction can partially restore structural organization—but not consistently tensile strength—suggests that timing, dose, and interaction with mechanical loading are critical determinants of treatment efficacy[25]. Moreover, downregulation of *Col1a1*, *Col3a1*, and elastin implicates elastin as a previously underrecognized player in the elasticity and energy storage of tendons affected by hormonal decline[24]. This dissociation between histological and biomechanical outcomes highlights an important translational gap.

Estrogen receptors and their functional role in tendons

The presence of ERα and ERβ in human tendon tissue underscores that estrogen directly modulates local tendon biology rather than exerting effects solely through systemic pathways[18]. Evidence for receptor-specific function is strongest in genetically modified animal models. Studies involving ERβ knockout models highlight this receptor's role in maintaining collagen architecture and preventing adipogenic infiltration[27-29]. These findings are internally consistent across models but have not yet been comprehensively confirmed in human tissue studies.

Activation of PPARγ in the absence of ERβ suggests a potential mechanistic link between estrogen signaling and tendon fatty degeneration—one that may have relevance to both rotator cuff disease and chronic tendinopathies[28,29]. Nevertheless, species-specific differences in receptor expression and signaling pathways limit direct extrapolation to human disease. Understanding receptor subtype–specific pathways could guide development of targeted therapies that preserve tendon health in theory without the systemic risks of hormone replacement.

Therapeutic implications

Hormonal therapies and tendon health

Hormone replacement therapy (HRT) remains the most

Study	Population	Key findings	Implications
Estrogen deficiency and tendons			
Structural and biomechanical tendon vulnerabilities postmenopause			
Kara et al.[20]	Human (n = 1443)	Age, hypertension, osteoporosis and sarcopenia are significant predictors of supraspinatus tendon tears (p <0.05).	Postmenopause-related systemic conditions increase tendon tear risk.
Yekta et al.[21]	Human (n = 73)	Achilles and gastrocnemius medialis stiffness were lowest in osteosarcopenic women (p < 0.05); lower stiffness was linked to poorer balance.	Reduced tendon stiffness in osteosarcopenia increases fall susceptibility.
Nogara et al.[22]	Human (n = 400)	Estrogen receptor-beta (ERβ) single nucleotide polymorphism (SNP) rs4986938 allele A is significantly associated with increased posterior tibial tendon (PTT) dysfunction risk (p = 0.0450), especially in postmenopausal women; no association found for rs1256049 SNP. Genetic risk may also be important in men.	Genetic estrogen receptor variants may elevate tendinopathy risk postmenopause.
Pontin et al.[23]	Human (n = 184)	XbaI SNP in estrogen receptor-alpha (ERα) gene associated with PTT tendinopathy (p = 0.01); A/A genotype may increase risk; no association with PvuII SNP.	
Mechanistic role of estrogen deficiency in tendon healing			
Matsumoto et al.[24]	Rats (n = 30)	qPCR showed that Col1a1 (p <0.001), Col3a1 (p = 0.001), and Eln (p = 0.001) expression in the rotator cuff were all significantly lower in 48-week-old rats compared with 12-week-old rats, with no significant differences at intermediate ages.	Estrogen deficiency lowers Eln expression, suggesting elastin as a biomarker for postmenopausal tendon degeneration.
Tashjian et al.[25]	Mice (n = 72)	Estrogen and testosterone improved structure of tendon enthesis (p ≤0.01); no change in biomechanical strength; testosterone restored activity levels; hormones regulated distinct healing pathways, including reduced inflammation.	Sex hormones enhance repair quality, not necessarily strength.
Sander and Connizzo[26]	Mice	Sex differences in ECM remodeling were present even without hormones (chromosomal basis). Hormone responses were sex-dependent; estrogen and progesterone had complementary but independent effects on ECM turnover. (p <0.05)	Both sex and hormonal changes shape tendon remodeling postmenopause.
Estrogen receptors and their functional role in tendons			
Hsieh et al.[27]	Rats	ERβ expression increased in tendinopathy and was associated with disease severity (p <0.01); mechanical stress and estrogen deficiency synergistically worsened tendon degradation (p <0.001).	ERβ is vital for tendon healing; its deficiency or dysfunction impairs repair and worsens structure, especially under stress
Bian et al.[28]	Mice	ERβ deficiency impairs Achilles tendon healing (p <0.01), weakens mechanics (p <0.001), and reduces collagen I deposition (p <0.001) via disrupted IRF5-CCL3 signaling in ECM remodeling phase.	
Bian et al.[29]	Mice	ERβ deletion impaired Achilles tendon healing, causing worse histology (p <0.01) and increased adipocyte accumulation (p <0.01) via peroxisome proliferator-activated receptor γ activation.	ERβ in tendons modulates stem cell fate to avoid fatty infiltration, and may be a therapeutic target.
Therapeutic implications			
Hormonal therapies and tendon health			
Wang et al.[30]	Rats	17β-Estradiol (E2) improved tendon healing dose-dependently by enhancing tendon matrix composition, reducing inflammation and apoptosis, and activating ERβ and PI3K/Akt signaling.	Estradiol may improve tendon healing, dose-dependently.
McMillan et al.[31]	Human (n = 132)	In individuals with BMI <25, MHT combined with exercise and education led to significantly better VISA-G scores and secondary outcomes than placebo at baseline, 12 weeks, and 52 weeks.	Menopausal hormonal treatment of GTPS offered greater benefits for those with lower BMI. Emphasizing education on tendon compression and load management enhances the effectiveness of both active and passive interventions.
Estrogen-like compounds as therapeutics			
Tashjian et al.[32]	Mice (n = 33)	Diethylstilbestrol enhanced tendon healing in repaired rotator cuff tendons by increasing osteogenic, angiogenic, and tendon maturation markers (p <0.02), restoring fibrocartilage structure closer to intact tendons.	Synthetic nonsteroidal estrogens may enhance tendon healing.
Carroll et al.[33]	Rats (n = 42)	Genistein improved tendon mechanical function (modulus, energy density) in estrogen-deficient rats (p <0.05); effects mainly influenced genes related to cell proliferation (Tnmd, Pcna, Timp1) (p <0.05) rather than collagen remodeling.	Dietary phytoestrogens in soybeans may support tenocyte proliferation.
Wu et al.[34]	Rats	Ginsenoside Rg1 promoted tendon healing by reducing inflammation and apoptosis (p <0.05), enhancing cell proliferation and migration (p <0.05), and upregulating matrix-related genes via IGF1R and MAPK pathways. Effects were estrogen receptor–dependent.	Ginseng-derived compounds may promote tendon healing (estrogen receptor–dependently).
Maman et al.[35]	Rats	E2, vitamin D, and some isoflavones increased cell proliferation via ERβ and vitamin D receptor (not ERβ), but did not effect or decreased collagen-1 and scleraxis expression.	Some compounds stimulate cell growth without improving matrix production.
Other interventions for postmenopausal tendon health			
Veronesi et al.[36]	Rats	Adipose-derived mesenchymal stromal cells (ADSCs) enhanced tenocyte healing and proliferation in estrogen-deficient conditions (p <0.0005); Allogenic (healthy) ADSCs outperformed autologous (OVX) ADSCs (p <0.005). Decorin (p <0.0005) and Tenascin C (p <0.05) expression was higher with OVX ADSCs.	Stem cell therapies may aid postmenopausal tendon repair, especially allogenic cells.
Albayrak et al.[37]	Human (n = 52)	Connective tissue massage improved menopausal symptoms, hot flashes, and emotional status short-term (p ≤0.05).	Tendon massage may offer hormone-mimicking relief in menopause.
Jacob et al.[38]	Rats (n = 20)	Swimming training in menopausal rats increased myotendinous junction evagination length (p <0.001) and promoted tissue reorganization; menopause alone reduced muscle-tendon interface and sarcomere lengths (p <0.0001); exercise mitigated some menopause-related structural declines.	Exercise may mitigate menopause-related tendon degradation.

Table 3. *Summary of studies investigating estrogen deficiency and tendon health.*

Abbreviations: ADSCs, adipose-derived mesenchymal stromal cells; BMI, body mass index; Col1a1, collagen type I alpha 1 chain; Col3a1, collagen type III alpha 1 chain; E2, 17β-Estradiol, ECM, extracellular matrix; ERα, estrogen receptor alpha; ERβ, estrogen receptor beta; GTPS, greater trochanteric pain syndrome; IRF5-CCL3, interferon regulatory factor 5 – C-C motif chemokine ligand 3 signaling pathway; MOCP, monophasic oral contraceptive pill; MHT, menopausal hormonal treatment; OVX, ovariectomized; PI3K/Akt, phosphoinositide 3-kinase/protein kinase B signaling pathway; PTT, posterior tibial tendon; qPCR, quantitative polymerase chain reaction; SNP, single nucleotide polymorphism; Tnmd, tenomodulin; Timp1, tissue inhibitor of metalloproteinases 1.

studied and biologically plausible intervention to counteract postmenopausal tendon decline. The overall strength of evidence is moderate, with consistent biochemical and histologic effects but variable functional and biomechanical outcomes. The preponderance of evidence suggests that HRT favorably influences collagen metabolism and tendon morphology, though biomechanical benefits are inconsistent[12,14,30]. This inconsistency likely reflects variability in study design, patient characteristics, and the absence of standardized exercise protocols. Notably, multiple studies suggest a synergistic effect between estrogen therapy and mechanical loading, reinforcing the concept that tendon health depends on both hormonal and biomechanical inputs[15,16]. This interaction aligns with load-remodeling principles, whereby optimal strain magnitude and contraction modality appear necessary to stimulate favorable tendon adaptation[40], particularly in hormonally altered states. Future investigations should clarify optimal timing, dose, and combination strategies to balance efficacy with cardiovascular and oncologic safety considerations.

Estrogen-like compounds as therapeutics

Estrogen analogs and selective estrogen receptor modulators such as raloxifene offer promising alternatives that may mimic estrogen's local effects on tendon tissue while minimizing systemic exposure[32,33]. Current evidence supporting these agents is almost entirely preclinical. Their observed stimulation of collagen turnover and attenuation of degenerative changes suggest that selective receptor modulation could be leveraged therapeutically. However, outcomes are primarily molecular or histologic, with limited demonstration of durable biomechanical improvement. In parallel, non-estrogenic compounds such as melatonin have been shown to improve collagen organization and modify biomechanical properties in the tendons of ovariectomized models, although structural recovery was incomplete[41]. Defining receptor subtype selectivity, tissue distribution, and long-term outcomes will be essential to determine whether these agents can effectively bridge the gap between full hormone replacement and non-hormonal management.

Other interventions for postmenopausal tendon health

Beyond hormonal pathways, mechanical and biological therapies appear to hold complementary value. Exercise interventions, such as swimming training in menopausal rats, may mitigate menopause-related tendon degradation[38]. The evidence for exercise is indirect but biologically plausible, supported by broader literature on mechanotransduction in tendon adaptation[42]. Importantly, tendon adaptation is highly dependent on mechanical load remodeling[40]. Recent literature emphasizes that tendon strain, stiffness, and force–elongation behavior are dynamically regulated by resistance loading protocols, contraction type, and strain magnitude[40]. However, outcomes remain equivocal due to variability in exercise prescription and loading parameters, highlighting the need for standardized, high-quality protocols to optimize tendon remodeling responses[40].

Meanwhile, early-stage investigations into stem cell–based or biologic therapies hint at the potential to restore tendon matrix composition even in the absence of hormonal restoration[36], though these findings remain exploratory. Injection-based therapies, particularly high-volume injections (HVI), have demonstrated clinically meaningful reductions in pain, tendon thickness, and neovascularity in Achilles tendinopathy, with corticosteroid-augmented formulations showing superior short-term improvements in function[43]. While not menopause-specific, these data provide translational insight into how targeted biologic or mechanical modulation at the tendon interface may complement systemic hormonal strategies. Importantly, though HVI has demonstrated short-term safety, long-term structural outcomes and hormone-specific subgroup analyses remain lacking[43].

Furthermore, tendon massage may offer hormone-mimicking relief in menopause[37], but current outcomes are symptom-based rather than tendon-specific. These approaches may represent a new frontier for individualized postmenopausal tendon care—especially for patients unable or unwilling to pursue systemic hormone therapy—provided future studies incorporate rigorous tendon-specific structural and functional endpoints.

Limitations

Several important limitations constrain the interpretation and generalizability of the current literature. First, the majority of evidence derives from preclinical animal or *in vitro* models, which, while mechanistically informative, may not fully replicate human tendon biology or menopausal physiology. Second, randomized controlled trials in humans are few, limiting the ability to draw definitive conclusions about the efficacy of hormonal or non-hormonal interventions. Third, study outcomes are highly heterogeneous, encompassing structural, biochemical, biomechanical, and patient-reported measures, which complicates synthesis and cross-study comparisons. Fourth, many studies are small in sample size, reducing statistical power and increasing susceptibility to chance findings. Fifth, the literature may be subject to publication bias, as studies demonstrating significant or positive effects are more likely to be published, potentially overestimating intervention efficacy. Finally, the review was not prospectively registered, which may increase risk of reporting bias.

Quality assessment

Overall, the evidence base consists of a mixture of moderate-to-high quality clinical studies and preclinical studies with greater methodological uncertainty. Human

observational studies generally demonstrated moderate to high quality, with several studies achieving high NOS scores. The randomized controlled trials were generally well conducted but still presented some concerns related to blinding limitations and reporting of allocation procedures. Most animal studies were rated as having an unclear risk of bias due to incomplete reporting of methodological safeguards such as randomization and blinding. This pattern is common in preclinical literature but nonetheless limits confidence in the internal validity of some mechanistic findings. *In vitro* studies provided valuable mechanistic insights but were constrained by simplified experimental conditions that may not fully replicate the complex mechanical and hormonal environment of tendon tissue *in vivo*. Consequently, the mechanistic conclusions drawn from preclinical models should be interpreted cautiously and considered complementary to the more robust evidence derived from human studies.

Synthesis and future directions

Taken together, the convergence of mechanistic, genetic, and interventional data supports a meaningful—though incompletely defined—role for estrogen signaling in tendon health across the menopausal transition, highlighting key opportunities for translational research and intervention development. This body of evidence demonstrates consistent molecular and cellular effects of estrogen deficiency on extracellular matrix remodeling, collagen turnover, and inflammatory regulation, with growing—but more heterogeneous—associations observed in human structural, biomechanical, and clinical outcomes. While preclinical models provide strong biological plausibility and internal consistency, translation to clinical practice remains constrained by limited longitudinal human data, variability in hormone exposure, and differences in mechanical loading and comorbidity profiles. Future studies integrating well-phenotyped human cohorts with standardized tendon-specific outcomes, alongside mechanistically informed interventions that account for receptor subtype specificity and biomechanical context, will be essential to clarify causality and therapeutic potential. Such efforts may ultimately enable more precise, individualized strategies to preserve tendon integrity and optimize musculoskeletal health in postmenopausal populations.

CONCLUSION

From an orthopedic perspective, menopause-related estrogen decline is best understood as a modifier of tendon biology rather than a sole causal agent in tendon degeneration. It influences tendon cell signaling, extracellular matrix turnover, load response, and healing dynamics, with variable effects on injury risk, surgical outcomes, and rehabilitation potential depending on bio mechanical and systemic contexts. Tendons appear directly responsive to hormonal signaling, and both estrogen receptors and sex hormones likely play key roles in maintaining tendon structure and function in preclinical models and observational studies. While hormonal replacement, estrogen-like compounds, and other therapies show potential for mitigating tendon decline, the magnitude and consistency of their effects vary by dose, interaction with physical activity, and comprehensive healing of structural matrix support. Though promising, many of these findings remain preliminary, with heterogeneous methodologies and limited longitudinal human evidence, and more clinically relevant research is needed to clarify best practices for preserving tendon integrity in postmenopausal women. Taken together, the literature underscores a complex interplay of hormonal, genetic, and mechanical factors shaping tendon health. Future directions include refining diagnostic imaging, clarifying exercise and loading protocols tailored to tendon adaptation, tailoring rehabilitation strategies, and integrating biologic augmentation into surgical strategies to improve long-term outcomes for postmenopausal women with tendon pathology.

REFERENCES

1. Wright VJ, Schwartzman JD, Itinoche R, Wittstein J. The musculoskeletal syndrome of menopause. Climacteric. 2024;27(5):466–472. doi: 10.1080/13697137.2024.2380363
2. Nedergaard A, Henriksen K, Karsdal MA, Christiansen C. Menopause, estrogens and frailty. Gynecol Endocrinol. 2013;29(5):418–423. doi: 10.3109/09513590.2012.754879
3. Bergamin F, Civera M, Rodriguez Reinoso M, Burgio V, Ruiz OG, Surace C. Worldwide incidence and surgical costs of tendon injuries: A systematic review and meta-analysis. Muscle Ligaments and Tendons Journal. 2023;13(01). doi: 10.32098/mltj.01.2023.05
4. Abate M, Schiavone C, Di Carlo L, Salini V. Prevalence of and risk factors for asymptomatic rotator cuff tears in postmenopausal women. Menopause. 2014;21(3):275–280. doi: 10.1097/GME.0b013e31829638e3
5. Grimaldi A, Fearon A. Gluteal tendinopathy: Integrating pathomechanics and clinical features in its management. J Orthop Sports Phys Ther. 2015;45(11):910–922. doi: 10.2519/jospt.2015.5829
6. Lagas IF, Nijst BKJF, Hartgens F, De Bie RA, Vis M, Verhaar JaN, et al. Lower extremity tendinopathies are associated with metabolic and chronic diseases: A systematic review. Muscles, Ligaments and Tendons Journal. 2024;14(1). doi: 10.32098/mltj.01.2024.10
7. Bryant AL, Clark RA, Bartold S, Murphy A, Bennell KL, Hohmann E, et al. Effects of estrogen on the mechanical behavior of the human achilles tendon in vivo. J Appl Physiol (1985). 2008;105(4):1035–1043. doi: 10.1152/japplphysiol.01281.2007
8. Circi E, Akpinar S, Balcik C, Bacanli D, Guven G, Akgun RC, et al. Biomechanical and histological comparison of the influence of oestrogen deficient state on tendon healing potential in rats. Int Orthop. 2009;33(5):1461–1466. doi: 10.1007/s00264-009-0778-1
9. Torricelli P, Veronesi F, Pagani S, Maffulli N, Masiero S, Frizziero A, et al. In vitro tenocyte metabolism in aging and oestrogen deficiency. Age (Dordr). 2013;35(6):2125–2136. doi: 10.1007/s11357-012-9500-0
10. Hart DA, Achari Y. Alterations to cell metabolism in connective tissues of the knee after ovariohysterectomy in a rabbit model: Are there implications for the postmenopausal athlete? Br J Sports Med. 2010;44(12):867–871. doi: 10.1136/bjsm.2008.054296
11. Faria A, Gabriel R, Abrantes J, Bras R, Moreira H. Biomechanical properties of the triceps surae muscle-tendon unit in young and postmenopausal women. Clin Biomech (Bristol). 2011;26(5):523–528. doi: 10.1016/j.clinbiomech.2010.12.011
12. Irie T, Takahata M, Majima T, Abe Y, Komatsu M, Iwasaki N, et al. Effect of selective estrogen receptor modulator/raloxifene analogue on proliferation and collagen metabolism of tendon fibroblast. Connect Tissue Res. 2010;51(3):179–187. doi: 10.3109/03008200903204669
13. Frizziero A, Vittadini F, Gasparre G, Masiero S. Impact of oestrogen deficiency and aging on tendon: Concise review. Muscles Ligaments Tendons J. 2014;4(3):324–328.

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14. Hansen M, Kongsgaard M, Holm L, Skovgaard D, Magnusson SP, Qvortrup K, et al. Effect of estrogen on tendon collagen synthesis, tendon structural characteristics, and biomechanical properties in postmenopausal women. J Appl Physiol (1985). 2009;106(4):1385–1393. doi: 10.1152/japplphysiol.90935.2008
15. Finni T, Kovanen V, Ronkainen PH, Pollanen E, Bashford GR, Kaprio J, et al. Combination of hormone replacement therapy and high physical activity is associated with differences in achilles tendon size in monozygotic female twin pairs. J Appl Physiol (1985). 2009;106(4):1332–1337. doi: 10.1152/japplphysiol.91439.2008
16. Cook JL, Bass SL, Black JE. Hormone therapy is associated with smaller achilles tendon diameter in active post-menopausal women. Scand J Med Sci Sports. 2007;17(2):128–132. doi: 10.1111/j.1600-0838.2006.00543.x
17. Hansen M, Kjaer M. Influence of sex and estrogen on musculotendinous protein turnover at rest and after exercise. Exerc Sport Sci Rev. 2014;42(4):183–192. doi: 10.1249/JES.0000000000000026
18. Bridgeman JT, Zhang Y, Donahue H, Wade AM, Juliano PJ. Estrogen receptor expression in posterior tibial tendon dysfunction: A pilot study. Foot Ankle Int. 2010;31(12):1081–1084. doi: 10.3113/FAI.2010.1081
19. Prisma statement: Prisma 2020. Available at: https://www.prisma-statement.org/prisma-2020. Last access date: 02/26/2026.
20. Kara M, Kara O, Durmus ME, Analay P, Sener FE, Citir BN, et al. The relationship among probable sarcopenia, osteoporosis and supraspinatus tendon tears in postmenopausal women: The sarcosp study. Calcif Tissue Int. 2024;114(4):340–347. doi: 10.1007/s00223-024-01183-7
21. Yekta EB, Torkaman G, Aghaghazvini L. Comparative study on muscle-tendon stiffness and balance impairment in postmenopausal women: A focus on osteosarcopenia and osteoporosis. Aging Clin Exp Res. 2024;36(1):232. doi: 10.1007/s40520-024-02888-3
22. Nogara PRB, Godoy-Santos AL, Fonseca FCP, Cesar-Netto C, Carvalho KC, Baracat EC, et al. Association of estrogen receptor beta polymorphisms with posterior tibial tendon dysfunction. Mol Cell Biochem. 2020;471(1-2):63–69. doi: 10.1007/s11010-020-03765-z
23. Pontin PA, Nogara PRB, Fonseca FCP, Cesar Netto C, Carvalho KC, Soares Junior JM, et al. Eralpha pvuii and xbai polymorphisms in postmenopausal women with posterior tibial tendon dysfunction: A case control study. J Orthop Surg Res. 2018;13(1):316. doi: 10.1186/s13018-018-1020-x
24. Matsumoto M, Uchida K, Tazawa R, Kenmoku T, Inoue K, Inoue G, et al. Impact of aging and estrogen deficiency on extracellular matrix-related gene expression in rotator cuff tendons: In vitro and in vivo rat model. JSES Int. 2025;9(5):1555–1561. doi: 10.1016/j.jseint.2025.05.021
25. Tashjian RZ, Zitnay J, Kazmers NH, Veerabhadraiah SR, Zelada AC, Honeggar M, et al. Estrogen and testosterone supplementation improves tendon healing and functional recovery after rotator cuff repair. J Orthop Res. 2024;42(2):259–266. doi: 10.1002/jor.25695
26. Sander AM, Connizzo BK. Estrogen and progesterone exhibit distinct yet coordinated roles in the regulation of tendon extracellular matrix remodeling. J Orthop Res. 2026;44(1):e70018. doi: 10.1002/jor.70018
27. Hsieh JL, Jou IM, Wu CL, Wu PT, Shiau AL, Chong HE, et al. Estrogen and mechanical loading-related regulation of estrogen receptor-beta and apoptosis in tendinopathy. PLoS One. 2018;13(10):e0204603. doi: 10.1371/journal.pone.0204603
28. Bian X, Liu T, Yang M, Gu C, He G, Zhou M, et al. The absence of oestrogen receptor beta disturbs collagen i type deposition during achilles tendon healing by regulating the irf5-ccl3 axis. J Cell Mol Med. 2020;24(17):9925–9935. doi: 10.1111/jcmm.15592
29. Bian X, Liu T, Zhou M, He G, Ma Y, Shi Y, et al. Absence of estrogen receptor beta leads to abnormal adipogenesis during early tendon healing by an up-regulation of ppargamma signalling. J Cell Mol Med. 2019;23(11):7406–7416. doi: 10.1111/jcmm.14604
30. Wang F, Shan H, Song G, Chen S, Zhang C, Liu Y, et al. 17beta-estradiol attenuates inflammation and tendon degeneration in a rat model of achilles tendinitis. Immunopharmacol Immunotoxicol. 2022;44(4):556–564. doi: 10.1080/08923973.2022.2065639
31. McMillan RM, Ganderton CL, Cook J, Semciw AI, Long DM, Pizzari T. Does menopausal hormone therapy, exercise, or both improve pain and function in postmenopausal women with greater trochanteric pain syndrome? A 2 x 2 factorial randomized clinical trial. Am J Sports Med. 2022;50(2):515–525. doi: 10.1177/03635465211061142
32. Tashjian RZ, Kazmers NH, Epperson RT, Honeggar M, Ma Y, Chalmers PN, et al. The effect of estrogen-like compound on rotator cuff tendon healing in a murine model. J Orthop Res. 2021;39(12):2711–2724. doi: 10.1002/jor.25000
33. Carroll CC, Patel SH, Simmons J, Gordon BD, Olson JF, Chemelewski K, et al. The impact of genistein supplementation on tendon functional properties and gene expression in estrogen-deficient rats. J Med Food. 2020;23(12):1266–1274. doi: 10.1089/jmf.2019.0293
34. Wu T, Qi W, Shan H, Tu B, Jiang S, Lu Y, et al. Ginsenoside rg1 enhances the healing of injured tendon in achilles tendinitis through the activation of igf1r signaling mediated by oestrogen receptor. J Ginseng Res. 2022;46(4):526–535. doi: 10.1016/j.jgr.2021.08.005
35. Maman E, Somjen D, Maman E, Katzburg S, Sharfman ZT, Stern N, et al. The response of cells derived from the supraspinatus tendon to estrogen and calciotropic hormone stimulations: In vitro study. Connect Tissue Res. 2016;57(2):124–130. doi: 10.3109/03008207.2015.1114615
36. Veronesi F, Della Bella E, Torricelli P, Pagani S, Fini M. Effect of adipose-derived mesenchymal stromal cells on tendon healing in aging and estrogen deficiency: An in vitro co-culture model. Cytotherapy. 2015;17(11):1536–1544. doi: 10.1016/j.jcyt.2015.07.007
37. Albayrak G, Cagliyan Turk A, Ozgul S. Effects of connective tissue massage on physical and emotional symptoms, insomnia, and quality of life in postmenopausal women: A randomized, sham-controlled trial. Maturitas. 2025;191:108149. doi: 10.1016/j.maturitas.2024.108149
38. Jacob CDS, Rocha LC, Neto JP, Watanabe IS, Ciena AP. Effects of physical training on sarcomere lengths and muscle-tendon interface of the cervical region in an experimental model of menopause. Eur J Histochem. 2019;63(3). doi: 10.4081/ejh.2019.3038
39. Abidin NZ. The “fat or fit paradox” in postmenopausal women: A cross-sectional study on the association between skeletal muscle mass, adiposity, and muscle strength. Muscle Ligaments and Tendons Journal. 2023;13(03). doi: 10.32098/mltj.03.2023.20
40. Kahraman Y. A critical review on tendon structure and load remodeling. Muscle Ligaments and Tendons Journal. 2023;13(2). doi: 10.32098/mltj.02.2023.04
41. Da Silva Rosa BL, Silva Pompêo GH, Melo Ramos C, Ferreira JH, Ruginsk SG, Pires Marques P, et al. Evaluation of the effect of melatonin on the calcaneal tendon of ovariectomized wistar rats. Muscles, Ligaments and Tendons Journal. 2023;13(4). doi: 10.32098/mltj.04.2023.01
42. Nakamichi R, Asahara H. The role of mechanotransduction in tendon. J Bone Miner Res. 2024;39(7):814–820. doi: 10.1093/jbmr/zjae074
43. Hassan R, Poku D, Miah N, Maffulli N. High-volume injections in achilles tendinopathy: A systematic review. Br Med Bull. 2024;152(1):35–47. doi: 10.1093/bmb/ldae015