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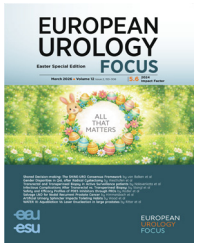

Mini Review

Physical Exercise for Erectile Dysfunction: A Mini review on Unresolved Controversies and the Path to Precision Prescription

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Abstract

Erectile dysfunction (ED) is increasingly recognized as an early marker of systemic vascular disease, yet the role of exercise as a therapeutic intervention remains surrounded by significant controversy. Although mechanistic studies suggest that exercise enhances endothelial function and nitric oxide bioavailability, clinical trials show highly variable outcomes across populations. Key unresolved debates include: optimal exercise modality (aerobic vs resistance training), dose-response relationships, the complex interplay between exercise and testosterone, genetic determinants of treatment response, and potential risks in athletic populations (particularly cyclists). This rapid review critically examines these controversies, highlighting where consensus is lacking and where conflicting evidence demands further investigation. We argue that exercise prescription for ED requires a precision medicine approach that considers individual physiology, training status, genetic variants, and comorbidity profiles. Future research must move beyond heterogeneous protocols toward mechanistically-driven, personalized interventions that optimize vascular, hormonal, and molecular adaptations while minimizing potential adverse effects in specific populations.

Patient summary: Exercise may improve erectile function, but the optimal prescription remains uncertain and should be personalized.

1. Introduction

Erectile dysfunction (ED) affects over 150 million men globally and functions as a sentinel marker for cardiovascular disease, with penile arterial insufficiency preceding coronary events by 2–5 yr [1]. The underlying pathophysiology, impaired nitric oxide (NO) signaling, endothelial dysfunction, and compromised cavernosal smooth muscle relaxation, directly parallels mechanisms targeted by exercise

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training [2], positioning exercise as an ideal nonpharmacological intervention.

Despite strong biological rationale, exercise prescription for ED lacks evidence-based guidelines and remains highly variable in clinical practice. Meta-analyses reveal profound heterogeneity, with International Index of Erectile Function (IIEF) improvements ranging from clinically negligible to comparable with phosphodiesterase-5 inhibitors (PDE5is) [3,4]. Emerging genetic data suggest individual response variability that current one-size-fits-all approaches entirely ignore [5]. This mini review addresses these controversies and proposes a precision medicine research framework.

2. The exercise prescription dilemma

The first unresolved debate concerns the exercise type. Aerobic training dominates ED research based on well-characterized mechanisms: enhanced endothelial NO synthase (eNOS) expression, improved arterial compliance, and reduced oxidative stress [6]. Meta-analytic evidence suggests moderate-to-vigorous aerobic exercise improves IIEF scores by 3–5 points [3], which is clinically meaningful but not universal. Resistance training receives disproportionately little attention despite plausible benefits, including improved insulin sensitivity, reduced visceral adiposity, and enhanced testosterone, with protocols remaining poorly standardized and effects on penile hemodynamics largely unexplored, leaving the critical question of whether strength gains translate to erectile improvements unanswered [7]. Allen (2019) [2] proposed that different exercise modalities exert differential effects on erectile function mechanisms: aerobic exercise primarily enhances endothelial function through vascular adaptations and resistance training acutely elevates testosterone and improves body image, while combat sports and group activities offer additional psychological benefits including stress reduction and improved self-esteem. Perhaps the most glaring deficiency is the absence of systematic dose-response data. Exercises employ wildly divergent protocols: intensity ranging from 40–85% maximal heart rate, session duration from 30 to 60 min, frequency from 3 to 7 d weekly, and intervention length from 8 wk to 6 mo [3,4]. This variation exists without systematic justification or validation of optimal parameters. In addition, without dose-response curves stratified by baseline erectile function, comorbidity burden, and fitness level, clinicians prescribe exercises based on generalized cardiovascular guidelines, a square-peg-round-hole approach that ignores ED-specific physiology.

The magnitude of erectile function improvement across randomized controlled trials varies considerably according to population characteristics, exercise modality, and intervention design (see Table 1).

Across all four studies, the consistent finding is that structured aerobic or interval exercise improves IIEF scores significantly more than the control conditions, regardless of the clinical population (obese, hypertensive, metabolic syndrome, or arterial ED). The methodological benchmark of the field remains a 24-mo lifestyle intervention in obese men, in which 31% achieved full erectile function recovery, the only trial to report complete recovery as a primary outcome [8]. A brief interval cycling program was sufficient to improve IIEF Erectile Function domain (IIEF-EF) scores, blood pressure, and cardiorespiratory fitness in hypertensive men, illustrating the dual cardiovascular-sexual benefit of aerobic training [9]. The Maresca et al [10] study is particularly noteworthy because it showed exercise adds clinically relevant benefit even in addition to an active pharmacological treatment (tadalafil), and the La Vignera et al [11] study is methodologically distinctive for using endothelial biomarkers (endothelial progenitor cells and endothelial microparticles) as mechanistic endpoints alongside the IIEF score.

3. The testosterone enigma

Testosterone's role in exercise-mediated erectile improvements remains contentious. Though severe hypogonadism (<300 ng/dl) clearly impairs function, the relevance of normal-range testosterone and transient exercise-induced elevations (20–40% increases lasting 15–60 min) is debated [12]. Three competing hypotheses exist: hormonal mediation (testosterone elevation drives improvements), receptor sensitivity (enhanced androgen receptor expression without elevated circulating levels), and testosterone-independent (vascular adaptations alone). Current evidence cannot discriminate between models. Acute resistance exercise elevates testosterone while chronic high-volume endurance training paradoxically suppresses it. Establishing testosterone's mechanistic contribution requires causal mediation analyses quantifying both acute hormonal responses and chronic training adaptations [2].

4. Precision medicine: genetic stratification and molecular biomarkers

The most promising avenue for resolving conflicting trial results involves genetic heterogeneity. A recent study demonstrated that eNOS gene polymorphisms (T-786C, G894T, and intron 4 VNTR) significantly predict baseline erectile function and PDE5i response in patients with cardiovascular diseases [5]. These variants modulate NO bioavailability, the central mechanism for both penile erection and exercise-induced vascular adaptation. Beyond eNOS, polymorphisms in *ACE* and *BDKRB2* genes, together with circulating micro ribonucleic acid (miRNA) profiles, may further modulate endothelial function and vascular NO signaling in exercise contexts. Collectively, such biomarkers could enable precision stratification of exercise interventions, identifying clear responders, partial responders requiring combination therapy (eg, exercise plus PDE5i), and nonresponders who may benefit from alternative modalities [13]. Although validated in cardiovascular rehabilitation, this precision framework is absent from exercise-ED trials, where genetic profiling could individualize prescriptions and resolve conflicting results.

5. When exercise becomes the problem

While exercise generally improves ED, prolonged competitive cycling may cause perineal numbness and vascular compromise through sustained pressure, with studies reporting 13–24% ED prevalence in competitive cyclists versus no elevated risk in recreational cyclists, suggesting dose-dependent effects [14]. Beyond cycling, excessive

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Table 1 – Exercise interventions and erectile dysfunction: evidence from four randomized controlled trials

Study	*N*	Exercise group (EG)	Control group (CG)	Duration	Effect (ΔIIEF)	Magnitude
Esposito et al [8]	110	*N* = 55; diet + physical activity program (walking, swimming, aerobic games); individualized caloric reduction (≈1700–1900 kcal/d); monthly sessions with nutritionist and trainer; obese men (BMI ≥ 30)	*N* = 55; general oral/written information on healthy food and exercise; no individualized program; sedentary obese men	24 mo	EG: +3.01 (13.9→17.0) CG: +0.1	Moderate EG: 31% regained normal function (IIEF ≥ 22)
Lamina et al [9]	43	*N* = 22; interval cycle ergometer training; 60–79% HR max reserve; 45–60 min/session; 3 sessions/wk; hypertensive men aged 50–70 yr	*N* = 21; sedentary; no physical activity during study period; matched hypertensive men on methyldopa	8 wk	EG: +3.64 (11.5→15.1) CG: +0.85	Moderate EG: Significant group difference ($p = 0.000$); CRP reduction correlated ($r = -0.588$)
Maresca et al [10]	20	*N* = 10; tadalafil 5 mg/d + structured exercise (cycle ergometer or treadmill; 65% VO_2peak; 30 min; 3×/wk); metabolic syndrome patients	*N* = 10; tadalafil 5 mg/d only; generic information about exercise usefulness; no structured program	2 mo	EG: +9.3 (10.8→20.1) CG: +3.0	High EG: 100% IIEF improvement versus 40% CG; added value of exercise = +5.9 pts ($p < 0.001$)
La Vignera et al [11]	70	*N* = 50; standard aerobic protocol; 150 min/wk moderate intensity; 30 min bouts; HR 40–60% max; Mediterranean diet; patients with arterial erectile dysfunction aged 48–62 yr	*N* = 20; mediterranean diet only; no aerobic physical activity; matched middle-aged men with vascular erectile dysfunction	3 mo	EG: +5.5 (11.0→16.5) CG: 0	High EG: significant improvement in PSV and endothelial markers (EPC, and EMP) ($p < 0.05$)

The ΔIIEF values represent the within-group change from baseline to post-intervention in the exercise group, with the control group's change shown for contrast. The "magnitude" column reflects both the raw score change and, where reported, the proportion of participants achieving clinically meaningful improvement.
BMI = body mass index; CRP = C-reactive protein; EMP = endothelial microparticles; EPC = endothelial progenitor cells; HR = heart rate; IIEF = International Index of Erectile Function; PSV = peak systolic velocity; VO_2peak: the highest oxygen consumption.

training volume may paradoxically impair erectile function through multiple mechanisms: chronic cortisol elevation, suppressed gonadotropin release, overwhelming oxidative stress, and sleep deprivation affecting testosterone production [2]. The "exercise-hypogonadal male condition" describes athletes experiencing testosterone suppression from high training loads. Allen (2019) [2] recommends that exercise programs avoid overtraining, with resistance training limited to twice weekly at high intensity to prevent testosterone suppression while maximizing physiological gains. Defining safe upper limits for exercise volume in ED management is crucial but unexplored.

6. Exercise-PDE5i synergy: complementary or redundant?

PDE5is remain the pharmacological cornerstone of ED treatment with established efficacy and safety [15]. However, since both exercise and PDE5i target the NO-cyclic guanosine 3', 5'-monophosphate pathway through distinct mechanisms, their combined use raises critical questions regarding potential synergy versus therapeutic redundancy [15]. Several studies suggest additive benefits, with combined tadalafil and aerobic exercise producing greater IIEF improvements than either intervention alone in patients with metabolic syndrome, and similar synergistic effects were observed particularly in men with diabetes and obesity [2]. Exercise could and probably should replace PDE5i as the first-line treatment option for ED [16], given that exercise interventions show the largest effect sizes among all treatments and can elicit sustainable cardioprotection extending beyond the training period [2].

7. Conclusion

Exercise holds tremendous promise for ED management, targeting vascular, metabolic, and potentially hormonal mechanisms underlying ED. However, current evidence remains plagued by heterogeneity, inadequate sample sizes, and failure to account for individual variability. These controversies carry direct clinical implications for millions of men seeking nonpharmacological ED treatment.

A paradigm shift is essential: from one-size-fits-all prescriptions toward precision medicine integrating clinical phenotype, genetic variants, molecular biomarkers, and training status. Advancing precision exercise prescription requires multicenter dose-response trials varying intensity, volume, and modality stratified by ED severity; genotype-guided interventions comparing tailored versus standard prescriptions; longitudinal miRNA profiling correlating changes with erectile outcomes; athletic population studies linking training metrics with hormonal profiles; three-arm trials comparing exercise monotherapy, PDE5i, and combined approaches; and comprehensive testosterone dynamics studies employing causal mediation analyses [2,7,8].

Allen (2019) [2] proposes specific exercise prescription guidelines for ED: high-intensity whole-body resistance training twice weekly, moderate-intensity aerobic exercise twice weekly, and group-based sport activities combining aerobic and anaerobic elements once weekly. This combination optimizes vascular adaptations through aerobic

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exercise, testosterone increases through resistance training, and psychological benefits (stress reduction, anxiety management, and body image improvement) through group activities and combat sports. The path forward requires interdisciplinary collaboration among andrologists, exercise physiologists, geneticists, and sports medicine specialists to transform exercise from a generic recommendation into a precision therapeutic tool that optimizes vascular, hormonal, and molecular adaptations while improving both erectile function and overall cardiometabolic health.

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