

Letter to Editor

Rethinking Gender in Orthopedics: From Biological Dimorphism to Precision Musculoskeletal Care



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Introduction

Orthopedics has traditionally approached sex differences as a matter of anatomical scale—bone size, muscle mass, and ligamentous laxity. However, emerging evidence suggests that sex and gender are not peripheral modifiers but central biological and socio-clinical determinants shaping musculoskeletal health, injury patterns, treatment response, and long-term outcomes [1, 2]. It is now imperative to reframe orthopedics through a sex- and gender-informed precision lens.

Biological sex influences skeletal architecture, hormonal milieu, inflammatory response, and tissue regeneration [3]. Estrogen signaling plays a crucial role in bone remodeling and ligament homeostasis [4], partially explaining the higher prevalence of anterior cruciate ligament injuries in female athletes [5] and accelerated bone loss observed after menopause [6]. Landmark data from the [World Health Organization \(WHO\)](#) emphasize the disproportionate burden of osteoporosis and fragility fractures in women [7]; however, emerging studies indicate that outcomes in men may be under-recognized and undertreated [8].

Beyond biology, gender—as a socio-cultural construct—affects exposure risk, access to care, pain report-

ing, and rehabilitation adherence [9]. For instance, disparities in total joint arthroplasty utilization and referral timing have been reported, even when disease severity is comparable [10]. Investigations published in journals such as *The Journal of Bone and Joint Surgery* and *The Lancet* increasingly call for stratified analyses rather than pooled data that obscure clinically meaningful sex-based differences [11].

A particularly underexplored dimension is in molecular orthopedics. Sex chromosomes influence immune signaling and mitochondrial function [12], which may modify outcomes in trauma, infection, and implant integration. Integrating multi-omics data with artificial intelligence offers an opportunity to identify sex-specific biomarkers predicting fracture healing, prosthesis survival, or osteoarthritis progression [13]. This aligns with the broader movement toward precision medicine, championed by initiatives such as the National Institutes of Health Sex as a Biological Variable policy [14].

Sex-aware orthopedics should not reinforce binary reductionism. Rather, it demands methodological rigor: adequate representation, predefined subgroup analyses, and transparent reporting [14, 15]. Clinical trials must move beyond post hoc comparisons and incorporate sex-specific hypotheses in study design.

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In this evolving paradigm, orthopedics is no longer solely about biomechanics—it is about biological context. Recognizing sex and gender as integral variables refines, rather than fragments, the field. The future of musculoskeletal care may well depend on how effectively we integrate these dimensions into research, surgical planning, and rehabilitation strategies.

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