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Review

Role of endocrine-immune dysregulation in osteoporosis, sarcopenia, frailty and fracture risk

Cherian Joseph [a], Anne M. Kenny [a], Pamela Taxel [a,b], Joseph A. Lorenzo [a,b], Gustavo Duque [c], George A. Kuchel [a,*]

[a] *UConn Center on Aging, University of Connecticut Health Center, MC-5215, 263 Farmington Ave., Farmington, CT 06030-5215, United States*
[b] *Division of Endocrinology, University of Connecticut Health Center, MC-5215, 263 Farmington Ave., Farmington, CT 06030-5215, United States*
[c] *Division of Geriatric Medicine, McGill University, Canada*

Abstract

Osteoporosis, a key predictor of hip fractures can be treated using a variety of safe and effective interventions. Nevertheless, optimally effective strategies for the prevention of hip fractures must also incorporate efforts to address a broad range of other potentially reversible factors. Hyperthyroidism, anticonvulsants, caffeine and smoking may decrease bone mass and increase fracture risk at any age. In older individuals it is important to also consider additional risk factors, including long-acting benzodiazepines, poor vision and sarcopenia. The presence of sarcopenia, an age-related decline in muscle bulk and quality enhances the risk of frailty and possibly also hip fracture, particularly if associated with diminished functional mobility, lower quadriceps strength and poor balance or body sway. In this review we examine evidence which indicates the presence of endocrine-immune dysregulation in both osteoporosis and sarcopenia. Post-menopausal declines in serum estrogen and androgen levels contribute to increases in local bone levels of cytoclastic cytokines, followed by increased osteoclastogenesis and bone loss. Similarly, the presence of decreased gonadal hormones and IGF-1, combined with unusually high peripheral levels of cytokines, inflammatory mediators and coagulation markers all enhance the risk of sarcopenia and frailty. We propose that a translational

* Corresponding author. Tel.: +1 860 679 3956; fax: +1 860 679 1307.
E-mail address: kuchel@uchc.edu (G.A. Kuchel).

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research approach which emphasizes common pathophysiologic mechanisms in osteoporosis and sarcopenia could accelerate the speed of discovery of effective strategies for both frailty and hip fracture prevention.

Keywords: Hormones; Inflammation; Cytokines; Estrogen; Androgen; Bone; Muscle; Mobility

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1. Risk factors and prevention strategies for hip fractures

The major focus of medical research has traditionally been on the development of strategies to treat disease and to prevent mortality. Given current and projected demographic trends, it has become imperative that systematic efforts be undertaken to also prevent and delay disability among growing numbers of older individuals. Hip fractures represent a particularly common and significant cause of excess mortality, as well as sustained disability among older women and men. For example, older adults experience a 20–25% excess mortality in the year following a hip fracture (Cooper et al., 1993). Moreover, hip fractures commonly herald the development of disability which is often new and sustained (Marottoli et al., 1992), with