

GUT MICROBIOTA AS A MODULATOR OF BONE REMODELING: MECHANISTIC INSIGHTS AND THERAPEUTIC IMPLICATIONS IN OSTEOPOROSIS

Vinicius Willian Calderon da Silva

Gustavo Silveira Pires; Rafael de Oliveira Tabian; Vitor Piacenti Padovan; Filipe Gabriel Januario

RESUMO

Introduction: Osteoporosis (OP) is a multifactorial metabolic disease characterized by reduced bone mineral density (BMD) and impaired bone microarchitecture, leading to increased fracture risk. Recent evidence supports the gut microbiota (GM) as a central regulator of bone homeostasis through immune, endocrine, and metabolic pathways, forming the gut-bone axis. Dysbiosis has been associated with systemic inflammation, altered intestinal permeability, impaired nutrient absorption, and hormonal dysregulation, all contributing to enhanced osteoclastogenesis and bone loss. **Objective:** To analyze the mechanisms linking gut microbiota to bone remodeling and to evaluate the therapeutic potential of microbiota modulation in osteoporosis. **Materials and Methods:** A narrative review was conducted using PubMed, prioritizing recent studies (2020-2026) while including foundational evidence without temporal restriction. The search strategy combined descriptors such as “gut microbiota,” “osteoporosis,” “bone remodeling,” “probiotics,” and “short-chain fatty acids” using Boolean operators. Experimental, clinical, and translational studies addressing immunological, endocrine, metabolic mechanisms and microbiota-targeted therapies were included. **Results:** The gut microbiota modulates bone remodeling through interconnected pathways. Immunologically, dysbiosis promotes pro-osteoclastogenic signaling via increased Th17 cells and inflammatory cytokines (e.g., TNF- α , IL-17), whereas microbial metabolites such as short-chain fatty acids (SCFAs) enhance regulatory T cells and suppress osteoclast differentiation. Endocrine interactions involve modulation of estrogen metabolism, the GH/IGF-1 axis, parathyroid hormone (PTH), and gut-derived serotonin, highlighting the relevance of the enteroendocrine-bone axis. Metabolically, microbiota improves calcium bioavailability and regulates bile acid signaling pathways, including TGR5-mediated effects on bone preservation. Experimental evidence from germ-free and antibiotic-treated models demonstrates significant alterations in bone mass and turnover following microbiota disruption, while probiotic interventions (e.g., *Lactobacillus* and *Lactocaseibacillus* strains) have shown anti-inflammatory and bone-protective effects in animal models and emerging clinical studies. Meta-analytical data suggest that probiotic supplementation may improve bone turnover markers in middle-aged and elderly populations, although heterogeneity remains. **Conclusion:** Gut microbiota modulation represents a promising adjunctive strategy in osteoporosis management. Current evidence suggests that microbiota-targeted interventions may be associated with improvements in bone density and remodeling markers; however, these effects vary according to experimental models, studied populations, and types of intervention. Further large-scale, well-controlled clinical trials are required to establish causal relationships and therapeutic applicability.

Palavras-chave: Gut Microbiota Osteoporosis Bone Remodeling Dysbiosis.