

Title: Clinical evidence on autologous cell-based therapies for periodontal soft tissue regeneration: a systematic review (word count: 15)

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Abstract (word count: 294)

Objective: Periodontal soft tissue deficiencies compromise tissue stability, esthetics, and patient comfort. Autologous cell-based therapies have emerged as a regenerative strategy aimed at restoring periodontal soft tissues; however, human clinical evidence remains limited and heterogeneous. This systematic review critically appraised human clinical evidence on autologous cell-based therapies for periodontal soft tissue regeneration.

Methods: A PRISMA-guided systematic review was conducted using PubMed/MEDLINE, Scopus, and Web of Science without year restrictions through January 2026. Human clinical studies evaluating autologous cell-based interventions for periodontal soft tissue regeneration were considered eligible. Study selection, data extraction, and risk of bias assessment were performed independently by multiple reviewers. Randomized trials were assessed using RoB 2 and non-randomized studies using ROBINS-I. Due to methodological heterogeneity, a narrative synthesis was performed. Ethical approval: Not applicable.

Results: Six clinical studies published between 2007 and 2015 were included (three randomized trials and three non-randomized clinical studies; 9–18 participants per study). All eligible studies evaluated ex vivo–expanded autologous gingival fibroblasts delivered through biomaterial carriers, commonly collagen-based scaffolds, combined with mucogingival surgical approaches, predominantly coronally advanced flap procedures. Clinical improvements were generally observed across intervention and comparator groups, including recession reduction, increased keratinized tissue dimensions, and improved attachment-related outcomes. However, comparative studies did not demonstrate consistent superiority over control procedures without cells or established graft-based approaches. Risk of bias ranged from “some concerns” in randomized trials to moderate-to-serious risk in non-randomized studies. Substantial heterogeneity across indications, comparators, outcomes, and follow-up periods (3–12 months) prevented quantitative synthesis through meta-analysis.

Conclusion: Autologous cultured gingival fibroblast–based therapies are clinically feasible and show favorable short-term outcomes. However, current evidence remains limited, heterogeneous, and at meaningful risk of bias, preventing conclusions regarding superiority over established periodontal plastic surgery. Well-designed randomized clinical trials with standardized outcomes and longer follow-up are needed.

Keywords: Gingival Fibroblasts; Gingival Recession; Tissue Engineering; Periodontal Plastic Surgery

Conflicts of Interest: The authors declare no conflicts of interest.