International Platform of Registered Systematic Review and Meta-analysis Protocols

Miao et al. INPLASY protocol 202560106. doi:10.37766/inplasy2025.6.0106 Downloaded from https://inplasy.com/inplasy-2025-6-0106/

INPLASY

Meta-analysis of the effects of compressive stress on osteoblasts and osteoclasts growth

INPLASY202560106

doi: 10.37766/inplasy2025.6.0106

Received: 26 June 2025

Published: 27 June 2025

Miao, TT; Ni, CL; Meng, QJ; Cheng, HX; Wei, Y.

Corresponding author:
Yuan Wei

wei0yuan@126.com

Author Affiliation:
Affiliated Stomatology Hospital of Anhui Medical College.

ADMINISTRATIVE INFORMATION

Support - High-throughput sequencing of subgingival microbiota in adolescent orthodontic patients and lncRNAs associated with osteogenic differentiation of osteoblasts in an inflammatory environment. Project number: 2023AH052590.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202560106

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 June 2025 and was last updated on 2**7** June 2025.

INTRODUCTION

Review question / Objective This study aimed to systematically assess the impact of compressive stress on the growth of osteoblasts and osteoclasts through a meta-analysis of existing literature. The focus was on understanding how compressive stress affects cell proliferation, differentiation, and overall bone metabolism.

Condition being studied Recent studies have increasingly indicated that mechanical stimulation, especially compressive stress, significantly influences the function and behavior of bone cells[5, 6]. Compressive stress, as a physical environmental factor, not only affects the proliferation, differentiation, and mineralization of bone cells but also regulates the bone remodeling process[7], thereby playing an important role in bone density, bone strength, and overall bone health.

METHODS

Search strategy This systematic review was conducted in accordance with the PRISMA 2020 guidelines [36]. The specific search strategies are as follows: PubMed: The search was performed using the keyword combination “osteoblast” AND “osteoclast” AND “mechanical stress” AND (“growth” OR “proliferation” OR “differentiation”), ensuring that only English-language articles were included, covering research on cell proliferation, differentiation, and gene expression. Web of Science: The same keywords “osteoblast” AND “osteoclast” AND “mechanical stress” AND ("cell proliferation" OR "cell differentiation") were used, with the "topic" field selected for precise searches. All articles were peer-reviewed academic papers. CNKI: The search used Chinese keywords “成骨细胞” AND “破骨细胞” AND “压应力” AND (“生长” OR “增殖” OR “分化”), to retrieve relevant articles from Chinese journals. ScienceDirect: The search used

keywords “osteoblast” AND “osteoclast” AND “mechanical stress” AND (“growth” OR “proliferation”), limited to the biomedical and materials science fields.

Participant or population N/A.

Intervention N/A.

Comparator N/A.

Study designs to be included Data were synthesized using RevMan 5.4 and R 4.1.4. Standardized Mean Difference (SMD) was used as the effect size. A random-effects model was primarily applied due to expected heterogeneity. Statistical heterogeneity was assessed using I^2 values, and subgroup analysis was performed when applicable (e.g., cell type, species).N/A.

Eligibility criteria To ensure high reliability, strict literature inclusion and exclusion criteria were applied:
Inclusion Criteria: 1. Original experimental studies assessing the effects of compressive stress on osteoblast and/or osteoclast growth. 2. Studies employing in vitro or in vivo models and evaluating cell proliferation, differentiation, or gene expression. 3. Studies with sufficient quantitative data (mean, SD, or extractable effect size). 4. Articles published in English or Chinese peer-reviewed journals.
Exclusion Criteria: 1. Studies not involving osteoblasts or osteoclasts. 2. Studies lacking quantitative data or adequate control groups. 3. Review articles, conference abstracts, or editorials. 4. Studies with insufficient methodological details or unclear compressive stress parameters.

Information sources To evaluate the impact of compressive stress on osteoblast and osteoclast growth, this study conducted an extensive literature search across multiple electronic databases, including PubMed, Web of Science (WoS), CNKI (China National Knowledge Infrastructure), and ScienceDirect. All literature searches were limited to publications from January 2000 to May 2024, and only English or Chinese-language articles were included.

Main outcome(s) A total of 1,267 articles were retrieved from PubMed, Web of Science, CNKI, and ScienceDirect. After deduplication in EndNote, 910 articles remained. Initial screening removed studies that did not meet the research topic or quality standards, leaving 710 articles. After secondary screening, 16 studies [13-28] were included in the meta-analysis (Figure 1). Reasons for exclusion at each stage have been detailed and visualized in the PRISMA flow diagram (Figure 1), including duplication, irrelevant topic, insufficient outcome data, and unclear methodology. The overall bias risk for the included studies was low, with all trials being evaluated as having low selection bias risk (Figure 2).

Quality assessment / Risk of bias analysis Risk of bias was assessed using a tailored tool for experimental studies, adapted from the Cochrane guidelines: 1. Randomization: Whether allocation was random. 2. Blinding: Whether outcome assessors were blinded. 3. Completeness: Whether data were reported fully. 4. Selective reporting: Whether any outcomes were selectively omitted. Each study was rated as low, unclear, or high risk across domains, and results were summarized in a bias risk graph (Figure 2).

Strategy of data synthesis Data were synthesized using RevMan 5.4 and R 4.1.4. Standardized Mean Difference (SMD) was used as the effect size. A random-effects model was primarily applied due to expected heterogeneity. Statistical heterogeneity was assessed using I^2 values, and subgroup analysis was performed when applicable (e.g., cell type, species).

Subgroup analysis The effect size for in-vitro studies was 1.05 (95 % CI: [0.78, 1.33]), demonstrating a robust positive impact of compressive stress on cell proliferation (Figure 4). The I^2 for this subgroup remained at 0 %, with a p-value of 0.99, confirming negligible heterogeneity and high consistency among studies. By contrast, the pooled effect for combined/animal studies was 0.66 (95 % CI: [0.18, 1.14]), indicating a modest yet favourable influence. Although heterogeneity was likewise minimal (I^2 = 0 %), the larger p-value (p = 0.16), indicating that the effect in animal experiments was less significant than in in vitro studies (Figure 4). Both meta-analyses showed a positive effect of compressive stress, but the in vitro studies yielded more significant results.

Sensitivity analysis 2.3.7Across the included studies, compressive stress was applied using a wide range of protocols. Although formal subgroup analyses based on loading magnitude, frequency, and duration were not feasible due to inconsistent reporting, key descriptive patterns were identified. Most in vitro studies applied compressive forces between 0.1 and 3 MPa, with durations ranging from 15 minutes to 72 hours and frequencies extending from static to dynamic loading up to 1 Hz.

Miao et al. INPLASY protocol 202560106. doi:10.37766/inplasy2025.6.0106 Downloaded from https://inplasy.com/inplasy-2025-6-0106/

In terms of cell origin, ten studies utilized primary cells (e.g., rat calvarial osteoblasts, murine bone marrow-derived osteoclasts), while four studies employed immortalized cell lines such as MC3T3-E1 and RAW264.7. Regarding species, twelve studies were rodent-based, and only one used human-derived cells. Due to the limited number of studies per subgroup, statistical comparisons were not conducted. However, qualitatively, stronger biological responses appeared more frequent in studies using primary cells and rodent models. These trends, while suggestive, require validation through further investigations with more standardized reporting of loading protocols and cell sources (Figure 5).

Country(ies) involved China.

Keywords Bone remodeling, Compressive stress, Osteoblasts, Osteoclasts, Meta-analysis.

Contributions of each author

Author 1 - Tingting Miao.
Author 2 - Chengli Ni.
Author 3 - Qianjiao Meng.
Author 4 - Huixin Cheng.
Author 5 - Yuan Wei.

Miao et al. INPLASY protocol 202560106. doi:10.37766/inplasy2025.6.0106 Downloaded from https://inplasy.com/inplasy-2025-6-0106/