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What is the best protocol to prepare platelet-rich fibrin in oral surgical procedures? A systematic review protocol with planned network meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202560059

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 June 2025 and was last updated on 9 February 2026.

INTRODUCTION

Review question / Objective The objective of this systematic review is to evaluate the effectiveness of various platelet-rich fibrin protocols used in oral surgical procedures. To this end, the study will address the following focused questions: I) What is the best protocol for preparing platelet-rich fibrin (PRF) for oral surgical procedures? II) What is the current level of scientific evidence related to the different PRF preparation protocols, considering only their application in oral surgical procedures?

Rationale The concept of biological signature suggests that the biological properties of platelet-rich fibrin may be totally modified as a result of the preparation method.1 In vitro studies showed that the number of platelet cytokines, leukocyte cytokines, and the quality of fibrin architecture of platelet concentrate significantly diverged among the different protocols.2-3 Therefore, the combination of different protocols for analytical purposes could lead to misinterpretations once clinical outcomes vary significantly between two platelet concentrates. To our knowledge, this systematic review will be the first study to analyze each protocol separately and combine the evidence from RCTs using a frequentist weighted least squares model to determine which of the available protocols produces better clinical outcomes for oral surgical procedures.

Condition being studied Healing and postoperative complications in oral surgical procedures.

METHODS

Search strategy The electronic search strategy was last updated on February 5, 2026, to ensure completeness and alignment with the finalized eligibility criteria. The full and detailed search strategies for all databases are available as Supplementary Material accompanying this protocol, allowing full transparency, reproducibility, and methodological verification.

Participant or population Health patients requiring different oral surgical procedures. No other restrictions on sex, gender, or ethnicity were placed on the population of the study.

Intervention Platelet-rich fibrin produced by different medical devices and protocols without biochemical blood handling. The platelet concentrate must be prepared without any anticoagulant, bovine thrombin, or any other gelling agent.

Comparator Different Platelet-rich fibrin protocols will be compared against each other and with placebo or no treatment group.

Study designs to be included Studies in humans, including only randomized clinical trials.

Eligibility criteria Randomized clinical trials reporting direct comparisons between natural healing with one or more platelet-rich fibrin protocols, such as leukocyte and platelet-rich fibrin (L-PRF), or advanced platelet-rich fibrin (A-PRF) in oral surgical procedures will be selected. Studies will be selected according to the PICOS criteria (Participant, intervention, comparator, outcomes, and study design) outlined in the referred sections. Additionally, we will exclude studies without a detailed description of the method to prepare platelet-rich fibrin. We will include only studies that reported the following surgical procedures: third molar surgery; orthognathic surgery; surgical treatment of bisphosphonate-associated osteonecrosis of the jaw; sinus lift surgery; treatment of oroantral communications; alveolar preservation after tooth extractions; dental implants; alveolar bone grafting; temporomandibular joint surgery; and alveolar and palate cleft surgery.

Information sources We will search the following electronic bibliographic databases: EMBASE, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science. The reference lists of the articles identified will be cross-checked. Furthermore, studies from the 'grey literature' will be screened through the following trial registry platforms: Current Controlled Trials (http:// www.controlled-trials.com), ClinicalTrials.gov (http://www.clinicaltrials. gov), and EU Clinical Trials Register (https:// www.clinicaltrialsregister.eu/ctr-search/search). A manual search will be done in the relevant journals of dentistry. If necessary, the searches will be re-run just before the final analyses, and further studies will be retrieved for inclusion.

Main outcome(s) We will include any clinical outcomes related to bone and soft healing. Similarly, if available in included studies, surrogate outcomes used as substitutes for clinically meaningful outcomes will be summarized.

Additional outcome(s) We will include any patient-reported outcomes, such as pain or quality of life. Additionally, all adverse events reported will be summarized.

Data management The studies will be imported into Endnote 2025 software (Thompson Reuters, Philadelphia, PA, USA), where duplicates will be automatically removed. All analyses will be performed using the software R version 4.5 or the latest available version for Mac OS X computer system. The package "netmeta" will be used to run network meta-analysis. This package is available from the Comprehensive R Archive Network (CRAN).

Quality assessment / Risk of bias analysis Risk of Bias 2 (ROB2) tool according to the methods described by the Cochrane Collaboration.

Strategy of data synthesis A frequentist network meta-analysis will be performed using direct and indirect evidence from eligible comparisons. We will provide a quantitative and narrative synthesis to summarize the level of evidence of different methods to prepare platelet-rich fibrin clots. We will provide summaries of intervention effects for each study by calculating standardized mean differences or mean differences in continuous outcomes, and odds ratios or risk ratios in dichotomous outcomes. We will pool the results using a fixed or random-effects meta-analysis based on the heterogeneity. Heterogeneity will be assessed using both the tau^2 test and the I^2 statistic. We will consider an I^2 value greater than 50% indicative of substantial heterogeneity. The heterogeneity within designs and between designs will be analyzed. Additionally, the assumption of transitivity and similarity based on clinical and methodological characteristics will be assessed. The inconsistency will be explored using the Net Heat Plot. We will also assess evidence of publication bias.

Subgroup analysis None planned.

Sensitivity analysis None planned.

Language restriction Studies published in any language will be selected.

Country(ies) involved Brazil, United States.

Keywords platelet-rich fibrin; PRF; oral surgery; maxillofacial surgery; centrifugal forces; centrifugation device; systematic review.

Dissemination plans The study's findings will be disseminated through peer-reviewed academic journal.

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