BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
Volume 21, Issue 10

DOI: 10.58240/1829006X-2025.21.10-358

REVIEW ARTICLE

EVALUATION OF PAIN IN PALATAL WOUND IN PATIENTS TREATED WITH REINFORCED GELATIN SPONGE: A SYSTEMATIC REVIEW

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Received: *Sep 24. 2025;* ***Accepted:*** *Oct 30, 2025;* ***Published:*** *Nov 16 ,2025*

ABSTRACT

Background: Autogenous soft tissue grafts harvested from the palate are frequently used in periodontal plastic surgery but are associated with postoperative pain and donor-site morbidity due to healing by secondary intention. Various materials have been tested to minimize discomfort, with reinforced gelatin sponge (GS) showing promising results owing to its bioactive, absorbable, and hemostatic properties.

Aim: This systematic review aimed to evaluate the effectiveness of reinforced GS compared with plain GS in reducing postoperative pain and enhancing wound healing following palatal graft harvesting.

Methods: A comprehensive search was performed in PubMed, Scopus, Web of Science, EMBASE, Semantic Scholar, ScienceDirect, and Google Scholar for randomized controlled trials (RCTs) published up to January 2025. Studies comparing reinforced GS with plain GS for palatal wound management were included. Risk of bias was assessed using the Cochrane Risk of Bias 2 (ROB 2) tool, and certainty of evidence was graded using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.

Results: Three RCTs (n = 165) were included. All studies reported improved pain control with reinforced GS, particularly when combined with cyanoacrylate, hyaluronic acid, or melatonin. The certainty of evidence was moderate for pain and low for wound healing.

Conclusion: Reinforced GS significantly enhances postoperative comfort and healing compared with plain GS, warranting further large-scale RCTs.

***Keywords*:** gelatin sponge, cyanoacrylate, hyaluronic acid, melatonin, palatal wound, pain control

INTRODUCTION

Autogenous soft tissue grafts, harvested either with or without the epithelial layer, are extensively employed to reconstruct soft tissue deficiencies surrounding teeth, dental implants, and edentulous ridges[1]. These grafts are indicated for a variety of clinical purposes, including coverage of gingival recession defects, augmentation of the width and thickness of keratinized gingiva, management of peri-implant mucosal recession, and correction of soft tissue deficiencies in partially edentulous areas [2,3]. Among various donor sites, the palate is most frequently utilized because of its predictable anatomy and abundance of keratinized tissue. However, harvesting grafts from the palate leaves an open wound that heals by secondary intention, resulting in postoperative pain, bleeding, and discomfort, which contribute significantly to donor-site morbidity[4]. Consequently, management of the palatal wound following graft harvesting becomes essential to improve patient comfort and accelerate wound healing [5].

Several materials and techniques have been developed to reduce postoperative morbidity at palatal donor sites, including periodontal dressings, acrylic stents, haemostatic agents, low-level laser therapy, photobiomodulation, cyanoacrylate (CY) tissue adhesives, and hyaluronic acid (HA) [6]. These interventions aim either to shield the wound from external trauma or to promote faster healing. Conventional dressings primarily act as passive mechanical barriers, whereas newer bioactive dressings actively modulate the wound healing process by influencing cellular and molecular pathways involved in repair [7]. Despite the availability of multiple options, there is limited consensus on which approach provides optimal

pain control and enhances wound healing outcomes.

Gelatin sponge (GS), a thermally denatured derivative of collagen obtained from animal sources, exhibits excellent biocompatibility, absorbability, and haemostatic properties [8]. Its porous structure facilitates platelet aggregation and clot formation, making it an ideal wound dressing material. Additionally, it has been shown to promote osteoblastic proliferation and human mesenchymal stem cell differentiation, suggesting its potential role in enhancing tissue regeneration[9,10]. To further improve its clinical performance, various bioactive agents have been incorporated into GS. Reinforcement with cyanoacrylate enhances wound sealing and provides a bacteriostatic, hemostatic, and adhesive barrier that reduces postoperative bleeding and pain [11]. Similarly, the addition of hyaluronic acid accelerates re-epithelialization, modulates inflammation, and promotes angiogenesis, thereby enhancing wound healing and reducing discomfort [12]. Melatonin-reinforced gelatin sponges offer an additional advantage by exerting antioxidant and anti-inflammatory effects that stimulate collagen deposition and angiogenesis [13,14].

Given the increasing application of reinforced GS for palatal wound management, it is essential to synthesize existing evidence to determine their efficacy in postoperative pain control. This systematic review, therefore, aims to evaluate and compare the effectiveness of plain versus reinforced GS in reducing pain and promoting healing in palatal wounds following autogenous soft tissue graft harvesting.

METHODOLOGY

Study Design and Protocol Registration

This systematic review was designed and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines[15]. The focused research question was structured using the PICO framework: Population – patients with palatal wounds; Intervention as reinforced gelatin sponge; Comparator as plain gelatin sponge; and Outcome as postoperative pain reduction assessed using the Visual Analogue Scale (VAS). The review protocol was registered in the PROSPERO database (Reference ID: CRD42025646203)

Eligibility Criteria

Studies were considered eligible for inclusion if they were randomized controlled trials that evaluated the efficacy of reinforced GS compared with plain GS for pain management in palatal donor sites after gingival graft harvesting. Only studies published in English were included. Case reports, case series, letters to the editor, review articles, and studies without pain assessment as an outcome measure were excluded. Studies that used other adjunctive interventions, such as laser therapy or platelet concentrates without a GS control, were also excluded.

Search Strategy

An extensive electronic literature search was conducted in three major databases, PubMed, Scopus, Web of Science, EMBASE, Semantic Scholar, Sciencedirect, and Google Scholar to identify relevant articles published up to January 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to gelatin sponge, palatal wound, and wound healing. Boolean operators ("AND" and "OR") were applied to optimize the search. The PubMed search string was formulated as: ("gelatin" OR "gelatine") AND ("sponge" OR "sponges") AND ("palatal" OR "palate") AND ("wound healing"). In addition to electronic searches, a manual screening of reference lists of included studies and relevant review articles was performed to identify any additional eligible publications not captured electronically. All retrieved studies were imported into reference management software, and duplicates were removed before screening.

Study Selection

Two reviewers (RK and PB) independently screened the titles and abstracts of all identified studies. Full-text versions of potentially relevant studies were obtained for detailed assessment. Discrepancies between the reviewers regarding study inclusion were resolved by discussion and consensus with a third reviewer (KA). Studies fulfilling the inclusion criteria were included for qualitative synthesis. The selection process was documented through a PRISMA flow diagram illustrating the number of studies identified, screened, and excluded at each stage.

Data Extraction

Data were extracted independently by two reviewers using a standardized template developed in Microsoft Word (Microsoft Corp., Redmond, WA, USA). Extracted information included the author's name, year of publication, country, study design, sample size, demographic characteristics of participants, type of reinforcement agent used, intervention protocol, comparator, outcome measures (VAS pain scores), follow-up duration, and principal findings. The third reviewer verified all entries for accuracy and completeness to minimize bias and transcription errors.

Assessment of Risk of Bias

The methodological quality of the included studies was evaluated using the Cochrane Risk of Bias 2 (ROB 2) tool for randomized controlled trials[16]. Each study was assessed across multiple domains, including randomization, deviations from intended interventions, missing outcome data, measurement of outcomes, and selective reporting. Each criterion was graded as low risk, some concerns, or high risk of bias by two reviewers (KA and PR). Inter-reviewer reliability was quantified using Cohen's kappa statistic, and disagreements were resolved through consensus.

Assessment of Certainty of Evidence

The overall certainty of evidence for the primary outcome was appraised using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework [17]. The evidence was initially rated high,

followed by potential downgrading based on five domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Two reviewers (PR and SSS) performed the initial GRADE evaluation, which was subsequently reviewed and finalized through consensus among all authors.

Data Synthesis

Given the heterogeneity in study designs, reinforcement materials, and outcome reporting, a quantitative meta-analysis was not feasible. Therefore, a qualitative synthesis was undertaken to summarize the direction and magnitude of the effects observed across the included studies. The results were organized descriptively to highlight differences in pain reduction and wound healing outcomes between reinforced and plain GS groups.

RESULTS

Characteristics of Study Settings

Three RCTs met the inclusion criteria, which were conducted in Italy, Turkey, and Egypt, providing a broad geographical representation [18-20]. The characteristics of the included studies are summarized in Table 1. In two studies, a single autogenous free gingival graft was harvested from the posterior palate, whereas one study harvested two adjacent grafts for recession coverage [18-20]. Following graft harvesting, two studies used both plain GS and reinforced variants, having HA and/or CY, to cover the palatal wound, stabilized with 5-0 non-absorbable sling sutures [18,19]. The third study used melatonin-loaded GS secured with a flowable composite stent [20]. The use of a stent in both control and test groups may have influenced the primary outcome by providing equal physical protection to the wound, potentially affecting pain scores on the VAS.

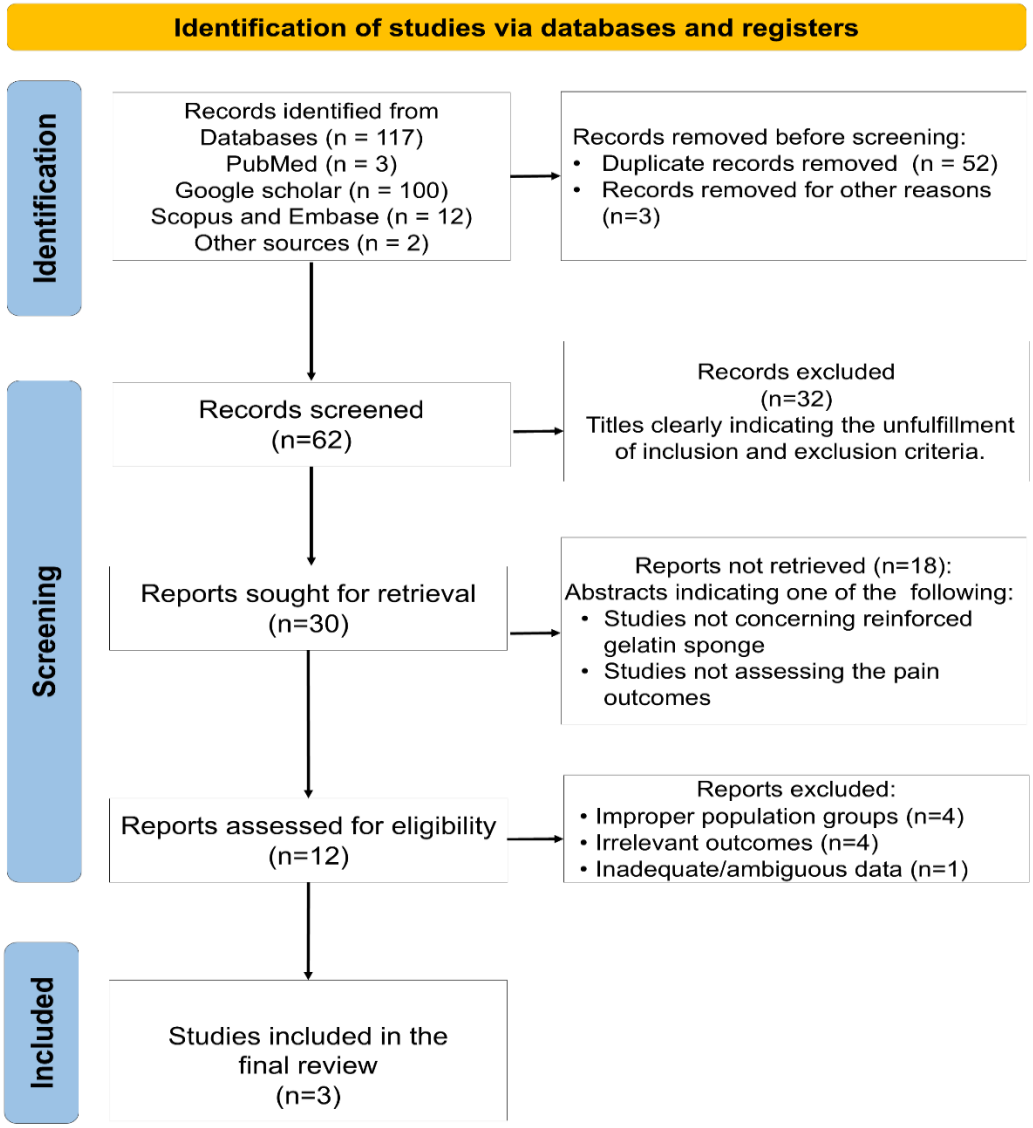

Figure 1. PRISMA Flow Diagram indicating the selection process of the articles in the present systematic review

Table 1. Characteristic data excluded from the included studies

Sr. No.	Author (Year)	Country	Study Design / Sample Size	Intervention (Test Group)	Control Group	Primary Outcome(s)	Secondary Outcome(s)	Conclusion	Inference
1	Hanife Merva Parlak et al (2023) [18]	Turkey	RCT (n = 89)	GS + CY (n = 22); GS + HA (n = 23); GS + HA + CY (n = 21)	GS (n = 23)	Pain (VAS)	Analgesic intake, secondary bleeding, epithelialization, colour match	GS reinforced with HA + CY enhanced wound healing and reduced morbidity by lowering pain and analgesic use.	HA + CY + GS group showed statistically significant VAS reduction compared with other groups on days 7 and 14 ($p < 0.001$).
2	Lorenzo Tavelli et al (2018) [19]	Italy	RCT (n = 50)	CY (n = 10); Periodontal dressing (n = 10); GS (n = 10); GS + CY (DLP) (n = 10)	Sutures (n = 10)	Pain (VAS)	Analgesic consumption, palatal healing score, willingness to repeat treatment	GS reinforced with CY reduced postoperative pain and discomfort versus conventional methods.	Postoperative palatal pain was significantly lower in the GS + CY (DLP) group compared with control ($P < 0.01$).
3	Salma Nabil Hussein et al (2024) [20]	Egypt	RCT (n = 26)	Melatonin-loaded GS (n = 13)	Placebo-loaded GS (n = 13)	Pain (VAS)	Wound healing (clinical + histologic)	Melatonin-reinforced GS showed anti-inflammatory potential in reducing pain and enhancing healing.	Test group demonstrated greater, though non-significant, pain reduction during first 7 days.

Abbreviations: GS = Gelatin Sponge; CY = Cyanoacrylate; HA = Hyaluronic Acid; VAS = Visual Analogue Scale; DLP = Double-Layer Protection; RCT = Randomized controlled trial

Characteristics of Interventions

In all studies, autogenous free gingival grafts were harvested from the posterior palate to cover gingival recession defects. The donor sites were managed with plain GS or its reinforced forms containing CY, HA, HA + CY, or melatonin. Two studies utilized GS + CY for palatal wound coverage, while one study compared multiple reinforced variants, including GS + HA, GS + HA + CY, and melatonin-reinforced GS. This heterogeneity reflects the clinical versatility of GS as a wound dressing and the growing interest in bioactive reinforcement agents to enhance its healing potential.

Characteristics of Outcome Measures

Pain was the primary outcome measure across all three studies, assessed using the VAS. In two studies, pain scores were recorded daily from postoperative day 1 to 7 [18,20,] while one study extended evaluation to days 10 and 14 [19]. Wound healing was evaluated as a secondary parameter in two studies [18,20]. In one, epithelialization was measured using 3 % hydrogen peroxide on postoperative days 7, 14, 21, and 28 [18], whereas another used histological examination on days 7 and 14 to assess tissue organization and healing progression [20].

Characteristics of Outcomes

All included studies reported superior pain control with reinforced GS compared with plain GS. In one RCT, GS + CY significantly reduced donor-site morbidity, pain levels, and analgesic consumption. Another study demonstrated that GS

+ HA + CY yielded the greatest reduction in VAS scores ($p < 0.001$). The third study observed improved pain control with melatonin-loaded GS. Although the pain reduction was not statistically significant, the trend favored melatonin reinforcement.

Risk of bias

Each study demonstrated a low risk of bias across all evaluated domains. The randomization procedures were clearly described, ensuring appropriate allocation concealment and minimizing selection bias. None of the studies reported deviations from intended interventions, and all maintained adherence to prespecified protocols. Outcome data were complete, with no evidence of attrition or exclusions that could influence results. Pain assessment using the VAS was standardized and objectively applied across all participants, indicating low risk in outcome measurement. Additionally, the studies reported all prespecified outcomes, with no signs of selective reporting. Overall, the methodological quality of the included RCTs was robust, indicating that the synthesized evidence can be considered reliable and internally valid for drawing conclusions about the efficacy of reinforced gelatin sponge in palatal wound pain control.

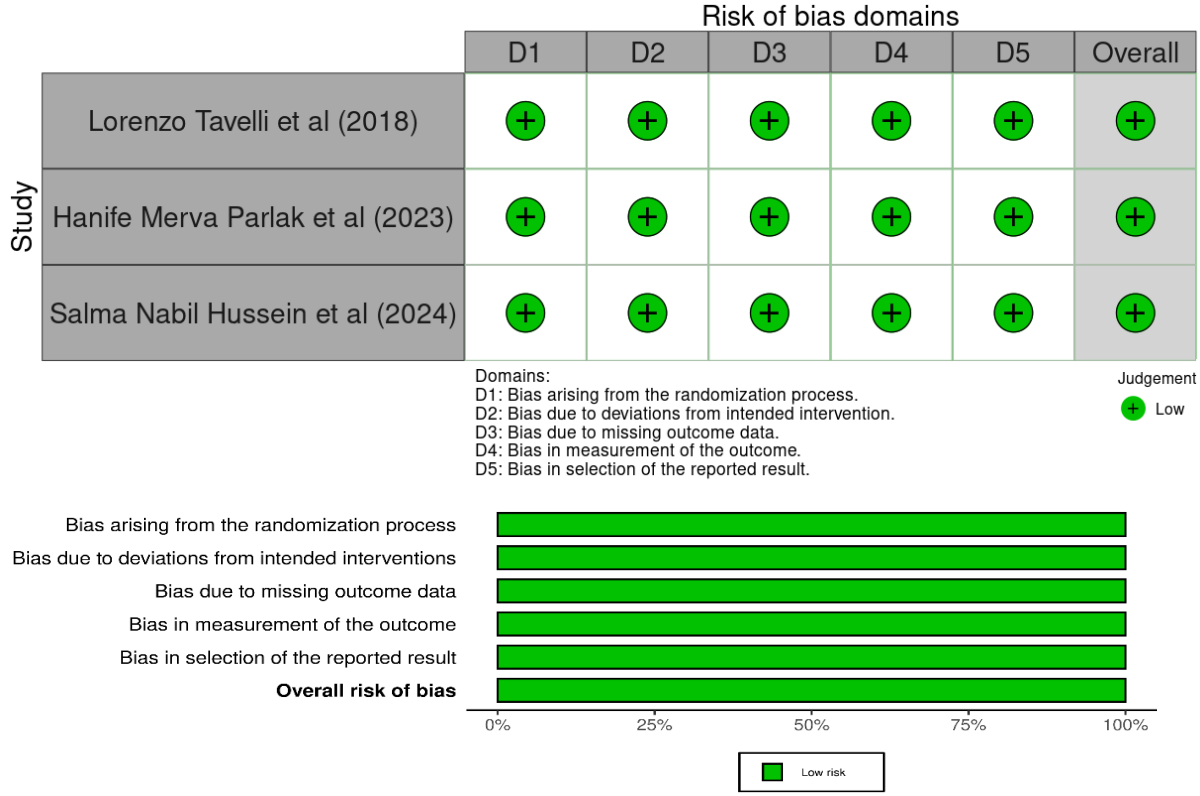

Figure 2. Risk of Bias Assessment of Included Randomized Controlled Trials

Certainty of Evidence

The overall certainty of evidence was appraised using the GRADE framework. For the primary outcome, postoperative pain reduction measured using the VAS, the certainty of evidence was rated as moderate. All three randomized controlled trials demonstrated low risk of bias, consistent direction of results favoring reinforced gelatin sponge, and direct clinical relevance. However, the evidence was downgraded by one level due to imprecision resulting from relatively small sample sizes (total n = 165) and wide or unreported confidence intervals in two studies.

For the secondary outcome of wound healing, the certainty of evidence was judged as low. Although findings from two studies indicated improved epithelialization and tissue recovery with reinforced gelatin sponge, heterogeneity in assessment methods (clinical scoring vs histological analysis) led to inconsistency. Additionally, small participant numbers and limited reporting of statistical measures contributed to imprecision.

No evidence of publication bias or indirectness was identified, and all studies directly addressed the clinical question. In summary, while reinforced gelatin sponge demonstrates favorable outcomes in postoperative pain control and potential for enhanced wound healing, the certainty of evidence remains moderate for pain and low for wound healing, underscoring the need for further high-quality, large-scale RCTs with standardized outcome reporting.

Table 2. Summary of Evidence Certainty Assessment (GRADE Framework)

Outcome	No. of Studies (Participants)	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Comments
Pain reduction (VAS)	3 (n = 165)	RCTs	Not serious	Not serious	Not serious	Serious	Unlikely	**Moderate**	Downgraded by one level for small sample sizes and wide confidence intervals.
Wound healing	2 (n = 115)	RCTs	Not serious	Serious	Not serious	Serious	Unlikely	**Low**	Limited data and varied evaluation methods (clinical vs histological).

DISCUSSION

The findings of this systematic review indicate that the use of reinforced GS in palatal wound management following autogenous graft harvesting offers a significant reduction in postoperative pain and improved wound healing when compared with plain GS. All included randomized controlled trials consistently reported favorable outcomes with GS reinforced using CY, HA, or melatonin, demonstrating its potential as an effective bioactive dressing material. These outcomes can be attributed to the unique biological and physicochemical properties conferred by the reinforcement agents that enhance the inherent hemostatic and biocompatible characteristics of GS.

CY, a tissue adhesive with strong polymerization and hemostatic capabilities, plays a dual role in wound protection and microbial barrier formation. Its sealing ability prevents bacterial penetration and fluid leakage, thereby minimizing inflammatory responses and pain at the donor site [21]. Tavelli et al. (2018) reported significantly lower postoperative VAS scores and reduced analgesic consumption in the GS + CY group compared to the control, highlighting the clinical benefits of incorporating CY into GS dressings [19]. The bacteriostatic nature of cyanoacrylate, combined with its capacity to form an impermeable protective film, provides a stable environment conducive to rapid epithelialization and tissue remodeling [22].

The synergistic effect of HA and CY, as demonstrated by Parlak et al. (2023), further enhanced wound healing outcomes[18]. HA is a naturally occurring glycosaminoglycan that promotes angiogenesis, fibroblast migration, and collagen synthesis, while simultaneously reducing inflammatory cell infiltration [23,24]. The combination of the regenerative capacity of HA with the sealing properties of CY resulted in superior pain control and accelerated tissue healing, indicating that dual reinforcement may provide an optimal biological and mechanical interface for wound repair. Similarly, melatonin-loaded GS, as evaluated by Hussein et al. (2024), exhibited anti-inflammatory and antioxidant properties that modulate cytokine release and oxidative stress, facilitating a faster transition from the inflammatory to the proliferative phase of healing [20,25]. Although statistical significance was not reached, the overall trend supported melatonin's beneficial role in reducing postoperative discomfort. The results across all studies show clinical consistency; however, the small sample sizes, short follow-up durations, and variation in reinforcement types introduce some degree of heterogeneity. Despite this, all studies demonstrated low risk of bias and moderate certainty of evidence for pain control, strengthening the reliability of these findings. Collectively, these outcomes suggest that reinforced GS can significantly improve patient comfort, reduce analgesic dependency, and accelerate palatal wound healing. Further large-scale, multicentric randomized trials with standardized reinforcement formulations and uniform outcome measures are warranted to establish definitive clinical guidelines for its routine use in periodontal plastic surgery.

CONCLUSION

Reinforced GS demonstrated superior outcomes in postoperative pain control and wound healing compared to plain GS in palatal donor sites. The addition of CY, HA, or melatonin enhanced the hemostatic, anti-inflammatory, and regenerative properties of GS, resulting in reduced morbidity and greater patient comfort. Although all RCTs showed consistent results with low risk of bias, the certainty of evidence was rated moderate due to limited sample sizes. Further large-scale

trials with standardized protocols are recommended to validate these findings and guide clinical application.

DECLARATIONS

Competing interests
No conflicts of interest regarding this study.
Funding Not funding

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