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Concentrated Growth Factors for Periodontal Regeneration in Severe Periodontitis: Clinical Efficacy and Inflammatory Modulation

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ABSTRACT

To evaluate the efficacy of concentrated growth factors (CGF) combined with guided tissue regeneration (GTR) in patients with severe periodontitis.

This retrospective study included 220 patients with severe periodontitis undergoing periodontal regenerative surgery. After propensity score matching, 85 patients treated with CGF plus GTR and 85 treated with GTR alone were analyzed. Overall clinical response, postoperative pain, gingival thickness, alveolar bone parameters, and gingival crevicular fluid levels of IL-17, IL-23, and IL-10 were assessed.

The CGF group showed a significantly higher overall response rate than the GTR-alone group (94.12% vs 75.29%). Pain scores were significantly lower in the CGF group on postoperative day 1, with no significant differences on days 3 and 7. At 3 months, improvements in gingival thickness, alveolar bone height, width, and gray values were greater in the CGF group, although differences were not significant at 6 months. CGF treatment reduced IL-17 and IL-23 levels and increased IL-10 levels; these changes correlated with improvements in gingival and bone regeneration.

CGF combined with GTR may enhance early periodontal tissue regeneration, reduce immediate postoperative pain, and modulate local inflammation in severe periodontitis. Further randomized controlled trials are needed to establish long-term benefits.

Keywords: Cytokines; Gingival crevicular fluid; Guided tissue regeneration; Periodontitis; Platelet-rich fibrin; Wound healing

INTRODUCTION

Severe periodontitis is a biofilm-associated inflammatory disease in which loss of periodontal attachment and alveolar bone can eventually compromise tooth retention.[1,2] When deep intrabony defects remain after non-surgical treatment, regenerative surgery may be considered. Guided tissue regeneration (GTR) uses a barrier membrane to exclude rapidly proliferating epithelial and connective-tissue cells from the defect and to preserve space for periodontal regeneration.[3,4] The clinical response is variable, however, and depends on defect configuration, wound stability, plaque control, smoking, and the inflammatory state of the site.[5,6]

Concentrated growth factors (CGF) are an autologous platelet-rich fibrin preparation produced by programmed centrifugation of whole blood. The

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resulting fibrin matrix contains platelets, leukocytes, and a range of growth factors, and can be shaped to fill or cover a surgical defect.[7,8] Experimental work has shown effects on periodontal ligament cells and gingival fibroblasts,[9,10] while early clinical studies suggest that CGF may improve healing when used with regenerative procedures.[11,12] Most studies have been small, and it remains uncertain whether the apparent benefit is sustained or mainly reflects faster early healing.

Periodontal repair also occurs within a changing local immune environment. The IL-23/IL-17 pathway is implicated in periodontal inflammation and bone resorption, whereas IL-10 has anti-inflammatory and bone-protective actions.[13] We therefore measured these cytokines in gingival crevicular fluid (GCF) as markers of local inflammatory balance. They were not intended as direct measures of factors released by CGF. This study compared GTR with and without adjunctive CGF in a retrospective cohort, with particular attention to the timing of gingival and bone changes and their association with GCF cytokine changes.

MATERIALS AND METHODS

Study Population and Design

This single-center retrospective cohort study used records from 220 consecutive patients with severe periodontitis who underwent periodontal regenerative surgery between January 2022 and December 2024 at Dongfang Hospital, Beijing University of Chinese Medicine, Beijing, China. Patients were categorized according to the procedure documented in the clinical record: GTR with adjunctive CGF (n=97) or GTR alone (n=123). Treatment decisions had been made during routine care; no intervention was assigned for this study. One treated tooth was analyzed for each patient. Written informed consent for treatment and the research use of anonymized clinical data was available for all participants.

Inclusion criteria comprised: (1) diagnosis of severe periodontitis according to established criteria;14 (2) radiographic evidence (CBCT) of vertical bone defect depth≥4 mm; (3) tooth mobility grade≤II; (4) age between 18 and 35 years; and (5) completion of the 9-month follow-up. Exclusion criteria were: (1) aggressive periodontitis; (2) systemic diseases (eg, diabetes, autoimmune disorders); (3) pregnancy or lactation; (4) antibiotic or immunosuppressant use within 3 months prior to enrollment; and (5) previous periodontal regenerative therapy.

Treatment Protocols

All patients first underwent supragingival and subgingival instrumentation and root planing. Surgery was scheduled after the plaque index had fallen below 20% and bleeding on probing was present at fewer than 15% of sites. A modified Widman flap was raised, the defect was thoroughly debrided, and the root surface was planed. A resorbable bilayer collagen membrane (Bio-Gide; Geistlich Pharma AG, Wolhusen, Switzerland) was trimmed to cover the defect. In the CGF group, 20 mL of venous blood was collected immediately before surgery into additive-free sterile tubes and processed in a Medifuge centrifuge (Silfradent Srl, Santa Sofia, Italy) using the manufacturer's programmed cycle. The fibrin-rich layer was isolated; part was cut into 1–2 mm^3 fragments and placed in the intrabony defect, and the remainder was compressed into a membrane and positioned over the grafted area. Flaps were closed without tension. Both groups received amoxicillin 500 mg three times daily for 7 days and 0.12% chlorhexidine rinse twice daily for 4 weeks, together with standardized oral-hygiene instructions. Follow-up visits were scheduled at 1, 3, 6, and 9 months.

Data Collection and Outcome Measures

The main clinical outcome was a composite response assessed 9 months after surgery and adapted from published periodontal regenerative outcome frameworks[15]. An excellent response required a probing depth of 3 mm or less, no bleeding on probing, and at least 50% radiographic defect fill. A good response required a probing-depth reduction of at least 2 mm, improvement in bleeding on probing, and 30%–49% radiographic defect fill. All other outcomes were classified as poor responses. The overall response rate was calculated as the proportion of excellent and good responses. Radiographic defect fill (%) was calculated on standardized CBCT images as [(baseline defect depth − 9-month residual defect depth)/baseline defect depth]×100%. CBCT gray value was analyzed separately and was not used in this calculation. Gingival thickness, alveolar bone height and width, and CBCT gray value were measured on standardized images at baseline and at 3 and 6 months. Gingival thickness was measured on the buccal aspect 4 mm apical to the cementoenamel junction. CBCT gray values were

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reported as scanner-dependent arbitrary units (AU), not Hounsfield units. Change scores were calculated as follow-up minus baseline. Postoperative pain was recorded on days 1, 3, and 7 using a 0–10 visual analog scale. GCF was collected at baseline and at 3 and 6 months. After isolation and removal of supragingival plaque, an absorbent paper strip was placed at the mesiobuccal site of the target tooth for 30 seconds; strips contaminated with blood were discarded. Samples were stored at −80°C until analysis. IL-10, IL-17, and IL-23 were measured with enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN, USA). Cytokine concentrations were expressed in pg/mL. For cytokines, Δ denotes the follow-up concentration minus the baseline concentration.

Statistical Analysis

Data were analyzed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA) and R version 4.2.0. Continuous variables were expressed as mean±standard deviation and compared by the independent-samples t test. Categorical variables were reported as number and percentage; the χ^2 test or Fisher exact test was selected according to the data distribution. Pearson correlation analysis was performed separately in each treatment group to examine the relationships between 3-month cytokine changes and periodontal regeneration measures. All tests were 2-sided, and $p<0.05$ was considered significant.

Because treatment had not been randomly assigned, propensity score matching was used. Propensity scores were estimated by logistic regression using age, sex, smoking history, baseline alveolar bone loss, and baseline gingival thickness. Patients were matched at a 1:1 ratio by nearest-neighbor matching with a caliper of 0.02 using the MatchIt package in R.

RESULTS

Baseline Characteristics After Propensity Score Matching

Prior to PSM, significant differences ($p<0.05$) were observed between the 2 groups in age, tooth location, alveolar bone height and width, and baseline IL-17 levels. After PSM, 85 patients were successfully matched in each group (CGF group and control group). Comparison of baseline characteristics between the matched groups revealed no significant differences ($p>0.05$) for any variable, confirming the effective elimination of confounding bias through matching (Table 1).

Comparison of Clinical Efficacy Between Groups

The overall response rate was significantly higher in the CGF group compared to the control group (94.12% vs 75.29%; $\chi^2=11.826$; $p<0.001$) (Table 2).

Comparison of Postoperative VAS Scores between Groups

The CGF group reported significantly lower VAS scores on postoperative day 1 compared to the control group ($p<0.001$). No statistically significant differences in VAS scores were observed between the groups at postoperative days 3 and 7 ($p>0.05$) (Table 3).

Comparison of Changes in Periodontal Parameters from Baseline

At the 3-month postoperative assessment, the CGF group demonstrated significantly greater increases in gingival thickness, alveolar bone height, alveolar bone width, and alveolar bone gray value compared to the control group (all $p<0.001$). However, by the 6-month assessment, the differences in the increments of these parameters between the 2 groups were no longer statistically significant ($p>0.05$) (Table 4).

Comparison of Changes in Gingival Crevicular Fluid Immune Mediator Levels from Baseline

At 3 months post-surgery, the changes (Δ) in GCF levels of IL-17 (ΔIL-17), IL-23 (ΔIL-23), and IL-10 (ΔIL-10) were significantly greater in the CGF group compared to the control group (all $p<0.001$). Specifically, the CGF group exhibited a greater reduction in pro-inflammatory mediators (ΔIL-17, ΔIL-23) and a greater increase in the anti-inflammatory mediator (ΔIL-10). By 6 months post-surgery, the differences in the changes of these immune mediators between the 2 groups were not statistically significant ($p>0.05$) (Table 5).

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Table 1. Comparison of baseline characteristics before and after propensity score matching.

Variable	Before PSM				After PSM			
	CGF group (n = 97)	Control group (n=123)	t/χ^2	*p*	CGF group (n=85)	Control group (n=85)	t/χ^2	*p*
Age, y	28.52±3.87	30.18±4.21	3.109	0.002	29.08±3.95	29.12±4.05	0.071	0.943
Gender (male/female)	51/46	74/49	1.292	0.256	45/40	44/41	0.024	0.877
Body mass index, kg/m^2	22.41±1.83	22.75±1.97	1.377	0.170	22.53±1.88	22.60±1.91	0.259	0.796
Smoking history, n (%)	25 (25.8)	46 (37.4)	3.426	0.064	23 (27.1)	25 (29.4)	0.118	0.731
Tooth position (anterior/molar)	38/59	68/55	5.932	0.015	35/50	37/48	0.101	0.751
Gingival thickness, mm	1.68±0.32	1.75±0.35	1.582	0.115	1.71±0.33	1.70±0.34	0.205	0.838
Alveolar bone height, mm	4.85±0.71	4.62±0.68	2.398	0.017	4.73±0.69	4.75±0.70	0.191	0.849
Alveolar bone width, mm	3.42±0.58	3.58±0.62	1.942	0.053	3.51±0.60	3.49±0.59	0.221	0.825
Bone gray value, AU	623.15±78.42	605.83±82.17	1.586	0.114	612.34±80.25	614.89±79.63	0.218	0.828
GCF IL-17, pg/mL	7.25±1.83	7.91±2.05	2.548	0.012	7.58±1.94	7.63±1.97	0.169	0.866
GCF IL-23, pg/mL	15.38±3.72	16.21±4.05	1.614	0.108	15.79±3.88	15.85±3.92	0.102	0.919
GCF IL-10, pg/mL	32.17±6.84	30.85±7.12	1.427	0.155	31.52±6.95	31.46±7.01	0.056	0.955

BMI: body mass index; CGF: concentrated growth factors; GCF: gingival crevicular fluid; AU: arbitrary unit; IL: interleukin; PSM: propensity score matching.

Table 2. Comparison of clinical efficacy between groups.

Group	Excellent response, n (%)	Good response, n (%)	Poor response, n (%)	Overall response rate, n (%)
CGF group (n=85)	52 (61.18)	28 (32.94)	5 (5.88)	80 (94.12)
Control group (n=85)	31 (36.47)	33 (38.82)	21 (24.71)	64 (75.29)
χ^2	NA			11.826
p	NA			<0.001

CGF: concentrated growth factors.

Table 3. Comparison of postoperative VAS scores between groups.

Group	Postoperative day 1	Postoperative day 3	Postoperative day 7
CGF group (n = 85)	3.42±0.85	2.15±0.73	0.78±0.42
Control group (n = 85)	4.26±1.12	2.38±0.81	0.92±0.51
t	5.327	1.934	1.892
p	<0.001	0.055	0.061

CGF: concentrated growth factors; VAS: visual analog scale.

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Table 4. Comparison of changes in periodontal parameters from baseline.

Group	Gingival thickness gain, mm		Alveolar bone height gain, mm		Alveolar bone width gain, mm		Bone gray value gain, AU	
	3-month	6-month	3-month	6-month	3-month	6-month	3-month	6-month
CGF group (n=85)	0.52±0.12	0.61±0.15	1.83±0.41	2.75±0.58	0.89±0.23	1.32±0.35	86.34±22.15	132.47±34.82
Control group (n=85)	0.38±0.10	0.58±0.14	1.42±0.36	2.68±0.55	0.62±0.19	1.28±0.33	63.15±18.42	128.92±32.75
t	8.264	1.432	7.183	0.895	8.516	0.783	7.892	0.735
p	<0.001	0.154	<0.001	0.372	<0.001	0.435	<0.001	0.464

CGF: concentrated growth factors; AU: arbitrary unit.

Table 5. Comparison of changes in GCF immune mediator levels from baseline.

Group	ΔIL-17, pg/L		ΔIL-23, pg/L		ΔIL-10, pg/L	
	3-month	6-month	3-month	6-month	3-month	6-month
CGF group (n = 85)	−3.28±0.85	−4.15±1.12	−6.72±1.83	−8.93±2.35	+8.45±2.12	+11.26±3.05
Control group (n = 85)	−1.95±0.62	−3.87±1.05	−4.13±1.24	−8.35±2.18	+5.32±1.58	+10.84±2.92
t	−12.846	−1.792	−10.572	−1.635	11.385	0.952
p	<0.001	0.075	<0.001	0.104	<0.001	0.343

CGF: concentrated growth factors; GCF: gingival crevicular fluid; IL: interleukin. All cytokine concentrations and their changes are expressed in pg/mL. Δ indicates the follow-up concentration minus the baseline concentration.

Correlation Analysis between Immune Mediator Changes and Regeneration Indices

Within the CGF group, a significant positive correlation was observed between ΔIL-10 and alveolar bone height gain (p<0.001), as well as between ΔIL-10 and bone gray value gain (p=0.004). Conversely, the changes in pro-inflammatory mediators ΔIL-17 and ΔIL-23 showed significant negative correlations with gingival thickness gain (both p<0.001). No significant correlation was found between ΔIL-23 and bone regeneration indices (bone height gain, bone gray value gain; p>0.05). In contrast, within the control group, no significant correlations were detected between any of the changes in immune mediators (ΔIL-10, ΔIL-17, ΔIL-23) and the regeneration indices (gingival thickness gain, alveolar bone height gain, bone gray value gain; all p>0.05). Furthermore, the absolute values of the correlation coefficients (r) in the control group were generally lower than those observed in the CGF group (Table 6).

Table 6. Correlation analysis between immune mediator changes and regeneration indices.

Group	Variable	Gingival thickness gain		Alveolar bone height gain		Bone gray value gain	
		r	*p*	*r*	*p*	*r*	*p*
CGF group	ΔIL-10	0.18	0.099	0.42	<0.001	0.31	0.004
	ΔIL-23	−0.35	<0.001	−0.18	0.092	−0.14	0.196
	ΔIL-17	−0.38	<0.001	−0.21	0.057	−0.17	0.121
Control group	ΔIL-10	0.09	0.412	0.15	0.173	0.11	0.318
	ΔIL-23	−0.11	0.325	−0.09	0.432	−0.08	0.478
	ΔIL-17	−0.12	0.282	−0.08	0.467	−0.06	0.602

CGF: concentrated growth factors; IL: interleukin.

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DISCUSSION

In the present study, GTR combined with CGF resulted in a higher clinical response rate than GTR alone after propensity score matching. Patients receiving CGF also had less pain on the first postoperative day. At 3 months, the increases in gingival thickness, alveolar bone height and width, and CBCT gray value were greater in the CGF group. The changes in IL-10, IL-17, and IL-23 showed a similar pattern. However, the differences in tissue measurements and cytokine levels were no longer significant at 6 months. These findings suggest that CGF mainly influenced the early course of periodontal repair. It may have shortened the time needed for wound maturation rather than producing a clearly greater final tissue gain.

The early period after regenerative surgery is important because the clot, flap, and barrier membrane remain sensitive to movement, plaque contamination, and wound opening. GTR maintains a protected space within the defect, but it does not directly remove the inflammatory influence inside the wound. Early soft-tissue closure is therefore required to protect the underlying regenerative area.[16] Complications such as flap dehiscence and membrane exposure may disturb healing and reduce the expected clinical benefit.[17] In this study, the earlier gains observed with CGF may indicate faster stabilization of the operated site. Although the continuous tissue measurements became similar at 6 months, an earlier response may still be useful by reducing the duration of the vulnerable postoperative period.

The associations between cytokine changes and gingival thickness were mainly found for IL-17 and IL-23. In the CGF group, a larger decrease in these mediators was accompanied by a greater gain in gingival thickness. The same relationship was not found for alveolar bone height or gray value. IL-23 is involved in the maintenance of the TH17 response, while IL-17 may increase the production of matrix-degrading enzymes. IL-17A signaling has been shown to promote MMP-2 and MMP-9 expression, which may accelerate degradation of extracellular matrix.[18] Persistent activity of this pathway may interfere with collagen deposition and organization in gingival connective tissue. Local inflammatory reactions around oral tissues and biomaterials may also affect fibroblast behavior and wound stability.[19] The present results therefore indicate that suppression of this inflammatory pattern may be more closely related to soft-tissue healing than to radiographic bone formation.

The fibrin structure of CGF may help to retain platelets, leukocytes, and soluble factors within the defect. It also provides a temporary matrix that can support cell migration. TGF-β and related mediators participate in fibroblast proliferation, matrix formation, and regulation of inflammatory cells.[20] Reduction of IL-23/IL-17 activity may further provide a more suitable environment for gingival repair. The importance of this pathway in periodontal inflammation has been reported previously.[21] However, the present data cannot determine whether cytokine reduction occurred before gingival thickening or resulted from improved wound healing. GCF was assessed at 3 and 6 months, while the main inflammatory events probably developed during the first days and weeks. Differences in host inflammatory responses, including variation in IL-10-related pathways, may also have affected the observed cytokine levels.[22]

A different association was noted for bone-related outcomes. In the CGF group, the increase in IL-10 was positively correlated with alveolar bone height gain and CBCT gray-value gain. IL-10 may reduce inflammatory damage to osteogenic cells and limit signals that favor osteoclast development. In an experimental scaffold model, higher IL-10 levels were found together with increased OPG expression and bone-formation markers.[23] This supports the possibility that control of local inflammation may be favorable for bone repair. CGF has also shown regenerative activity in pulp and other dental tissues, suggesting that its biological influence is not restricted to gingival healing.[24] Nevertheless, radiographic changes cannot confirm true periodontal regeneration, and IL-10 should not be regarded as the direct cause of the observed bone gain.

Platelet-derived growth factors may be more effective when excessive inflammation is controlled. PDGF-BB can promote recruitment and osteogenic differentiation of mesenchymal cells,[25] whereas IGF-related pathways participate in matrix formation and mineralization.[26] In the present study, the rise in IL-10 and the improvement in bone measurements occurred during the same early period. This may indicate that the local environment became more favorable for growth-factor activity. However, PDGF, TGF-β, VEGF, and other CGF components were not measured. No

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mediation analysis was performed. The results only show a relationship between an anti-inflammatory GCF pattern and early radiographic improvement.

The lower pain score in the CGF group was limited to postoperative day 1. There was no significant difference on days 3 and 7. This finding indicates an effect on the immediate postoperative response rather than prolonged analgesia. The IL-23/IL-17A/TRPV1 pathway has been related to nociceptor sensitization and mechanical pain.[27] IL-23-related neutrophil activity may also contribute to edema and local tissue pressure.[28] In addition, the fibrin matrix may cover the defect and reduce mechanical irritation during the first postoperative hours. Both mechanisms are possible. However, cytokines were not measured on the day when pain was assessed, and information on additional analgesic use, swelling, and flap tension was not complete. Therefore, the relationship between cytokines and pain remains an indirect explanation.

From a clinical point of view, CGF may be considered when early wound stabilization is particularly important. The results also suggest that soft- and hard-tissue healing may not have the same inflammatory pattern. IL-17 and IL-23 were more closely related to gingival thickness, while IL-10 was associated with bone measurements. This observation may be useful for future studies but cannot support treatment selection according to cytokine levels. Basic factors such as plaque control, defect morphology, flap stability, clot protection, and tension-free closure remain essential. Experimental research has shown that CGF-containing scaffolds may support angiogenic and osteogenic signaling,[29] and platelet-rich fibrin matrices can provide a mixture of cells, proteins, and regenerative mediators.[30] CGF should nevertheless be regarded as an adjunct and not as a substitute for correct surgical technique.

The absence of significant differences at 6 months is also relevant. It may indicate that patients treated with GTR alone continued to heal and eventually approached the tissue level observed in the CGF group. This could explain part of the inconsistent results reported for platelet concentrates. Studies differ in the type of platelet preparation, centrifugation procedure, defect anatomy, combined graft material, surgical technique, and time of outcome assessment.[31] A study evaluating only a late time point may not detect a temporary early advantage. The present findings should therefore not be generalized to all CGF preparations or to every periodontal regenerative procedure.

Several limitations should be noted. Treatment was selected during routine clinical practice rather than assigned randomly. Propensity score matching reduced the measured baseline differences but could not control unrecorded factors, including operator judgment, small variations in flap management, oral-hygiene compliance, and use of postoperative medication. Detailed anatomical information was incomplete. The number of residual bony walls, defect angle, exact defect-depth distribution, and tooth-specific morphology were not systematically recorded. These characteristics may have influenced both treatment selection and regenerative outcome.

The biological assessment was also limited to IL-10, IL-17, and IL-23. It did not include the main growth factors released from CGF or the cellular composition of the local inflammatory response. Sampling at 3 and 6 months provided little information about the first postoperative weeks. In addition, the study was conducted at one center and included a relatively young population without important systemic diseases. Its findings may not apply directly to older patients or patients with diabetes and other conditions affecting periodontal healing. The 9-month follow-up was insufficient for assessment of attachment stability, recurrence, or tooth survival. CBCT measurements also cannot demonstrate histological formation of new cementum, periodontal ligament, and alveolar bone.

Future randomized studies should record defect morphology in detail and use standardized CGF preparation and surgical procedures. Repeated GCF sampling during the first postoperative days and weeks may help clarify whether changes in cytokines precede clinical improvement. Longer follow-up is also needed to determine whether faster early healing results in better long-term attachment stability or tooth retention.

In conclusion, CGF used as an adjunct to GTR was associated with a higher clinical response, less immediate postoperative pain, and faster early improvement in gingival and radiographic measurements. The changes in IL-10, IL-17, and IL-23 suggest that this early response occurred together with alteration of the local inflammatory environment. As the differences in tissue gain were no longer present at 6 months, CGF appears to accelerate early recovery rather than clearly increase the final regenerative level.

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STATEMENT OF ETHICS

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Dongfang Hospital, Beijing University of Chinese Medicine (approval No. DF202251101). Written informed consent for treatment and the research use of anonymized clinical data was obtained from all participants.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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DATA AVAILABILITY

The de-identified data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to institutional approval and applicable privacy regulations.

AI ASSISTANCE DISCLOSURE

OpenAI ChatGPT was used for English-language editing and stylistic revision after the scientific content and statistical results had been prepared by the authors. All AI-assisted text was reviewed and revised by the authors, who take full responsibility for the manuscript. AI tools were not used for study design, data collection, or statistical analysis.

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