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Evaluation of gingival crevicular fluid and peri-implant sulcus fluid levels of periostin: A preliminary report

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Abstract

Background: Periostin is a protein present in alveolar bone and periodontal ligament whose function is related to response to external forces. The aims of this study are to detect levels of periostin in peri-implant sulcular fluid (PISF) and gingival crevicular fluid (GCF) and to evaluate the relationship between periostin, pyridinoline cross-linked carboxyterminal telopeptide of Type I collagen (ICTP), and C-terminal cross-linked telopeptide of Type I collagen (CTX) levels and clinical inflammatory symptoms and duration of functional loading.

Methods: The study population comprised nine women and four men with mean age 43.23 ± 12.48. Twenty "bone-level designed" dental implants (DIs) placed in molar or premolar sites, without any signs of peri-implant bone loss and with a restoration in function for at least 12 months, were included in the study with 20 contralateral natural teeth (NT) as controls. Clinical parameters and restoration dates of the implants were recorded. PISF, GCF, ICTP, CTX, and periostin levels were evaluated using enzyme-linked immunosorbent assay.

Results: ICTP, CTX, and periostin levels were similar between DI and NT groups. There were no statistically significant differences between PISF and GCF values. When implants were grouped as healthy (gingival index [GI] = 0) and inflamed (GI ≥0), ICTP levels and PISF volume were lower in healthy implants compared with the inflamed group. Both periostin and CTX levels were negatively correlated with functioning time, suggesting less bone remodeling around DIs at later stages of functioning.

Conclusion: Findings of this study suggest collagen breakdown products may be used as markers to evaluate peri-implant metabolism.

KEYWORDS

Dental implants, inflammation, pathogenesis, gingival crevicular fluid

Several well defined clinical parameters are being used for evaluation of dental implants (DIs); however, early detection of the inflammatory process prior to occurrence of clinical signs is essential for early diagnosis and preventing further tissue breakdown.[1] Peri-implant sulcular fluid (PISF) is the osmotically mediated exudate originating from the vascular plexus of the gingiva and is considered the analog of gingival crevicular fluid (GCF) of natural teeth (NT).[2,3] During inflammation in GCF higher inflammatory mediators and tissue degradation components present, therefore, GCF may help to represent early detection of peri-implant inflammatory changes.[3] Through evaluation of the

components of PISF and correlation of these data with clinical symptoms, peri-implant diseases can be detected and treated before detectable clinical signs appear.[4] In this context, several components in PISF have been investigated, including inflammatory markers (cytokines and prostaglandins), tissue degradation components (matrix metalloproteinases and acute phase proteins), mineralized tissue components, and bone turnover markers.[5–8]

Similar to periodontal diseases, biofilm is considered the primary etiologic factor for initiation and progression of peri-implant diseases, and inflammatory mediators induced by bacterial challenge are responsible for the pathogenesis of peri-implant mucositis and peri-implantitis.[9–11] In periodontitis, bone loss around teeth is regarded as a biofilm-mediated infection, and it is also believed that bone loss around an implant (peri-implantitis) is also a result of a similar infectious process.[12] Because Type I collagen comprises 90% of the organic matrix of bone, breakdown products of collagen are released into the circulation during bone resorption and may be detected in serum and/or urine.[13] Pyridinoline cross-linked carboxyterminal telopeptide of Type I collagen (ICTP) and C-terminal cross-linked telopeptide of Type I collagen (CTX) are two fragments of C-telopeptide collagen that have been characterized.[14–16] A significant relationship between ICTP levels and several bone-metabolic diseases, such as postmenopausal osteoporosis, has been reported.[16] In a pilot study using beagle dogs in a ligature-induced experimental periodontitis model, it was reported that ICTP levels in GCF were elevated 2 weeks after disease onset, and notable radiographic bone loss was detected at 4 weeks, reflecting the promising role of ICTP in defining future bone loss.[17] From this point of view, ICTP levels have been investigated for NT and DIs, and increased ICTP levels were reported in periodontal inflammation that presented clinically with higher attachment and bone loss.[18] In clinical studies, Tümer et al.[8] and Arikan et al.[19] compared ICTP levels for healthy and inflamed DIs, and the results indicated elevated ICTP levels in PISF of DIs that showed peri-implantitis.

Periostin, originally termed as osteoblast specific factor-2, is a matricellular protein mainly expressed in periosteum, periodontal ligament (PDL), and on the alveolar bone surface in adults.[20] It has been shown to play a functional role in wound repair, cardiovascular diseases, bone and tooth remodeling, and tooth morphogenesis.[21–23] A significant role of periostin has been demonstrated in maintenance of PDL integrity under mechanical loading,[24] and it has been shown to be related to the orthodontic tooth movement process as well.[25] To determine effects of periostin on human PDL (hPDL) cells in inflammatory conditions, Padial-Molina et al.[26] subjected hPDL cells to different concentrations of periostin under inflammatory challenge using tumor necrosis factor (TNF)-α and *Porphyromonas gingivalis* lipopolysaccharide (LPS). Their results revealed that, when subjected to inflammatory mediators and bacterial virulence factors, periostin acts as a key factor for periodontal integrity and is involved in important cellular events, such as cell proliferation, migration, and activation of the survival-signaling pathway. Periostin expression by hPDL fibroblasts was shown to be decreased, indicating a possible role of periostin in periodontal disease progression.[26] Balli et al.[27] investigated levels of periostin in GCF and serum of patients with different stages of periodontal disease (healthy, gingivitis, and periodontitis) and a decrease in levels of GCF periostin with increasing severity of inflammation was recorded, which may suggest a contributory role of periostin in tissue breakdown. Similarly, Aral et al.[28] performed a clinical study in 72 patients with chronic periodontitis (CP) and aggressive periodontitis (AgP) and reduced GCF periostin levels were detected in patients with CP and AgP compared with healthy controls. To the best of the authors' knowledge, no studies that investigate PISF periostin level and its correlation with peri-implant inflammation exist in the literature.

Thus, the aims of this clinical study are: 1) to evaluate levels of periostin, ICTP, and CTX for DIs and NT and 2) to investigate their relationship with peri-implant/periodontal inflammation and duration of functional loading.

1 | MATERIALS AND METHODS

Data for this study were taken from 13 individuals (four males and nine females, aged 27 to 65 years; mean age: 43.23 ± 12.48 years), who lost their teeth due to caries and endodontic problems, at the Department of Periodontology, Faculty of Dentistry, Hacettepe University, Ankara, Turkey, from 2012 to 2013. A total of 20 DIs inserted in the posterior region (four maxillary first premolars, five maxillary second premolars, three maxillary first molars, one first mandibular premolar, one mandibular second premolar, and six mandibular molars) and 20 contralateral NT were evaluated. All DIs included were "bone-level designed," restored with cement-retained crowns, and had been subjected to functional loading with natural dentition or fixed dental restorations in the opposing arch for at least 12 months. DIs supporting fixed bridges or overdentures and with any signs of peri-implantitis were excluded from the study. Patients with periodontitis history, bruxism, pregnancy, lactation, systemic conditions related to peri-implant/periodontal status, diabetes mellitus, or with a history of cardiovascular and metabolic bone disease were also excluded. The study procedure was explained in detail, and written informed consent was obtained from patients. The study protocol was approved by the Ethics Committee of Hacettepe University, Ankara, Turkey (HEK 12/196 to 05).

1.1 | Surgical and prosthetic procedures

Local anesthesia was applied, and a midcrestal incision with sulcular releasing incisions at adjacent teeth was performed. Full-thickness flaps were reflected and osteotomies were prepared for the premolar or molar sites as determined before the surgical procedure. All implants had a bone level design and were placed in pristine bone. At least 1 mm of intact bone was present at buccal and lingual/palatal sites after insertion of DIs. Short implants (≤8 mm),[29] narrow implants (<3.5 mm),[30] implants placed immediately, and implants placed in combination with bone grafting procedures were not included. All implants were placed in prosthetically driven positions using two-stage DI surgical protocol, and second-stage surgery was performed after 12 weeks of healing. The definitive fully occluding metal-ceramic crowns were fabricated and cemented onto abutments after 3 months of healing.

1.2 | Clinical evaluation

Clinical parameters were recorded for each DI and NT site at four sites using a periodontal probe.* Probing depth (PD), clinical attachment level (CAL), plaque index (PI),[31] gingival index (GI),[31] and gingival bleeding time index (GBTI)[32] were recorded. In addition to clinical parameters, the total duration of functional loading (months) for DIs was also noted. All clinical measurements were performed by an experienced clinician (AA).

1.3 | Peri-implant sulcus fluid/GCF sampling

Before clinical evaluation (except PI), to eliminate any circadian effects, PISF/GCF samples were obtained between 8:00 and 10:00 am by the method described by Rüdin et al.[33] Briefly, after isolation of the sampling area with cotton rolls, the supragingival plaque was removed and the sites were gently air dried to eliminate any contamination with plaque or saliva. To avoid any effect on PISF/GCF volume, extreme care was taken to minimize mechanical trauma while sampling.[34] Standardized paper strips were inserted at 1-mm depth at the entrance of the peri-implant sulcus, regardless of the PD, for 30 seconds. For each DI/NT, samples were taken at four sites (mesial, mid-buccal, distal, and palatal/lingual). Strips contaminated by blood were excluded from the sampling group. After 30 seconds of sampling time, paper strips were immediately transferred to a previously calibrated device.† Care was taken to minimize the period between sampling and the transfer of the paper strips to the device to eliminate the risk of evaporation.[34] PISF volume was electronically measured in the proprietary units of the measuring device and then converted to microliters using a software program.‡ The PISF/GCF samples were placed in sterile Eppendorf tubes and carefully wrapped to be stored in −80°C until laboratory analysis.

1.4 | Quantification of ICT, CTX, and periostin in PISF/GCF

To determine the levels of ICTP, CTX, and periostin in PISF, paper strips were placed in sterile tubes and stored at −80°C. Paper strips were cut, and their content was extracted by adding 500 μL of sterilized phosphate-buffered saline. Samples were studied using commercially available enzyme-linked immunosorbent assay (ELISA) kits§¶# by following the instructions of the manufacturer. Minimum detection level or lower level of detection values for ELISA kits were as follows: 1) for ICTP, 1.56 ng/mL; 2) for CTX-I, 0.156 ng/mL; and 3) for periostin, 1.56 ng/mL. Each sample was measured in duplicate.

For detection of human periostin and human CTX, the ELISA protocols were the same and can be summarized as follows. Reagents and samples were prepared and brought to room temperature. One hundred microliters of sample or standard solution was added to wells, followed by incubation for 2 hours at 37°C. Liquid in each well was removed, and 100 μL of biotin-antibody was added, followed by incubation for 1 hour at 37°C. The liquid was aspirated, and the wells were washed three times. One hundred microliters of horseradish peroxidase (HRP)–avidin was added to each well, followed by incubation for 1 hour at 37°C. The liquid was aspirated, and the wells were washed five times. Ninety microliters of tetramethylbenzidine substrate was added to each well, followed by incubation for 20 minutes at 37°C in a dark place. After addition of 50 μL of stop solution to each well, a microplate reader set at 450 nm was used. Sample concentrations were calculated using absorption values and the standard curve.

For detection of human ICTP levels, 50 μL of sample or standard solution and 50 μL HRP-avidin were added to each well, followed by incubation for 1 hour at 37°C. The liquid was aspirated, and the wells were washed three times. Fifty microliters of substrate A and 50 μL of substrate B were added to each well, followed by incubation for 15 minutes at 37°C in a dark place. After addition of 50 μL of stop solution, a microplate reader set at 450 nm was used. Sample

* Michigan O Color-Coded Probe, Hu-Friedy, Chicago, IL.

† Periotron 8000, Oraflow, Hewlett, NY.

‡ MLCONVERT.EXE, Oraflow, Hewlett, NY.

§ Human periostin ELISA kit (CSB-E16444h), Cusabio, Wuhan, China.

¶ Human C-telopeptide of Type I collagen (ICTP) ELISA Kit (CSB-E10363h), Cusabio.

Human cross-linked carboxy-terminal telopeptide of Type I collagen (CTX-I) ELISA Kit (CSB-E11224h), Cusabio.

TABLE 1 Clinical and biochemical parameters for DIs and NT

Clinical and Biochemical Parameters	DIs, mean ± SD (n = 20)	NT, mean ± SD (n = 20)	*P* Value
PD, mm	2.3 ± 0.68	1.95 ± 0.49	0.07
CAL, mm	2.33 ± 0.68	2.76 ± 1.12	0.14
PI	0.42 ± 0.32	0.4 ± 0.36	0.68
GBTI	1.05 ± 0.76	0.63 ± 0.58	0.06
GI	0.48 ± 0.54	0.42 ± 0.45	0.76
PISF/GCF volume, μL	0.74 ± 0.47	0.45 ± 0.22	0.06
Duration, months	22.63 ± 12.09		
ICTP, ng/mL^{-1}	6.22 ± 9.57 (0.17 to 39.52)	4.51 ± 6.45 (0.17 to 20.56)	0.62
CTX, ng/mL	3.69 ± 3.56 (0.08 to 10.33)	4.80 ± 3.15 (0.55 to 12.19)	0.17
Periostin, ng/mL	14.13 ± 20.53 (0.89 to 70.75)	13.96 ± 16.56 (4.21 to 66.03)	0.08

Duration = duration of functional loading.

concentrations were calculated using absorption values and the standard curve.

1.5 | Statistical analyses

Mann–Whitney *U* test was performed for comparison of study groups. Correlations were performed using Spearman correlation coefficient (ρ). *P* values < 0.05 were considered statistically significant for all parameters. A difference between DI and NT can be detected at an α level of 0.05, with a statistical power of 75%. However, a difference between maxillary and mandibular DIs can be detected at an α level of 0.05, with a statistical power of 45%. Software was used for all statistical analyses and power calculations.*

2 | RESULTS

Data demonstrating clinical parameters are represented in Table 1. No statistical differences were noted between test (DIs) and control sites (NT) regarding PD, CAL, PI, GBTI, GI, and PISF/GCF volume, indicating the homogeneity of the study population (Table 1).

When DIs were grouped as healthy (GI = 0) and inflamed (GI > 0), statistical differences were noted in PISF volume and ICTP, representing higher values for the inflamed sites (PISF volume: 0.55 ± 0.44 μL versus 0.91 ± 0.45 μL; ICTP: 3.20 ± 5.92 ng/mL^{-1} versus 9.25 ± 11.74 ng/mL^{-1}, $P < 0.05$ for healthy and inflamed sites, respectively). There were no statistical differences for any of the other parameters evaluated (Table 2).

For NT, statistical differences were detected for PD, demonstrating higher values for the inflamed sites (2.13 ± 0.49 versus 1.72 ± 0.40, $P < 0.05$). Similar to DIs, higher ICTP levels were detected for inflamed NT sites (5.44 ± 6.66 ng/mL^{-1} versus 3.37 ± 6.39 ng/mL^{-1}, $P < 0.05$) (Table 2).

When DIs were classified based on the location (maxilla versus mandible), although higher values were recorded in ICTP, CTX, and periostin for DIs in the mandible, no statistical differences were detected between groups for any of the parameters evaluated ($P > 0.05$) (Table 3).

For DI, a negative correlation was detected between duration of functional loading, periostin ($r = -0.54$, $P = 0.03$), and CTX ($r = -0.54$, $P < 0.05$). In addition, GI was positively correlated with ICTP ($r = 0.52$, $P < 0.05$). Similar to DI, a positive correlation was reported between ICTP and GI ($r = 0.52$, $P = 0.01$) for NT.

3 | DISCUSSION

Structural differences in surrounding mucosa have been reported for peri-implant and periodontal tissues.[35] Unlike the perpendicularly oriented fibers in the periodontium, collagen fibrils are parallel in peri-implant tissues, and tissue apical to junctional epithelium is characterized with more collagenous, less vascular, and lower fibroblast content, which may contribute to the increased susceptibility of DIs to inflammation.[35,36] Therefore, early detection of any inflammatory changes around DIs is essential for prevention and treatment of peri-implant diseases at earlier stages. By way of its content and volumetric changes during inflammation, PISF/GCF offers great potential in reflecting inflammatory changes and tissue loss.[5,37] In the present study, significantly higher levels of ICTP were detected for inflamed DI and NT when compared with healthy controls. Similarly, Oringer et al.[38] reported elevated levels for ICTP in GCF of patients with gingivitis and periodontitis, increasing with the severity of disease progression, as well as a positive correlation with the presence of several pathogenic species (*Tannerella forsythia*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Prevotella nigrescens*, and *Treponema denticola*). These findings suggest that specific pathogens may lead to an inflammatory response that results in release of inflammatory mediators and osteoclastic resorption detected by elevated ICTP. ICTP levels of DI and its correlation with subgingival pathogens was investigated, which demonstrated a significant correlation with the presence of some species (*T. forsythia, Campylobacter rectus, Peptostreptococcus micros*, and *P. nigrescens*) responsible for peri-implant disease progression

* SPSS for Windows, SPSS, Chicago, IL.

TABLE 2 Comparison of clinical and biochemical parameters among healthy and inflamed DIs and Teeth

Clinical and Biochemical Parameters	DIs			NT		
	GI = 0, mean ± SD (n = 10)	GI > 0, mean ± SD (n = 10)	*P* Value	GI = 0, mean ± SD (n = 10)	GI > 0, mean ± SD (n = 10)	*P* Value
PD, mm	2.12 ± 0.62	2.47 ± 0.73	0.31	1.72 ± 0.40	2.13 ± 0.49*	0.03*
CAL, mm	2.15 ± 0.61	2.5 ± 0.74	0.27	2.27 ± 0.96	3.15 ± 1.12	0.10
PI	0.32 ± 0.33	0.52 ± 0.28	0.11	0.30 ± 0.39	0.47 ± 0.33	0.16
GBTI	0.8 ± 0.79	1.3 ± 0.67	0.14	0.44 ± 0.72	0.77 ± 0.41	0.11
PISF/GCF volume, μL	0.55 ± 0.44	0.91 ± 0.45*	0.02*	0.37 ± 0.25	0.50 ± 0.19	0.38
Duration, months	20.55 ± 10.41	25.28 ± 14.37	0.78			
ICTP, ng/mL^{-1}	3.20 ± 5.92 (0.17 to 19.06)	9.25 ± 11.74* (1.241 to 39.52)	0.02*	3.37 ± 6.39 (0.17 to 19.24)	5.44 ± 6.66* (1.06 to 20.57)	0.03*
CTX, ng/mL	2.64 ± 2.76 (0.08 to 8.34)	4.753 ± 4.09 (0.08 to 10.33)	0.4	3.73 ± 3.27 (0.55 to 8.87)	5.674 ± 2.92 (1.497 to 12.198)	0.23
Periostin, ng/mL	5.085 ± 4.32 (0.89 to 16.84)	23.18 ± 26.26 (1.69 to 70.76)	0.11	11.29 ± 15.38 (4.21 to 50.8)	16.15 ± 17.90 (4.35 to 66.03)	0.18

Duration = duration of functional loading.

*$P < 0.05$: statistically significant difference.

TABLE 3 Comparison of clinical and biochemical parameters among DIs classified by location

DIs, Clinical and Biochemical Parameters	Maxilla, mean ± SD (n = 12)	Mandibular, mean ± SD (n = 8)	*P* Value
PD, mm	2.52 ± 0.67	1.97 ± 0.57	0.09
CAL, mm	2.54 ± 0.66	2.00 ± 0.61	0.13
PI	0.43 ± 0.37	0.40 ± 0.22	0.96
GBTI	1.16 ± 0.71	0.87 ± 0.83	0.40
GI	0.39 ± 0.54	0.59 ± 0.53	0.38
PISF volume, μL	0.57 ± 0.34	0.97 ± 0.55	0.07
Duration, months	25.56 ± 14.34	18.85 ± 7.88	0.41
ICTP, ng/mL^{-1}	5.518 ± 10.92 (0.17 to 39.52)	7.29 ± 7.67 (0.17 to 19.06)	0.43
CTX, ng/mL	3.35 ± 3.52 (0.08 to 10.33)	4.20 ± 3.82 (0.31 to 10.33)	0.51
Periostin, ng/mL	10.40 ± 19.42 (0.89 to 70.75)	19.73 ± 22.17 3.24 to 64.74	0.28

Duration = duration of functional loading.

and ICTP.[38] Tümer et al.[8] reported a trend of increase in PISF ICTP levels for implants with signs of peri-implantitis. Supporting the findings of these studies, in a clinical study including 39 DIs, increased total amounts of ICTP for DIs were reported in the peri-implantitis group.[19] Similar to previous studies,[8,39] a positive correlation was detected between ICTP and GI in the present study, both for NT and DIs. Elevated levels of ICTP with the degree of inflammation suggest ICTP can be a possible marker for identification of disease severity and progression.

Studies have revealed a specific role for periostin during early phases of fracture healing in the recruitment of progenitor cells and osteoblastic differentiation and bone formation.[40,41] These reports indicate the potential role of periostin in bone remodeling and turnover. Padial-Molina et al.[42] investigated messenger RNA expression and levels of periostin in hPDL cultures subjected to biomechanical loading and bacterial virulence factors (TNF-α and *P. gingivalis* LPS) in vitro. Their results indicated that, under biomechanical loading and bacterial challenge, both expression and protein levels of periostin are increased in the early period of exposure, followed by a significant decrease with disease progression. In a recent study,[43] changes in periostin levels following surgical periodontal treatment were evaluated to determine the role of periostin in wound healing. A total of 22 patients with CP and AgP (case group) and periodontally healthy individuals (control) were recruited. Tissue biopsies, GCF, whole saliva, and serum samples were taken before and after surgical procedures. Their results demonstrated a significant increase in periostin levels after surgery, most dominantly in the diseased group, and this increase returned to baseline levels after 2 and 4 weeks as the wound healed. Although this early increase after surgery was found to be related to elimination of bacterial challenge and inflammatory factors, the following decrease was attributed to the maturation of the wound, which may lead to a decrease in periostin levels, possibly due to the deposition of periostin into extracellular matrix and formation of mature collagen. In contrast to the present results, previous studies reported decreased periostin levels in patients with gingivitis.[27] Patients with CP[27,28] and AgP[28] showed a decrease in periostin levels with progression of disease. The decrease in periostin levels with progression of

periodontal disease was explained by two mechanisms: first, bacterial challenge may alter the expression of periostin, and secondly, disease progression decreases PDL cells (one of the important cells responsible for periostin production), which might lead to a decrease in periostin levels.[44] In the present study, DIs and NT with signs of peri-implantitis and periodontitis were excluded, so present findings may only reflect the gingivitis/peri-implant mucositis in which early inflammatory mechanisms take place without irreversible loss of supporting tissues. This may be the reason for conflicting results.

In a mouse study investigating orthodontic tooth movement, Rangiani et al.[25] reported a great reduction of tooth movement and bone formation in the absence of periostin and detected higher periostin levels on the compression side than the tension side, indicating the essential role of periostin in bone remodeling. In the same study, collagen degradation also was delayed in the periostin knockout mice, suggesting that periostin plays an active role in collagen remodeling. Rios et al.[24,45] reported alveolar bone defects, external root resorption, and diminished cementoblast attachment to root surface in periostin null mice subjected to mechanical loading. In the absence of mechanically challenging environmental conditions, no defects developed, supporting the idea that periostin plays a major role in maintaining the integrity of tissues under loading conditions. In the present study, under functional loading, a negative correlation was detected between duration of functional loading and periostin, possibly explained by the decreased remodeling of DIs following functional loading.

Although the sample size was limited and findings were statistically not significant, PISF periostin, ICT, and CTX levels were higher for DIs in the mandible compared with DIs in the maxilla. When the possible roles of ICTP, periostin, and CTX during bone remodeling are taken into account, higher levels detected in the mandible may be attributed to the shorter mean duration of functional loading of DIs in the mandible (18.85 $\pm$ 7.88 versus 25.56 $\pm$ 4.34 months).

One of the limitations of the present study was the limited number of DIs, due to the specific inclusion criteria that included restoration type (single crowns) and the use of contralateral teeth as controls, which limited further comparisons between DIs at different stages of functional loading. Moreover, present interpretations about the comparison of maxillary and mandibular DIs requires caution due to the limited number of DIs in groups. Further studies including more DIs at different stages of functional loading (early, moderate, late) are needed to clarify the role of periostin in bone remodeling around DIs. Another limitation of the data obtained in this research was the high variation of investigated markers within the same implant groups. High variation in the present study results may suggest that levels of these markers may also be dependent on other factors, like occlusal loads and bone remodeling, in addition to clinical inflammation, which was the main scope of this research.

The following results can be taken from the present and previous studies: periostin plays a role in the early inflammatory phase of peri-implant/periodontal diseases, possibly due to the acute bacterial challenge and related immune response. However, as the disease progresses and a chronic challenge is abundant, periostin decreases with the severity of the disease.[27,28,44] During healing of periodontal defects, after removal of bacterial challenge, an early increase was reported, supporting the role of periostin in restoring and maintaining the integrity of periodontal tissues. After maturation of the wound, possibly due to the integration of periostin into the matrix, periostin decreases to baseline levels. Under in vitro diseased conditions, it has been reported that periostin increases hPDL cell migration and proliferation, which may be a target for new studies on novel periostin-containing biologic agents.[26]

4 | CONCLUSIONS

Within the limitations of this preliminary study, it can be concluded that periostin and ICTP can be used as markers of peri-implant inflammatory processes and bone remodeling after functional loading of DIs similar to natural dentition. Further clinical studies including a more comprehensive study involving DIs at different stages of functional loading (early, moderate, late) or inflammation (healthy, peri-implant mucositis/gingivitis, periodontitis/peri-implantitis) are needed to clarify the exact role of these markers in peri-implant inflammation and bone remodeling.

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