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ORIGINAL ARTICLE

Associations of alveolar bone loss and interleukin-1β levels in one- and two-stage surgical procedures: a randomized prospective trial

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ABSTRACT

Objective: Dental implants have been widely and successfully used in recent years as an alternative treatment for removable and fixed dental prostheses. The aim of this randomized prospective study was to determine the alveolar bone loss rate (ABLR) and IL-1β levels in one- and two-stage surgical procedures.

Materials and methods: This study included 40 patients with a single missing tooth in the posterior mandible; dental implants were inserted using a one-stage surgical procedure (Group I) or a two-stage surgical procedure (Group II). All clinical periodontal parameters were recorded; peri-implant crevicular fluid (PICF) samples were collected before loading (T0) and during the third (T1) and sixth (T2) months after loading. ABLR values were evaluated at T0 and T2 by using dental tomography. PICF was analysed after T2 samples were collected. The study was registered through clinicaltrials.gov; identifier NCT03045458.

Results: This study found that, the probing pocket depth was found to be significantly higher in Group I than Group II at both T1 and T2 ($p < .05$). There was no significant difference in other clinical parameters between the groups ($p > .05$). There was a significant difference between Group I ABLR values at T0 and T2 ($p < .05$). The PICF IL-1β levels were not significantly different between groups ($p > .05$).

Conclusions: Within the limitations of the short observational period and small sample size of this study, two-stage implant placement shows comparable clinical outcomes to implants placed using a one-stage placement protocol.

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Dental tomography; interleukin-1β; one- and two-stage dental implants; peri-implant crevicular fluid

Introduction

Dental implants are increasingly being used to restore partial and complete edentulism [1–3]. Various factors affect the success of dental implants, so patients should be carefully evaluated before the treatment procedure. All risk indicators, such as poor oral hygiene, history of periodontitis, diabetes, smoking, alcohol consumption and genetic traits should be considered [4]. Additionally, critical success factors are careful treatment planning and a surgical procedure to prevent peri-implant disease and implant failure [5].

Different surgical techniques, including one- or two-stage surgical procedures can be performed. In a one-stage surgical procedure, the healing cap is connected directly. In a two-stage surgical procedure, the fixture is subperiosteally placed and covered with a cover screw, which is replaced with a healing abutment in a second surgery. There are advantages and disadvantages in both procedures. In one-stage procedure, the dental implant penetrates the oral mucosa; but in two-stage procedure, the dental implant is completely buried under the oral mucosa during the healing phase. Two-stage procedures reduce the risk of undesirable loading onto the implants, but require a second, minor, surgical operation to connect the healing abutments, as well as more time prior to initiation of the prosthetic phase for tissue-healing before the second surgical operation [6].

Dental implant success is critical for both patients and society. The current criteria for implant evaluating are based on clinical and radiographic changes. The consensus of the first European Workshop on Periodontology suggested that success depends on a mean alveolar bone loss level of less than 1.5 mm during the first year after the prosthetic phase, and less than 0.2 mm of annual bone loss thereafter. Therefore, evaluation of the initially achieved alveolar bone loss rate (ABLR) in the most coronal position possible is a crucial factor for the long-term success of dental implant treatment [7].

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In addition, different diagnostic parameters are used to evaluate peri-implant disease in serum, saliva and crevicular fluid. Inflammatory products of periodontal disease are present in crevicular fluid. In recent years, researchers have analysed peri-implant crevicular fluid (PICF) to detect potential host markers; PICF is a primary parameter used to diagnose disease activity and determine the prognosis [8,9]. Pro-inflammatory cytokines may induce alveolar bone resorption around dental implants [10,11]. IL-1β may be a critical marker for dental implant survival [1]. Some studies have shown that the PICF IL-1β level is closely related to peri-implantitis [10–12]. Other studies have shown that IL-1β level increases in gingival crevicular fluid (GCF) and periodontal tissues in the presence of periodontal diseases, and the correlation between IL-1β levels and the severity of the disease is apparent [12–14]. Guncu et al. [15] evaluated the effect of inflammation on the level of IL-1β in PICF. They divided samples into two groups: with and without inflammation, and found significantly higher levels of IL-1β in PICF with peri-implantitis compared to samples from healthy implants. Yaghobee et al. [9] suggested that levels of IL-1β in PICF with peri-implantitis are significantly higher than levels around healthy implants.

In the last few decades, cone-beam computed tomography (CBCT) has been used to create three-dimensional images. CBCT is appropriate for imaging of the craniofacial area. It provides clear images of highly contrasted structures and is extremely useful for assessing bone [16,17].

There are no studies in the literature that assess ABLR using both CBCT and PICF IL-1β levels in implants inserted using one- or two-stage surgical procedures. The aim of this study was to determine the level of alveolar bone loss and IL-1β in PICF in one- or two-stage surgical procedures.

Clinical relevance: Different surgical techniques can affect the success of dental implants. ABLR is one of the most important criteria for the assessment of implant success. The PICF IL-1β levels are an additional important factor that increases in peri-implantitis. Thus, it is important to clinically evaluate both of parameters during in the follow-up period.

Materials and methods

Study population

The present study included 40 healthy patients (Group I: 12 males, eight females; Group II: 12 males, eight females; mean age, 30.75 ± 8.58 years) missing one tooth from the mandible. Patients visited the Department of Periodontology, Dicle University, Diyarbakir, Turkey, between 2010 and 2011. All patients were informed in detail about the study protocol and were asked to sign informed consent forms. All participants voluntarily gave informed consent. Ethics committee approval for this study was obtained from the Dicle University Ethics Committee for this study (D.Ü.D.F.E.K.2010/02), and the study was registered through clinicaltrials.gov; identifier NCT03045458.

The inclusion criteria were as follows: (1) missing first molar tooth in the mandible, (2) a history of edentulism in the area of implant treatment area of at least 6 months, (3) age greater than 18 years and (4) voluntary provision of informed consent. Exclusion criteria were as follows: (1) poor mouth hygiene, (2) untreated, uncontrolled caries and/or periodontal disease, (3) severe systemic diseases that might contraindicate intervention, such as uncontrolled diabetes mellitus, coagulation disorders or immunocompromised status, (4) history of chemotherapy within 5 years prior to surgery, (5) history of radiation of head or neck region, (6) history of other metabolic bone diseases, (7) current need for bone grafting in the planned implant area, (8) history of bone grafting in the planned implant area, (9) smoking, alcohol or drug abuse, (10) bruxism or (11) pregnancy or lactation.

Study design

This study was designed as a prospective, randomized, controlled (parallel) study. Randomization was performed prior to surgery by opening a sequentially numbered sealed envelope corresponding to the patient recruitment number. Investigators received randomization instructions only after enrolling a subject and immediately prior to surgery. The participants were randomly divided into two groups. A one-stage surgical procedure was performed on 20 patients (Group I); a two-stage surgical procedure was performed on the other 20 patients (Group II). The primary outcome of the study was a change in alveolar bone level at the implant site between T0 (before loading, 3 months after placement of the implant) and T2 (6 months after loading), as measured by CBCT. The secondary outcomes between T0, T1 (3 months after loading) and T2 were changes in the level of IL-1β PICF, probing depth (PD), modified plaque index (mPI), modified gingival index (mGI) and modified bleeding index (mBI). The CONSORT flow chart of the study is shown in Figure 1, and the protocol for the trial and CONSORT checklist are available as Data S1.

Surgical procedure

Standard plus and bone level, sand-blasted, large grit, acid-etched (SLA) surface, titanium dental implant (Straumann AG, Waldenburg, Switzerland) systems were used. All implants in the present study were 12 mm in length and 4.8 mm in diameter, and all were inserted by the same periodontist (TTY). Pre-surgical radiographic evaluation was conducted using CBCT. Before surgery, the patient's mouth was rinsed with chlorhexidine mouthwash. After local anaesthesia, a full thickness flap was reflected, and an osteotomy was prepared in each first mandibular molar sites. Group I received tissue-level (platform-switching) implants; Group II received bone-level dental implants (Figure 2). After implant placement, 3.0 silk sutures (Sterisilk, SSM Sterile Health Products, Inc., Istanbul, Turkey) were used to close flap. Three months later, second-stage surgery was performed and each implant was exposed into the oral cavity. The cover screw was removed and replaced with healing abutments. The second surgery in the bone level implants was performed 3 months later. After 3 months, both one-stage and two-stage implants

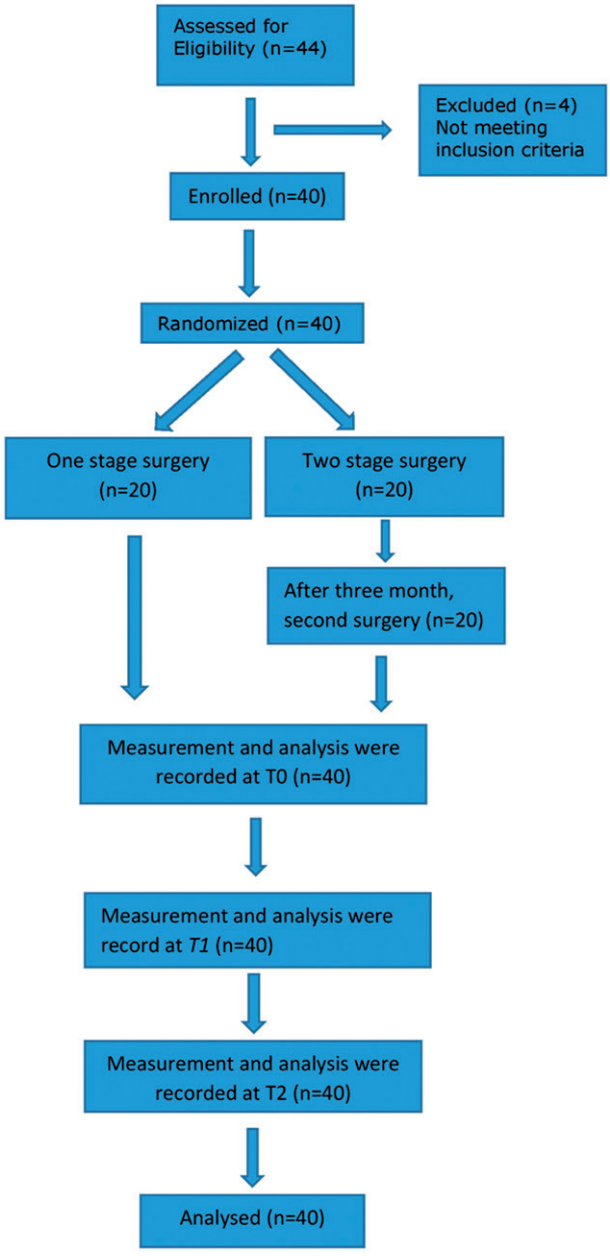

Figure 1. CONSORT flow chart of this prospective, randomized, controlled (parallel) study. The participants (n:40) were randomly divided into two groups. Group I: A one-stage surgical procedure. Group II: two-stage surgical procedure.

were loaded. Patients in both groups were enrolled in a monthly periodontal/peri-implant maintenance program after abutments were connected; full mouth scaling was performed around all natural teeth and implant surfaces. Oral hygiene instructions regarding regular tooth brushing were provided and patients were encouraged to floss their teeth and peri-implant surfaces daily. No implant failures or adverse were reported during the study.

Clinical measurements

The clinical measurements were performed by the same periodontist (TTY). Regarding clinical parameters of PD [18], mPI [19], mGI [20] and mBI [19] were recorded to evaluate the clinical status of the dental implants. All measurements were performed at four sites around each dental implant before loading, 3 months after placement of the implant (T0) and after loading in the third (T1) and sixth (T2) month. The median of the four measurements at each implant was used for statistical analysis. A Williams periodontal probe was used for clinical measurements.

Radiologic evaluation

Radiologic evaluations were conducted by the same periodontist (TTY). Image analysis was performed using KaVo 3D eXam Vision software (KaVo Dental GmbH, Biberach an der Riss, Germany). ABLR values were measured in millimetres from a fixed reference point on the implant (implant shoulder to the most coronal position of the crestal bone contacting the implant). All measurements were performed at four sites (mesial, distal, buccal and lingual) around each dental implant, at T0 and T2. The four values were then averaged for each dental implant.

PICF sampling and determination of PICF IL-1β

PICF sampling was performed three times using previously described methods at T0, T1 and T2 [15]. The mPI was recorded before PICF sampling. Supragingival plaque was carefully removed using sterile curettes, and then surfaces were mildly dried and isolated using cotton rolls to reduce

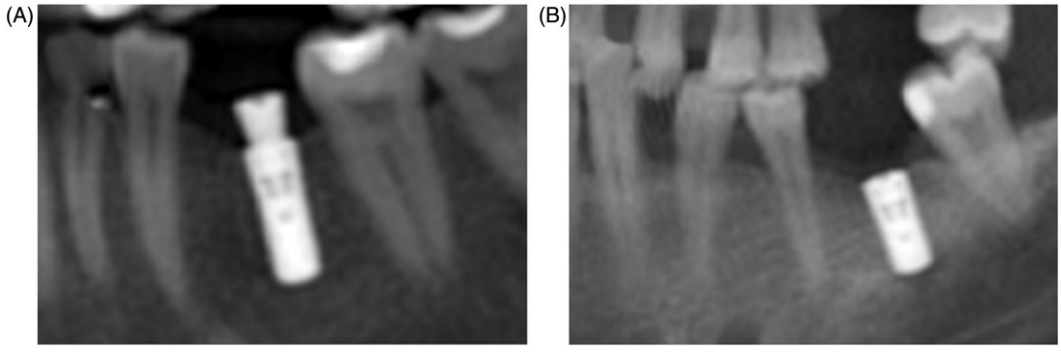

Figure 2. Twenty tissue-level (platform switching) (A) and 20 bone-level (B) dental implants 12 mm in length and 4.8 mm in diameter were inserted in the present study.

any contamination by plaque and saliva. Filter paper strips (PerioPaper, Oraflow, Inc., Plainview, NY) were gently inserted into the peri-implant crevice for 30 s at the mesial, distal, buccal and lingual sites of the implant. Papers with visible blood contamination were discarded. To eliminate the risk of evaporation, the four strips with PICF were immediately placed in sterile, firmly wrapped Eppendorf tubes and stored at −20 °C until the day of laboratory analysis. The IL-1β concentration at each dental implant was determined using an IL-1β enzyme-linked immunosorbent assay (ELISA) kit (Thermo Fisher Scientific, Inc., Waltham, MA) according to the manufacturer's instructions and using human recombinant standards. The assay sensitivity of IL-1β is 1 pg/mL and assay ranges between 3.9 and 250 pg/mL.

Statistical analysis

The sample size was predicated by assuring that the primary study objective had adequate power to assess the non-inferiority hypothesis. Under these assumptions, PROC POWER (SAS Version 9.2, SAS Institute, Inc., Cary, NC) required a sample size of 18 evaluable subjects in each treatment group. The data outside the confidence interval of the mean value were considered as outlier. Therefore, a sample size of 40 subjects was considered sufficient to meet the primary objective of this study. Although the study was powered for the primary outcome variable, the secondary outcome variables each retained 90% power to demonstrate non-inferiority, assuming that the treatments were truly equal.

The assumption of normal distribution of the data was analysed using the Kolmogorov–Smirnov test, and the homogeneity of the data was analysed using Levene's test. A repeated measures analysis of variance was used for within-group comparisons of the repeated measures at three different times, and a Bonferroni multiple comparison test was used to determine the difference between the results of each period. The relationship between the variables was investigated using the Spearman rank correlation analysis. Intergroup differences were analysed using a two-sample *t*-test; a p value$<.05$ was considered as statistically significant. The association between the IL-1β and the ABLR was analysed with univariate logistic regression models.

Results

The mean age of the patients (12 males, eight females in Group I, 12 males, eight females in Group II) was 30.75 ± 8.58 years in this study (Table 1).

Table 1. Demographic characteristics of the participants.

	One stage	Two stage	*p*
N	20	20	1.00
Age	30.75 ± 8.58	37.00 ± 11.814	.63
Gender	12 male	12 male	1.00
	8 female	8 female	1.00

Analysis of clinical parameters

Clinical parameters are summarized in Figure 3. Significant differences were found in the PD between T0 and T2 in Group I ($p = .009$), and in the mBI between T0 and T2 ($p = .023$) (Figure 3). The mean PD values were significantly

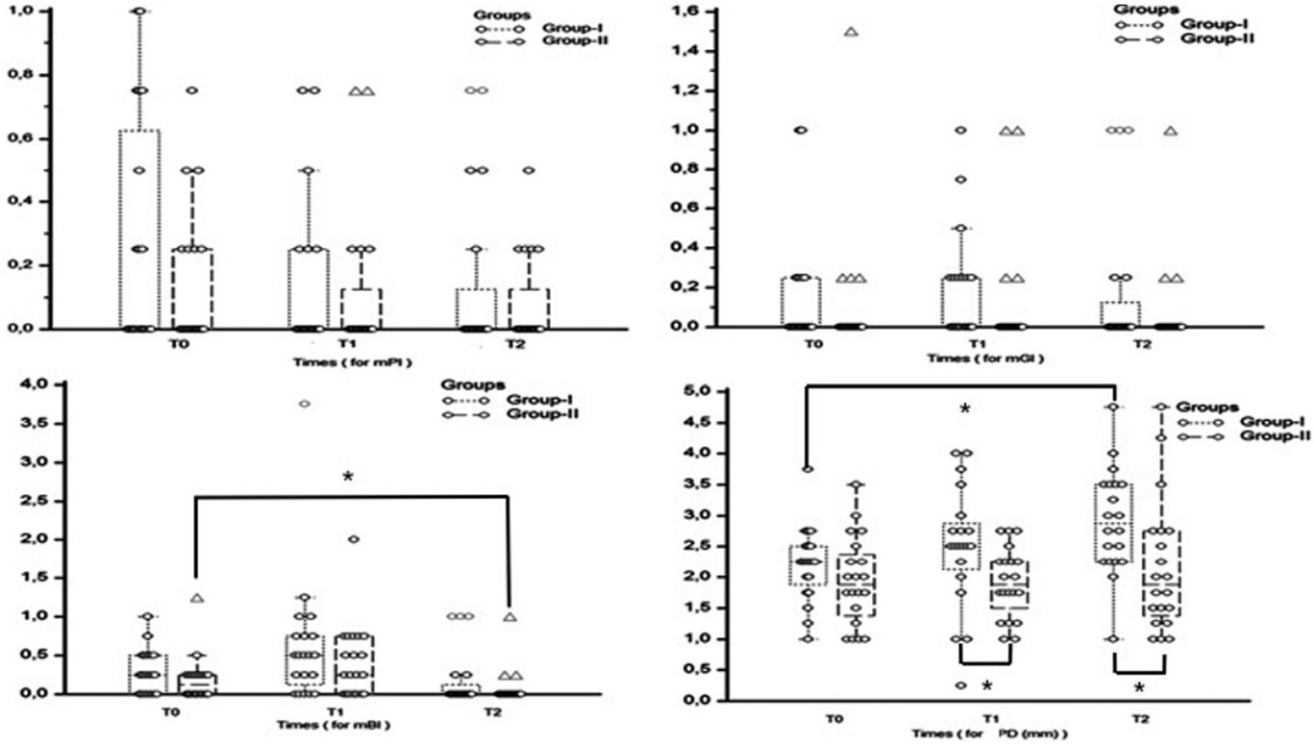

Figure 3. The time-dependent change results of the clinical parameters. The different symbols (circle and triangle) within the same columns show outlier values. Statistically significant differences were found in the PD between T0 and T2 in Group I ($p = .009$), and in the mBI between T0 and T2 in Group II ($p = .023$). The mean values of PD between Group I and Group II were significantly different [T1 ($p = .028$); T2 ($p = .016$)]. $^{*}p < .05$.

different between Group I and Group II [T1 ($p = .028$); T2 ($p = .016$)] (Figure 3).

Analysis of ABLR

Analysis of the time-dependent changes in ABLR revealed a significant difference between the mean ABLR values for T0 and T2 in Group I ($p = .005$) (Table 2). There were also statistically significant correlations between the mPI and ABLR at T2 in Group I. Although ABLR values were higher in Group I than Group II at both T0 and T2, these differences were not statistically significant (Table 2).

Analysis of the PICF IL-1β levels of Group I and Group II

The time-dependent changes in PICF IL-1β levels were not statistically significant in Group I or Group II ($p > .05$) (Figure 4). Intergroup comparisons revealed that the average values for IL-1β levels at T0, T1 and T2 in Groups I and II were not statistically significant ($p > .05$) (Figure 4). There were significant correlations in Group I between the mGI and IL-1β levels at T1; the PD and IL-1β levels at T2; and the mBI and IL-1β levels, and the PICF and IL-1β levels at T2 in Group I. There was also a significant correlation in Group II between the PICF and IL-1β levels at T0, the PD and IL-1β levels at T1, and the PD and IL-1β levels at T2 in Group II. This study did not detect significant associations between ABLR and IL-1β in Groups I and II ($p > .05$) (Figure 5).

Table 2. The comparison of time-dependent change results of ABLR, both intra-group and inter-group.

	ABLR T0 Mean ± SD	ABLR T2 Mean ± SD	*p*
I. Group ($n = 20$)	4.11 ± 6.11	6.22 ± 6.66	.005*
II. Group ($n = 20$)	3.69 ± 4.34	4.81 ± 4.31	.365
p	.803	.37	

ABLR (%): alveolar bone loss rate.
All data presented are mean ± standard deviation (SD) values.
*$p < .05$.

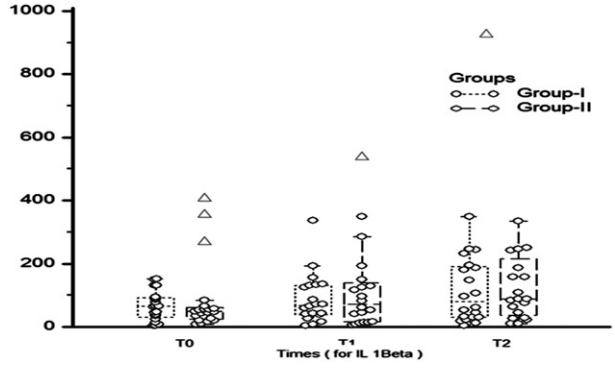

Figure 4. The level of IL-1β in Group I (A) and Group II (B). The different symbols (circle and triangle) within the same columns show outlier values. The time-dependent changes in PICF IL-1β levels were not statistically significant in Group I or Group II ($p > .05$). No statistically significant difference was detected between Group I and II ($p > .05$).

Discussion

In the present study, dental implants inserted using one- or two-stage surgical procedures were compared using clinical, radiological and biochemical evaluations. This study showed that the PD was significantly higher in Group I. Although there were no statistically significant differences between the groups, ABLR mean values were higher at T0 and T2 in Group I than in Group II; when intra-group changes were evaluated, ABLR mean values at T0 and T2 differed significantly in Group I. There were no differences in PICF IL-1β levels between Groups I and II at any time point.

Becker et al. reported that increased PD is a critical indicator, suggesting a high risk of an infection developing in the implant mucosa [21]. In this study, when inter-group clinical parameters were analysed, the only statistically significant difference was observed in the PD values at T0 and T2 between the one-stage and two-stage dental implants at T1 and T2. However, there was no difference in ABLR values between the groups, showing that the differences were related to the soft tissue around the dental implants and implant structure or to the dental implant surgery procedure. The differences in PD were likely to be due to the different implant designs: one has a neck, one does not. In Group I, the dental implant's neck was the platform switch. Bone level dental implants were used in Group II. The high PD value in Group I may not be related to any pathological condition. This result also suggests that different surgical techniques affect periodontal parameters such as the PD; this may also explain why implant structure (tissue level or bone level) is affected by the PD. A high PD is expected in a two-stage surgical procedure. In two-stage surgery, keratinized tissue may reduce the probability of implant exposure during healing [22]. Contrary to our results, Nemli et al. reported that one-stage implants had significantly lower PD results than two-stage implants [23].

One of the most important factors for long-term implant success is the level of bone crest surrounding the implant. Crestal bone loss can lead to increased bacterial accumulation, resulting in peri-implantitis. Different approaches have been described in the literature for preservation of the marginal bone height, including platform switching and modifications in alveolar crest placement level [24,25]. In platform switching, it was assumed that by inward positioning of the implant/abutment junction a biological width was established and therefore bone resorption at the implant-abutment junction associated with the inflammatory cell infiltrate was reduced [26,27]. This was supporting the present higher ABLR values detected in Group I and in this group's higher ABLR values may be due to the different design of the fixture itself. The osseointegration process in the mouth area is completed after dental implants are inserted in the one-stage procedure, and this issue raises questions about this technique. Moreover, Gulati et al. suggested that the amount of alveolar bone loss increases, particularly when this process is completed in the oral medium [7]. Similar to our results, Enkling et al. reported that no differences between bone loss associated with healing were found between one- and two-stage surgical procedures [28].

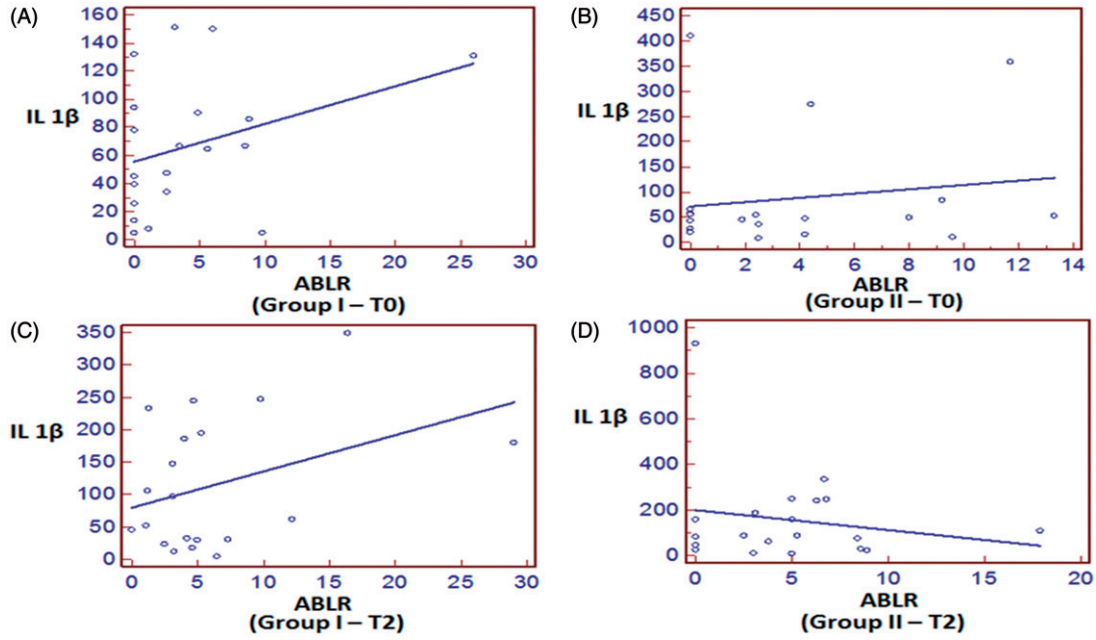

Figure 5. The relationship between IL-1β and ABLR in Group I (A, C) and Group II (B,D) at T0, T2. No significant association was detected between ABLR and IL-1β in both groups.

Previous studies have determined that ABLR is greater in one-stage implants because there is a micro space or a cavity at the bone level of the dental implants during two-stage surgical procedures [29,30]. Ericsson et al. inserted dental implants by using one- and two-stage surgical procedures in patients who had lost one tooth from the maxillary anterior region. At the one-year follow-up, the clinical findings showed that, the amount of alveolar bone loss in the one-stage surgical procedure group was 0.08 mm; there was 0.05 mm alveolar bone gain in the two-stage surgical procedure group [31]. Conversely, Nemli et al. reported that one-stage implants exhibited significantly lower bone loss than two-stage implants [23]. Similar to the present study, Weber et al. evaluated the changes in levels of the alveolar bone between one- and two-stage implants and found that the level of alveolar bone loss was similar for both surgical procedures [32]. Cecchinato et al. found that the peri-implant bone-level change did not differ between one- and two-stage surgical procedures during 1- and 2-year of follow-ups [33].

In our study, the ABLR in Group I differed significantly between T0 and T2 in Group I. There were no differences between groups at T0 and T1. Accordingly, the difference between the two groups in this study is thought to be related to the dental implant surgery procedure, the shape of the implant, and the neck of the implant structure.

In the present study, the probable relationship between radiological and clinical parameters was analysed. There was a positive relationship in Group I between the mPI and ABLR at T2. Furthermore, there was a positive relationship in Group II between the keratinized soft tissue level and ABLR at T0. Heckmann et al. [34] reported that the bone loss around dental implants is related to the mBI, PI and exudates, and they also reported that keratinized mucosa loss causes this inflammatory variance.

The laboratory findings in the present study revealed that the PICF IL-1β level increased over time in both groups, but this increase was not statistically significant. This result is congruent with studies that have confirmed that the PICF IL-1β level increases over time [35]. The difference between intergroup PICF IL-1β levels was not statistically significant. Interleukin levels were not statistically different in this study; finding may be related to the low number of samples. IL-1β is a pro-inflammatory cytokine that plays a major role in periodontal destruction [9,15]. The biologic effects of IL-1β depend on its tissue concentration. In periodontal tissue, IL-1β causes bone destruction and induces the production of tissue destructive-proteinases [9]. This result was related to the ABLR value; PICF IL-1β level is increased, resulting in time such as both ABLR Group I and Group II, but this increase was not significant between groups for PICF IL-1β or ABLR. Similarly, to this study, Ata-Ali et al. [36] reported a significant relationship between PICF IL-1β levels and the clinical inflammatory response in peri-implant tissues.

According to our study protocol, both groups had monthly periodic follow-ups, and oral hygiene was maintained by cleaning the plaque from the peri-implant area. This periodic interference reduces the risk and severity of infection in the peri-implant area. Therefore, because of the similarity of the quantitative PICF IL-1β levels in both groups, the differences between the groups were not significant. Our findings related to PICF IL-1β levels are congruent with studies that have shown the relationship between periodontal parameters and PICF IL-1β levels, and are also congruent with their interpretations [37–39].

A limitation of this study was that the follow-up period was limited to six months, and therefore we evaluated the short-term outcomes of different surgical procedures. Long-term clinical follow-up studies may be useful. This study could be planned as a split-mouth study to eliminate possible individual factors. The short-term results of this study revealed that two-stage implants showed comparable clinical results to one-stage implants. The PD was significantly higher

in Group I, and the ABLR mean values for T0 and T2 were significantly different. Although there were no statistically significant differences between the groups, the ABLR mean values were higher in Group I and there were no differences in PICF IL-1β levels between Groups I and II. The present results suggest that two-stage surgical procedures improve the success rate of dental implants. However, advanced studies related to this subject are necessary.

Acknowledgements

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Declaration of Helsinki Declaration and its later amendments or comparable ethical standards.

Disclosure statement

The authors report no conflicts of interest related to this study. The authors alone are responsible for the content and writing of this article.

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