A Randomized Controlled Clinical Trial of Edentulous Patients Treated with Immediately Loaded Implant-Supported Mandibular Fixed Prostheses

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ABSTRACT

Purpose: A 1-year blinded two-arm parallel randomized controlled clinical trial was conducted to test the null hypothesis that immediate loading of four dental implants between the mental foramina with a fixed prosthesis has no benefits compared with the conventional loading technique in terms of implant success and clinical function.

Materials and Methods: Forty-five patients, completely edentulous in the mandibles seeking implant-supported prostheses at the Faculty of Dentistry, University of Toronto, were recruited. Four TiUnite dental implants (NobelBiocare®, Göteborg, Sweden) were placed following the one-stage surgical protocol. Immediately after surgery, the patients were randomly assigned to either study arms by a third independent party. In the experimental arm (EA), existing mandibular denture was converted into an interim implant-supported fixed bridge (ISFB) on the same day of surgery. In the control arm (CA), the mandibular denture was hollowed out and relined with a soft tissue reline. The implants were loaded with the permanent ISFB at least 3 months postsurgery. Patients were assessed by a calibrated independent investigator at 2, 6, and 12 months following completion of treatment.

Results: A total of one hundred sixty implants were placed. Due to anatomical limitations, one patient was excluded from the study. Four patients in the EA did not receive intervention as allocated and were transferred to the CA. Implant success rate was comparable between the two arms and exceeded 96%. Marginal bone loss was statistically significantly more in the immediate loading arm, −0.296 mm versus −0.037 mm (intention to treat: $p = .002$; per protocol: $p = .021$). The relatively early intervention and insertion of the final prosthesis in the immediate arm, when bone healing and remodeling process had not yet been completed, might explain the difference in the amount of bone loss.

Conclusion: Immediate loading of four dental implants with a fixed prosthesis in the edentulous mandible is a feasible treatment option and leads to a substantial improvement in perceived oral health status.

KEY WORDS: edentulous mandible, fixed implant prosthesis, immediate loading, implant, randomized controlled trial

INTRODUCTION

The high success rate and consequently the widespread use of dental implants for prosthetic rehabilitation have led to revision of numerous aspects of the original treatment protocols including the timing of implant loading.[1,2] Immediate implant loading is defined as implant placement with primary stability and prosthetic loading with a provisional prosthetic tooth at the same clinical visit.[3] It might be speculated that the ultimate goal of the immediate loading protocol is to reduce the number of surgeries, which would clearly lead to decrease in morbidity and would shorten the time frame for both surgery and prostheses insertion. The latter should therefore translate into faster achievement of masticatory functional occlusion and improved aesthetics without affecting the high success rates that have been reported for endosseous dental implants. As laudable as

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these concepts are, in order for immediate loading protocols to be deemed successful, consideration should be given to several key factors pertaining to the surgical and prosthodontic aspects of immediate loading protocol. These factors include primary implant stability,[4–6] implant geometry and surface topography integration,[7–9] surgical technique,[10,11] bone quality and quantity,[12–15] prosthesis design, and occlusal forces.[16–20]

In light of the potential risks outlined above, it is understandable that the earliest trials focused on the use of immediately loaded implants were undertaken with caution. Some investigations were done so that in addition to the placement of implants that were going to be loaded immediately, submerged implants were placed to act as a backup in case of failure of the immediately/early-loaded ones so as to reduce the potential for postsurgical morbidity.[16,21,22]

The more recent short- and medium-term studies have reported invariably higher success rates (90–100%) for immediately loaded implants when combined with fixed prostheses.[23–25] These high success rates were attributed to several factors, such as ensuring balanced occlusion and equal distribution of forces between the loaded implants especially when incorporating cantilevers in the prosthesis designs.[17,23,26–29]

Moreover, in order to reduce surgical morbidity as well as costs of implants (associated both with treatment and posttreatment), there has been increasing interest in the reduction of the number of implants for the support of prostheses. Indeed, this too has now become an important area of study with several studies focused on the determination of how many fixtures are necessary to provide successful support of their overlying prostheses.[17,21,24,26,30,31]

As mentioned above, a number of clinical studies have attempted to investigate the efficacy of the immediate loading concept as a feasible treatment modality. However, most studies had no control groups, to which outcomes of the immediate loading treatment could be compared, thus limiting the validity of the conclusions reached. More importantly, very few of these are well-reported randomized controlled clinical trials. We therefore have decided to conduct the current randomized controlled trial (RCT) with the following objectives:

1 to determine whether four dental implants in the mandible can be loaded immediately, thereby providing successful implant-supported fixed prostheses;
2 to evaluate implant success, clinical function, and prognosis of implant-supported fixed prostheses.

The *null* hypothesis is as follows: there is no increase in the failure rates of prostheses and immediately loaded implants in comparison with implants placed with a delayed loading protocol.

MATERIALS AND METHODS

The sample size was calculated by comparing means and standard deviations (SDs) of bone loss around implants that were loaded immediately or implants that were loaded after osseointegration has been achieved (i.e., delayed loading). Mean peri-implant bone loss for immediately loaded implants was based on a previous study that presented bone loss data based on 60 implant measurement sites from 12 patients.[32] The mean value for peri-implant bone loss during the first year was 0.9 mm (SD 1.1 mm). Subsequently, these data were compared with bone loss results for the mandible from another study. The mean bone loss during the first year of loading was 0.09 mm (SD 0.55 mm).[28]

The study power set at 80% and a significance level of $p = .05$. Accordingly, it was estimated that a minimum of 18 patients were required per arm. Thus, the proposed number of 22 patients per arm was chosen to allow for dropouts during follow-up.

This was a parallel RCT. The Human Ethics Board of the University of Toronto approved the treatment protocol. Forty-two subjects (24 females and 18 males) were recruited from new patients seeking treatment at the Faculty of Dentistry, University of Toronto, Canada. Both treatment protocols were discussed with the patients and a consent form was signed by the patient and countersigned by a witness.

The two study arms consisted of the experimental arm (EA), where patients underwent the immediate loading protocol, and the control arm (CA), where patients were treated using the standard delayed loading protocol.

Randomization of Patients into the Two Study Arms

Patients were assigned randomly to one of the two study arms using a randomization list that was generated by an independent party. A sealed numbered randomization envelope assigned to each patient was opened only when the implant-placement surgery had been completed in

order to eliminate any possible operator bias during surgery. Following opening of the randomization envelope and the allocation of the patient to either of the study arms, the investigator signed and dated the envelope.

Preoperative Protocol for Both Study Arms

Prior to implant surgery, each patient and each proposed prosthetic site was assessed by a prosthodontist. Inclusion and exclusion criteria are listed in Table 1. They were similar to those used for selection of patients in the past studies.[23,33–35]

Clinical Intervention: Prosthesis Preparation, Surgical Protocol, and Prosthodontic Protocol

Prosthesis Preparation. The current maxillary and mandibular dentures were optimized. If they were found to be inadequate, new prostheses were fabricated.

Surgical Protocol. The surgical protocol followed is the standardized, validated one. The surgery was carried out under local anesthetic and antibiotic coverage. A crestal incision in the mandible was made, extending about 1 cm beyond the mental foramina. Then, the mucoperiosteum was elevated and the implant site was prepared. Four TiUnite dental implants (NobelBiocare®, Göteborg, Sweden) were placed between the mental foramina.

Immediately following surgery, the initial stability of the implants was assessed by hand testing using a torque wrench (torque value ≥35 Ncm).

Right after surgery, allocation to either arm of the study was determined using the randomization envelope.

Experimental Arm (EA). Permanent multiunit abutments (NobelBiocare®) were installed on the four implants and torqued to 20 Ncm with a standardized manual torque wrench, and the soft tissues were then sutured. The location of the implants was indicated on the mandibular denture using Fit Checker (GC America®, Alsip, IL, USA). Then, four multiunit temporary copings (NobelBiocare®) were installed on the implants, and the surgical site was protected using rubber dam. The temporary copings were picked up using the mandibular denture as a tray in cold-cured acrylic resin (ProBase, Ivoclar Vivadent Inc., Mississauga, ON, Canada). In order to minimize the amount of exothermic heat generated during the curing process, a minimum amount of acrylic resin was used, and intraoral water coolant was circulated constantly. The mandibular denture was then converted into an interim implant-supported fixed prosthesis. This was inserted the same day as implant-placement surgery. The occlusion was evaluated and refined when necessary. The fabrication of the permanent implant-supported prosthesis was initiated 2 weeks after surgery following previously established protocols.[2]

Control Arm (CA). Healing abutments (NobelBiocare®) placed on the four implants and the soft tissues were then sutured. The mandibular denture was hollowed out and relined with a soft tissue reline material (COE-SOFT™, GC America®). The soft tissue reline material was adjusted so that it was not resting on the healing abutments in order to prevent loading of the implants. The permanent implant-supported fixed prosthesis fabrication process was initiated 3 to 4 months postsurgery.

Patients were assessed regularly and in a blinded fashion by a calibrated, independent investigator at 2, 6, and 12 months following completion of treatment.

During follow-up visits, prosthesis and implant success was evaluated using the criteria proposed by Zarb and Albrektsson.[36] Osseointegration was evaluated by torquing the implants with a standardized torque wrench set at 20 Ncm. If an implant was shown to be mobile or painful while torquing, it was considered a failure and removed.

Radiographic Imaging and Bone Measurements

Standardized long-cone intraoral periapical radiographs were used to assess peri-implants bone levels. These radiographs were taken at the insertion of the permanent mandibular implant-supported fixed prosthesis stage (baseline) and during the 12-month recall visit.

Management of Radiographs. Photographs of the individual radiographs were taken with a digital camera (Nikon Coolpix 995, Melville, NY, USA) mounted on a copy stand for stability at 8″ distance from the radiograph. The illuminated area was masked off, leaving only the area for the size of a periapical radiograph uncovered, allowing for accurate light meter reading for each individual density.

TABLE 1 Patients' Inclusion and Exclusion Criteria

Inclusion Criteria
1. The patient is at least 18 years of age or older.
2. The patient is edentulous in the mandible and subjectively desires an implant-supported screw-retained fixed prosthesis.
3. The teeth at the implant site have been extracted or lost at least 3 months prior to the date of implant placement.
4. No guided bone regeneration or guided tissue regeneration procedures had been performed at the implant sites.
5. The bone quality and quantity allow placement of four TiUnite dental implants (NobelBiocare®), of at least 3.75 mm in diameter and 10 mm in length between the two mental foramina without the use of concurrent bone augmentation techniques.
6. The patient committed to participating in the 3-year follow-up examinations of this study.

Exclusion Criteria	
Primary exclusion criteria	
a. Systemic exclusion criteria	*b. Local exclusion criteria*
1. Presence of a medical condition requiring prolonged use of steroids.	1. Presence of a local inflammation, including untreated periodontitis.
2. Presence of a history of leukocyte dysfunction and deficiencies.	2. Presence of a history of local irradiation therapy.
3. Presence of a history of bleeding disorder.	3. Presence of osseous lesion.
4. Presence of a history of neoplastic disease requiring the use of radiation or chemotherapy.	4. Presence of any unhealed extraction sites (less than 3 months postextraction of teeth in intended sites).
5. Presence of a history of renal failure.	5. Presence of persistent intraoral infection.
6. Presence of a metabolic bone disorder.	6. Inadequate oral hygiene or lack of motivation for adequate home care.
7. Presence of a history of uncontrolled endocrine disorder.	
8. Presence of a physical handicap that would interfere with the ability to perform adequate oral hygiene.	
9. The use any investigational drug or device within the 30-day period immediately prior to implant surgery.	
10. Presence of a history of drug abuse.	
11. Heavy smokers (>20 cigarettes per day) or cigar equivalents or chewing tobacco equivalents.	
12. Presence of conditions or circumstances, which in the opinion of the investigator, would prevent completion of study participation or interfere with the analysis of study results (e.g., history of noncompliance or unreliability).	
13. Advanced age and/or compromised general health such that the long surgical and prosthodontic appointments required for the standard implant-supported fixed prosthesis protocol are too demanding.	
14. Presence of psychiatric contraindications (Blomberg and Lindquist, 1983). These include psychotic syndromes, severe character disorders, and neurotic syndromes. Patients who might demand unrealistic outcomes were also excluded from participation in this investigation.	
Secondary exclusion criteria (*at implant-placement surgery*)	
1. Lack of sufficient bone for the procedure.	
2. Inability to place implants according to protocol requirements.	

The resultant images were then processed stored and measured using public domain software (ImageJ, U.S. National Institute of Health, Bethesda, MD, USA) on a DELL Inspiron 640 m computer using the technique described and validated previously.[37]

Crestal Bone Measurements. The measurement of bone level was performed by a calibrated investigator in a blinded fashion (i.e., blinded as to patient name and the chronology of the radiographic series by random presentation of the implant images). The mean of two

measurements for each site was utilized for statistical analysis of changes in crestal bone level.

The vertical distance in millimeters from the apical edge of the implant collar to the most apical initial point of contact observed between the implant and the bone was measured at the mesial and distal sites. The effects of any misalignment of the film plane relative to the implant long axis on apparent crestal bone position were accounted for by using the known thread pitch of the implant to calibrate the measurements for each implant.

Statistical Analysis

Chi-square and Fisher's exact tests of association were used to evaluate differences between the treatment arms with respect to demographic variables. Students' *t*-tests were used to determine significant differences between treatment arms with respect to continuous variables: age, duration of edentulism in the maxilla and mandible for all patients, number of years smoke-free, and number of years smoked for former and current smokers, respectively.

To assess the primary outcome, tests of noninferiority were used. A margin of equivalence was set at 1 mm of bone loss. Variance estimates for bone loss were calculated, adjusting for within-patient correlation using Taylor linearization, to prevent artificially small variance estimates.

All analyses comparing the two treatment arms were conducted using both the Intention To Treat (ITT) and the Per Protocol (PP) analyses.

The SAS 9.1.3 (Cary, NC, USA) software was used. Statistical significance was determined when p was $<.05$.

RESULTS

Patient Demographics

The process of participants' enrollment, allocation of interventions, withdrawals, and timing of outcome measures is shown in the Consolidated Standards of Reporting Trials (Figure 1).

The mean (±SD) age of the patients was 61.5 ± 10.35 years. Twenty-four (57.5%) of the participants were female and 18 (42.5%) were male. Demographic data of the patients in both study arms are shown in Figures 2 and 3. Patient characteristics between the two treatment arms did not differ significantly, suggesting successful randomization.

The majority of patients had a conventional complete denture in the maxilla (32 patients), seven had a removable partial denture, and two had implant-supported fixed prostheses.

Fifty-five percent of the patients suffered some chronic medical condition and were on medications. Current smokers accounted for 20.0% of the patients. Among smokers, 65.5% smoked one pack/day, and the mean years of smoking were 29.39 years (Figure 3.3).

Out of the one hundred sixty-eight implants placed, one hundred sixty (95.2%) were placed by the same surgeon. One prosthodontist restored 85% of the patients.

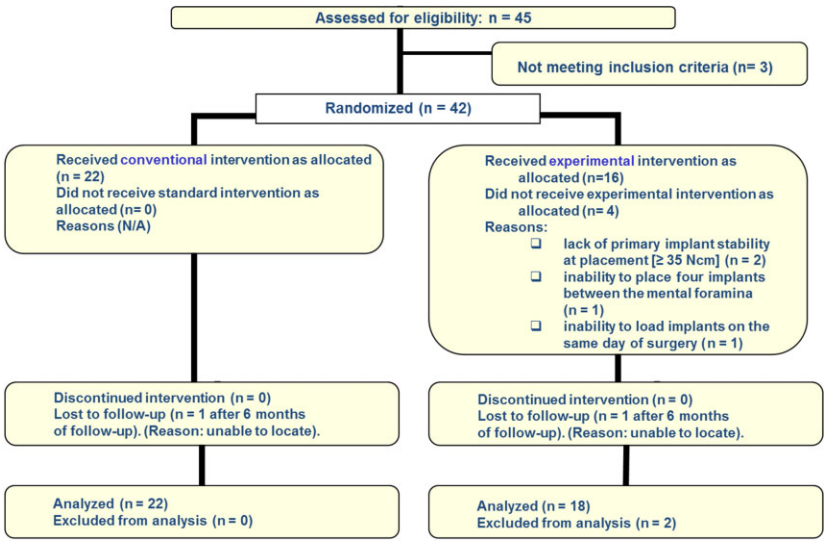

Figure 1 Consolidated Standards of Reporting Trials flow diagram of participants, withdrawals, and timing of outcome measures.

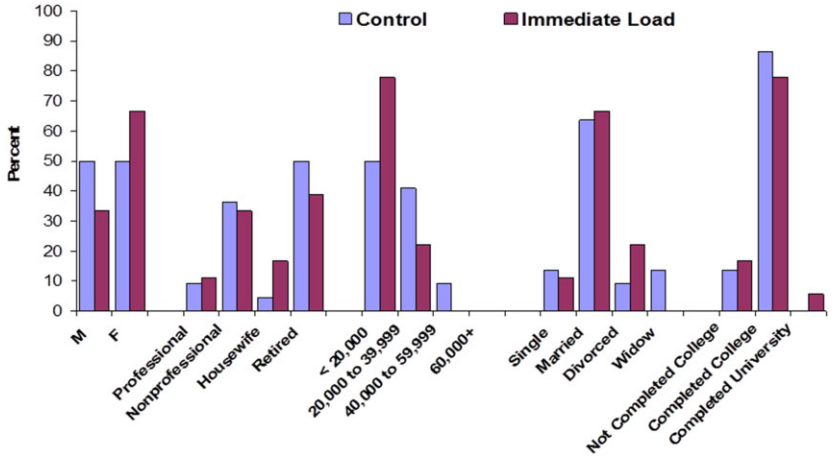

Figure 2 Patient demographic data (gender, social status, average annual income, marital status, education level).

The Lekholm and Zarb classification was used to assess jawbone morphology. Eighty-three percent of the patients had bone quality type 2 or 3 (Figure 4). No or minor (<5 mm) reduction of cortical bone was required to place the dental implants.

Patient Exclusion and Dropout

In one patient, the surgeon was not able to place all four implants between the mental foramina due to anatomical limitations. Consequently, the patient was excluded from the study and received an implant-supported mandibular overdenture. One implant in one patient and two in another failed the initial stability test. As a result, it was planned that the patients would be restored following the conventional loading protocol. One of the two patients, however, lost the implant that failed the initial stability test 6 weeks postsurgery and was lost to follow-up. Another male patient developed a sudden gag reflex right after implant-placement surgery and showed signs of anxiety, and so the prosthodontist was not able to implement the immediate loading protocol, i.e., load the implants on the same day of surgery. The patient was reassured and was treated following the conventional loading protocol.

One implant failed in two patients in the immediate load arm and two implants failed in one patient in the control arm. Another implant failed in one patient who was treated following the conventional protocol because

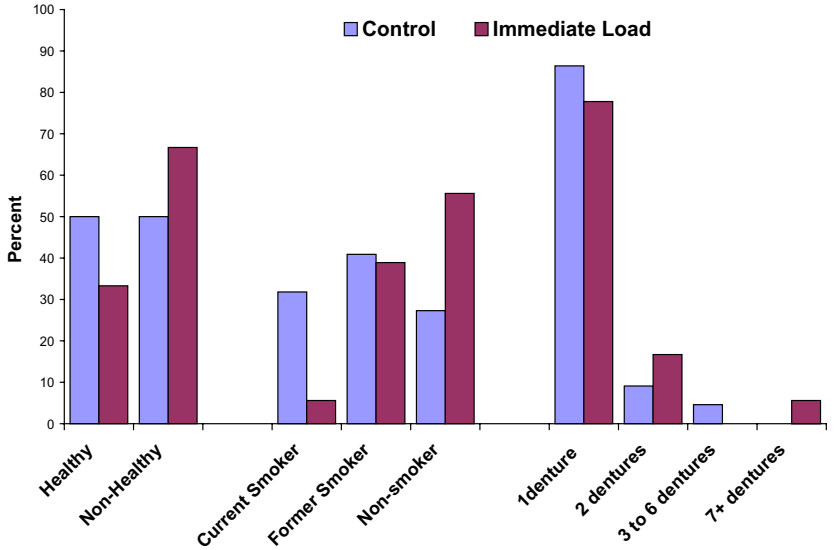

Figure 3 Patient demographic data (health status, smoking history, and number of dentures).

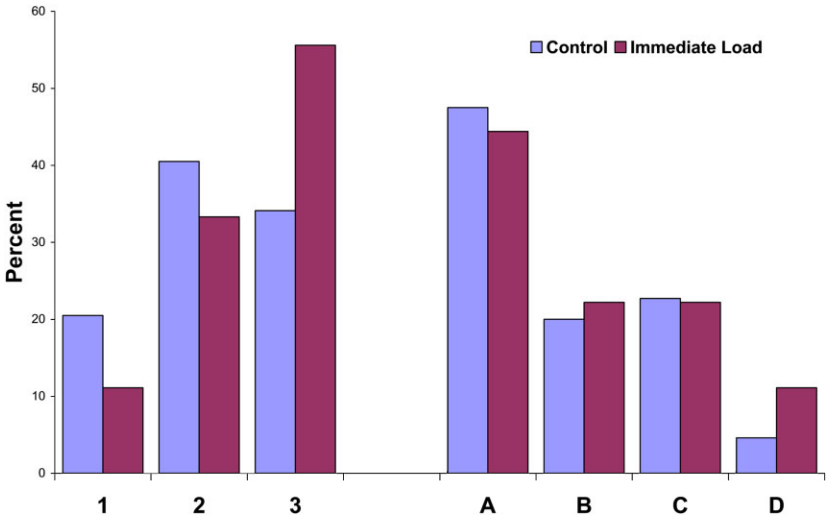

Figure 4 Bone morphology of anterior mandible (bone quality: 1, 2, and 3; bone quantity: A, B, C, and D).

of the inability to implement the immediate loading protocol as mentioned previously. All implant failures occurred between 6 and 8 weeks postimplant-placement surgery. The patients were not excluded from the study, and all lost implants were replaced and loaded with implant-supported fixed prostheses. There were no implant failures following insertion of the permanent fixed prostheses.

Implant Success Rate

Overall, one hundred sixty implants were placed between the mental foramina; one hundred thirty-five were 3.75-mm-wide implants, one was 3.3 mm wide, and the remaining 24 implants were 4 mm in diameter. Implant length ranged between 10 and 15 mm, with the majority being 15 mm (75.6%). No statistically significant difference was found between the two arms in terms of implant diameter distribution ($p = .103$).

The implant success rates are shown in Table 2. No statistically significant differences were observed between the two arms.

Bone loss analysis for the two arms of the study showed that there was statistically significantly more bone loss during the first year of loading in the immediate loading arm (mean −0.296) as compared with the conventional loading one (mean −0.037) (Table 3) (Figure 5). This significant difference was confirmed when both PP and ITT analyses were carried out ($p = .021$ and $p = .002$, respectively). Moreover, there was no significant interaction between site (distal vs mesial) and intervention arm (Figure 6).

Except of the positive correlation between patient's age and bone loss in the immediate loading arm ($p < .010$), there were no significant correlations between bone loss and any of the patients' demographic variables when each arm was analyzed separately and when data from both arms were pooled together (Table 4).

TABLE 2 Implant Success Outcome 1 Year Postloading

	ITT		PPA		
Implant Failure	Control	Immediate	Control	Immediate	Total
No	93 (96.88%)	62 (96.88%)	86 (97.73%)	69 (95.83%)	155
Yes	3 (3.13%)	2 (3.13%)	2 (2.27%)	3 (4.17%)	5
Total	96	64	88	72	160

Fisher's exact test, $p = .6581$.
ITT, intention to treat; PPA, per protocol analysis.

TABLE 3 Mean Peri-implant Marginal Bone Loss 1 Year Postloading (mm)

	Control				Immediate				
	Sites	Mean Bone Loss	Lower CL$^{\Delta}$	Upper CL$^{\Delta}$	Sites	Mean Bone Loss	Lower CL$^{\Delta}$	Upper CL$^{\Delta}$	*F* Value *p* Value*
Overall bone loss	148	−0.037	0.104	−0.178	121	−0.296	−0.078	−0.514	Overall effect of site ITT: $F(1,35) = 11.27$ $p = .002$ PPA: $F(1,35) = 5.80$ $p = .021$
Distal	72	−0.031	0.156	−0.218	60	−0.267	−0.021	−0.512	Site by intervention interaction
Mesial	76	−0.042	0.104	−0.188	61	−0.325	−0.101	−0.549	ITT: $F(1,35) = 0.09$ $p = 0.761$ PPA: $F(1,35) = 0.021$ $p = .885$

CL$^{\Delta}$, CL = Confidence Level.

DISCUSSION

The success rate of the immediately loaded TiUnite dental implants 1 year postloading was around 96%, while the prosthesis survival rate was 100%. This figure was not significantly different from the success rate of the conventionally loaded TiUnite dental implants (97%) and is comparable with what has been reported in the literature.[23,38–40] Furthermore, the reduction in the number of immediately loaded mandibular implants from six to four in the current study did not lower the success rate for the implants. In fact, the success rate reported in this study was comparable with success rates reported in the literature when five or six dental implants were immediately loaded.[16,39,41–45] Consequently, our findings show that four TiUnite dental implants can be loaded immediately with fixed prostheses in the mandible with success. It is important to stress, however, that implant placement was confined to the zone of the anterior mandible, an area that has been shown to provide the most favorable implant outcomes and prognosis.[24,25,37] This reduction in the number of implants has a significant impact on shortening treatment time, decreasing potential surgical morbidity, and reducing initial and possibly long-term costs for the patient as this usually means fewer implants and implant hardware to be used and maintained.

Five out of one hundred sixty implants placed failed. Four out of those five implants were placed in

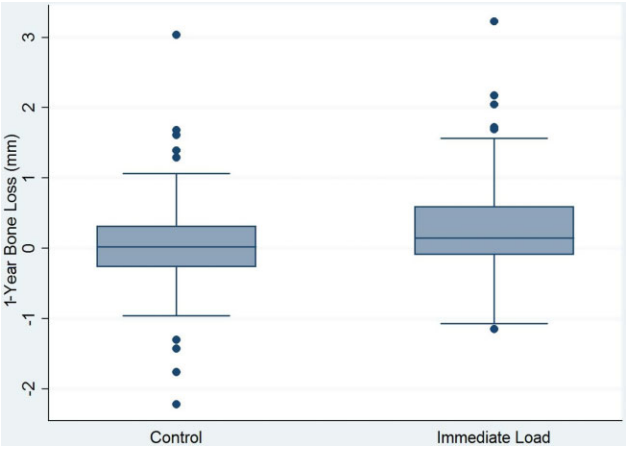

Figure 5 Mean overall peri-implant marginal bone loss 1 year postloading.

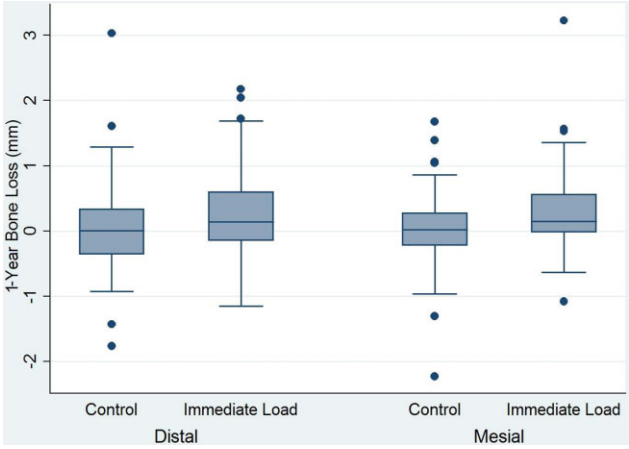

Figure 6 Mean peri-implant marginal bone loss by site 1 year postloading.

TABLE 4 Linear Regression for Overall Mean Bone Loss (mm/year) and Patients' Demographics

		Adjusted		
Factor		Beta	SE	Sig.
Intercept		−0.258	0.790	0.845
Age		0.008	0.005	0.161
Gender	Female	0.137	0.161	0.396
	Male			
Smoking history	Former/current smokers	0.160	0.137	0.303
	Nonsmoker			
Years edentulous prior to implant surgery	0 to <1 year	−0.192	0.152	0.274
	1–10 years	−0.072	0.128	0.659
	>10 years			
Implant length		−0.020	0.490	0.695
Jawbone quality*	1	−0.101	0.179	0.573
	2	−0.054	0.116	0.641
	3			
Jawbone quantity*	A	0.072	0.259	0.948
	B	0.254	0.250	0.573
	C	0.089	0.270	0.459
	D			

*Using Lekholm and Zarb classification.
SE, standard error.

type 1 bone according to the Lekholm and Zarb classification. These findings correlate with data reported by others.[46,47]

Although the difference in bone loss between the two study arms was statistically significant, bone loss of 0.296 mm during the first year of loading is well below 1 mm, the maximum acceptable amount of peri-implant bone loss suggested by Zarb and Albrektsson.[36] Furthermore, the average bone loss observed in this study is similar to that reported by other researchers.[23,29,39,48] In the immediate loading arm, the majority of the final implant-supported fixed prostheses were inserted 3 months following implant-placement surgery, while in the control arm the final prostheses were inserted within an average of 4.5 months after implant placement. The peri-implant marginal bone level baseline radiographs were taken at prosthesis insertion. The relatively early intervention and insertion of the final prosthesis in the immediate arm, when bone healing and remodeling process had not yet been completed, might explain the difference in the amount of bone loss identified when comparing the two study arms during the first year of loading.

Of note is that the use of up to 12-mm cantilevers on the distal extensions bilaterally did not compromise clinical outcomes. Careful organization of the occlusion is the most important factor to consider when planning cantilevers on immediately loaded dental implants. Group function occlusion was aimed for with lighter central point contact on the cantilever teeth.

Due to the nature of their design, randomized controlled clinical trials are generally adequate for measuring the efficacy of a given modality of treatment but not its effectiveness. This is mainly because those types of studies are carried out under "ideal" conditions. The patients included in these studies are usually those who have optimal health and are usually monitored closely over the duration of the study. In our study, however, patients were *not* excluded based on the presence of medical conditions except of those conditions that are well established to be considered as absolute contraindications for treatment with dental implants in routine clinical practice (e.g., bleeding disorder). Furthermore, we did not eliminate patients with possible risk factors for implant failure such as smoking habit (≤10 cigarettes/day) and bruxism so that this further parallels clinical practice as it were. Therefore, it might be concluded that although this is an idealize randomized controlled clinical trial, the data reported here possess external validity.

CONCLUSION

The *null* hypothesis of which there is no increase in the failure rates of prostheses and immediately loaded implants in comparison with implants placed with a delayed loading protocol was not rejected. The prosthesis survival rate 1 year postloading in the immediate and the control loading arms was the same (100%). No statistically significant difference in implant success rate was observed between the two study arms.

The high clinical success rate in this randomized controlled clinical trial contributes to a growing body of evidence that supports the use of immediate loading protocols for dental implants using mandibular implant-supported fixed prostheses. This treatment modality should reduce treatment time, cost, and surgical morbidity significantly.

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