Single Implant Treatment in Healing versus Healed Sites of the Anterior Maxilla: A Clinical and Radiographic Evaluation

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ABSTRACT

Purpose: The aim was to document the Nobelreplace tapered TiUnite® (Nobel Biocare, Göteborg, Sweden) implant system used by experienced clinicians in daily practice for replacing single maxillary anterior teeth and to compare the clinical and radiographic outcome between implants installed in healing sites (early implant placement) and fully healed sites (conventional implant placement) after on average two and a half years of function.

Material and Methods: A cross-sectional study in patients who had been treated by two periodontists and two prosthodontists in 2006 and 2007 was conducted. Surgical treatment involved standard flap elevation without releasing incisions and restorative procedures included cemented crowns in all patients. Only straightforward single implant treatments in healing sites (6–8 weeks following tooth extraction) and fully-healed sites (≥6 months following tooth extraction) were considered with both neighboring teeth present and without the need for hard and/or soft tissue grafting. Clinical and radiographic analyses of all implants were performed by a blinded clinician who had not been involved in the treatment.

Results: Forty-nine of the 53 eligible single implants (22 early and 27 conventionally placed implants) in 44/48 patients were available for scrutiny. There was no significant difference in implant survival between early (95%) and conventionally (93%) installed implants ($p = 1.000$). Mean bone level to the implant-abutment interface was 1.25 and 1.02 mm for early and conventional implant placement, respectively ($p = .220$). In spite of fairly low plaque levels (26%), overall peri-implant bleeding was quite prevalent (36%). Mean peri-implant probing depth was 3.3 mm. Five restorations had experienced technical complications.

Conclusions: Single Nobelreplace tapered TiUnite® implants installed in healing as well as in healed sites of the anterior maxilla are predictable. Both strategies seem equally successful in terms of implant survival, bone remodeling, clinical response, and risk for complications.

KEY WORDS: conventional, dental implant, early, single tooth

INTRODUCTION

Patients expect a long-lasting, functional, and esthetic solution to replace one or more missing teeth in the anterior maxilla. Dental implants have been increasingly used to meet these demands. The traditional protocol included a healing period of several months after tooth extraction followed by another load-free period of 3–6 months following implant surgery.[1] With respect to single-tooth replacements in the esthetic area, data on this concept have been reported for several implant systems mainly comprising case series studies.[2–7] For this indication, TiUnite® implants have been poorly

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documented. The commonly used Nobelreplace® tapered (Nobel Biocare, Göteborg, Sweden) implant system with its TiUnite® (Nobel Biocare, Göteborg, Sweden) surface may not even show any documentation in this field.

The long healing period following tooth removal along with the recommended load-free period following implant insertion were obvious drawbacks of the aforementioned protocol. As a result, one focus point of research became the progressive shortening of the total treatment period and, as such, early implant placement was introduced with even potentially superior esthetic results when compared with conventional implant treatment.[8] Evidently, this could impose potential risks in terms of treatment outcome because the alveolar ridge is in a healing state after a period of only 6–8 weeks following tooth removal. Difficulties include a correct 3-D implant positioning, primary implant stability and uncertain hard and soft tissue outlines because dimensional changes of the alveolar ridge have not reached a steady state yet.[9] Based on these aspects, it is obvious that surgical experience is warranted when early implant placement is pursued.

In a recent systematic review by den Hartog and colleagues[10] only two studies comparing early with conventional single implant treatment in the anterior maxilla could be identified.[5,8] These studies were based on the Astra Tech® (Mölndal, Sweden) and Biomet 3i® (Palm Beach, USA) implant system, respectively. Evidently, this information is scarce, may be incomplete in terms of clinical response parameters and does not necessarily apply to other implant systems.

The aim of this study was to document the Nobelreplace tapered TiUnite® system used by experienced clinicians in daily practice for replacing single maxillary anterior teeth and to compare the clinical and radiographic outcome between implants installed in healing sites (early implant placement) and fully healed sites (conventional implant placement) after on average two and a half years of function.

MATERIALS AND METHODS

Patient Selection

This study included clinical and radiographic data on patients who had been treated for single tooth implants in 2006 and 2007. The patients were selected on the basis of the following selection criteria:

1. All surgical and restorative treatments performed by two experienced periodontists, respectively, prosthodontists at the Dental Clinic of the Free University in Brussels (VUB) or private practice
2. Early (6–8 weeks following tooth removal) or conventional (at least 6 month following tooth removal) single implant treatment in the anterior maxilla (regions 15–25) using Nobelreplace tapered TiUnite® implants
3. Natural teeth present both mesial and distal to the implant
4. Willingness to come in for additional evaluation and informed consent

Implant treatments including hard and/or soft tissue grafting prior to or at the time of implant surgery were excluded. The study was conducted in accordance with the Helsinki declaration of 1975 as revised in 2000, and the protocol was approved by the ethical committee of the University Hospital in Brussels (UZ Brussel).

Surgical Procedure

A clinical case is shown in Figure 1. In all patients, implant surgery was preceded by screening and a comprehensive clinical and radiographic examination. Thereupon, a treatment plan was proposed to the patient. The surgical procedure was identical for early and conventional implant placement and always included antibiotic and analgesic therapy (amoxicillin/clavulanic acid 500 mg and ibuprofen 600 mg), both started 1 hour pre-operatively. Oral disinfection was performed using a 0.2% chlorhexidine digluconate mouthwash (Corsodyl®, GlaxoSmithKline, Genval, Belgium). Following local anesthesia, a standard mucoperiosteal flap was elevated including sulcular incisions at both teeth facing the single-tooth gap via a palatally oriented crestal incision. Vertical releasing incisions were never performed. Thereupon, all patients received one or more commercially available implants (Nobelreplace tapered TiUnite®). A correct 3-D positioning of the implant principally as described by Buser and colleagues[11] was considered of pivotal importance. That is, in the mesiodistal dimension a minimum distance of 2 mm between the implant shoulder and the neighboring tooth was pursued. In the orofacial dimension, the implant shoulder was positioned palatal to the point of emergence at the adjacent teeth. In the apicocoronal dimension, the implant shoulder was located at the level

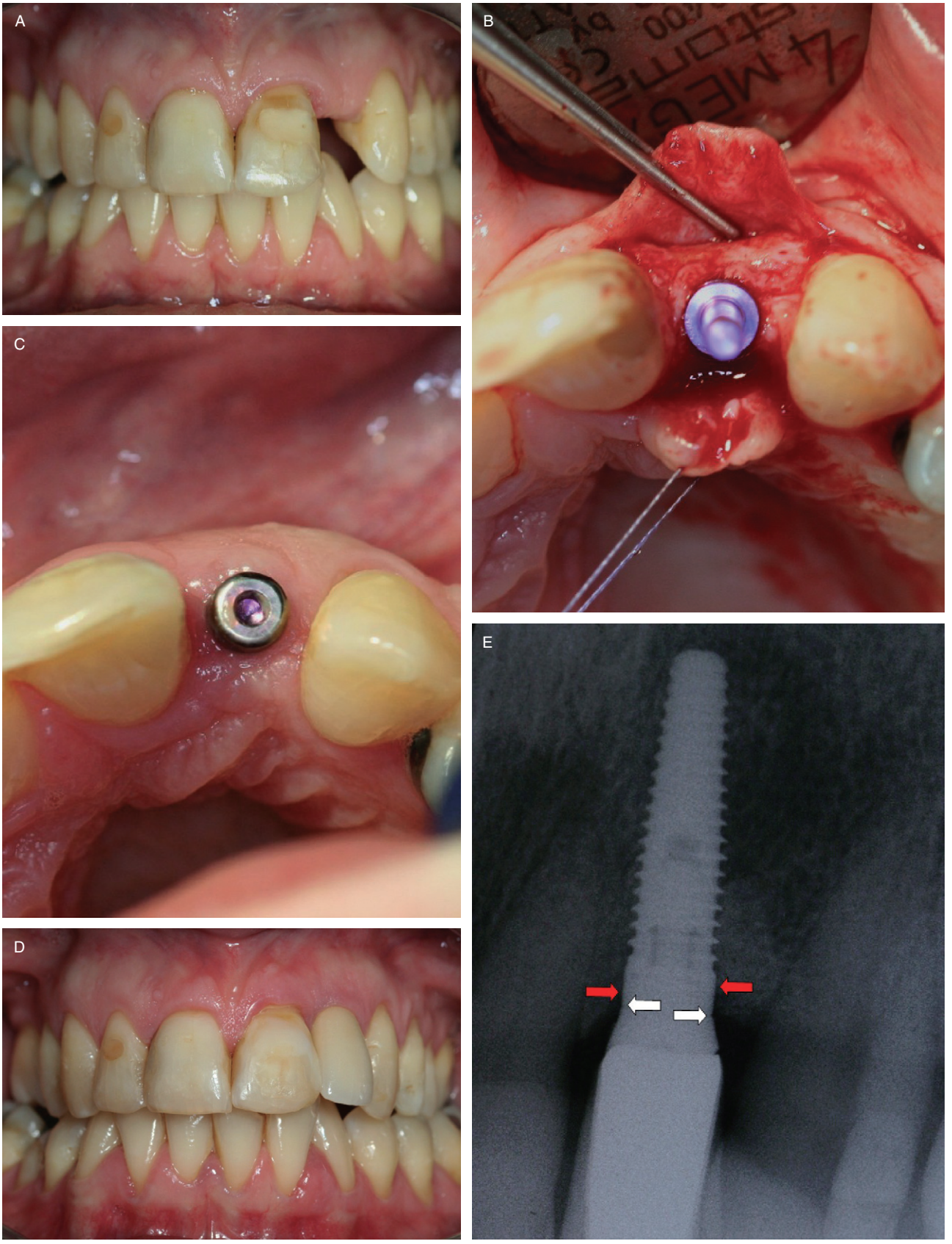

Figure 1 Clinical case illustrating single implant treatment. *A*, Pre-operative view of a missing lateral maxillary incisor (agenesis). *B*, Standard mucoperiosteal flap elevation with a direction indicator in situ (see text for details). *C*, Small-diameter healing abutment to be replaced by a wide-diameter healing abutment after 3 months of osseointegration. *D*, Result after 20 months of function. *E*, Radiography with white arrows at the level of the implant-abutment interface and red arrows indicating the first bone-to-implant contact.

of the alveolar crest usually corresponding to a 1–2-mm apical position from the cement–enamel junction of the neighboring teeth. Sites were occasionally underprepared to ensure primary implant stability. This allowed for a one-stage procedure in all cases. At the time of surgery, small-diameter healing abutments were placed with an appropriate height depending on the thickness of the soft tissues. The mucoperiosteal flap was sutured at the mesial and distal aspect (Vicryl®, 5/0, Johnson & Johnson, St-Stevens-Woluwe, Belgium). Post-operative instructions included continued antibiotic treatment for 5 days and analgesic therapy. Oral disinfection was recommended for 2 weeks. Sutures were removed between 1 and 2 weeks post-operatively. Following 3 months of osseointegration, the small-diameter healing abutments were replaced by wider abutments and the patient was referred to the prosthodontist for restorative treatment.

Restorative Procedure

An open tray impression coping (Nobel Biocare, Göteborg, Sweden) was attached and a pre-selected disposable tray (Coe disposible impression tray, GC America, Alsip, IL, USA) was appropriately perforated. The implant impression was made using a polyether impression material (Impregum Penta®, 3M Espe, Seefeld, Germany). On the master model, the final configuration of the restoration was defined by means of a wax-up, thereby essentially copying the clinical crown of the contralateral tooth. The choice of the abutment material (titanium or ceramic) was left to the discretion of the prosthodontist and included the Aesthetic Abutment® or Procera® Abutment (Nobel Biocare, Göteborg, Sweden). Abutment dimensions were selected on the basis of implant angulation and depth of the implant shoulder in reference to the midfacial soft tissue margin. A distance of the latter to the abutment-crown interface of about 1 mm was pursued to avoid deep cementation. The minor palatal position of the implant in reference to the point of emergence at the neighboring teeth allowed for a flat to slightly concave emergence profile of the cosmetic porcelain. No attempt was made to condition the soft tissues by means of a provisional crown in any of the patients. All restorations were cemented using temporary cement (Temp-Bond NE, Kerr, Scafati, Italy). Oral hygiene instructions were reinforced following installation of the crown.

Clinical Evaluation

All patients were clinically re-examined in June 2009 by one blinded clinician who had not been involved in the treatment. Besides implant survival, which was considered a primary outcome variable, the following secondary parameters were registered at the implant restoration as well as at the contra-lateral tooth:

1. Plaque score. A score (0 = no visible plaque; 1 = visible plaque) was given at four sites per tooth and implant (mesial, midfacial, distal, palatal)
2. Probing depth was measured to the nearest 0.5 mm at four sites per tooth and implant (mesiofacial, facial, distopalatal, palatal) using a manual probe (PCPUNC 15, Hu-Friedy®, Leimen, Germany)
3. Bleeding on probing. A score (0 = no bleeding; 1 = bleeding) was given at four sites per tooth and implant (mesial, midfacial, distal, palatal)

Radiographic Evaluation

Following clinical evaluation standard intra-oral radiographs were made of all implants using the long-cone paralleling technique and a plastic X-ray holder (XCP Bite Block, Dentsply Rinn, Elgin, IL, USA). All radiographs were scanned (300 dpi) and digitized (SprintScan 35 Plus, Polaroid, Cambridge, MA, USA). Marginal bone levels (distance from the implant-abutment junction to the first visible bone-to-implant contact) were determined mesial and distal to the implant by the use of a computer program (Vixwin 2000 v1.11, Dentsply Gendex, Lake Zurich, Switzerland) (Figure 1E). In order to determine intra-examiner repeatability and inter-examiner reproducibility 20 radiographs were analyzed twice by one blinded clinician who analyzed all the radiographs of the study and once by another clinician.

Complications

Patients were asked if any complication occurred in the follow-up period and patient records were scrutinized for biologic complications (abscess, fistula) and technical complications (loosening of the abutment screw, loss of retention of the crown, fracture of components). In addition, each restoration was clinically evaluated.

Statistical Analysis

The implant was used as the statistical unit in all analyses. The Fisher's exact test was adopted to compare the

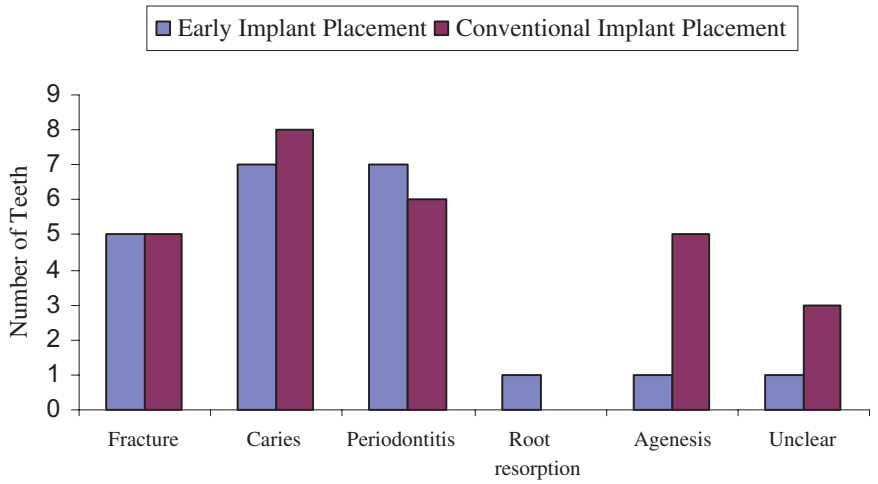

Figure 2 Reasons for tooth loss for early and conventional implant placement.

distribution in terms of smokers, reasons for tooth loss, implant location, implant diameter, implant length, restoration material and implant survival between early and conventional implant placement. Intra-examiner repeatability and inter-examiner reproducibility on marginal bone levels were assessed using percent agreement within 0.2 mm deviation, Pearsson correlation coefficients and the Wilcoxon signed ranks test. The Mann-Whitney test was used to compare the time from treatment to evaluation, clinical and radiographic parameters (plaque score, bleeding on probing, probing depth, bone level) between early and conventional implant placement. The Wilcoxon signed ranks test was performed to identify differences between implants and contra-lateral teeth. The level of significance was set at 0.05.

RESULTS

From the 48 patients who met the selection criteria, 44 (19 men, 25 women; mean age 52; age range 23–76) participated for the clinical and radiographic examination. One patient cancelled her appointment because of illness and three did not show up at their appointment.

22 early implant placements could be evaluated. One subject received 2 implants and 4 patients were smokers (≥10 sigarettes per day). The mean time from surgery to evaluation in this group was 30 months (SD 9; min 17, max 41).

27 conventional implant placements were assessed in 23 patients. 19 subjects received one implant, 4 patients were provided with two implants. The sample included 3 smokers. The mean number of months between implant placement and evaluation was 31 (SD 8; min 18, max 41). There was no significant difference neither in the number of smokers ($p = .685$), nor in the time span from surgery to evaluation between the two groups ($p = .529$).

Figure 2 shows the reasons for tooth loss sorted per treatment strategy. There was no significant difference in the distribution of the factors causing tooth failure between early and conventional implant placement ($p = .555$). Overall, caries and periodontitis were the most prevalent reasons for tooth loss.

Figure 3 shows implant locations sorted per treatment strategy. There was no significant difference in the distribution of these locations between early and conventional implant placement ($p = .890$). Irrespective of the treatment, at least half of the implants were installed in the premolar region.

Table 1 provides details on implant diameter and length sorted per treatment strategy. There were no significant differences in terms of these implant characteristics between early and conventional implant placement ($p \geq .338$). Implants with a regular platform (4.3 mm) and standard length (13 mm) were most often inserted.

All but two crowns were metal-ceramic restorations. The two full-ceramic restorations were connected onto implants installed in fully healed bone. There was no significant difference in restoration material between early and conventional implant placement ($p = .491$).

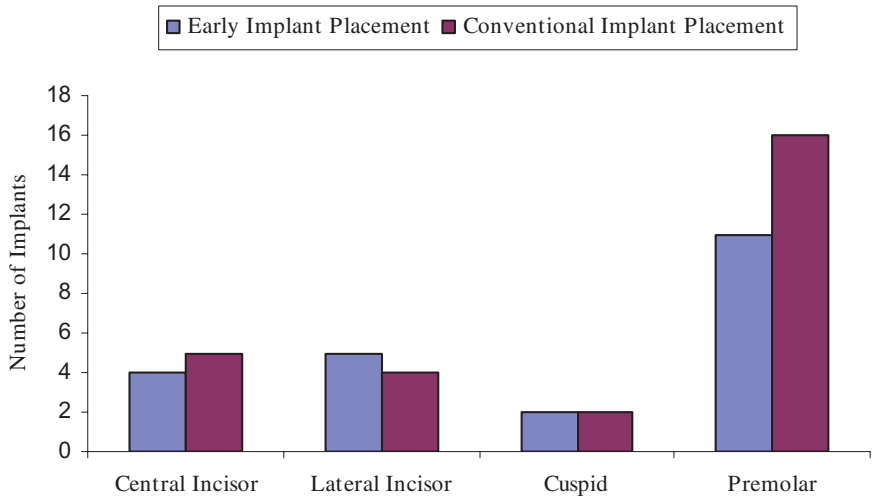

Figure 3 Distribution of implants by location for early and conventional implant placement.

Clinical Results

Of the 49 implants included in the present study, three were lost pointing to an overall implant survival rate of 94%. All the failures occurred within the first 3 months following surgery without clinical signs of infection. In the early placement group, the one failure was in a non-smoking male patient of 51 years old and it concerned a 4.3 × 10 mm implant in a premolar position. In the conventional placement group, one of the two failures was in a smoking male patient of 48 years old and it related to a 4.3 × 10 mm implant in a premolar position. The second implant loss occurred in a non-smoking male patient of 51 years old and included a 4.3 × 10 mm implant in a premolar position. These result in an implant survival rate of 95% and 93% after 2 years of function for implants installed in healing, respectively, fully healed sites. The difference was not significant ($p = 1.000$).

TABLE 1 Distribution of Implants by Diameter and Length

	Diameter (mm)	Length (mm)			
		10	13	16	Total
Early implant placement	3.5	1	4	0	5
	4.3	7	7	1	15
	5	1	1	0	2
Total		9	12	1	22
Conventional implant placement	3.5	0	2	2	4
	4.3	8	10	3	21
	5	0	2	0	2
Total		8	14	5	27

As shown in Table 2 overall plaque levels were fairly low at implants (26%) and contra-lateral teeth (29%) indicating good oral hygiene. The difference between implants and teeth was not significant ($p = .537$). However, in spite of this observation, peri-implant bleeding was quite elevated pointing to 36%, which was substantially higher than the bleeding tendency at contra-lateral teeth (22%) ($p = .008$). The overall probing depth at implants was 3.3 mm and was also significantly higher than the corresponding value at contra-lateral teeth (2.7 mm) ($p < .001$). There were no significant differences in terms of plaque levels, bleeding on probing or probing depth between early and conventionally installed implants ($p \geq .195$).

Radiographic Results

The intra-examiner repeatability on marginal bone levels was high (90% agreement within 0.2 mm deviation; Pearsson correlation coefficient: 0.982 – $p < .001$; Wilcoxon signed ranks test: $p = .709$), as was the inter-examiner reproducibility (85% agreement within 0.2 mm deviation; Pearsson correlation coefficient: 0.978 – $p < .001$; Wilcoxon signed ranks test: $p = .737$).

Digital analysis of the radiographs showed mean bone level of 1.25 mm (standard deviation [SD] 0.60; min 0.40, max 2.40) in the early placement group as assessed by the distance from the implant-abutment interface to the first bone-to-implant contact. The corresponding value for the conventional placement group was 1.02 mm (SD 0.60; min 0.00, max 2.36). There was no significant difference in bone level between early and conventional implant placement ($p = .220$).

TABLE 2 Comparison of Clinical Parameters between Implants and Contra-Lateral Teeth

	Implant Plaque	Implant BoP	Implant PD	Tooth Plaque	Tooth BoP	Tooth PD
Mean (SD)	26.4 (17.9)	36.3 (21.1)	3.3 (0.7)	28.5 (21.7)	22.2 (20.6)	2.7 (0.4)
Min	0	0	2.0	0	0	2.0
Max	50	75	4.8	75	75	3.5

SD, standard deviation; BoP, bleeding on probing; PD, probing depth.

The cumulative percent of bone level is shown in Figure 4 for each group. According to the success criteria of Albrektsson and Isidor[12] (1.5-mm bone remodeling during the first year of function and maximum 0.2 mm annually thereafter) 81% of the early and 90% of the conventionally placed implants can be classified as successful after on average 30, respectively 31 months of function.

Complications

All complications were of technical nature. In the early placement group, one porcelain fracture occurred and three crowns lost retention. In the conventional placement group, one metal-ceramic crown lost retention. There was no significant difference in the number of complications between early and conventional implant placement ($p = .318$).

DISCUSSION

Hitherto, a number of review articles have been published on the clinical outcome of single implant treatment showing implant survival rates surpassing 95% after 2–5 years of function.[13–15] As these do not specifically report on single implants in the anterior maxilla, they may not fully apply to the present topic. In this regard, a recent systematic review by den Hartog and colleagues[10] may be more relevant to consider. Their systematic search revealed that the number of clinical

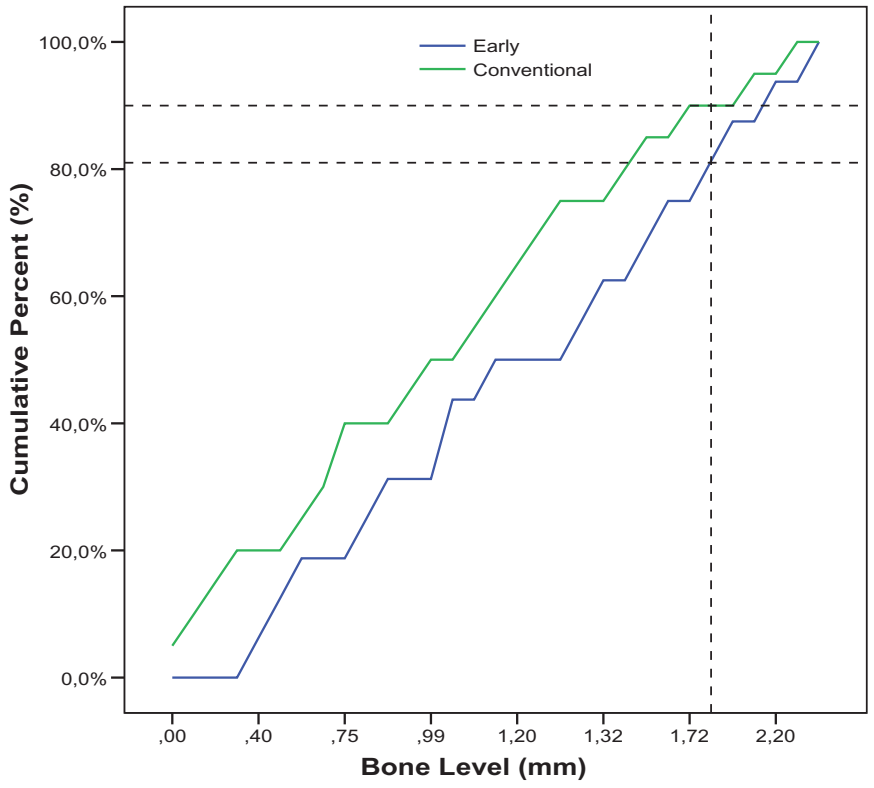

Figure 4 Cumulative percent of bone level for early and conventional implant placement.

studies comparing early with conventional single implant treatment in the anterior maxilla is very scarce and that available studies show incomplete data. Although a limited amount of studies have been published using Nobelreplace® tapered implants for immediate single-tooth replacement,[16,17] the system lacks long-term documentation and is clearly underexposed to research when it comes to other treatment modalities. The purpose of this study was to document the Nobelreplace® tapered system used by experienced clinicians in daily practice for replacing single maxillary anterior teeth and to compare the clinical and radiographic outcome between implants installed in healing sites and fully healed sites after on average two and a half years of function.

Of the 49 implants included in the present study, three were lost within the first 3 months following surgery. Interestingly, all failures related to 10-mm implants in a premolar position. Even though these findings suggest a clustering of failures, the observation is probably coincidental. After all, short TiUnite® implants (6–8.5 mm) conventionally installed in the severely resorbed maxilla may yield survival rates up to 97% after 2 years of function as reported by Renouard and Nisand.[18] One should also take into account that more than half of the implants were located in a premolar position. Clearly, there are no data indicating higher failure of implant treatment in this area.

In our study, conventional implant placement resulted in an implant survival rate of 93%. Other studies reporting on the survival of single TiUnite® implants in non-augmented healed sites after at least 2 years of function indicated a 94–100% survival rate.[19,20] Also the Straumann® (Basel, Switzerland) and Astra Tech® (Mölndal, Sweden) implant system seem to enjoy comparable survival rates for this indication.[2,7] In the present study, early implant placement resulted in only one failure, leading to a survival rate of 95%. There was no significant difference between early and conventionally installed implants in terms of this primary outcome variable, which is supported by the results of a recent meta-analysis by den Hartog and colleagues[10] based on limited data up to 1 year of function. In their report, immediate/early and conventional implant placement yielded survival rates of 94%, respectively, 93% using a conventional loading protocol.

As shown by den Hartog and colleagues,[10] it is clear that a number of studies did not systematically provide information on clinical parameters such as plaque, bleeding tendency, and probing depth. In our patients, plaque levels were fairly low at implant and corresponding tooth sites, indicative of good oral hygiene. Concurrently, bleeding on probing was nearly 40% at implant sites in both groups, which is in agreement with ample studies.[3,5,18,21] This proportion was substantially higher than the corresponding value at contra-lateral natural teeth (about 20%) and could be explained by the microgap at the level of the implant-abutment interface inducing microbial leakage and a pumping effect, ultimately creating an inflammatory cell infiltrate and local bone resorption.[22,23] In addition, a second inflammatory cell infiltrate is formed just below the level of the peri-implant sulcus at the abutment-crown interface. Still, some reports indicated no to rare bleeding tendency on peri-implant probing, hereby contrasting our and aforementioned observations by others.[2,7,24] In this regard, possible disparities in probing forces should be taken into account. At least in the periodontal literature, it has been described that the average probing force generated by various clinicians nearly reaches 0.5 N and that inter-individual variability is high.[25]

In the present study, the mean probing depth at implant sites amounted to 3.3 mm. There was no significant difference between conventional and early implant placement, which is in line with Schropp and colleagues.[8] Probing depth at contra-lateral natural teeth was slightly, yet significantly smaller as shown by our data. This is in agreement with other studies on single implants in the anterior maxilla comparing implants with contra-lateral natural teeth and demonstrates once again the fundamental differences between implants and teeth at the transmucosal level.[3,21] Essentially, these reflect a disparity in biologic width around implants and teeth.[26] Interestingly, Cardaropoli and colleagues[6] and Zarone and colleagues[7] described a mean probing depth at implant sites of only 2.5 mm; whereas, Schropp and colleagues[8] reported over 4 mm following comparable conventional single implant treatment in the anterior maxilla. Besides differences in the implant system used, possible disparities in probing force could explain once again the observed inconsistencies among these studies. Evidently, probing force is a methodological variable difficult to control in a study when standard manual probes are used.

Besides implant survival, bone remodeling was considered another primary outcome variable in our study.

We observed a mean distance of 1.05 mm between the implant-abutment interface and the first bone-to-implant contact for conventionally installed implants after on average 31 months of function. According to the internationally accepted success criteria by Albrektsson and Isidor[12], 90% of these implants may be considered successful. These results are in line with other studies reporting on single TiUnite® implants in non-augmented healed sites: De Bruyn and colleagues[20] described a 1.35-mm bone loss after an average 38 months of function and Turkyilmaz and colleagues[19] showed a 1.11-mm bone remodeling after 4 years of function. Also, Zarone and colleagues[7] showed comparable results pointing to a 1.20-mm bone loss 2 years after conventional placement of a single one-piece Straumann® implant in the premaxilla. However, data on the Astra Tech® implant system indicated virtually no remodeling after 2 years of function as shown by Palmer and colleagues,[4] which clearly contrasts these and our findings. Although differences in the methodology to determine bone loss exist among the studies, this observation suggests that some systems seem to induce less bone remodeling than others. In this regard, it should be taken into account that bone remodeling is a complex phenomenon which is influenced by a number of factors. These relate to the macro- and microgeometry of the implant collar and implant-abutment interface, among others.[26] Unlike Astra Tech® implants, the Nobelreplace® tapered implants included in this study showed a turned implant collar without retention elements, a flat-to-flat connection and no diameter reduction of the abutment at the level of the implant-abutment interface. On the other hand, our data may not fully reflect bone loss as we only analyzed radiographs at one point in time. Long-term prospective studies documenting actual bone loss from the moment of implant installation would be valuable in this respect.

An important observation was that implants inserted in healing sites performed just as well as those installed in completely healed bone in terms of bone remodeling with a mean level of 1.25 mm for early installed implants after an average 30 months of function. This is in line with the results of the two available studies comparing early with conventional single implant treatment in the anterior maxilla.[5,8]

With respect to complications, one porcelain fracture and four retention losses of the crown occurred in the period from treatment to evaluation. Thus, only technical complications were reported relating to 10% of the restorations. As shown by a systematic review, these complications may be common for single-implant restorations affecting nearly one-fifth after 4 years of function.[13] According to the literature, fistula represent the most prevalent biologic complication. These seem mainly related to cemented provisional restorations and subside after placement of the definitive crown.[8,16,27] Obviously, we did not encounter this complication in our study because no provisional restorations had been installed.

Because neither the patient, nor the clinicians were aware of the fact that a study would be conducted at the time of treatment, we believe our results truly reflect daily practice. On the other hand, we acknowledge that some caution may be indicated when interpreting our data as this was not a randomized controlled study, yet a cross-sectional investigation based on data of patients who had been retrospectively recruited. Systematic error inflicted by selection bias may be considered one of the most important drawbacks of a non-randomized clinical study and renders research findings inaccurate, if present. We believe our study did not suffer from selection bias because patients were included on the basis of strict selection criteria hereby ensuring homogeneous and comparable study samples. As such, we only considered straightforward single implant cases in cooperative patients with both neighboring teeth present and without the need for hard and/or soft tissue grafting. Since these procedures are often required in the incisor/cuspid area because of pronounced resorption and for esthetic purposes, it should not be surprising that more than half of the single tooth gaps were located in a premolar position. Another point favoring homogeneity in our investigation was the fact that the number of clinicians was kept minimal only including two experienced surgeons sharing the same philosophy when it comes to the need for hard and/or soft tissue grafting. Similarly, all restorative procedures had been performed by two experienced prosthodontists, both working together with their dental technician. Especially variability in terms of clinicians providing restorative therapy and dental technicians may compromise the overall esthetic treatment outcome, as suggested by others.[28] Esthetics was clearly not addressed in the present report. Additional studies comparing early with conventional single implant treatment in the anterior maxilla should definitely focus on this aspect of treatment outcome.

Based on the results of the present study, single Nobelreplace tapered TiUnite® implants installed in healing as well as in healed sites of the anterior maxilla are predictable. In addition, both strategies are equally successful in terms of implant survival, bone remodeling, clinical response, and risk for complications after on average two and a half years of function.

CONFLICT OF INTERESTS AND SOURCE OF FUNDING

The authors declare that they have no conflict of interests. The study was supported by the dental department of the Free University of Brussels (VUB).

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