DR. ONUR ETOZ (Orcid ID : 0000-0003-0246-8224)
DR. KRISTINA BERTL (Orcid ID : 0000-0002-8279-7943)
PROF. NURDAN OZMERIC (Orcid ID : 0000-0003-1098-8318)
DR. ANDREAS STAVROPOULOS (Orcid ID : 0000-0001-8161-3754)

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How old is old for implant therapy in terms of implant survival and marginal bone levels after 5-11 years?

Onur ETÖZ*[1,2], Kristina BERTL*[1,3], Edmund KUKLA[4], Christian ULM[3], Nurdan OZMERİC[2], Andreas STAVROPOULOS[1,5,6]

1) Department of Periodontology, Faculty of Odontology, University of Malmö, Sweden
2) Department of Periodontology, Gazi University, Turkey
3) Division of Oral Surgery, University Clinic of Dentistry, Medical University of Vienna, Austria
4) Comprehensive Center Unit, University Clinic of Dentistry, Medical University of Vienna, Austria
5) Division of Conservative Dentistry and Periodontology, University Clinic of Dentistry, Medical University of Vienna, Vienna, Austria
6) Division of Regenerative Dental Medicine and Periodontology, University Clinics of Dental Medicine (CUMD), University of Geneva, Geneva, Switzerland

* Authors contributed equally in terms of workload.

Author contribution:

Dr. Etoz contributed to the collection and interpretation of the data; Dr. Bertl contributed to the conception and design of the study, analysis, and interpretation of the data; Dr. Kukla contributed to the collection and interpretation of the data; Dr. Ulm and dr. Ozmeric contributed

to the interpretation of the data. Dr. Stavropoulos contributed to the conception and design of the study, and interpretation of the data;
all authors contributed to drafting and/or critically revising the manuscript.

Corresponding author: Andreas Stavropoulos, Professor & Director, Division of Regenerative Dental Medicine and Periodontology, University Clinics of Dental Medicine (CUMD), University of Geneva, Geneva, Switzerland.
email: andreas.stavropoulos@unige.ch

Abstract

Aim

To evaluate implant survival and marginal bone levels (MBL_{evel}) at least 5 years after implant installation in patients ≥ 65 years old.

Methods

Patient records were screened retrospectively for the following inclusion criteria: (1) ≥ 65 years of age at the time of implant installation, and (2) ≥ 5-year radiographic follow-up or registered implant loss. Association between patient- and implant-related data with radiographically assessed data [i.e., implant survival, mean MBL_{evel} (i.e., average of mesial and distal level), maximum marginal bone loss (i.e., either mesial or distal loss; maximum MBL_{oss})] were statistically evaluated by mixed effects multi-level regression models.

Results

Two-hundred-eighteen implants in 74 patients were included with a mean follow-up of 6.2 years (range: 5 to 10.7 years); 4 early and 6 late implant losses have been registered (implant survival rate: 95.4%). Mean MBL_{evel} and maximum MBL_{oss} was 1.24 ± 0.9 mm and 1.48 ± 1.0 mm, respectively. Maximum MBL_{oss} < 2 mm, 2 to 5 mm, and ≥ 5 mm was found in 70.7, 28.8, and 0.5% of the implants, respectively. For both, mean MBL_{evel} and maximum MBL_{oss}, age presented a slightly protective effect (mean MBL_{evel}: Coef. -0.041, p = 0.016; maximum MBL_{oss}: Coef. -0.045, p = 0.014).

Conclusion

The high implant survival rate (95.4%), low mean MBL_{evel} (1.24 mm), and low frequency of maximum MBL_{oss} ≥ 5 mm (0.5%) observed herein after 5 to 11 years follow-up, suggest that older age should not be considered as a limiting factor for implant treatment.

Keywords

Elderly patient; aging; dental implant; risk factor; implant survival; marginal bone loss.

Introduction

Life expectancy and thus the elderly population is increasing due to an improved health care and increased personal wealth. Despite improved efforts for dental prophylactic measures, increased age is associated with higher number of lost teeth (Feine et al. 2002; Müller et al. 2007; Schimmel et al. 2017). Tooth loss leads to impaired chewing function, which in turn may result in poor nutrition intake, and in general reduced quality of life (Fontijn-Tekamp et al. 2000; Sheiham et al. 2001). Although installation of dental implants has become a common treatment choice for replacing missing teeth (Trullenque-Eriksson & Guisado-Moya 2014; Klinge et al. 2018), elderly patients choose implant treatment less often compared with other age groups (Zitzmann et al. 2007; Visser et al. 2011). This may be because elderly patients are often reluctant to the surgical intervention for implant installation due to higher costs or limited knowledge about dental implant treatment itself (Tepper et al. 2003; Müller et al. 2012). Nevertheless, it can be expected that independent elderly in high income countries will choose dental implants increasingly often in the future (Meijer et al. 2001; Madianos et al. 2016; Schimmel et al. 2017).

A potential concern regarding dental implant therapy in elderly patients is the risk of compromised wound healing (Zarb & Schmitt 1994; Bartold et al. 2016). Wound healing might be compromised due to aging itself, but also due to a higher prevalence of chronic diseases in this group of patients, which are interfering with the wound healing process (Wood et al. 2004; Chrcanovic et al. 2014). Recently it was reported that ageing does not seem to compromise osseointegration in terms of higher numbers of early implant losses (EIL) (Bertl et al. 2019). However, compromised wound healing is not the only concern in terms of dental implant therapy in elderly patients; the ability to maintain a sufficient oral hygiene, to seek regularly supportive treatment, and to handle removable restorations appear even more important for a successful treatment outcome and avoidance of biological complications on the long-term (Schimmel et al. 2017). Nevertheless, the use of dental implants in elderly patients is, in general, considered as a predictable treatment option (Jemt 1993; de Baat 2000; Schimmel et al. 2017; Srinivasan et al. 2017; Schimmel et al. 2018), but long-term results (i.e., ≥ 5 years of follow-up) are still relatively rare.

The present study aimed to evaluate implant survival and marginal bone levels/loss at least 5 years after implant installation in patients ≥ 65 years old.

Methods

Study population

The study protocol of the present retrospective long-term cohort study was approved by the ethics committee of the Medical University of Vienna (EK-Nr. 1980/2016) and reporting complies with the STROBE guidelines (Appendix 1). The dental records of all patients, who received dental implants at the Division of Oral Surgery (Medical University of Vienna, Austria) between 10/2006 and 12/2012, were screened for the following inclusion criteria: (1) ≥ 65 years of age at the time of implant installation, and (2) ≥ 5 year radiographic follow-up after implant installation or registered implant loss. This specific timeframe was chosen to allow a 5-year follow-up at the time of screening. Further, it should be noted that the population included herein is also part of a previous publication (Bertl et al. 2019).

Patient- and implant-related parameters

The following patient-related data was extracted: (1) age and (2) smoking status at the time of implant installation, (3) gender, (4) periodontal diagnosis [i.e., periodontally healthy, periodontally diseased and staged according to the 2017 World Workshop on the classification of periodontal and peri-implant diseases and conditions (Tonetti et al. 2018), or edentulous], and (5) presence / absence of relevant systemic diseases [i.e., diabetes, osteoporosis, rheumatoid arthritis, inflammatory bowel diseases, and hyperthyroidism]. Further, the following implant-related parameters had been recorded: (1) number of implants per patient, (2) implant region (i.e., upper / lower / posterior / anterior), (3) implant diameter (i.e., ≤ 3.5 / 3.5 to 4.5 / ≥ 4.5 mm), (4) implant length (i.e., < 10 / ≥ 10 mm), (5) implant type (i.e., bone level / tissue level), (6) implant connection type (i.e., internal / external), (7) bone augmentation prior to or simultaneously to implant installation, (8) type of supra-structure (i.e., fixed / removable), (9) supra-structure with single or multiple units (i.e., fixed or removable dental prosthesis on multiple connected implants / removable supra-structure combining implants and teeth / removable supra-structure on multiple, not connected implants), (10) type of opposing dentition (i.e., natural teeth / implant-borne prosthesis / removable prosthesis), (11) follow-up period after implant installation, (12) timeframe between implant installation and delivery of the supra-structure, and (13) loading time.

Radiographic parameters

Panoramic and periapical radiographs and data from the dental records were used for extracting the following outcome parameters: (1) implant loss (i.e., EIL or late implant loss with EIL occurring before prosthetic restoration and late implant loss thereafter), (2) mean marginal bone level (i.e., mean of the mesial and distal level; mean MBL_{evel}), and (3) maximum marginal bone

loss (i.e., either mesial or distal loss; maximum MBL_{oss}). Further, maximum MBL_{oss} was categorized as follows: (1) < 2 mm, (2) 2 to 5 mm, and (3) ≥ 5 mm maximum MBL_{oss}.

Radiographs (i.e., panoramic and/or periapical radiographs) from the time of implant installation (i.e., baseline) and last available follow-up were used for measuring MBL_{evel}. Since the present study is retrospective, the periapical radiographs were not standardized, however all of them – as a standard in this clinic – were taken with the parallel technique. The radiographs were first calibrated based on the known implant length. Thereafter, the mesial and distal corners of the implant shoulder and the most coronal bone-to-implant contact / MBL_{evel} at the mesial and distal aspect were marked, and their distance was linearly measured parallel to the implant surface (Figure 1). The difference between the baseline and follow-up radiographs represented MBL_{oss} or in seldom cases marginal bone gain (MBG_{ain}). A single examiner (O.E.) assessed the radiographs under standardised conditions (i.e., on the same computer screen with the same settings, in a darkened room) with an image analysis program (Photoshop CC, Adobe Systems). Radiographs were assessed in a random sequence (i.e., baseline and follow-up radiographs of the same implant were not judged one after the other). Previously, a calibration session of the main examiner together with 2 co-authors (K.B., A.S.) was performed by assessing 30 radiographs displaying different implant systems and MBL_{evel}. Intra-observer repeatability was assessed by re-measuring 15% of all radiographs with a 2 weeks interval.

Statistical analysis

Statistical analysis comprised descriptive analysis and mixed effects multi-level regression models to analyse any effect of the assessed parameters on mean MBL_{evel} and maximum MBL_{oss}. For descriptive analysis, the cohort was additionally subdivided into 4 age groups at the time of implant installation: (1) 65 to 69.9 years, (2) 70 to 74.9 years, (3) 75 to 79.9 years, and (4) ≥ 80 years. Due to the limited number of implant losses no regression analysis was performed on "implant loss" as primary outcome parameter.

By means of mixed effects multi-level regression analyses with a random intercept model where implants were nested within patients using an unstructured covariance structure any associations between the primary outcome parameters ("mean MBL_{evel}" and "maximum MBL_{oss}") and various secondary outcome parameters (i.e., age, gender, smoking status, periodontal diagnosis, systemic diseases, number of implants per patient, implant region, -diameter, -length, -type, implant connection type, necessity of bone augmentation, type of supra-structure, supra-structure with single or multiple unit, type of opposing dentition, follow-up period after implant installation,

timeframe between implant installation and delivery of the supra-structure, loading time) were assessed in 2 steps. First, each secondary outcome parameter was tested in a univariate approach. Thereafter, all parameters being relevant predictors based on a 0.20-level in the univariate analyses were combined in the final multivariate model. The effects of these predictors on both primary outcome parameters were assessed by Wald and LR test. Intra-observer repeatability was tested with the intra-class correlation coefficient (ICC 1.1). Statistical analysis was performed using SPSS Version 24.0 (SPSS Inc., Chicago, IL, USA) and STATA (StataCorp LLC, USA) and p-values < 0.05 were considered as statistically significant.

Results

Study population

218 implants in 74 patients (51.4% female) were included in the present retrospective long-term cohort study, with most of the patients (i.e., 56.8%) being between 65 and 70 years old at the time of implant installation. Mean follow-up was 6.2 ± 1.2 years, ranging from 5 to 10.7 years. Few patients smoked at the time of implant installation and/or reported any systemic disease (i.e., < 10%), while most of the patients (i.e., 83.8%) were either edentulous or treated for periodontitis prior to implant installation. For details see Table 1.

Implant characteristics

Forty-three patients received less than 4 implants, 22 patients 4 implants, and 9 patients more than 4 implants. 40.8% of the implants were placed in the lower posterior, and 27.1% in the lower anterior. In 41 cases (18.8%) some kind of bone augmentation procedure was performed. The majority of the implants were between 3.5 and 4.5 mm (68.8%) in diameter. Furthermore except for 2 tissue level implants, implants were bone level implants and except for 7 implants with an external connection, implants had an internal connection. About 85% of the implants were restored with a fixed supra-structure and in 71% of the implants multiple implants/units were combined in the prosthetic restoration; interestingly, for more than half of the implants a removable restoration was present in the opposing dentition. For details see Table 1.

Early and late implant losses

In 9 patients (3 female) 4 EIL (i.e., after < 0.4 years; 1.8% on the implant level) and 6 late (i.e., after 1.7 to 5.5 years; 2.8% on the implant level) implant losses were registered resulting in a survival rate of 87.8 and 95.4% on the patient and implant level, respectively. All patients experiencing implant loss had a history of periodontitis (i.e., stage 3 or 4) but were not classified as multimorbid and none were smoking at the time of implant installation (Table 2). Due to the

low number of either early or late implant losses a random-effects logistic regression analysis was not meaningful.

Radiographic outcome

Radiographs representing baseline where only orthopantomograms; at follow-up, 178 orthopantomograms and 30 periapical radiographs were available. Reliability evaluation showed a high degree of intra-observer repeatability; i.e., ICC was 0.926 and 90.3% of the re-measurements deviated maximum 0.5 mm, while the deviation of the remaining 9.7% was within 0.7 mm.

Based on 208 implants, mean MBL_{evel} and maximum MBL_{oss} was 1.24 ± 0.9 mm (range: 0.4 mm MBG_{ain} to 5.0 mm MBL_{oss}) and 1.48 ± 1.0mm (range: 0.2 mm MBG_{ain} to 5.6 mm MBL_{oss}), respectively. Interestingly, compared to the younger age cohorts, mean MBL_{evel} was > 50% less in the cohort ≥ 80 years of age; however, only 17 implants were included in this cohort (Figure 2). Maximum MBL_{oss} < 2, 2 to 5, and ≥ 5 mm was observed in 70.7%, 28.8%, and 0.5% of the implants, respectively (Figure 3).

The results of the univariate and multivariate regression analyses for mean MBL_{evel} and maximum MBL_{oss} are reported in Table 3 and 4, respectively. In terms of mean MBL_{evel}, only age, implant region, implant length, and follow-up period after implant installation appeared relevant in the univariate analysis (i.e., $p < 0.02$; Table 3) and age and implant length remained significant in the final multivariate model (Table 4). Specifically, higher age had a slightly protective effect on mean MBL_{evel} (Coef. -0.041, $p = 0.016$), while higher implant length (i.e., ≥ 10 mm) resulted in slightly increased mean MBL_{evel} (Coef. 0.571, $p = 0.048$). In terms of maximum MBL_{oss} the same 4 parameters (i.e., age, implant region, implant length, and follow-up period after implant installation) presented with a p-value < 0.20 in the univariate analysis (Table 3), however, only age remained statistically significant in the final multivariate model (Table 4); i.e., age also had slightly protective effect on maximum MBL_{oss} (Coef. -0.045, $p = 0.014$). Considering for both primary parameters (mean MBL_{evel} and maximum MBL_{oss}) the overall effects of the 4 predictors (i.e., age, implant region, implant length, and follow-up period after implant installation) based on a LR test only age presented with statistical significance (mean MBL_{evel}: $p = 0.0213$; maximum MBL_{oss}: $p = 0.0197$).

Discussion

In the present retrospective cohort study in a university setting, high implant survival rate (95.4%), low mean MBL_{evel} (1.24 mm), and low frequency of severe MBL_{oss} (i.e., ≥ 5 mm; 0.5%) was observed 5 to 11 years after implant placement in patients ≥ 65 years of age; in fact, age appeared to have a slight but statistically significant protective effect in terms of mean MBL_{evel} and maximum MBL_{oss}.

The high implant survival rate observed herein is in accordance with what was presented in meta-analyses of studies assessing implant treatment in elderly patients. Specifically, in patients ≥ 65 years old a post-loading implant survival rate of 96.2 and 91.2% was calculated after 5 and 10 years in function, respectively (Srinivasan et al. 2017), and in geriatric patients (i.e., ≥ 75 years) a survival rate of 97.3 and 96.1% was found after 1 and 5 years, respectively (Schimmel et al. 2018). These rates of implant survival are overall comparable to those reported for the general population: 97.2 and 95.2% for single tooth implants (Jung et al. 2012) and 95.6 and 93.1% for implants supporting fixed dental prostheses (Pjetursson et al. 2012) after 5 and 10 years, respectively. In this context, in the original studies included in the above-mentioned systematic reviews, information on EIL, i.e., implant loss before functional loading of the implants, was often missing. It may thus be argued that the high implant survival rates in the above-mentioned studies is because EIL is not always captured in those numbers. The combination of several factors, such as compromised wound healing due to aging, higher prevalence of chronic diseases, and/or higher medication intake, might affect the wound healing process in this group of patients (Wood et al. 2004; Chrcanovic et al. 2014); thus, EIL could indeed be more frequent in the elderly. Nevertheless, in the present group of patients, the rate of EIL was quite low (i.e., 1.8% on the implant level). Further, a previous study based on a larger group of patients from this clinic (i.e., the patients included herein are part of this previous publication) assessed specifically EIL (Bertl et al. 2019); in 444 patients ≥ 65 years of age at the time of implant installation with 1517 implants, EIL rate was 0.66% on the implant level. In the same study (Bertl et al. 2019), 347 patients of the elderly group were also matched to a younger patient cohort (i.e., < 55 years old at implant installation), based on specific criteria; EIL was shown to be 1.44 vs. 2.59%, respectively, in the matched cohorts. In another retrospective study (Engfors et al. 2004) on 133 patients aged ≥ 80 years with 761 implants only 6 early implant failures (i.e., 0.8% on the implant level) were recorded; the control group consisting of 115 patients aged < 80 years (mean age: 65 years) with 670 implants registered also 6 early implant losses (i.e., 0.9% on the implant level).

One explanation for the low implant loss rates in the elderly may be that those finally receiving dental implants are probably selected more carefully by their dentist and are in general healthier

than those choosing another type of prosthetic solution or no treatment. Indeed, the population evaluated herein cannot be considered as multimorbid; i.e., the prevalence of smoking and any systemic disease (e.g., diabetes or osteoporosis) did not exceed 8%. Only the periodontitis prevalence (primarily stage 3 and 4) was relatively high with almost 85% (including the edentulous patients); however, the treatment standards of this department require a successful periodontal treatment before any implant installation is considered. Altogether, one might argue that the missing effect of any systemic disease might be at least partly due to the small number of patients being actually diseased in the present group of patients (Table 1). This lack of effect of systemic condition on implant survival agrees well with the results of a previous systematic review (Schimmel et al. 2018) on the impact of systemic medical conditions on implant therapy in the elderly. In that study, mainly patients after radiotherapy in the head and neck region and those receiving high-dose antiresorptive therapy due to cancer, respectively metastases, presented a higher risk for implant-related complications and failures. Other diseases, such as cardiovascular disease or diabetes mellitus type II (if well controlled), or patients receiving low-dose antiresorptive therapy for osteoporosis presented high implant survival rates. Nevertheless, care should be taken for patients on long-term bisphosphonate intake (i.e., > 36 months) or with comorbidities, since there is risk for medication related osteonecrosis of the jaws (Stavropoulos et al. 2018). In perspective, it has to be pointed out that presence / absence of any systemic disease herein was recorded only once at the time of implant installation but not thereafter. Thus, possible changes over time are not captured herein. Similarly, no effect of smoking on the outcome parameters assessed was observed, although it has been clearly described that smoking affects the outcome of implant therapy negatively (i.e., higher failure rate and increased MBL_{oss}) (Chrcanovic et al. 2015); this is probably due to the fact that only a small number of the patients included in this study were smoking.

Concerns about implant therapy in elderly regard not only the early wound healing process but also the capability of the patients to perform proper oral hygiene measures in the long-term, thus preventing peri-implant diseases. In the present study, MBL_{oss} was used as surrogate for peri-implantitis. The mean MBL_{evel} was overall < 1.5 mm with an even decreasing tendency for increasing age; i.e., mean MBL_{evel} and maximum MBL_{oss} of patients ≥ 80 years of age was only about 0.5 and 1.0 mm, respectively. Indeed, more than two thirds of the implants showed maximum MBL_{oss} < 2 mm and in about one third maximum MBL_{oss} was within 2 and 5 mm; only a single implant was recorded with maximum MBL_{oss} ≥ 5 mm (Figure 3). Even lower values and a similar trend for potentially better outcomes in patients ≥ 80 years of age was reported in a previous retrospective study (Park et al. 2017). After 2 to 17 years of follow-up, only 71 out of 882

implants showed a mean MBL_{evel} of 2.1 mm. In fact, the mean MBL_{evel} was highest in the age group 65 to 69 years and lowest in patients older than 80 years of age; i.e., in the latter group none out of 22 implants suffered any MBL_{oss}. Furthermore, the systematic review on prospective studies including elderly patients ≥ 65 years of age, already mentioned above (Srinivasan et al. 2017), reported a MBL_{oss} of 0.7 and 1.5 mm after 5 and 10 years, respectively; however, it is important to note that this data was based only on a single study (Hoeksema et al. 2016). Compared to younger populations (i.e., mean age < 65 years) with at least 5 years of follow-up, more or less comparable values are reported (Roccuzzo et al. 2008; Zetterqvist et al. 2010; Hasegawa et al. 2016; den Hartog et al. 2017). In this context in the present study MBL_{evel} was measured on radiographs taken immediately after implant installation and at last control. Consequently, MBL_{oss} measurements herein include the physiologic bone remodelling occurring after implant installation up to the first year of loading. Considering the results of the 2017 World Workshop on the classification of periodontal and peri-implant diseases and conditions, up to 2 mm of MBL_{oss} might be considered as physiologic bone remodelling (Renvert et al. 2018). Consequently, less than 30% of the patients herein might be considered suffering from peri-implant disease. This value is not much different from what was reported for the prevalence of peri-implantitis in the general population (i.e., 22% but with thresholds for MBL_{oss} varying from > 0.4 to > 5 mm) (Derks & Tomasi 2015), indicating that the elderly are not more prone to this complication compared to younger patients. Nevertheless, even if these results appear encouraging to place implants in elderly patients, one should keep in mind, that almost 60 and 25% of the current population has been < 70 and < 75 years of age, respectively, at time of implant installation. Thus, approximately 5 years later, most of them were < 80 years of age. Hence, a relevant proportion of the current study population was most likely still able to perform sufficient oral hygiene and follow recommendations and attend follow-ups. In perspective, elderly patients should be closely followed, contact to the caregivers sought, and the possibility for a back-off strategy allowing later on – if necessary – to switch to a low-maintenance prosthesis kept (Schimmel et al. 2017).

In the present study, both panoramic and periapical radiographs were used. Previous studies, comparing panoramic and periapical radiographs indicated periapical radiographs as the “gold standard” for measuring MBL_{evel} around dental implants (Sirin et al. 2012; Kühl et al. 2016); however, panoramic radiographs have been described as viable alternative (Gutmacher et al. 2016), especially in cases with implants in the lower anterior region (Zechner et al. 2003). Herein, panoramic radiographs were used at both baseline and at follow-up, for the vast majority of the implants (i.e., 86%); this limits any possible impact on the findings of this study from a potential

bias due to using different types of radiographs at different timepoints. In this context, another limitation of the present study was the relatively small number of implant losses; i.e., due to the small number of early (n = 4) and late (n = 6) implant losses a random-effects logistic regression analysis was not meaningful and hence, the herein recorded potential predictors could neither be related to early nor late implant loss.

In conclusion, the high implant survival rate (95.4%), low mean MBL_{evel} (1.24 mm), and low frequency of maximum MBL_{oss} ≥ 5 mm (0.5%) observed herein after 5 to 11 years follow-up, suggest that older age should not be considered as a limiting factor for implant treatment.

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Table legends

Table 1. Characteristics of the patient cohort (n = 74) and implant-related data (n = 218).

Table 2. Patient characteristics and implant-related data of the failing implants.

Table 3. Results of the univariate regression analyses for both primary parameters (i.e., mean MBL_{evel} and maximum MBL_{oss}).

Table 4. Results of the multivariate regression analyses for both primary parameter (i.e., mean MBL_{evel} and maximum MBL_{oss}).

Figure legends

Figure 1. Measurements of the MBL_{evel} from the implant shoulder to the bone level after calibration by the implant length (a) at baseline (i.e., day of implant installation) and (b) at last available follow-up (i.e., after 8.2 years in this specific case). The red dots are indicating the mesial and distal aspect of the implant shoulder and the green dots the most coronal bone-to-implant contact at the mesial and distal aspect of the implant. Further, the red dotted line indicates the calibration for the implant length and the green lines indicate the extent of the marginal bone loss (i.e., the distance between the red and green dots).

Figure 2. Mean MBL_{evel} (a) and maximum MBL_{oss} (b) of the 4 age cohorts (mean ± standard deviation). The number of implants per group is given in white letters in the bars.

Figure 3. Examples of cases and frequency distribution of maximum MBL_{oss} in 3 categories: (a) < 2, (b) 2 to 5, and (c) ≥ 5 mm maximum MBL_{oss} at last follow-up.

Appendix legends

Appendix 1. STROBE Statement—checklist of items that should be included in reports of observational studies.

Table 1. Characteristics of the patient cohort (n = 74) and implant-related data (n = 218).

Patient-related data	
Mean age in years* [mean ± SD (min; max)]	70.7 ± 4.8 (65; 84)
Age cohorts in years* [n (%)]	
65-69.9	42 (56.8)
70-74.9	18 (24.3)
75-79.9	8 (10.8)
> 80	6 (8.1)
Gender [female; n (%)]	38 (51.4)
Smoking status* [yes; n (%)]	6 (8.1)
Periodontal diagnosis [n (%)]	
Periodontally healthy	12 (16.2)
Edentulous	16 (21.6)
Periodontitis stage 1	0 (0.0)
Periodontitis stage 2	1 (1.4)
Periodontitis stage 3	12 (16.2)
Periodontitis stage 4	33 (44.6)
Systemic disease* [present; n (%)]	
Diabetes mellitus	6 (8.1)
Osteoporosis	6 (8.1)
Rheumatoid arthritis	3 (4.1)
Inflammatory bowel disease	2 (2.7)
Hyperthyroidism	1 (1.4)
Implant-related data	
Implants per patient [n (%)]	
1	18 (8.2)
2	30 (13.8)
3	30 (13.8)
4	88 (40.4)
5	10 (4.6)
6	42 (19.2)
Implant region [n (%)]	
Upper posterior	51(23.4)
Upper anterior	19 (8.7)
Lower posterior	89 (40.8)
Lower anterior	59 (27.1)
Implant diameter [mm; n (%)]	
≤ 3.5	38 (17.4)
3.5 to 4.5	150 (68.8)
≥ 4.5	30 (13.8)
Implant length [mm; n (%)]	
< 10	14 (6.4)
≥ 10	204 (93.6)
Implant type [n (%)]	
Tissue level	2 (0.9)
Bone level	216 (99.1)
Implant connection type [n (%)]	
Internal	211 (96.8)
External	7 (3.2)
Bone augmentation prior to or simultaneously to implant installation [yes; n (%)]	41 (18.8)
Type of supra-structure [n (%)]	
Fixed	181 (84.5)
Removable	33 (15.5)
Supra-structure with single or multiple units [n (%)]	
Single implant restoration	62 (29.0)
Fixed or removable dental prosthesis on multiple connected implants	132 (61.6)
Removable supra-structure combining implants and teeth	1 (0.4)
Removable supra-structure on multiple, not connected implants	19 (9.0)
Type of opposing dentition [n (%)]	
Natural teeth	73 (34.1)
Implant-borne restoration	21 (9.8)
Removable restoration	120 (56.1)
Follow-up period after implant installation in years [mean ± SD (min; max)]	6.2 ± 1.2 (5.0 - 10.7)
Timeframe between implant installation and delivery of the supra-structure in years [mean ± SD (min; max)]	0.5 ± 0.2 (0.2; 1.7)

Loading time in years [mean ± SD (min; max)]	5.9 ± 1.1 (4.3; 10.2)

max, maximum; min, minimum; SD, standard deviation.
** At the time of implant installation.*

Table 2. Patient characteristics and implant-related data of the failing implants.

Type of implant loss	Patient related data			Implant-related data							
	Age* Gender	**Systemic diseases***	**Periodontal diagnosis Smoking status***	**Number of implants per patient**	**Implant position**	**Implant length / diameter (mm)**	**Implant type Implant connection type**	**Bone augmentation prior to or simultaneously to implant installation**	**Type of supra-structure Supra-structure with single or multiple units Type of opposing dentition**	**Follow-up period after implant installation (years)**	**Timeframe between implant installation and delivery of the supra-structure (years) Loading time (Years)**
Early implant loss	83 Male	None	Periodontitis stage 4 NS	1	24	13 / 4.3	Bone level Internal	None	-	0.08	-
	70 Female	None	Periodontitis stage 4 NS	6	44	9.5 / 3.8	Bone level Internal	None	-	0.31	-
	69 Male	None	Periodontitis stage 3 NS	1	25	13 / 3.5	Bone level Internal	None	-	0.35	-
	69 Male	None	Periodontitis stage 4 NS	1	31	13 / 3.5	Bone level Internal	None	-	0.36	-
Late implant loss	81 Male	Diabetes, Osteoporosis	Periodontitis stage 4 NS	1	34	10 / 4.3	Bone level Internal	None	Fixed Multiple implants Removable	1.84	0.36 1.48
	76 Female	None	Periodontitis stage 4 NS	1	15	10 / 4.3	Bone level Internal	Sinus lift	Removable Multiple implants Removable	2.84	0.83 2.01
	72 Male	Hyper- thyroidism	Periodontitis stage 4 NS	4	23	13 / 4.3	Bone level Internal	None	Fixed Multiple implants Removable	5.45	0.46 4.99
	67 Female	None	Periodontitis stage 4 NS	2	26	13 / 4.3	Bone level Internal	Sinus lift	Fixed Single implant Natural dentition	1.73	0.61 1.12
					27	10 / 4.3	Bone level Internal	Sinus lift	Fixed Single implant Natural dentition	1.73	0.61 1.12
	66 Male	Diabetes	Periodontitis stage 4 NS	1	14	13 / 4.3	Bone level Internal	Block graft	Fixed Single implant Natural dentition	5.18	na° > 3.50

Na, not available; NS, non-smoker.
** At the time of implant installation. ° The exact time-point is unknown, because the crown was delivered at the referring dentist.*

Table 3. Results of the univariate regression analyses for both primary parameters (i.e., mean MBL_{evel} and maximum MBL_{oss}).

Parameter		Mean MBL_{evel}				Maximum MBL_{oss}			
		Coef.	p-value	95% CI		*Coef.*	p-value	95% CI	
				lower	upper			lower	upper
Age*	*Years*	**-0.043**	**0.013**	**-0.077**	**-0.009**	**-0.046**	**0.013**	**-0.083**	**-0.010**
Gender	*Male*	0.0				0.0			
	Female	0.048	0.781	-0.291	0.387	0.112	0.547	-0.253	0.477
Smoking status*	*No*	0.0				0.0			
	Yes	0.272	0.318	-0.261	0.804	0.222	0.450	-0.355	0.800
Periodontal diagnosis	*Periodontally healthy*	0.0				0.0			
	Edentulous	0.232	0.396	-0.305	0.769	0.142	0.633	-0.440	0.723
	Periodontitis stage 3°	-0.081	0.796	-0.697	0.535	-0.147	0.667	-0.814	0.521
	Periodontitis stage 4	0.064	0.804	-0.438	0.565	0.070	0.801	-0.473	0.613
Diabetes mellitus*	*No*	0.0				0.0			
	Yes	-0.210	0.571	-0.936	0.516	-0.222	0.579	-1.005	0.562
Osteoporosis*	*No*	0.0				0.0			
	Yes	0.263	0.408	-0.360	0.885	0.221	0.521	-0.452	0.894
Rheumatoid arthritis*	*No*	0.0				0.0			
	Yes	0.146	0.707	-0.613	0.904	0.044	0.917	-0.775	0.863
Inflammatory bowel disease*	*No*	0.0				0.0			
	Yes	-0.378	0.494	-1.459	0.704	-0.454	0.445	-1.621	0.712
Hyperthyroidism*	*No*	0.0				0.0			
	Yes	0.670	0.329	-0.677	2.017	0.670	0.366	-0.784	2.124
Implants per patient	*Number*	0.035	0.551	-0.080	0.150	0.029	0.649	-0.095	0.153
Implant region	*Upper posterior*	**0.0**				**0.0**			
	Upper anterior	**0.273**	**0.209**	**-0.153**	**0.700**	**0.272**	**0.247**	**-0.188**	**0.732**
	Lower posterior	**-0.024**	**0.895**	**-0.335**	**0.383**	**-0.036**	**0.855**	**-0.423**	**0.351**
	Lower anterior	**0.285**	**0.155**	**-0.107**	**0.677**	**0.301**	**0.163**	**-0.122**	**0.723**
Implant diameter	*≤ 3.5 mm*	0.0				0.0			
	3.5 to 4.5 mm	-0.071	0.707	-0.442	0.300	-0.010	0.960	-0.411	0.391
	≥ 4.5 mm	-0.079	0.741	-0.544	0.387	-0.080	0.755	-0.584	0.423
Implant length	< 10 mm	**0.0**				**0.0**			
	≥ 10 mm	**0.648**	**0.029**	**0.065**	**1.231**	**0.687**	**0.033**	**0.057**	**1.317**
Implant type	Tissue level	0.0				0.0			
	Bone level	-0.464	0.536	-1.934	1.006	-0.500	0.537	-2.086	1.087

Implant connection type	Internal	0.0				0.0			
	External	-0.452	0.304	-1.315	0.411	-0.380	0.505	-1.253	0.617
Bone augmentation prior to or simultaneously to implant installation	*No*	0.0				0.0			
	Yes	0.076	0.687	-0.294	0.446	0.036	0.858	-0.363	0.435
Type of supra-structure	*Fixed*	0.0				0.0			
	Removable	0.014	0.953	-0.443	0.471	0.014	0.953	-0.443	0.471
Supra-structure with single or multiple units	*Single implant restoration*	0.0				0.0			
	Fixed or removable dental prosthesis on multiple connected implants	0.079	0.630	-0.243	0.401	0.048	0.789	-0.300	0.396
	Removable supra-structure combining implants and teeth	-0.201	0.825	-1.991	1.589	-0.162	0.870	-2.096	1.772
	Removable supra-structure on multiple, not connected implants	0.032	0.914	-0.559	0.624	0.109	0.737	-0.529	0.747
Type of opposing dentition	Natural teeth	0.0				0.0			
	Implant-borne restoration	0.355	0.219	-0.211	0.922	0.369	0.238	-0.244	0.981
	Removable restoration	0.225	0.201	-0.120	0.571	0.226	0.236	-0.148	0.599
Follow-up period after implant installation	*Years*	**-0.096**	**0.165**	**-0.232**	**0.040**	**-0.109**	**0.146**	**-0.255**	**0.038**
Timeframe between implant installation and delivery of the supra-structure	*Years*	-0.409	0.220	-1.063	0.245	-0.413	0.252	-1.120	0.293
Loading time	*Years*	-0.083	0.247	-0.223	0.057	-0.095	0.215	-0.246	0.055

CI, confidence interval; Coef., coefficient; maximum marginal bone loss, maximum MBL_{oss}; mean marginal bone level, mean MBL_{evel}.
** At the time of implant installation.*
° The single patient classified as periodontitis stage 2 was included in the group of patients classified as periodontitis stage 3.
Potential predictors are indicated in bold ($p < 0.20$).

Table 4. Results of the multivariate regression analyses for both primary parameter (i.e., mean MBL_{evel} and maximum MBL_{oss}).

Parameter		**Mean MBL_{evel}**				**Maximum MBL_{oss}**			
		Coef.	**p-value**	**95% CI**		***Coef.***	**p-value**	**95% CI**	
				lower	**upper**			**lower**	**upper**
Age*	*Years*	**-0.041**	**0.016**	**-0.074**	**-0.008**	**-0.045**	**0.014**	**-0.080**	**-0.009**
Implant region	*Upper posterior*	0.0				0.0			
	Upper anterior	0.291	0.175	-0.129	0.712	0.293	0.206	-0.161	0.748
	Lower posterior	0.000	0.999	-0.345	0.345	-0.064	0.735	-0.435	0.307
	Lower anterior	0.238	0.213	-0.137	0.613	0.249	0.226	-0.154	0.652
Implant length	< 10 mm	0.0				0.0			
	≥ 10 mm	**0.571**	**0.048**	**0.005**	**1.136**	0.588	0.058	-0.020	1.197
Follow-up period after implant installation	*Years*	-0.091	0.164	-0.220	0.037	-0.104	0.143	-0.242	0.035

CI, confidence interval; Coef., coefficient; maximum marginal bone loss, maximum MBL_{oss}; mean marginal bone level, mean MBL_{evel}.
** At the time of implant installation. Significant predictors are indicated in bold ($p < 0.05$).*

Appendix 1. STROBE Statement—checklist of items that should be included in reports of observational studies.

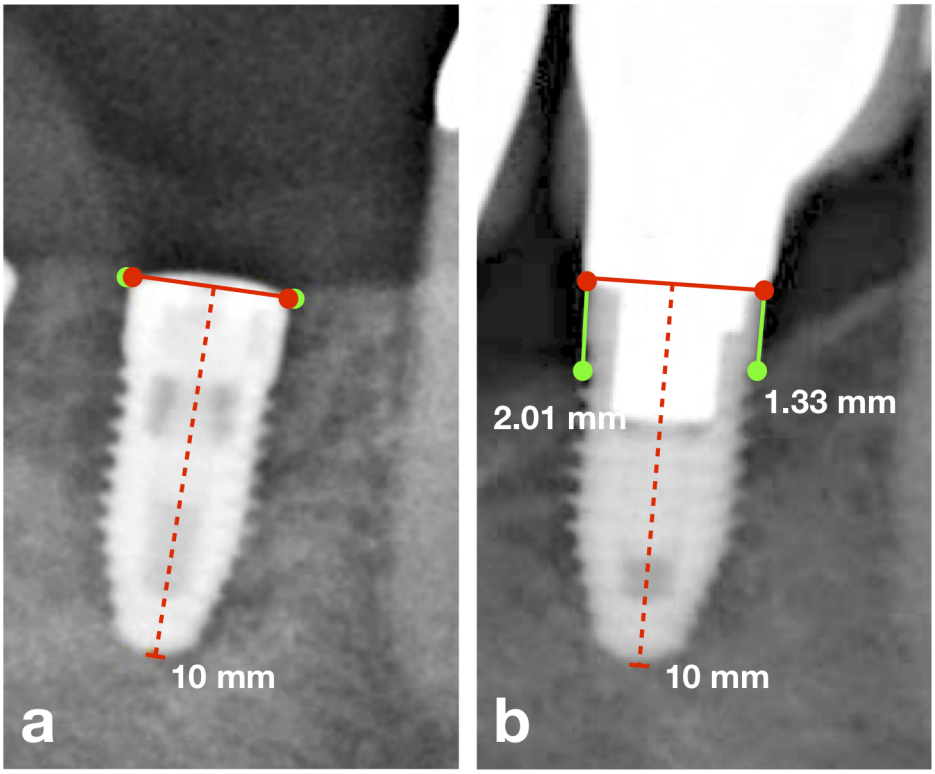
	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.



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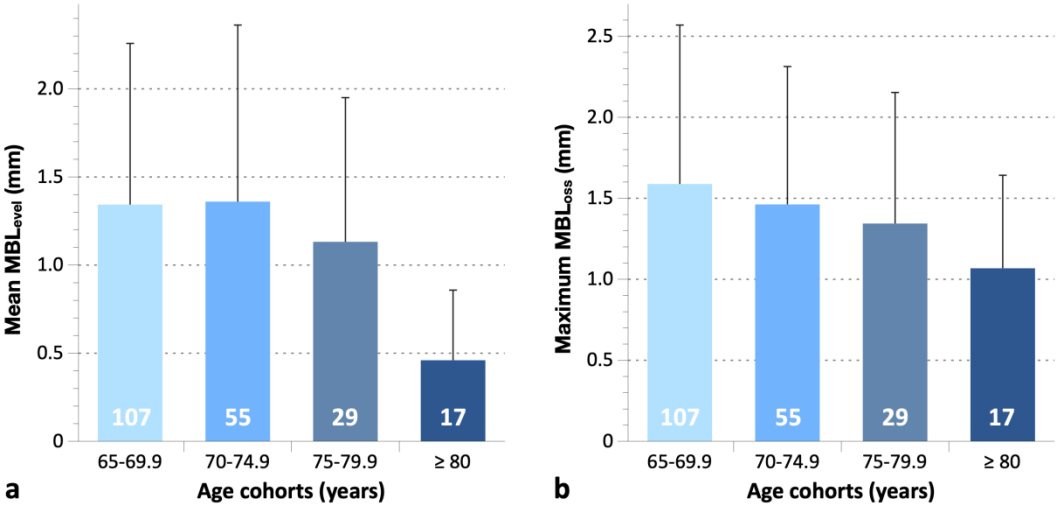

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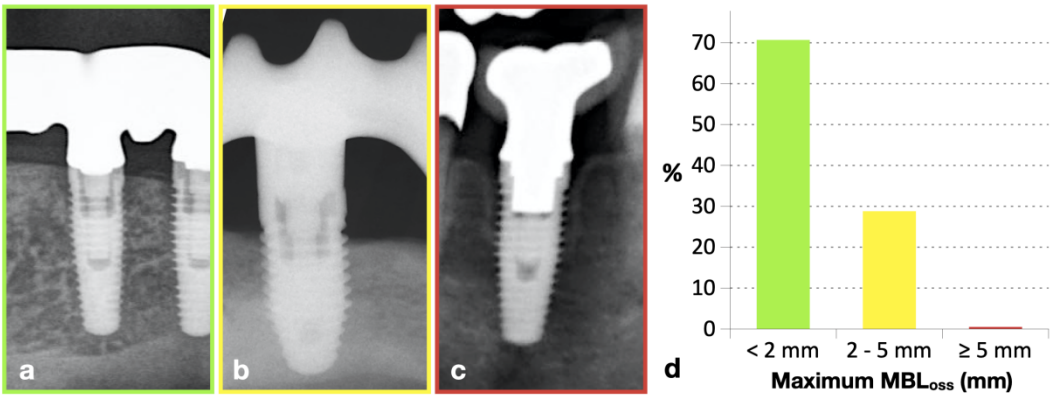

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