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How old is old for implant therapy in terms of early implant losses?

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Abstract

Objectives: To assess, retrospectively, whether older age has an impact on implant osseointegration when compared with younger age.

Methods: All patients ≥65 years old at implant installation, in an university setting over a time-period of 11.5 years, with complete anamnestic data and follow-up until prosthetic restoration were included, and any early implant loss (EIL; i.e. lack of osseointegration prior to or at the time-point of prosthetic restoration) was recorded. Further, one implant, from each of the elderly patients, was attempted matched to one implant in a younger patient (35 to <55 years old at implant installation) from the same clinic based on (a) gender, (b) implant region, (c) smoking status and (d) bone grafting prior to/simultaneously with implant installation. The potential impact of various local and systemic factors on EIL in the entire elderly population, and in the matched elderly and younger patient group was statistically assessed.

Results: Four hundred forty-four patients ≥65 years old (range 65.1–91.3; 56.8% female) receiving 1,517 implants were identified; 10 patients had one EIL each (implant/patient level: 0.66/2.25%). Splitting this patient cohort additionally into four age groups [65–69.9 (n = 213), 70–74.9 (n = 111), 75–79.9 (n = 80) and ≥80 (n = 40)], EIL was on the implant level 0.41, 0.83, 0.34 and 2.26%, respectively, (p = .102) and on the patient level 1.41, 2.70, 1.25 and 7.50%, respectively, (p = .104); multilevel analysis showed weak evidence of association of increasing age with higher EIL rate (p = .090). Matching was possible in 347 cases, and 5 (1.44%) and 9 (2.59%) EIL in the elderly and younger patients, respectively, were observed (p = .280). EIL could not be associated with any systemic condition or medication intake.

Conclusions: Elderly patients ≥65 years old presented a similarly low EIL rate as younger patients 35 to <55 years old, while patients ≥80 years old may have a slight tendency for a higher EIL rate. Hence, ageing does not seem to compromise osseointegration, and if at all, then only slightly and at a later stage of life.

KEYWORDS

dental implant, early implant loss, elderly population, osseointegration

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1 | INTRODUCTION

Current data indicate that about 20% of the European population is ≥65 years old and about 6% is ≥80 years old (Eurostat, 2018); the prognosis is that these percentages will continue to grow in the future. Taking this into account, together with the fact that implant-supported restorations significantly improve not only oral health-related quality of life (Reissmann, Dard, Lamprecht, Struppek, & Heydecke, 2017), but also health-related quality of life (Naito et al., 2006) in general, elderly patients seeking implant treatment are and will remain a significant part of daily clinical work (Schimmel, Müller, Suter, & Buser, 2017). In a recent systematic review of prospective trials on implant treatment in elderly patients (i.e. patients being ≥65 years old at the time-point of implant installation), implant survival rates of 98% and 91% after 1 and 10 years of loading, respectively, were calculated (Srinivasan, Meyer, Mombelli, & Müller, 2017). These rates are similar to those previously reported for the general population; for example, the survival rate of implants supporting single crowns is >97% and 95% after 5 and 10 years, respectively, and that of implants supporting fixed dental prostheses is >95% and 93%, respectively (Hjalmarsson, Gheisarifar, & Jemt, 2016; Jung, Zembic, Pjetursson, Zwahlen, & Thoma, 2012; Pjetursson, Thoma, Jung, Zwahlen, & Zembic, 2012). Furthermore, another systematic review reported that implant loss rates of older patients (i.e. ≥60 years old) did not differ significantly from those of younger patients (i.e. ≤54 years old) (Sendyk et al., 2017).

In this context, several factors associated with ageing may compromise implant osseointegration; for example, elderly patients—compared with younger patients—show higher rates of systemic diseases (e.g. diabetes) and more often receive medication/treatment (e.g. bisphosphonates, radiotherapy) that interfere with wound healing in general and bone healing in particular (Bartold, Ivanovski, & Darby, 2016; Chambrone, Mandia, Shibli, Romito, & Abrahao, 2013). Further, ageing per se influences negatively several stages of the implant integration process, in terms of both soft and hard tissue healing. Briefly, the early inflammatory stage of healing is delayed/prolonged due to the generally increased inflammatory response in the elderly compared to younger adults; similarly, the proliferative phase of healing is delayed/prolonged, among other factors, due to the reduced numbers of stem cells and amount of growth factors in the elderly (Bartold et al., 2016). Nevertheless, there is limited information on early implant losses (EIL) in the elderly, that is implant losses prior to loading—an ultimate sign of compromised osseointegration. Indeed, in the original studies included in the above-mentioned systematic reviews (Sendyk et al., 2017; Srinivasan et al., 2017), information on EIL was often missing, while the number of elderly patients in most of the original studies was general rather small (i.e. mostly <50). Further, in studies with larger elderly patient numbers presenting rates of EIL of 4.5% to 9.7% on the implant and patient level, respectively, reporting did not include any comparisons to younger patients (Engfors, Ortorp, & Jemt, 2004; Kowar, Eriksson, & Jemt, 2013). Consequently, lack of significant differences between elderly and younger patients, in terms of survival rates of already osseointegrated implants, as reported above, and lack of comparative data, obviously does not exclude the possibility that significant differences in terms of EIL do exist between elderly and younger patients, but simply are erroneously not captured.

Thus, information on EIL in the elderly is rather scarce in the currently existing literature. Therefore, the aim of the present study was to assess, retrospectively, EIL rate in a large elderly patient cohort, that is ≥65 years old at the time-point of implant installation, and compare it with that in a matched younger patient cohort, that is 35 to <55 years old at the time-point of implant installation.

Clinical Relevance

Scientific rationale for the study: Information on early implant loss (EIL; i.e. lack of osseointegration prior to or at the time-point of prosthetic restoration) in the elderly is rather scarce in the currently existing literature.

Principal findings: EIL in patients ≥65 years old at implant installation was similarly low as in younger patients 35 to <55 years old (1.44% vs. 2.59%, respectively), matched for gender, implant site, smoking and bone grafting. A weak evidence of association of increasing age with higher EIL rate was observed, with patients ≥80 years old showing a rate of EIL of 2.25% and 7.5% on the implant and patient level, respectively, compared with patients 65–79 years old that showed rates of 0.34%–0.83% and 1.25%–1.70%, on the implant and patient level, respectively; yet, this is based on a limited number of EIL cases (i.e. 1–3) in the various age subgroups. EIL could not be associated with any systemic condition or medication intake, in this relatively healthy elderly patient cohort.

Practical implications: Age per se should not be considered as a limiting factor for implant therapy, but it should be taken into account that patients ≥80 years old may have a slight tendency for a higher risk of EIL than slightly younger patients.

2 | MATERIALS AND METHODS

The present retrospective cohort study is based on dental records of the University Clinic of Dentistry, Medical University of Vienna, Austria, which were selected automatically (electronically) based on information from the payment system of the clinic, from 01/2005—where all dental records became digital—to 06/2016. All treatments were performed in the Division of Oral Surgery, by experienced oral surgeons, and the predominant implant types installed were NobelReplace and Replace Select. The study protocol was approved by the ethics committee of the Medical University of Vienna (EK-Nr.

1980/2016); reporting in the present manuscript complies with the STROBE guidelines.

2.1 | Patient population

2.1.1 | Elderly patient cohort

The dental records of all patients who had paid/received an implant between 01/2005 and 06/2016 were ≥65 years old at the time-point of implant installation, were extracted and manually screened twice by two examiners (M.E. and M.K.) for complete anamnestic data (i.e. records on systemic diseases and medication intake) and follow-up until prosthetic restoration. Patients with records indicating history of head and neck cancer and/or immune deficiency due to immunosuppressant medication were excluded.

The following parameters were extracted: (a) age, (b) gender, (c) implant region, (d) EIL, that is lack of osseointegration prior to placement of the prosthesis and occlusal loading (yes/no; primary outcome variable), (e) bone augmentation prior to or simultaneously with implant installation (yes/no), (f) smoking status at the time-point of implant installation (yes/no), (g) history of periodontitis, that is presence of bone loss judged on panoramic radiographs or if the patient was completely edentulous (yes/no; please note that as standard at the University Clinic, all patients were periodontally healthy or periodontal disease was treated and considered as under control at the time-point of implant installation), (h) presence of diabetes mellitus, osteoporosis or rheumatoid arthritis (yes/no) and (i) regular intake of bisphosphonates, statins, selective serotonin reuptake inhibitors (SSRI), proton-pump inhibitors (PPI), anticonvulsants, corticosteroids, antihypertensives, anticoagulants or non-steroidal anti-inflammatory drugs (NSAID) (yes/no).

2.1.2 | Younger patient cohort

Based on previous studies (Sendyk et al., 2017), which applied a difference of 10 years between younger and older patient cohorts, the "cut-off value" for the younger patients was defined as 55 years of age. One implant in each elderly patient was attempted to match with an implant installed in a patient 35 to <55 years old at the time-point of implant installation, by manually looking through an automatically generated list of dental records of all patients who had paid/received an implant at the same clinic and timeframe, on the basis of the following criteria: (a) gender, (b) implant region [i.e. upper anterior (tooth no. 13–23)/upper posterior/lower anterior (tooth no. 33–43)/lower posterior], (c) bone grafting prior to or simultaneously with implant installation (yes/no) and (d) smoking status (yes/no). Regarding elderly patients with ≥2 implants, the implant to be matched was chosen at random; if matching failed, another implant from the remaining ones in the same patient was again chosen at random and matching was attempted. When matching of one implant in a given patient was achieved, then the next patient in the list was attempted to match. Similar anamnestic data to those collected from the patients in the elderly patient cohort were also extracted in this younger patient group.

2.2 | EIL

From each EIL case, the following parameters were additionally extracted: (a) timing of implant installation, that is immediate/delayed, if within the same session as the tooth extraction or at some later time-point, respectively, (b) implant dimension, (c) implant type, (d) connection type, that is internal/external, (e) antibiotic prescription at the time-point of implant installation (yes/no), (f) post-operative healing type, that is submerged/non-submerged and (g) re-implantation at later time-point (yes/no, including time-point).

2.3 | Statistical analysis

Descriptive statistics were calculated for patient- and implant-related characteristics. To identify any potential differences/tendencies among the elderly and younger patients, both cohorts were sub-classified into 4 age sub-cohorts: (a) 65–69.9/70–74.9/75–79.9/ and ≥80 years of age in the elderly group, and (b) 35–39.9/40–44.9/45–49.9/50–54.9 years of age in the younger group. Fishers' exact test or chi-squared test was used to assess any potential differences: (a) between patients or implants, with and without an EIL, in the elderly patient cohort, (b) between the elderly and younger patient matched cohorts, and (c) among the 4 age sub-cohorts, separately for the elderly and younger matched patient cohorts regarding the various categorial parameters (i.e. age cohorts, gender, implant region, EIL, bone augmentation, smoking status, history of periodontitis, presence/absence of a systemic disease, medication intake). Patient-specific parameters have been compared on the patient level, while implant-specific parameters on the implant level. Additionally, several univariable random effects logistic regression analyses assessed any effect of the various predictors (i.e. age, gender, implant region, no. of implants per patient, bone augmentation, smoking status, history of periodontitis, presence/absence of a systemic disease, medication intake) on the primary outcome parameter (i.e. EIL) in the elderly patient cohort. Parameters significant at the $a = 0.20$ were considered for the final multivariable model, whereas age and gender were considered a priori confounders. Statistical analysis was performed using SPSS Version 24.0 (SPSS Inc.) and STATA 15.1 (StataCorp LLC), and p-values <.05 were considered as statistically significant.

3 | RESULTS

3.1 | Patient population

Out of 628 patients ≥65 years old at the time-point of implant installation, 444 patients could be included in the elderly patient cohort herein (mean age: 72.0 ± 5.7; range: 65–91 years; 56.8% female); most common reasons for exclusion were no follow-up after implant installation, that is prosthetic restoration was performed at the referring dentist,

and unclear anamnestic data. This elderly patient cohort received 1,517 implants (range: 1–12 implants per patient). Out of those 444 elderly patients, 347 could be matched with younger patients <55 years old (elderly/younger patient cohort: mean age 71.0 ± 5.0/46.5 ± 6.0, range 65 to 89/35 to <55 years, respectively; 55.9% female); most commonly, the remaining 97 patients could not be matched due to the low number of lower anterior implants in younger patients. Data on implant region, number of implants per patient, bone augmentation, smoking status, history of periodontitis, presence of systemic diseases and medication intake are presented in Table 1 for the elderly patient cohort (n = 444) and in Table 2 for the matched patient cohorts (n = 347 patients each in the elderly and younger patient cohort). The elderly patient cohort differed significantly from the matched younger patient cohort in several parameters (p < .01; Table 2); that is, elderly patients presented more often with a history of periodontitis, systemic disease (diabetes mellitus, osteoporosis, rheumatoid arthritis) and regular intake of several medications.

TABLE 1 Characteristics of the elderly patient cohort (n = 444) and implant-specific details (n = 1,517)

Patient characteristics	
Age	
Mean ± *SD* (min; max)	72.0 ± 5.7 (65; 91)
Cohorts [65–69.9/70–74.9/75–79.9/≥80 years of age; *n* (%)]	213/111/80/40 (48.0/25.0/18.0/9.0)
Gender [female; *n* (%)]	252 (56.8)
Smoking at the time-point of implant installation [*n* (%)]	48 (10.8)
History of periodontitis [yes; *n* (%)]	384 (86.5)
Systemic disease [present; *n* (%)]	
Diabetes mellitus	47 (10.6)
Osteoporosis	41 (9.2)
Rheumatoid arthritis	20 (4.5)
Medication intake [yes; *n* (%)]	
Bisphosphonates	31 (7.0)
Statins	94 (21.2)
Selective serotonin reuptake inhibitors	48 (10.8)
Proton-pump inhibitors	66 (14.9)
Anticonvulsants	16 (3.6)
Corticosteroids	23 (5.2)
Antihypertensives	198 (44.6)
Anticoagulants	31 (7.0)
Non-steroidal anti-inflammatory drugs	116 (26.1)
Implant characteristics	
Implants per patient [*n* (%)]	
1	61 (13.7)
2	115 (25.9)
3	30 (6.8)
4	170 (38.3)
5	17 (3.8)
6	24 (5.4)
7	9 (2.0)
8	5 (1.1)
9	4 (0.9)
10	7 (1.6)
11	1 (0.2)
12	1 (0.2)
Implant region [*n* (%)]	
Upper posterior/anterior	353 (23.3)/141 (9.3)
Lower posterior/anterior	573 (37.8)/450 (29.7)
Bone augmentation [yes; *n* (%)]	228 (15.0)

Abbreviation: *SD*, standard deviation.

3.2 | EIL

In the elderly patient cohort, 10 patients had one EIL each, that is EIL on implant and patient level was 0.66% and 2.25%, respectively. Specifically, EIL occurred in one patient each with 2, 7, and 8 implants, in two patients each with 3 and 5 implants, and in three patients with 6 implants. EIL rate in the 4 elderly patient sub-cohorts [i.e. 65–69.9 (n = 213), 70–74.9 (n = 111), 75–79.9 (n = 80) and ≥80 years old (n = 40), respectively] was 0.41%, 0.83%, 0.34% and 2.26%, respectively, on the implant level, and 1.41%, 2.70%, 1.25% and 7.50%, respectively, on the patient level; the difference in EIL rate between the ≥80 years sub-cohort and the 3 remaining sub-cohorts was not statistically significant (p = .102 and p = .104, on the implant and patient level, respectively; Figure 1). Similarly, the multivariable random effects logistic regression analysis for the elderly patient cohort indicated only weak evidence of association of higher EIL rate with increasing age (p = .090; Appendix S1). Further, no statistically significant differences between patients/implants with and without EIL and no significant effects, in regard to the various evaluated parameters, were observed within the elderly patient cohort (Table 3 and Appendix S1). In regard to the matched cohorts, five patients in the elderly group versus nine patients in the younger group experienced one EIL each, that is 1.44% versus 2.59%, respectively (p = .280; Figure 1). No statistically significant differences were observed between patients/implants with and without EIL, within the matched elderly and younger patient cohorts in regard to any of the evaluated parameters, although there was higher prevalence of diabetes mellitus, osteoporosis, and rheumatoid arthritis and regular medication intake in the elderly patients compared with the younger ones (p ≥ .174; Table 4). Further details on all EIL cases are listed in Table 5.

4 | DISCUSSION

The results of the present study, based on a relatively large patient sample, showed that EIL are not more frequent in elderly (≥65 years old) than in younger patients (<55 years old), and in general are seldom, that is <1% on implant and around 2.5% on patient level. Thus, this finding appears to correspond well to the currently existing

TABLE 2 Characteristics of the matched patient cohorts (n = 347 patients each in the young and elderly patient cohort; each patient contributed with one implant)

	Young patient cohort (<55 years of age)	Elderly patient cohort (≥65 years of age)
Age		
Mean ± *SD* (min; max)[a]	46.5 ± 6.0 (35; 55)	71.0 ± 5.0 (65; 89)
Cohorts[b] [*n* (%)]	56/75/92/124 (16.1/21.6/26.5/35.8)	171/104/49/23 (49.3/30.0/14.1/6.6)
History of periodontitis [yes; *n* (%)][a]	114 (32.9)	314 (90.5)
Systemic disease [yes; *n* (%)]		
Diabetes mellitus[a]	3 (0.9)	37 (10.7)
Osteoporosis[a]	1 (0.3)	28 (8.1)
Rheumatoid arthritis[a]	1 (0.3)	18 (5.2)
Medication intake [yes; *n* (%)]		
Bisphosphonates[a]	1 (0.3)	23 (6.6)
Statins[a]	9 (2.6)	71 (20.5)
Selective serotonin reuptake inhibitors[a]	11 (3.2)	38 (11.0)
Proton-pump inhibitors[a]	8 (2.3)	44 (12.7)
Anticonvulsants	3 (0.9)	11 (3.2)
Corticosteroids	10 (2.9)	21 (6.1)
Antihypertensives[a]	36 (10.4)	152 (43.8)
Anticoagulants[a]	2 (0.6)	27 (7.8)
Non-steroidal anti-inflammatory drugs[a]	9 (2.6)	85 (24.5)
	Matching criteria	
Gender [female; *n* (%)]	194 (55.9)	
Smoking at the time-point of implant installation [*n* (%)]	44 (12.7)	
Implant region [*n* (%)]		
Upper posterior/anterior	94 (27.1)/24 (6.9)	
Lower posterior/anterior	200 (57.6)/29 (8.4)	
Bone augmentation [yes; *n* (%)]	65 (18.7)	

Abbreviation: *SD*, standard deviation.
[a]Inter-group comparison (presented a statistically significant difference ($p < .01$).
[b]Young patient cohort: 35–39.9/40–44.9/45–49.9/50–54.9 years of age; elderly patient cohort: 65–69.9/70–74.9/75–79.9/>80 years of age.

knowledge on implant therapy in the elderly. As mentioned earlier, in a recent systematic review on implants in patients ≥65 years of age, post-loading implant survival rates of 98% at 1 year and 91% at 10 years were calculated (Srinivasan et al., 2017). Similarly, in another systematic review on implant losses in older (≥60 years old) versus younger (≤54 years old) patients, no significant differences were observed between the two groups in terms of implant survival (94% vs. 95%, respectively, based on four studies included) (Sendyk et al., 2017). However, the high survival rates reported in these reviews regarded mainly osseointegrated implants and EIL were not specifically addressed; in most of the original studies included in these reviews, information on EIL was often missing, while the number of elderly patients was in general rather small (i.e. mostly <50). Therefore, possible significant differences between elderly and younger patients in terms of EIL might have been overseen.

Older age per se is shown to negatively influence wound healing on several levels. Osseointegration follows the regular steps of osseous wound healing, starting with an inflammatory phase due to the surgical trauma of implant installation and is followed by a proliferative stage, where new tissue is formed. Older age is shown to influence the cells and mediators involved in these processes; elderly patients are producing larger amounts of inflammatory mediators and thereby show an increased/stronger inflammatory reaction, and consequently, a prolonged inflammatory phase is observed in the elderly compared with younger patients. Further, the number and function of stem cells, including growth factor production, are decreased with increasing age, resulting in reduced new bone tissue formation capacity and imbalanced remodelling, which in turn affects tissue maturation (Bartold et al., 2016; Bosshardt, Chappuis, & Buser, 2017; Chan & Duque, 2002; Gibon, Lu, & Goodman, 2016).

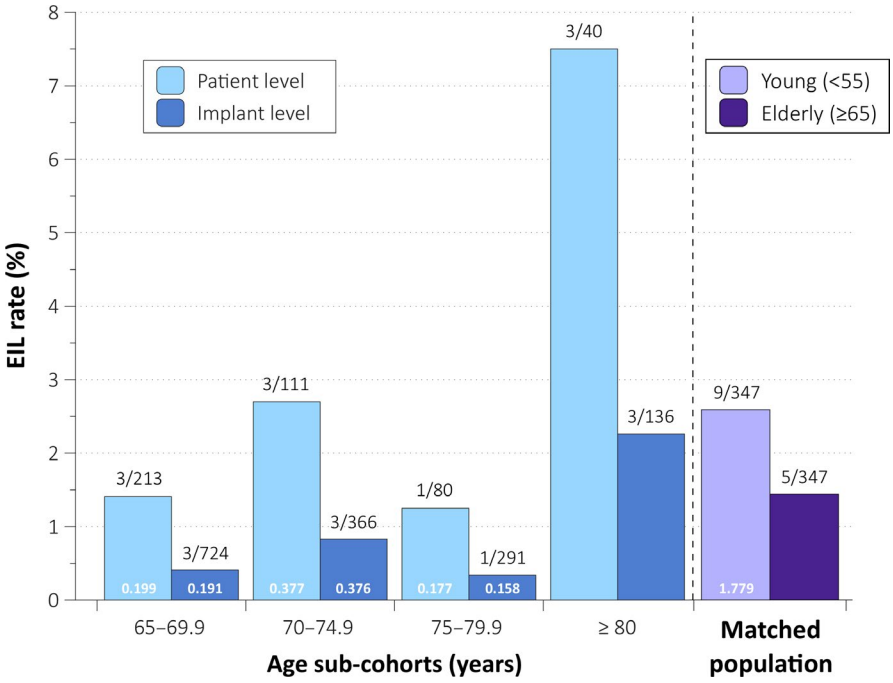

FIGURE 1 EIL rate (%) on the patient (light blue) and implant (dark blue) level in the elderly patient cohort (n = 444), divided into 4 sub-cohorts. The matched population (young patient cohort is displayed in light purple, elderly patient cohort in dark purple) consisted of 347 patients contributing with one implant each. The numbers on top of the bars present the actual numbers of EIL out of the total numbers of patients/implants, and the white numbers inside the bars represent the relative risk for EIL compared to the sub-cohort of patients ≥80 years of age or compared to the matched elderly patient cohort, respectively

TABLE 3 Frequency distribution of the various patient- and implant-related parameters in EIL and non-EIL cases, within the elderly patient cohort (i.e. 444 patients with 1,517 implants)

	EIL		
Patient characteristics	**No (n = 434)**	**Yes (n = 10)**	***p*-value**
Age cohorts (65–69.9/70–74.9/75–79.9/≥80 years of age; n)	210/108/79/37	3/3/1/3	.104
Gender (female/male; n)	249/185	3/7	.109
Smoking status at the time-point of implant installation (non-smoker/smoker; n)	383/48	9/1	1.000
History of periodontitis (no/yes; n)	60/374	0/10	.371
Systemic disease (no/yes; n)			
Diabetes mellitus	388/46	9/1	1.000
Osteoporosis	393/41	10/0	.609
Rheumatoid arthritis	414/20	10/0	1.000
Medication intake (no/yes; n)			
Bisphosphonates	403/31	10/0	1.000
Statins	342/92	8/2	1.000
Selective serotonin reuptake inhibitors	386/48	10/0	.610
Proton-pump inhibitors	369/65	9/1	1.000
Anticonvulsants	418/16	10/0	1.000
Corticosteroids	411/23	10/0	1.000
Antihypertensives	240/194	6/4	1.000
Anticoagulants	403/31	10/0	1.000
Non-steroidal anti-inflammatory drugs	318/116	10/0	.070
Implant characteristics	**No (n = 1,507)**	**Yes (n = 10)**	***p*-value**
Implant region (upper posterior/upper anterior/lower posterior/lower anterior; n)	350/140/571/446	3/1/2/4	.704
Bone augmentation (no/yes; n)	1,280/227	9/1	1.000

Abbreviation: EIL, early implant loss.

TABLE 4 Frequency distribution of the various patient- and implant-related parameters in EIL and non-EIL cases, in the matched patient cohorts

	Elderly patient cohort (≥65 years of age) Early implant loss			Younger patient cohort (<55 years of age) Early implant loss		
Patient and implant characteristics	**No (*n* = 342)**	**Yes (*n* = 5)**	***p*-value**	**No (*n* = 338)**	**Yes (*n* = 9)**	***p*-value**
Age cohorts[a] (*n*)	168/103/49/22	3/1/0/1	.499	54/72/92/120	2/3/0/4	.328
Gender (female/male; *n*)	193/149	1/4	.174	189/149	5/4	1.000
Smoking status at the time-point of implant installation (non-smoker/smoker; *n*)	299/43	4/1	.494	296/42	7/2	.319
History of periodontitis (no/yes; *n*)	33/309	0/5	1.000	229/109	4/5	.161
Systemic disease (no/yes; *n*)						
Diabetes mellitus	305/37	5/0	1.000	335/3	9/0	1.000
Osteoporosis	314/28	5/0	1.000	337/1	9/0	1.000
Rheumatoid arthritis	324/18	5/0	1.000	337/1	9/0	1.000
Medication intake (no/yes; *n*)						
Bisphosphonates	319/23	5/0	1.000	337/1	9/0	1.000
Statins	271/71	5/0	.588	329/9	9/0	1.000
Selective serotonin reuptake inhibitors	304/38	5/0	1.000	327/11	9/0	1.000
Proton-pump inhibitors	298/44	5/0	1.000	330/8	9/0	1.000
Anticonvulsants	331/11	5/0	1.000	335/3	9/0	1.000
Corticosteroids	321/21	5/0	1.000	328/10	9/0	1.000
Antihypertensives	191/151	4/1	.391	303/35	8/1	1.000
Anticoagulants	315/27	5/0	1.000	336/2	9/0	1.000
Non-steroidal anti-inflammatory drugs	257/85	5/0	.340	330/8	8/1	.213
Implant region (upper posterior/upper anterior/lower posterior/lower anterior; *n*)	92/23/199/28	2/1/1/1	.303	93/23/194/28	1/1/6/1	.724
Bone augmentation (no/yes; *n*)	277/65	5/0	.588	274/64	8/1	1.000

[a]Elderly patient cohort: 65–69.9/70–74.9/75–79.9/>80 years of age; Younger patient cohort: 35–39.9/40–44.9/45–49.9/50–54.9 years of age.

Indeed, it has been demonstrated in preclinical trials that osseointegration can be compromised in older age (Shirota et al., 1993; Takeshita, Murai, Ayukawa, & Suetsugu, 1997). For example, titanium implants placed in the tibia of old rats (1.5 years old) showed only about 1.5% bone-to-implant-contact (BIC) after 4 weeks of healing, compared with 40% and 29% BIC in young (1.5 months old) and adult (5.5 months old) rats, respectively (Takeshita et al., 1997). Furthermore, older age is associated with high rates of systemic diseases and elderly patients receive more often medications that interfere with wound healing in general and bone healing in particular (Bartold et al., 2016). Thus, the possibility of different EIL rates in the elderly and in younger patients appeared as a reasonable concern.

In this context, a variety of factors have been associated with an increased EIL rate; examples are—but not limited to—smoking, maxillary site, male gender, short implant length, implant type/brand, number of implants, immediate placement, need of bone grafting, non-submerged healing, history of periodontitis, the clinician and specific medication intake (Alsaadi, Quirynen, Komárek, & van Steenberghe, 2007; Antoun, Karouni, Abitbol, Zouiten, & Jemt, 2017; Berglundh, Persson, & Klinge, 2002; Bryant, 1998; Chrcanovic, Kisch, Albrektsson, & Wennerberg, 2016; Derks et al., 2015; Esposito, Grusovin, Loli, Coulthard, & Worthington, 2010; Hickin, Shariff, Jennette, Finkelstein, & Papapanou, 2017; Jemt, 2017; Manzano et al., 2016; Olate, Lyrio, de Moraes, Mazzonetto, & Moreira, 2010; Olmedo-Gaya, Manzano-Moreno, Cañaveral-Cavero, Dios Luna-del Castillo, & Vallecillo-Capilla, 2016; Palma-Carrió, Maestre-Ferrín, Peñarrocha-Oltra, Peñarrocha-Diago, & Peñarrocha-Diago, 2011; Pommer et al., 2011; Troiano et al., 2018). For example, PPI (Al Subaie et al., 2016; Chrcanovic, Kisch, Albrektsson, & Wennerberg, 2017; Wu et al., 2017), SSRI (Wu et al., 2014) and antidepressants in general (Chrcanovic et al. 2016), which are all rather common in the elderly, have been associated with an increased risk for implant failure. The matching procedure herein accounted for four factors, that is smoking, gender, jaw site and need of bone grafting, while some other factors did not vary or were controlled through the routines of the university clinic, that is mainly the same type of implant (i.e. NobelReplace/Replace Select) was installed by experienced oral surgeons; all periodontitis patients were considered generally successfully treated prior to implant installation, and diabetic patients were generally well controlled. Within this context, the absence of data on the reason of tooth loss for each single tooth cannot exclude the possibility that some/several of the teeth were lost due to

TABLE 5 Characteristics of all patients with EIL in the elderly and younger patient cohorts

Patient	Age	Gender	History of periodontitis	Smoking status	Medication intake Systemic disease	Position	Augmentation Timing of implant installation	Implant dimension Implant type Connection type	Antibiotic prescription Submerged/non-submerged healing Re-implantation
Elderly patient cohort (≥65 years of age)									
#1[a]	69.1	m	Yes	No	– –	31	– Immediate	13/3.5 Nobel Replace select straight Internal	Yes Open Re-implanted after 4 months
#2[a]	67.1	m	Yes	Yes	– –	23	– Delayed	11.5/4.3 Nobel Replace select tapered Internal	Yes Open Re-implanted after 3 months
#3[a]	68.7	m	Yes	No	– –	24	– Delayed	13/3.5 Nobel Replace select tapered Internal	Yes Closed Re-implanted after 4 months
#4[a]	70.2	f	Yes	No	– –	44	– Delayed	9.5/3.8 Xive S Plus Internal	No Open Re-implanted after 3 months
#5	74.8	m	Yes	No	AHD –	15	– Delayed	11.5/3.5 Nobel Replace select tapered Internal	No Open Re-implanted after 6 months
#6	73.7	f	Yes	No	– –	46	– Delayed	10/4.3 Nobel Replace Conical connection PMC Internal	Yes Open Re-implanted after 3 months
#7	75.3	f	Yes	No	– –	33	Intraoperative bovine BS Delayed	11.5/3.5 Nobel Replace select tapered Internal	No Open Re-implanted after 1 month
#8	81.0	m	Yes	No	Statins, AHD Diabetes	33	– Delayed	13/4.3 Nobel Replace select straight Internal	No Open Re-implanted after 5 months
#9[a]	82.9	m	Yes	No	AHD –	24	– Delayed	13/4.3 Nobel Replace select tapered Internal	Yes Open Re-implanted after 1.5 months
#10	88.9	m	Yes	No	PPI, statins, AHD –	43	– Delayed	11.5/4.3 Nobel Replace select tapered Internal	Yes Open Re-implanted after 1 month
Younger patient cohort (<55 years of age)									
#11	42.3	m	Yes	Yes	– –	23	– Delayed	13/4.3 Nobel Replace select tapered Internal	Yes Open Re-implanted after 8 months

(Continues)

TABLE 5 (Continued)

Patient	Age	Gender	History of periodontitis	Smoking status	Medication intake Systemic disease	Position	Augmentation Timing of implant installation	Implant dimension Implant type Connection type	Antibiotic prescription Submerged/non-submerged healing Re-implantation
#12	44.2	m	No	No	– –	33	– Delayed	13/3.5 Nobel Replace select tapered Internal	Na Open Re-implanted
#13	39.1	m	No	No	– –	37	– Delayed	13/4.3 Nobel Replace select tapered Internal	No Open Re-implanted after 4.5 months
#14	54.0	m	No	No	AHD –	36	– Delayed	11.5 13/4.3 Nobel Replace select tapered Internal	No Open Re-implanted after 11 months
#15	50.4	f	Yes	Yes	– –	24	– Delayed	13/4.3 Nobel Replace select tapered Internal	Yes Open Not re-implanted
#16	55.0	f	Yes	No	Constant NSAID users –	34	– Delayed	10/4.3 Nobel Replace Select tapered Internal	Yes Closed Not re-implanted
#17	40.6	f	Yes	No	– –	34	– Delayed	13/4.3 Nobel Replace Select tapered Internal	No Closed Re-implanted after 4 years
#18	35.9	f	No	No	– –	46	Autogenous bone block (2-step surgery) Delayed	Na	Na Open Re-implanted after re-augmentation
#19	52.1	f	Yes	No	– –	36	– Delayed	10/4.3 Nobel Replace Select tapered Internal	Yes Open Re-implanted after 2.5 months

Abbreviations: AHD, anti-hypertensive drugs; BS, bone substitute; Na, not available; NSAID, non-steroidal anti-inflammatory drug; PPI, proton-pump inhibitors; m, male; f, female.
[a]Indicates the patients included in the elderly matched cohort.

other reasons than periodontitis. However, due to the lack of specific data for all patients and based on the high prevalence of moderate or severe periodontitis in populations above 65 years of age (e.g. 92% in Germany; Holtfreter, Kocher, Hoffmann, Desvarieux, & Micheelis, 2010), it seemed reasonable to assume that all completely edentulous patients suffered from some degree of periodontitis. Nevertheless, other factors largely inherent with ageing could not be controlled (matched to), but were accounted for; indeed, in the present study population, the elderly patient cohort presented a significantly higher frequency of medication intake (bisphosphonates, statins, SSRI, PPI, antihypertensives, anticoagulants and NSAID) as well as higher prevalence of osteoporosis and rheumatoid arthritis, compared with the matched younger patient cohort. In the younger population, none of the investigated systemic diseases appeared in >1% and none of the medications was taken by more than 3.5% of the patients, except of antihypertensives (10%); so, the younger population, herein, should be considered as relatively healthy. No association of any of those parameters with EIL was observed in the present study, neither in the elderly nor in the younger patient group. Indeed, in both groups, a very low number of EIL were observed and in most cases of EIL, the various evaluated parameters (e.g. systemic disease, medication intake and bone augmentation) were not present. The rationale to use 2 cohorts with a minimum of 10 years of age difference, herein, was based on the assumption that if age had an effect, this would be easier to observe when using 2 distinct age groups. The rationale to select only one implant to represent each individual in the old versus younger group was to have balance in the groups for 4 conceptually relevant parameters (i.e. gender, region, smoking, augmentation). Further, the extent of therapy (i.e. number of implants installed) was not considered during matching herein, because it was anticipated that a large number of patients would not be able to match, due to the fact that younger patients would most likely bear a lower number of implants compared with the elderly ones. In this context, no effect of the number of implants per patient on EIL was observed in the elderly patient cohort. In perspective, a different valid approach to address the topic could have been using an unmatched sample and performing a simple regression analysis with age as the independent factor and correcting for the various parameters, or perform hierarchical analyses including all implants of a patient.

In this context, the elderly patients herein cannot be considered as a severely multi-medicated and/or multimorbid population. Specifically, only three types of medication have been taken by more than 20% (i.e. statins, antihypertensives and NSAID), while two medications were taken by 10%–20% of the elderly population (i.e. SSRI and PPI). Further, only 11% presented with diabetes mellitus and only 9% with osteoporosis that were also receiving treatment. It may indeed be that elderly patients seeking implant therapy are in generally relatively healthier than the average elderly population; a similar observation has been made in previous reports on implant therapy in the elderly (Compton et al., 2017; Kowar, Stenport, & Jemt, 2014). This may also partly explain the observation that the matched younger patient cohort herein presented an EIL rate almost 2 times higher than that in the elderly patients. Another possibility may be that elderly patients are more likely afraid of complications (Ellis et al., 2011; Müller et al., 2013) and, therefore, follow more carefully the post-operative instructions (e.g. avoiding wearing a removable prosthesis shortly after the operation). In general, control of all confounders is difficult to achieve in large patient cohorts and establishment of an implant register, as recently suggested (Klinge et al., 2018), may hopefully support a more complete risk factor analysis in the future.

Sixty-five years of age has been used as the cut-off to define elderly in several studies, including the systematic review of Srinivasan et al. 2017; still, one may argue that lack of significant differences between the elderly and younger patients reported previously and observed herein is because this cut-off age is simply too low. Indeed, the multilevel analysis for the elderly patient cohort indicated only weak evidence of association of increasing age with higher EIL rate; in the 40 patients ≥80 years old contributing with 136 implants herein, EIL was 2.3% on the implant and 7.5% on the patient level, compared with patients 65–79 years old that showed rates of 0.34%–0.83% and 1.25%–1.70%, on the implant and patient level, respectively. Nevertheless, it should not be forgotten that these percentages still represent a limited number of EIL cases (i.e. 1–3 per sub-cohort). In previous studies with relatively large numbers of patients ≥80 years of age, where EIL was reported, more or less similar failure rates as those observed herein were recorded (Engfors et al., 2004; Kowar et al. 2013). Specifically, in a retrospective evaluation of 133 patients with 761 implants, EIL was 4.5% on the implant level (Engfors et al., 2004), while in another analysis of 72 patients with 265 implants, seven patients had 1 EIL each (i.e. 9.7% on the patient level) (Kowar et al., 2013). Still, 92.5% of the patients ≥80 years old in the present study showed successful primary osseointegration and received the prosthetic restoration.

Considering the facts/limitations that the present study is of retrospective character, both elderly and younger patient groups were relatively healthy, the operators were experienced oral surgeons, and only few EIL were observed, it is nevertheless reasonable to conclude, that based on a relatively large number of elderly patients—when compared with patient numbers in previously published studies—ageing does not seem to compromise osseointegration, and if at all, then only slightly and at a later stage of life.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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