Influence of Medical and Geriatric Factors on Implant Success: An Overview of Systematic Reviews

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Purpose: To provide an overview of the influence of medical and geriatric factors on implant survival in order to form clinical recommendations for the practitioner. ***Materials and Methods:*** This narrative literature review was performed to address the following questions: *(1)* Is age (> 75 years) a risk factor for implant survival?; *(2)* Is diabetes mellitus a risk factor for implant survival?; and *(3)* Is antiresorptive therapy a risk factor for implant survival? The PubMed, Web of Knowledge (Thomson Reuters), and Google Scholar databases were searched for systematic reviews and research papers of evidence level II and above that were published up to February 2019 for each topic. ***Results:*** *(1)* Age > 75 years does not affect implant survival according to short-term follow up (1 to 5 years). However, polypharmacy should be considered in this patient group. *(2)* Diabetes mellitus is not a risk factor for implant survival in the short term, but there is no information on appropriate perioperative treatment and wound closure. There is little evidence in the literature on the success of bone grafting and progressive loading protocols in diabetic patients. *(3)* Implant therapy cannot be recommended in patients under high-dose bisphosphonate and antibody therapy. Bone grafting should be avoided under antiresorptive therapy. There are no treatment regimens available for patients with peri-implantitis receiving antiresorptive medication. ***Conclusion:*** This review suggests that the risk assessment for an implant patient should not be based on age, but rather on the patient's specific risk factors, such as former and current diseases and medication. *Int J Prosthodont 2021;34(suppl):s21–s26. doi: 10.11607/ijp.7000*

Edentulism is a common phenomenon in the elderly, a population conventionally defined as older than 65 years of age.[1] A distinction is further made between partial and total edentulism.[2] The prevalence of total edentulism ranges from 1.3% to 78.0% in elderly patients worldwide.[2] In Germany, the Robert-Koch Institute reports a total edentulism prevalence of 22% in the elderly age group.[3] According to an estimate by the World Health Organization, the elderly population will increase from 900 million to 2 billion by 2050.[4] An elderly patient does not necessarily have to be a geriatric patient, since genetics, environmental, and socioeconomic conditions, as well as lifestyle and overall health, influence the aging process, and these parameters lead to interindividual differences between chronologic and biologic age.[5–7] However, geriatric guidelines still define geriatric patients according to their chronologic age. A patient is defined as geriatric at over 80 years of age or at over 70 years of age with typical geriatric multimorbidity.[8] The main challenges in treating geriatric patients are multimorbidity combined with polypharmacy, reduced mobility, reduced dexterity and motor skills, and legal aspects.[9]

Total edentulism can be adequately restored with dental implants. Studies with an observation period of up to 20 years have demonstrated implant survival rates of > 90%.[10] However, it is well documented that implant survival is influenced by both medical and geriatric factors.[11] Advanced age, diabetes mellitus, and drug intake are discussed heterogenously as risk factors in the current literature.[12–16] Risks factors can impair surgical procedures, implant osseointegration, and postloading survival, and risk factors may accumulate over the patient's lifespan.[15] Therefore, clinical recommendations concerning the effects of medical and geriatric factors on implant survival should be evidence-based. Sackett distinguishes different levels of evidence,[17]

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ranging from a low level based on editorials, expert opinion (level V), and case series/reports (IV) to a medium level based on nonexpressive, descriptive studies (III) (Table 1). A high level of evidence is provided by well-designed controlled studies without randomization (II) or by randomized controlled trials (RCT) (Ib).[18] RCTs are summarized and interpreted in systematic reviews with meta-analyses (evidence level Ia).

This narrative review was conducted to provide an overview on medical and geriatric factors in the edentulous implant patient for the 2019 Oral Reconstruction International Expert Meeting to offer clinical recommendations for the practitioner.

The following questions were addressed:

1. Is age (> 75 years) a risk factor for implant survival?
2. Is diabetes mellitus a risk factor for implant survival?
3. Is antiresorptive therapy a risk factor for implant survival?

Table 1 Levels of Evidence According to Sackett

Systematic reviews with or without meta-analysis	Ia
Well-designed randomized controlled trials (RCTs)	Ib
Well-designed controlled studies without randomization	II
Non-expressive, descriptive studies	III
Case series/reports	IV
Editorials, expert opinions, consensus conferences	V

MATERIALS AND METHODS

Search Strategy and Data Extraction

An electronic search was conducted for each of the addressed topics. The PubMed database of the US National Library of Medicine, the Web of Knowledge of Thomson Reuters, and the Google Scholar database were screened for relevant articles (systematic reviews/meta-analyses) in the English language published up to February 2019. Data from relevant publications were extracted. A hand search in other databases was not performed. The overall findings were summarized in a narrative manner, and recommendations are based on available systematic reviews and research papers of evidence level II and above. The results were evaluated and revised in Working Group 1 and finally adopted in the plenum during the meeting.

RESULTS AND DISCUSSION

Age and Implant Survival

A current systematic review with meta-analyses analyzed implant survival in patients ≥ 75 years of age and identified 6,893 studies, of which 60 were included for further data analysis.[15] Studies with patients < 75 years of age; one-piece implants; zygomatic implants or pterygoid implants; postloading follow-up < 12 months; narrow-diameter implants or mini dental implants; and implants with turned or machined surfaces were excluded. Of these 60 studies, just 7 prospective RCTs were available and included in the meta-analysis. The mean age of the cohort was 79 to 87 years, with an observation period of 12 to 180 months. The authors concluded that the 1- to 5-year implant survival

Table 2 Data Relating to Age and Implant Survival

Study (first author)	Publication year	Loading Protocol	Implant system	Observation period (in months)	Number of patients (n)	Mean age (in years)
Becker	2016	Not specified	Nobel Biocare	12	31	83.0 (F = 16), 56.2 (M = 15)
Bressan	2014	Immediate	Ankylos	24	5	79.0
Cakarer	2011	Conventional	Astra-tech, Straumann, Nobel, Frialit, Swiss Plus, Biohorizons, Bio-Lok	Up to 60	16	75.56
de Carvalho	2013	Immediate	Nobel Biocare, Lifecore, Biomet 3i, Globtek	12–180	45	75+
Hoeksema	2015	Conventional	Straumann	120	7	75+
Maniewicz	2017	Early	Straumann	60	17	87.06
Müller	2015	Early	Straumann	60	18	75.53

Mean age and calculated implant survival are highlighted (red frame). Modified table reprinted with permission from Schimmel et al.[15]

rates (90.9% to 100%) were similar to those reported in younger cohorts (Table 2).[15] Data on associations between patient age and peri-implant marginal bone loss or peri-implantitis are not available, as long-term follow-up studies do not exist.

However, advanced age is correlated with age-related diseases. A current comprehensive study identified 92 age-related diseases accounting for 51.3% of all global burden among adults.[7] The most common systemic medical conditions are diabetes mellitus, neurocognitive impairment, cardiovascular disease, chronic respiratory disease, and cancer/neoplasms.[7] Age-related disease leads to consecutive medication intake. Today, the elderly represent 13% of the European population and consume nearly one-third of all prescriptions dispensed.[19] The most prescribed drugs in the Western hemisphere are metformin, lisinopril, levothyroxine, simvastatin, setraline, and omeprazole. Anticoagulants are among the top 50 prescribed drugs, and bisphosphonates (BPs) and antibodies are only among the 200 most commonly prescribed drugs.[20] Elderly patients often take more medication at the same time; if they use at least five drugs indicated for the treatment of a chronic disease over a 4-month period, it is defined as polypharmacy.[21] In current systematic reviews, there is no available evidence to define levothyroxine and simvastatin as risk factors. Omeprazole (proton pump inhibitors) and setraline (selective serotonin reuptake inhibitors) are classified as potential risk factors, but with a low level of evidence—only five studies were available, as demonstrated by a systematic review and a current additional clinical study on this topic.[22,23] It is currently not proven whether anticoagulants or novel direct oral anticoagulants represent a risk factor for implant survival. However, a postoperative bleeding risk should be considered in this patient group.[24,25]

In conclusion, based on a low to moderate level of evidence, an older age (> 75 years) does not affect implant survival in the short term (1–5 years), and polypharmacy should be considered in this patient group.

Diabetes Mellitus and Implant Survival

A current systematic review included seven clinical studies investigating the influence of diabetes mellitus (mainly type 2) on implant survival with a general observation period of 24 months (maximum of 60 months) in a population with a mean age of 29 to 81 years.[15] Calculated implant survival rates ranged between 86% and 100%, so diabetes mellitus cannot be classified as a risk factor for implant survival in the short term (Table 3). However, data on long-term and general perioperative treatment (medication [eg, antibiotic regime]) and wound closure are often not reported in the literature.[14] Further, there is little evidence for the success of bone grafting (in particular for extensive bone grafting procedures of large alveolar defects) and progressive loading protocols in diabetic patients.[26,27] Most studies regarding diabetic patients do not provide data on the hemoglobin A1c (HbA1c) metrics nor on the duration of the diabetes mellitus.[15] Glycemic control is monitored by HbA1c reflecting blood glucose concentrations over 3 to 4 months.[28] An HbA1c value of 6.5% is recommended for diabetic patients, and values > 6.5% define poorly adjusted diabetes mellitus.[29] There is some evidence that osseointegration may be delayed in diabetic patients if the diabetes mellitus is not well controlled.[30,31] With the duration of diabetes mellitus, the microvascular and macrovascular conditions

Total number of implants failed/ placed in the study period (n)	Number of patient (implants) dropouts during the study period (n)	Number of implants survived (total)	Calculated implant survival rate (SR%)	Edentulous state of the jaw rehabilitated	Prosthesis type
2/59	0 (0)	57 (59)	96.61	Not specified	Not specified
0/20	0 (0)	20 (20)	100.00	Completely edentulous	Complete fixed on 4 implants
1/42	0 (0)	41 (42)	97.62	Completely edentulous	2-IOD
1/45	0 (0)	44 (45)	97.77	Partially edentulous	Fixed
0/14	5 (10)	4 (4)	100.00	Completely edentulous	2-IOD
2/36	12 (24)	10 (11)	90.91	Completely edentulous	2-IOD
0/36	8 (16)	20 (20)	100.00	Completely edentulous	2-IOD

result in retinopathy, nephropathy, neuropathy, coronary heart disease, cerebrovascular disease, and peripheral vascular diseases.[32] These conditions can also be associated with additional medication (see Age and Implant Survival section).

In summary, based on a low level of evidence, diabetes mellitus is not a risk factor for implant survival up to 5 years after loading, but there is no information regarding the long-term survival of implants in these patients or the appropriate perioperative treatment (ie, medication, such as an antibiotic regime) and wound closure. Further, there is little evidence in the literature for the success of bone grafting and progressive loading protocols in diabetic patients. Therefore, complex surgical procedures and progressive loading protocols should be considered carefully.

Table 3 Data Relating to Diabetes Mellitus and Implant Survival

Study (first author)	Publication year	Study design	Investigated condition related to diabetes	Observation period (in months)
Aguilar-Salvaterra[a]	2016	Pros	HbA1c ≤ 6, Type 2	24
			HbA1c = 6.1–8.0, Type 2	24
			HbA1c = 8.0–10, Type 2	24
Alsaadi[a]	2008	CS	Type 1	n.r.
			Type 2	n.r.
Dowell[a]	2007	Cohort (Pros)	Type 2	4
			No	4
Erdogan[a]	2015	Pros	HbA1c = 6.1–7.5, Type 2	>12
			No	>12
Eskow[a]	2017	Observational	HbA1c = 6–7.9, Type 2	24
			HbA1c ≥ 8.0, Type 2	24
Oates[a]	2014	Cohort (Pros)	HbA1c ≤ 5.9, Type 2	12
			HbA1c = 6.0–8.0, Type 2	12
			HbA1c ≥ 8.1, Type 2	12
Peled[a]	2003	CS	Type 2 diabetes	60

Mean age and calculated implant survival are highlighted (red frame). The observation periods are short (maximum of 5 years, average 12 to 24 months), and the study designs are heterogenous. However, implant survival rates are high. Modified table reprinted with permission Schimmel et al.[15]

Antiresorptive Therapy and Implant Survival

Based on two systematic reviews including more than 30 articles on implant survival under BP or antiresorptive therapy (denosumab [Prolia, Xgeva; Amgen]), a low-dose BP treatment for osteoporosis does not affect implant survival after a short-term follow-up; however, it can lead to medication-related osteonecrosis of the jaw (MRONJ).[15,16] This devastating side effect should be considered during treatment, especially since the decreasing prescription rates of BPs for the treatment of osteoporosis in Germany is almost compensated by the increasing prescription rates of antiresorptive agents based on current drug surveys (Fig 1).[33–35] A perioperative antibiotic prophylaxis is strongly recommended for all patients under this medication.[36,37] For low-dose antibody therapy (denosumab) in patients with osteoporosis, there is no information on the survival of the implant, and the same implant healing as in BP patients is assumed. High-dose BP and antibody therapy lead to the highest incidence of MRONJ.[38,39] Therefore, implant therapy cannot be recommended. Bone grafting should be avoided under antiresorptive therapy.[38] There are no treatment regimens available for patients with peri-implantitis receiving antiresorptive medication.[40] Recommendations concerning the effects of antiresorptive therapy on implant survival are based on a moderate level of evidence.

CONCLUSIONS/FUTURE RESEARCH

This review suggests that the risk assessment of an implant patient should not be based on chronologic age, but rather on the patient's specific risk factors, such as former and current medications. The key to successful implantology is the correct assessment of risk factors. A careful and targeted medical history is mandatory and may require referral to a specialist.

Recommendations Regarding Age

An older age (> 75 years) does not affect implant survival after a short-term follow-up (1 to 5 years). However, polypharmacy should be considered in this patient group.

Recommendations Regarding Diabetes Mellitus

Current studies demonstrate that diabetes mellitus is not a risk factor for implant survival in the short term, but there is no information on appropriate perioperative treatment (medication) and wound closure. There is little evidence in the literature for the success of bone grafting and progressive loading protocols in diabetic patients. Therefore, complex surgical procedures should be considered carefully.

Number of patients (n)	Mean age (in years)	Total number of implants placed in the study period (n)	Total number of implants failed in the study period (n)	Number of implants survived (total)	Calculated implant survival rate (SR%)	Time of failure
33	59	33	0	33	100	n.a.
30	57	30	1	29	96.6	Late
22	61	22	3	19	86.3	Late
n.r.	56.2	1	1	0	0	Early
n.r.	56.2	24	1	23	95.83	n.r.
25	51–81	38	0	38	100	n.a.
10	29–61	12	0	12	100	n.a.
12	52.6	22	0	22	100	n.a.
12	49.5	21	0	21	100	n.a.
9	59.9	21	0	21	100	n.a.
11	59.9	38	2	36	94.74	n.r.
50	64	100	1	99	99	n.r.
4	64	94	1	93	98.9	n.r.
20	64	40	0	40	100	n.a.
41	n.r.	141	8	133	94.33	Early: 6; Late: 2

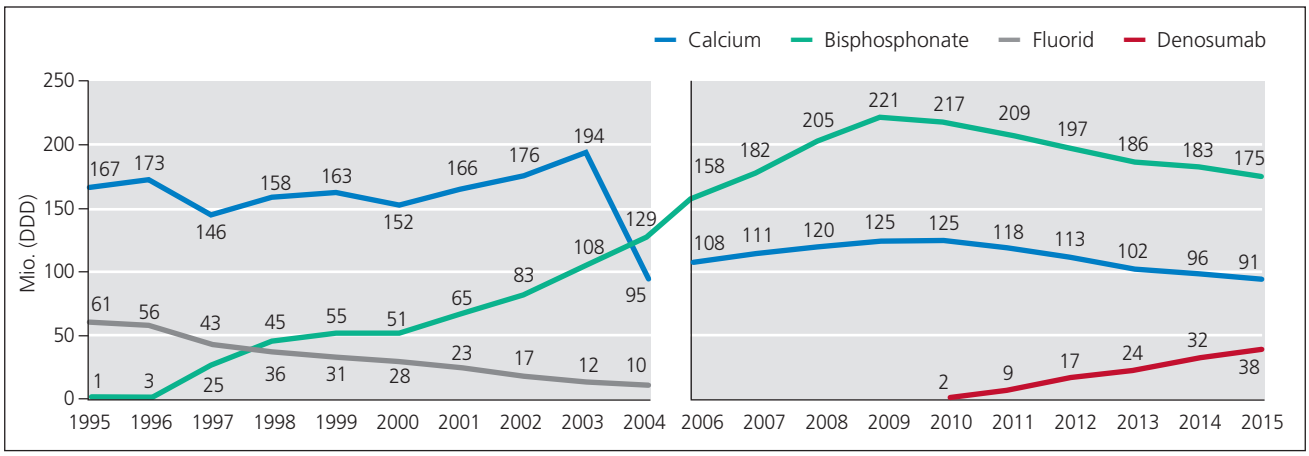

Fig 1 Decreasing prescription rate of bisphosphonates for the treatment of osteoporosis (green line) is almost compensated for by the increasing prescription rate of antiresorptive agents since 2009/2010 in Germany (red line). Composite figure based on Schwabe et al[35,36] and images reprinted with permission.

Recommendations for Antiresorptive Therapy

Oral, low-dose BP treatment for osteoporosis does not affect implant survival over a short-term follow-up, but can lead to MRONJ. For low-dose antibody therapy (denosumab) in osteoporosis, there is no information on the survival of the implant. The same implant healing as in low-dose BP patients is assumed. High-dose BP and antibody therapy lead to the highest incidence of MRONJ; therefore, implant therapy cannot be recommended. Bone grafting should be avoided under antiresorptive therapy. There are no treatment regimens available for patients with peri-implantitis receiving antiresorptive medication.

Based on the evidence found, it is suggested that the impact of commonly prescribed medications on implant survival and progression in peri-implantitis should be examined in clinical and preclinical studies. Future prospective longitudinal clinical studies should analyze the outcome of different bone grafting procedures and progressive loading protocols on implant success in diabetic patients (short and long term). Perioperative

treatment in diabetic patients (eg, antibiotics, wound closure, prosthetics) should be recorded for in-depth evaluation. Since no evidence is available regarding treatment regimens for patients with peri-implantitis receiving antiresorptive medication, further research has to focus on this condition.

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