Chapter 5

Dental Implants in the Medically Compromised Patient Population

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Additional information is available at the end of the chapter

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Abstract

As a result of the increase of the life expectancy, elder people live with diverse diseases or conditions like systemic disorders, immune-related disorders, and psychiatric issues. Consecutively, practicing clinicians are faced with serving dental implant treatments in such a population comprised of medical and demographic characteristics. Most commonly, implant therapy is performed among patients above middle ages; therefore, clinicians often encounter medically compromised patients. The patients are usually with adverse conditions like bleeding disorders, bone diseases, cardiovascular disease (CVD), and/or immunologic conditions like cancer therapy, steroid or immunosuppressive or antiresorptive medication, alcoholism, smoking, and many others. Nevertheless, only few conditions could be stated for contraindication to dental implant therapy. Besides the broad range of the mentioned dental implant comorbidities smoking seems less prevalent compared to the general population. Dental implants in smoking patients are certainly affected in relation to the failure rate, marginal bone loss, and some other risks of postoperative complications. Hence, smoking or other similar conditions could be accounted as a chronic systemic disorder just like diabetes mellitus or drug usage. Briefly, it seems that establishing the medical and demographic conditions prior to implant therapy along with controlling the systemic diseases or disorders may be more important than the presence of compromise.

Keywords: systemic diseases, dental implant success, contraindication

1. Introduction

Dental implant (DI) is broadly considered to be the ideal treatment of the tooth loss, which is mostly required in the aged population [1, 2]. The prevalent age-range for implant therapy has been reported above 40 years [2] or between 51 and 60 years [1], thus the patients who required

dental implant therapy are usually associated with systemic comorbidities. For both patients' and clinicians' benefit, systemic comorbidities of the patient should be well-diagnosed before DI therapy. Besides, treatment plan and patient selection should be carried out with reference to the clinical evidence. Patients should be ensured to inform thoroughly about the risks and precautions.

2. Systemic disorders and compromised conditions

2.1. Elderly population

Aging has an effect on biological activity via altering the inflammatory, regenerative, and remodeling phases of healing process. First, it makes inflammatory phase prolonged by promoting the release of inflammatory mediators. Second, it decreases new tissue formation in the regenerative phase by reducing angiogenesis and the number of mesenchymal stem cells, which are the progenitors of new bone formation. Last, it causes an imbalance in bone remodeling by changing cell activity, level of matrix metalloproteases, apoptosis, and collagen turnover [3]. Therefore, it may not be wrong to consider that aging causes a delay on osseointegration of dental implants.

In the literature, there are eligible studies that have been conducted for long-term time periods and the survival rate (SR) of dental implants is about 90% (**Table 1**). Furthermore, in a recent meta-analysis, SR has been reported to be 91.2% for up to 10 years [4]. On the other hand, considering the peri-implant pathology and bone level changes, studies have unsatisfactory results. According to the aforementioned meta-analysis [4], there is only one prospective clinical study that reports peri-implant marginal bone loss (MBL) after 10 years as 1.5 mm [5]. Additionally, another reviewer states that peri-implant mucositis and peri-implantitis are observed more commonly in totally edentulous patients, which are mainly ≥65 years old [3].

2.2. Tobacco smoking

Tobacco consumption is one of the main considerable patient-related systemic conditions for the patients who require DI. Though smoking is not a contraindication for DI therapy, there have been a lot of studies that report negative effects on DI outcomes.

According to the clinical studies (**Table 2**), there is a tendency to consider that implant failure is correlated with smoking habits. Most of the studies confirm the association between smoking and increased failure rate of implants in both short- and long-term periods. Besides, tobacco smoking has been proved to increase the failure rate of DI from 2.5- to 3-fold [9, 12]. However, there is only one study that has showed a higher survival rate of DI in smoker patients [13].

People who consume 10–20 cigarettes daily are often counted as heavy smokers in clinical studies. And despite a small number of studies that reveal the effect of the number of cigarettes on failure, it has been demonstrated that consuming the 6–15 cig/day doubled the risk of implant failure [9].

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Moy et al., 2005, Retrospective cohort [6]	2–20 years	541 subjects are aged >60 years (1140 total)	ND (4680 total)	82% (for aged >60 years)	–	Patients who are aged >60 years have higher risk for implant failure (RR = 2.24)
Manor et al., 2009, Retrospective cohort [7]	6 years	194 (2 equal groups for evaluating early and late failures)	294	–	Assigned as minor/moderate/major MBL	Old age may be a risk factor for late failures and risk is also more likely for men and posterior of jaws
Lee et al., 2010, Prospective [8]	2.7 years (mean)	35 subjects are >70 aged geriatric MCP with controlled systemic disease	118	–	MBL: 0.27 mm	Old age is not a risk factor for peri-implant MBL ($p = 0.484$)
Busenlechner et al., 2014, Retrospective [9]	8 years	2632 subjects are >50 years (61% out of 4316 total)	ND	95.3% for the age >70 years	–	Old age over 70 years is not associated with long-term implant success
Becker et al., 2015, Prospective [10]	7 years	31 aged subjects	84	94.6% for 13 patients with 40 implants	MBL: 0.1 mm (difference of 0–7 years' follow-up) PD: 2.6 mm	DI is successful in aged population, and MBL changes are comparable with the younger populations
Neves et al., 2016, Retrospective [2]	7.3 years (mean)	528 subjects are aged >40 years (721 total MCP subjects with the age range of 20–87)	ND (3998 total)	92.7% for the age <40, 85.3% for age >40, and 86.5% is overall SR (patient based)	33.8% of patients and 12.7% of implants have pathology	>40 age is a risk factor of implant loss (risk is higher for more than two times than <40 age), but is not a risk for peri-implant pathology
Prasad et al., 2016, Retrospective cohort [11]	5.7 years of mean	Approximately the half of 1091 total subjects is aged >60 years	ND (1918 total)	96.4% (implant based), 94.6% (patient based)	–	Age over 65 years is shown to have an increased risk of implant failure
Hoeksema et al., 2016, Prospective comparative [5]	10 years	(1) 52 subjects with age range of 35–50 years (2) 53 subjects with age range of 60–80 years	(1) 104 (2) 106	(1) 97.1% (2) 93.4%	MBL: 0.1 mm (1st year), 0.7 mm (5th year), 1.5 mm (10th year) PD: 3 mm for both groups at 10th year	Mandibular two-implant OD is equally successful in older patients compared with the younger patients without significant differences of the parameters
Srinivasan et al., 2016, Sys. Rev., meta-analysis [4] (includes 11 prospective studies)	1–10 years	206 subjects are aged ≥65 years	480	97.7% (1st year), 96.2% (5th year), 91.2% (10th year)	MBL: 0.1–0.3 mm (1st year), 0.7 mm (5th year), 1.5 mm (10th year)	Age alone should not be a limiting factor for DI therapy Reported complications are found inadequate for a meta-analysis

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Mean/total of values/subjects and considerations	1–20 years	4765 patients above middle ages	>1082	SR is 90% for long-term period	0.1 mm in the 1st, 1.7 mm in the 5th, and 1.5 mm in the 10th year follow-ups (out of 3 in available 8 studies)	Implant therapy is a successful treatment in the medically compromised patient

MCP, medically compromised patients; DI, dental implant; SR, survival rate; MBL, marginal bone loss; BoP, bleeding on probing; RR, risk ratio; ND, no data available; OD, overdenture.

Table 1. Studies that indicate dental implant outcomes in the elderly population.

Regarding the MBL, smoking seems to have a destroying effect by increasing the annual rate of MBL by 0.164 mm/year [14], and MBL is about 1.4 mm after 3 years with a statistically significant difference from people who do not smoke tobacco [15, 16].

As a result, tobacco smoking alone is not contraindicated for DI, and DI survival is about 90% for a long time period. On the other hand, smokers are under a higher risk of implant failure compared to the nonsmokers. Thus, clinicians should take into account other concomitant systemic factors which could increase the risk of failures.

2.3. Alcohol consumption

There is no evidence to suggest that alcoholism is a contraindication for DIs. SR of DI is similar to healthy population with a reasonable alcohol consumption. Nevertheless, alcoholism is claimed to increase the risk of complications for DI because it may cause many systemic disorders like liver disease, bleeding disorders and osteoporosis (OP), and it may impair immune response and some nutritional elements like folate and B vitamins, and it is often associated with tobacco smoking [28].

It is reported that consumption of >10 g of alcohol increases the MBL and decreases DI survival in humans [15]. Despite there are few studies available (**Table 3**) concerning the DI outcomes in patients who consumed high level of alcohol, further clinical studies with well-defined subjects are required for clarifying the relation.

2.4. Cardiovascular diseases

Cardiovascular disease (CVD) compromises the blood flow which may restrict oxygen or nutrients in the osseous tissue, thus is hypothesized to have higher risk of osseointegration failure [29–31]. Clinical studies and reviews demonstrate no evidence of contraindication related to DI success in patients with CVD (**Table 4**), and this disease is registered as a relative complication due to the risk of infective endocarditis. Antibiotic prophylaxis is necessary prior to the surgery [31] according to the guidelines of the American Heart Association's last publish [32, 33].

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Ekfeldt et al., 2001, Retrospective controlled study [17] (half of subjects lost at least half of their implants)	8 years	54 total (half part is smoker, and 9 of them defined as heavy smokers who consumed ≥10 cig/day)	ND	31 DI loss in 7 heavy smokers (at least half of their implants)	6% of implants had infection during healing in smokers	Except from instability associated with bad bone quality, implant losses mostly occur in patients with heavy smoking habits or bruxism. It is more prominent in post-loading period (22 implants had lost after loading in 7 patients of heavy smokers)
Moy et al., 2005, Retrospective [6]	2–20 years	173 smoker	ND	79.77% for smokers	–	There is a correlation between smoking and increased failure rate (RR = 1.56)
Galindo-Moreno et al., 2005, Prospective [15]	3 years	63 smoker	ND (514 total)	–	MBL is 1.36 mm in smokers	MBL is significantly related to tobacco smoking
Alsaadi et al., 2007, Retrospective [18]	Up to the abutment connection	ND (2004 total)	6946 total (343 heavy smoker who consumed >20 cig/day)	92.95% for heavy smokers	–	Smoking of >20 cig/day is shown significantly higher early implant failure when compared to no smoking groups
Holahan et al., 2008, Retrospective chart review [19]	5 years	24 smoker	83 in smokers	88% for smokers	–	Implants placed in smokers are 2.6 times more likely to fail than implants placed in nonsmokers
Sverzut et al., 2008, Retrospective [20]	<1 year	76 smoker (out of 650 total)	197 in smokers (1628 total)	97.19% for smokers, 96.68% for nonsmokers	–	Tobacco use alone cannot be considered as a factor for risk related to early implant failures
Alsaadi et al., 2008, Retrospective [21]	2 years	22 (>20 cig/day)	93 implants in patients who consumed >20 cig/day	93.94%	–	Smoking does not seem predominant player for late implant loss
Alsaadi et al., 2008, Prospective [22]	<1 year	90 smoker	95 in smokers	94.44%	–	Tendency for more early implant failures is noticed in smokers
Lee et al., 2011, Retrospective [23]	5 years	ND (95 total)	ND (249 total)	ND	ND	Implant failures are correlated with smoking
Cakarer et al., 2014, Retrospective [24]	5 years	ND	246 in smokers		–	Smoking is not affected the DI survival

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Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
				97.5% (6 failed out of 246 implant)		
Busenlechner et al., 2014, Retrospective [9]	8 years	1726 smoker	ND (13147 total)	76.5% for smokers (overall SR is 97%)	–	Smoking increases the failure rate by 3-fold 6–15 cig/day doubles the risk of implant failure
Tran et al., 2016, Retrospective chart review [12]	10 years	215 smoker	(2729 total)	–	–	Smoking increases the failure rate by 2.6-fold
Krennmair et al., 2016, Prospective cohort [16]	3 years	9 smoker (out of 44 total)	ND	–	1.45* mm in smokers	Smoking is risk factors for MBL (OR: 8.9)
Neves et al., 2016, Retrospective [2]	7.3 years of mean	476 smoker	ND	85.1% (patient based)	36.6% pathology rate (patient based)	Smoking is not associated with higher risk of implant failure and peri-implant pathology (>4 mm pocket depth with BoP or MBL)
Pedro et al., 2017, Analytical, observational, longitudinal study [25]	2–4 years	ND (18 total)	ND (57 total)	–	ND	Smoking has an influence on both mesial and distal bone loss (p = 0.037)
Niedermaier et al., 2017, Retrospective cohort [13]	7 years	141 smoker (out of 380 total)	ND (2081 total)	98.6% for smokers, 96.1% for nonsmokers	–	Smokers have a significantly higher DI survival rate than nonsmokers
Clementini et al., 2014, Systematic review and meta-analysis [14]	>1 year	478 smoker and 1207 nonsmoker	ND	ND	Smoking increases the annual rate of MBL by 0.164 mm/year	Smoking has a harmful effect on peri-implant bone loss. However, the level of evidence for oral implant therapy in patients with systemic conditions is very low
Mean/total of values/subjects	1–20 years	3520 patients with smoking habits (13 out of 17 available studies)	1057 implants in smokers (6 out of 17 available studies)	SR is about 90% for smokers	Apprx. 1.4 mm MBL after 3 years	Smoking has a negative impact on the success and survival of dental implants

Statistically significant difference with healthy groups.DI, dental implant; SR, survival rate; MBL, marginal bone loss; BoP, bleeding on probing; OR, odds ratio; RR, risk ratio; ND, no data available.

Table 2. Studies that indicate dental implant outcomes in patients with smoking habits.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Galindo-Moreno et al., 2005, Prospective [15]	3 years	23 alcohol users	ND	–	MBL: 1.66 mm	MBL is significantly related to a daily consumption of >10 g of alcohol
Gander et al., 2014, Retrospective [26]	20 months	33 (29 patients with SCC, 24 underwent mandibular reconstruction)	136 total	92.7% (at 1st year), 87.5% (after 20th month)	–	In head and neck oncology patients alcohol ($p = 0.001$) is associated with higher implant failure rate
Scully et al., 2007, Review [27]	ND	ND	ND	Similar to healthy population	–	May not be a risk for DI
Diz et al., 2013, Review [28]	ND	ND	ND	Similar to healthy population	–	May be at increased risk of complications for DI

MBL, marginal bone loss; ND, no data available; SR, survival rate; SCC, squamous cell carcinoma; DI, dental implant.

Table 3. Studies that indicate dental implant outcomes in patients with alcohol abuse.

DI surgery is suggested as a legitimate procedure for the patients at high risk for IE (such as aortic or mitral valve replacement or cyanotic congenital malformation) which under prophylactic antibiotic regime of 2 g amoxicillin orally at 1 hour preoperatively [34]. There is also evidence suggesting that this regimen significantly reduces failures of DIs though it is still unknown whether postoperative antibiotics are more beneficial, and which antibiotic is the most effective [33]. Reviewers stated the importance of concomitant bleeding or cardiac ischemia which could develop during DI insertion, therefore, procuring medical advice is recommended prior to the implant surgery [28]. As a matter of fact, recent myocardial infarction, stroke, and cardiovascular surgery are well-known contraindications for performing DI surgery [35].

According to the current literature, CVD does not hinder the osseointegration of DI [36, 37] and is not associated with higher risk of implant failure (**Table 4**). SR is about 89% up to 20 years (**Table 4**). However, the number of the studies that reports peri-implant health condition is insufficient. Unlike the other studies available, one study revealed that CVD has risk factors for peri-implant bone loss with the mean value of 1.38 mm after 3 years [16]. Further studies are needed in this respect.

2.5. Diabetes

As being the most prevalent endocrine disease, diabetes mellitus is a metabolic disorder that is generally diagnosed by the characteristic symptoms of polydipsia, polyuria, and polyphagia in correlation with exceeded blood glucose levels more than 200 mg/dL. It causes hyperglycemia due to a defect of insulin secretion [39], that insulin has an effect on the regeneration of bone matrix. In a diabetic patient, hyperglycemia reduces clot quality, number of osteoclasts, and collagen production, which are the keys of bone regeneration [30].

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Moy et al., 2005, Retrospective cohort [6]	2–20 years	1140 total (202 with hypertension, 106 with CVD, 75 with pulmonary disease)	ND (4680 total)	85% for hypertension, 85% for CVD	–	There is no correlation between hypertension, coronary artery disease, pulmonary disease and increased failure rate of DI
Alsaadi et al., 2007, Retrospective [18]	Up to the abutment connection	ND (2004 total)	ND (6946 total)	ND	–	Cardiac disease is not associated with increased incidence of the early failures
Alsaadi et al., 2008, Retrospective [21]	2 years	19 subjects with CVD	76 in subjects with CVD	90.79%	–	Cardiac problem does not seem a predominant player for late implant loss
Neves et al., 2016, Retrospective [2]	7.3 years of mean	222 subjects with CVD	ND	89.2% (patient based)	32% (patient based)	Cardiac disease is not associated with higher risk of implant failure and peri-implant pathology (>4 mm pocket depth with BoP or MBL)
Nobre et al., 2016, Retrospective [38]	5 years after loading	70 total (CVD subjects: 38 patients; non-CVD subjects: 32 patients)	352	CVD: 86.7%; non-CVD: 93.8%	MBL at 1st and 5th year is 0.95–1.52 mm in CVD; 0.78–1.54 mm in non-CVD group	Implant rehabilitations represent a valid treatment for diabetic patients with or without coexisting CVD, with a good risk/benefit ratio (nonsignificant differences between the groups)
Krennmair et al., 2016, Prospective cohort [16]	3 years	19 subjects with CVD (out of 44 total)	ND	–	1.38 mm in CVD*	CVD is risk factors for bone loss. (OR: 5.1)
Pedro et al., 2017, Analytical, observational, longitudinal [25]	2–4 years	ND (18 total)	ND (57 total)	–	ND	Heart diseases are not a contraindication for DI bone loss
Niedermaier et al., 2017, Retrospective cohort [13]	7 years	95 subjects with CVD (380 total)	ND (2081 total)	97.8%	–	DI survival in patients with cardiovascular problems does not differ from the healthy control subjects
Mean/total of values/ subjects	2–20 years	1533 patients with CVD (in 6 out of 8 available studies)	428 (in 2 out of 8 available studies)	Approx. 89% SR	0.95 mm at 1st year 1.38 mm at 3rd year 1.52 mm at 5th year	CVD may not pose a risk for dental implants

Statistically significant difference with healthy groups.CVD, cardiovascular disease; RD, rheumatic disorders; OR, odds ratio; MBL, marginal bone loss; ND, no data available; SR, survival rate.

Table 4. Studies that indicate dental implant outcomes in patients with cardiovascular diseases.

A decreased bone density is observed around the titanium implants in animal subjects, and implant survival is slightly reduced in poor metabolic control [28] with an average rate of 89% (**Table 5**). Yet no clinical evidence exists to establish an association of glycemic control with implant failure because of the insufficient identification and reporting of glycemic control in most of the published studies [40].

Though diabetes is not a contraindication for DI therapy, evaluating the HbA1c level of the patient and chlorhexidine mouth wash and antibiotic prophylaxis are recommended in order to reduce the relative risk of infection associated with diabetes [28, 30].

2.6. Bleeding disorders

There is no evidence to suggest that bleeding disorders (BDs) are contraindication for placement of DIs [28] or a contraindication for implant survival/success [31]. Since the risk of thromboembolism of interrupting or changing the antiplatelet therapy is higher than the risk of hemorrhage caused by dental implant surgery, invasive dental procedures including dental implant surgery are suggested to perform normally [42].

Considering the oral anticoagulant therapy (OAT), DI is not contraindicated in patients under an OAT [28, 31]. Minor DI surgery (that does not involve autogenous bone grafts, extensive flaps, or osteotomy preparations extending outside the bony envelope) is asserted to be safe regarding the risk of hemorrhage in patients who have an INR value of 2–4, and local hemostatic agents are suggested enough for these patients [43, 44]. On the other hand, it should be noted that some medications that are commonly used in dental practice (like metronidazole, erythromycin, and clarithromycin) may increase the anticoagulant effect of warfarin [31].

There are some additional precautions for the patients with inherited BDs such as taking medical advice previously, the replacement of deficient coagulation factor to reach a minimum level of 50% before surgery, slow injection of local anesthesia with vasoconstrictor, the use of antifibrinolytic agents (oral tranexamic acid and/or 5% tranexamic mouthwash) up to 7 days postsurgically, and the use of topical antiseptics (chlorhexidine or povidone iodine) in order to reduce the risk of local infection. Sinus lifting and bone graft procedures are recommended to be avoided, and consulting for the use of nonsteroidal anti-inflammatory drugs is advised as they may increase the risk of a dangerous hemorrhage [31].

Studies that analyze the bleeding risk and DI success after invasive DI surgeries are lacking (**Tables 6** and **7**). Studies are also required for evaluating whether anticoagulants have an effect on DI therapy negatively or which is the optimum drug or regimen.

2.7. Thyroid disorders

Thyroid hormones of triiodothyronine (T3) and thyroxine (T4) have been demonstrated to have influence on cortical bone healing than cancellous bone around titanium implants [47]. Thus, thyroid hormones-related disorders could be regarded as the considerable issues for evaluating the success of dental implants.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Moy et al., 2005, Retrospective cohort [6]	2–20 years	48 diabetic	ND	68.75% in diabetic patients	–	There is a correlation between diabetes and increased failure rate (RR = 2.75)
Alsaadi et al., 2007, Retrospective [18]	Up to the abutment connection	ND	ND	ND	–	Controlled diabetes type 2 is not associated with increased incidence of the early failures
Alsaadi et al., 2008, Retrospective [21]	2 years	9	33	100%	–	Diabetes type 2 does not seem predominant player for late implant loss
Busenlechner et al., 2014, Retrospective [9]	8 years	185 (4.3% out of 4316 total)	ND	95.1% for diabetes (overall 97%)	–	Diabetes is not associated with long-term implant survival (p = 0.928)
Neves et al., 2016, Retrospective [2]	7.3 years (mean)	56 diabetic	ND	92.9% (patient based SR)	26.8% patient based	Diabetes is not associated with higher risk of implant failure and peri-implant pathology (>4 mm PD with BoP/MBL)
Niedermaier et al., 2017, Retrospective cohort [13]	7 years	9	ND	91.9%	–	DI survival in diabetic patients does not differ from the healthy control subjects
Shi et al., 2016 Meta-analysis [41] (abstract available)	ND	252	587	ND	–	There is no difference between the failure rates of the patients with uncontrolled and well-controlled diabetes
Diz et al., 2013, Review [28]	ND	ND	ND	Slightly reduced in bad metabolic control	–	Evaluating the HbA1c level for patient selection, avoiding hypoglycemia, using chlorhexidine and antibiotic prophylaxis are recommended for diabetic patients
Oates et al., 2013, Review [40]	Unrestricted	–	–	Implant failure rates ranging from 0 to 9.1%	–	Clinical evidence is lacking for the association of glycemic control with implant failure, because the identification and reporting of glycemic control are insufficient or lacking in most of the published studies
Mean/total of values/subjects	2–20 years	559 diabetic patients (in 6 out of 7 available studies)	620 (in 2 out of 7)	Approx. 89% SR		Diabetes may interfere with the SC and SR pf implants

DI, dental implant; BoP, bleeding on probing; MBL, marginal bone loss; ND, no data available; SR, survival rate; RR, risk ratio; PD, pocket depth.

Table 5. Studies that indicate dental implant outcomes in patients with diabetes.

Author, year, study design	Objective of the study	No of patients	Conclusion related to surgical risks of DI
Clemm, 2016, Clinical comparative study [45]	Postoperative bleeding risk of patients continuing their anticoagulation therapy (antiaggregant, vit-K inhibitors, vitamin-K inhibitor withdrawal bridged with heparin, direct oral anticoagulants) and undergoing implant surgery and advanced bone grafting procedures	564 patients	**1.** No thromboembolic complication occurred **2.** The postoperative bleeding risk after implant surgery and/or bone grafting procedures is very low in patients continuing the anticoagulant therapy **3.** The invasiveness of the surgical procedure had no statistically significant effect on bleeding frequencies **4.** Patients taking vit-K inhibitors had a significantly higher risk of a postoperative bleeding compared to patients without any anticoagulant **5.** Most of the postoperative bleedings are easily controllable via local hemostatic measures

Table 6. Hemorrhagic risks in patients undergoing advanced implant surgery and bone grafting procedures.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Markovic et al., 2016, Randomized study [46]	1 year	20	80	100% for both groups	–	There is no difference between healing of the hydrophilic and hydrophobic TiZr implant surface. OAT influences the bone healing by resulting in lower ISQ at 3rd month in comparison with baseline values, although without compromising implant stability

OAT, oral anticoagulation therapy; ISQ, implant stability quotient; SR, survival rate.

Table 7. Studies that indicate dental implant outcome in patients with bleeding disorders or under an anticoagulant therapy.

Concerning the peri-implant pathology, thyroid disorders are reported to have the lowest potential risk compared to the other systemic disorders, in a recent clinical study [2] (**Table 8**). Due to the limited number of clinical studies that report DI outcomes in patients with thyroid disorders, it is hard to deduce a suggestion. Therefore, there is a certain need for further studies about the thyroid disorders.

2.8. Hepatitis

Concerning the dental implantology, hepatitis is one other disease which has not been studied widely yet. These infectious diseases impair immune system, increase oxidative stresses induced by the viral proteins, and cause virus-associated organ damage including liver fibrosis, steatosis, or hepatocellular carcinoma [48].

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Alsaadi et al., 2008, Retrospective [21]	2 years	25 Hypo- 6 Hyper-	111 Hypo- 22 Hyper-	93.69% Hypo- 86.36% Hyper-	–	Hypo- or hyperthyroidism does not seem a predominant player for late implant loss
Neves et al., 2016, Retrospective [2]	7.3 years of mean	37	ND	86.5% (patient based SR)	18.9% (patient based)	Thyroid disorders are associated with neither higher risk of implant failure nor peri-implant pathology (>4 mm PD with BoP or MBL)
Mean/total of values/subjects	Up to 7 years	68	133 (in one study available)			Further studies are required

BoP, bleeding on probing; MBL, marginal bone loss; ND, no data available; SR, survival rate; PD, pocket depth.

Table 8. Studies that indicate dental implant outcomes in patients with thyroid disorders.

Being one of the most spread and dangerous human pathogens, hepatitis C is shown to affect the oral conditions by increasing decays, gingival bleeding, and pocket depth due to the evident change in salivary flow [49].

Though hepatitis was indicated only as a possible risk factor previously [50], a present report is registered that hepatitis is the only risk factor for peri-implant pathology among the other systemic compromising factors such as cardiac diseases, thyroid disorders, diabetes, rheumatologic disorders, HIV infection, and smoking [2] (**Table 9**).

2.9. Bone diseases

Being the most frequent bone disorder, osteoporosis (OP) affects both bone mass and density. The effect is also more prominent in cancellous bone and in women [30].

Clinical studies have demonstrated that a SR of DIs in the patients with the diagnosis of OP is about 94% (**Table 10**). Despite a small number of studies that report peri-implant conditions, one study has presented a high rate of peri-implantitis in patients with OP (76.1%), but this rate does not differ from the healthy population or the patients with osteopenia [51]. Regarding the peri-implant MBL, one recent study has reported a mean value of 0.11 mm at first

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Neves et al., 2016, Retrospective [2]	7.3 years of mean	12 with hepatitis	ND	83.3% (patient based)	66.7% (patient based)	Hepatitis is not associated with higher risk of implant failure but it is a risk factor for peri-implant pathology (OR = 3.74) (>4 mm PD with BoP or MBL)

OR, odds ratio; BoP, bleeding on probing; MBL, marginal bone loss; ND, no data available; PD, pocket depth.

Table 9. Studies that indicate dental implant outcomes in patients with hepatitis.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Alsaadi et al., 2007, Retrospective [18]	Up to the abutment connection	ND	ND	ND	–	OP is found significantly associated with early implant failures (OR: 2.88)
Alsaadi et al., 2008, Retrospective [21]	2 years	19 subjects with OP	68	86.76%	–	OP does not seem predominant player for late implant loss
Holahan et al., 2008, Retrospective chart review [19]	5 years	41 with OP (21.4% of 192 total), 57 with OPN (29.7% of total)	ND	ND	–	OP or OPN is not a contraindication to DI. No association between BMD T-score and DI survival is found
Busenlechner et al., 2014, Retrospective [9]	8 years	151 subjects with OP (3.5% out of 4316 total)	ND	94.4% for OP-subjects (overall rate is 97%)	–	OP is not associated with long-term implant survival ($p = 0.661$)
Dvorak et al., 2011, Cross-sectional study [51]	6 years	47 subjects with OP, 16 with OPN, 140 are healthy controls	ND	81% for OPN, 87% for OP, 87% for the control	Peri-implantitis rates: 75% in the OPN, 76.1% in OP group, 76.5% in the control	There is no relation between (neither OPN nor OP) bone status and peri-implantitis or implant loss
Siebert et al., 2015, Comparative prospective [54]	1 year	24 women (the half was under iv. 5 mg zoledronic acid once-yearly, others without OP)	120	100%	ND	The mean MBL is similar for both groups. Immediate implant osseointegration can be successful in patients who received iv. zoledronic acid
Chow et al., 2016, Prospective [53]	5 year	79 subjects with OP	158	98.7%	MBL 0.65 mm BOP 49.6% PI 47.4%	OP is not a contraindication for DI, and reduced skeletal BMD is not associated with increased MBL. BOP is found significantly correlated with MBL
Niedermaier et al., 2017, Retrospective [13]	7 years	7 subjects	ND	94.1%	–	OP under the medication with BF seems to be a risk factor for success of DI
Temmerman et al., 2017, Prospective nonrandomized controlled multicenter [52]	1 year	20 subjects with OP, 28 control subjects	63 in OP-patients, 85 in control	98.4% is for OP group, 100.0% is for control group	MBL: 0.11 ± 0.49 mm for OP group; 0.05 ± 0.52 mm for control group (implant based)	DI in patients suffering from OP/OPN is a reliable treatment compared to healthy patients. Long-term follow-up is necessary

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Mean/total of values/subjects	1–8 years	388 (in 8 out of 9 available studies)	409 (in 4 out of 9 available studies)	94% SR in patients with OP	Mean MBLs are 0.11 mm at 1st year and 0.65 mm at 5th year follow-ups	Bone disease does not seem to be associated with the peri-implantitis or failure of DIs

OP, osteoporosis; OPN, osteopenia; OR, odds ratio; ND, no data available; BMD, bone mineral density; MBL, marginal bone loss; DI, dental implant; SR, survival rate.

Table 10. Studies that indicate dental implant outcomes in patients with bone diseases.

year [52], and one other has reported a mean of 0.65 mm at fifth year [53]. Additionally, bone status does not seem to be a predisposition for DI failures.

2.10. Rheumatologic disorders

Rheumatologic disorders encompass a large number of diseases and syndromes such as rheumatoid arthritis, osteoarthritis, and osteoporosis, which are the most common rheumatologic diseases (RDs) [2]. Different RDs could affect DI success in different ways [28]. For instance, rheumatoid arthritis (RA) has not stated a predominant player for late implant loss in one study [21]. However, together with the connective tissue disease, RA increases bone resorption when compared to the connective tissue disease alone [55].

Today, there are only a few number of clinical studies with limited amount of participants that evaluate the success of DIs in patients with RD. Although RD was shown as risk factor for peri-implant MBL in a recent prospective study [16], no relationship was found with the implant failure risk or peri-implant pathology in another study [2]. Therefore it can be concluded that any relation of RD in DI success is unclear, and there is a certain need for further studies with sufficient number of participants (**Table 11**).

2.11. Bisphosphonate therapy

Bisphosphonates (BFs) suppress the osteoclast function and therefore are used for the treatment of disorders causing abnormal bone resorption such as OP, malignancies (multiple myeloma, bone metastases of breast, or prostate cancer), or nonmalignant bone diseases (the most prevalent of osteoporosis and Paget disease) [30, 37].

According to the recent meta-analyses, the consumption of oral BF in patients with OP could only be assumed to be a relative contraindication for DI. Further, there is no evidence that any BFs have a negative impact upon implant survival. In this context, patients should be informed about the related risks and DI could be placed under optimum oral care conditions. On the contrary, in patients who are under BF treatment intravenously together with RT doses of above 50 Gy, DI placement was reported to be a contraindication [30, 56].

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Alsaadi et al., 2008, Retrospective [21]	2 years	6 patients with RD	28	100%	–	RA does not seem predominant player for late implant loss
Krennmair et al., 2016, Prospective [16]	3 years	6 patients with RD (44 total)	ND	–	1.61 mm in RD	RD is risk factors for bone loss (OR: 50.1)
Neves et al., 2016, Retrospective [2]	7.3 years (mean)	36 patients with RD	–	80.6% (patient based)	25% (patient based)	RDs are associated neither with higher risk of implant failure nor peri-implant pathology (>4 mm pocket depth with BoP or MBL). However, it is associated with a higher number of implant failures

RD, rheumatologic disease; RA, rheumatoid arthritis; BoP, bleeding on probing; MBL, marginal bone loss; DI, dental implant; SR, survival rate; ND, no data available; OR, odds ratio.

Table 11. Studies that indicate dental implant outcomes in patients with rheumatologic disorders.

In conclusion, BFs do not seem to have an adverse effect on DI survival under optimum oral care conditions, and OBFs are not associated with occurrence of osteonecrosis of jaws (ONJ) (**Table 12**).

2.12. Head and neck cancer

Squamous cell carcinoma, adenocarcinoma, and ameloblastoma are the most common malignancies that are encountered in the head and neck regions. These patients with malignancies frequently go under challenging adjuvant therapeutic procedures such as radiotherapy (RT) or chemotherapy (CT) in addition to the tumor surgery. Due to the aggressive nature of the cancer and challenging cancer therapies, it is difficult to manage the DI surgery and prosthetic procedures.

Furthermore, studies that evaluate the DI success in cancer patients are limited because most of the studies had a control group of patients who are under another cancer treatment (instead of a healthy control group) or have no control subjects to compare the success of dental implants. Therefore, the results are sufficient to achieve a conclusion regarding DI success (**Tables 13** and **14**). According to these clinical studies, CT does not seem to be associated with the higher DI failure when compared with the surgical treatment only. RT seems to be impairing the osseointegration process. Regardless of the cancer-treatment procedure, smoking and alcohol consumption in patients diagnosed with head and neck cancer yield higher implant failures. Additionally, there are no studies about implant therapy in patients with malignant diseases that are treated with BFs [64], and no study determined peri-implant conditions of DI in such patient population.

For improving the DI success in cancer patients, implant surgery is recommended to be performed at least 21 days prior to the initiation or following after 9 months of radiotherapy under a strict surgical asepsis and antimicrobial prophylaxis. Premature loading of the implants should be avoided [28, 31].

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Jeffcoat, 2006, Longitudinal single-blind controlled [57]	3 years	50 (the half is under OBF, the other half is not used BF)	210	100% for OBF, and 99.2% for control group	–	OBF usage is not associated with occurrence of ONJ compared to placebo
Martin et al., 2010, Cohort [58]	>1 year	589 aged women	ND	26 implants loss in 16 patients	–	Implant failure occurred as early as 4 weeks and as late as 11 years after placement
Famili et al., 2011, Retrospective [59]	1 year	211 women	347	98.7%	–	OBF therapy is not significantly affects implant success
Al-Sabbagh et al., 2015, Retrospective [60]	6 years	39	51	86.4%	–	It is suggested that there is a possible association between implant failure and not using of BF in elder patients (OR: 9.22)
Mozzati et al., 2015, Clinical chart review [61]	10 years	235 middle-aged women under OBPs for OP	1267	98.7% (implant based) 93.2% (patient based)	–	The risk for developing BRONJ associated to DI surgery remains low for patients receiving oral BPs. The use of procedures that could enhance healing such as platelet concentrates is recommended
Siebert et al., 2015, Comparative prospective [54]	1 year	24 women (half under iv. BF, others without OP)	120	100%	ND (MBL is similar)	Immediate implant osseointegration can be successful in a patient with OP using once-yearly infusion of 5 mg iv. zoledronic acid
Suvarna et al., 2016, Retrospective [62]	3 years	112 (58 patients on OBF therapy)	140	92%	–	No significant risk of implant failure is seen in patients on OBP therapy compared with healthy patients
Tallarico et al., 2016, Prospective [63]	3 years	32	98	98%	1.35 ± 0.21	No prosthesis failed during the entire follow-up, and no major complications were recorded. OBF therapy is not significantly affecting DI success in case of accurate treatment selection, minimally invasive surgical approach and constant follow-up
Ata-Ali et al., 2016, Systematic review and meta-analysis [56]	1–7 years	1288 patients (386 cases and 902 controls)	4562 (1090 DI in cases,	Ranged between 66.7 and 100% in BF users, 95.5	–	There is not enough evidence that BFs have a negative impact upon implant SR Further, prospective studies

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
			3472 in controls)	and 100% in nonusers		involving larger sample sizes and longer durations of follow-up are required to confirm these results
Mean/total of values/subjects	1–10 years	1238	2233 (in 7 out of 8 available studies)	SR is about 97% in patients who are under BFs therapy	1.35 mm at 3rd year follow-up (in one study available)	BFs do not seem to have an adverse effect on DI survival under an optimum oral care conditions, and OBFs are not associated with occurrence of ONJ

BF, bisphosphonate; OBF, oral bisphosphonate; OP, osteoporosis; BRONJ, BP-related osteonecrosis of the jaws; ONJ, osteonecrosis of the jaws; MBL, marginal bone loss; DI, dental implant; SR, survival rate; ND, no data available.

Table 12. Studies that indicate dental implant outcomes in patients who underwent bisphosphonate treatment.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Kovacs, 2001, Retrospective [65]	10 years (3 years of mean)	30 (received postsurgical adjuvant CT) and 17 (received only oncological surgery)	106 in CT group, 54 in surgery group	98.1% on implant basis	–	CT is not detrimental to the survival and success of DIs in the mandible
Cao and Weischer, 2003 [66] (abstract available)	?	27 total number of nonirradiated and irradiated patients	131 total	65% on patient basis	–	Implants and prostheses in irradiated patients have significantly lower survival rates than in nonirradiated patients
Korfage et al., 2011, Prospective [67]	5 years	50 (18 patients were treated with surgery only, 32 patients with RT in addition to the surgery)	195 (72 in surgery-, and 123 in surgery + RT)	98.6% for non-RT treated, 89.4% for RT-treated group	–	Implant loss is higher in patients with head and neck cancer who received RT posttumor surgery
Gander et al., 2014, Retrospective [26]	20 months	33 (29 patients with SCC, 24 underwent mandibular reconstruction)	136 total	92.5% (at 1st year), 87.5% (after 20th month)	–	Only smoking ($p = 0.016$) and alcohol abuse ($p = 0.001$) are associated with higher implant failure rates

SCC, squamous cell carcinoma; CT, chemotherapy; RT, radiotherapy; DI, dental implant; SR, survival rate; ND, no data available.

Table 13. Studies that indicate dental implant outcomes in head and neck oncology patients.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Moy et al., 2005, Retrospective cohort [6]	2–20 years	22 patients received RT	ND	68.18% in irradiated patients	–	There is a correlation between head and neck radiation and increased failure rate (RR = 2.73)
Alsaadi et al., 2008, Retrospective [21]	2 years	2 patients received RT	15 in irradiated patients	80%	–	RT is affected significantly the late implant loss (OR: 3.32)
Carr, 2012, Retrospective case series [69]	2 years	ND (412 total)	ND (1512 total)	ND	ND	Late implant failure is influenced by the local factor of "implant location" and the systemic factor of "radiotherapy"
Mancha, 2012, Retrospective [70]	5 years	30 RT-group, 20 control (non-RT treated oral cancer group)	225 in RT group, 130 in control group	92.6% for irradiated (48.3% for ORN-developed patients)	–	Irradiated patients have significantly higher implant loss than nonirradiated patients (p = 0.063)
Korfage et al., 2014, Retrospective [71]	14 years	164 patients with oral cancer (also 91 of them are smoker, 65 are nonsmoker)	318 in RT-group, 206 in nonirradiated group	91.5% for irradiated, 99.5% for nonirradiated	–	Implant loss is higher in irradiated patients ($p < 0.001$) but no significant difference is shown for bone loss assessed on panoramic radiographs Smoking is also not found associated with the occurrence of ORN
Rana et al., 2016, Retrospective [72]	5 years	46 patients with oral cancer	162	67% (52 implant had lost)		RT dose of <50 Gy units also showed significantly increased amount of implant survival rate
Nooh, 2013, Systematic Review [68]	1–14 years	944 patients with oral cancer	3775	88.9% (for 3357 implants)	–	In preimplantation RT, SR of DI is significantly higher for the mandible (93.3%) than for the maxilla (78.9%) or for grafted bone (87.5%) While RT dose above 55 Gy significantly decreased implant survival
Mean/total of values/subjects	1–20 years	284 patients with oral cancer (in 5 out of 6 available studies), 54 irradiated patients (in 3/6)	720 implants in irradiated patients (in 4 out of 6 available studies)	Approx. 83.07% SR in irradiated patients		RT, especially a dose above 50 Gy, negatively affects DI success

ORN, osteoradionecrosis; RT, radiotherapy; DI, dental implant; OR, odds ratio; RR, risk ratio; SR, survival rate; ND, no data available.

Table 14. Studies that indicate dental implant outcomes in patients who underwent radiation therapy.

2.12.1. Radiotherapy and hyperbaric oxygen therapy

RT reduces the cellular and vascular processes of healing, therefore it is assumed to impair the osseointegration and increase the risk of DI-related complications [31]. RT doses higher than 50 Gy are known to hinder osseointegration of DIs [30]. On the other hand, DI placement becomes contraindicated in patients who have received additional therapy of BFs intravenously or hormonal therapy, corticosteroids or immunosuppressive medication [30]. According to the data retrieved from the recent studies, it can be concluded that implant loss is clearly higher in irradiated patients (**Table 14**). The failures are more prominent in mandible or in grafted bone [68].

In the past, adjuvant hyperbaric oxygen therapy (HBO) treatment was shown to lead lower DI failure rates in cancer patients who underwent RT than those nonirradiated and irradiated patients [73]. Whereas, according to the recent clinical studies and reviews (**Table 15**), it seems that HBO has no positive effect on implant survival in irradiated patients. Therefore, this issue remains controversial.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Schoen et al., 2007, RCT [74]	1 year	26 (the half is HBO treated, others is control)	ND	85.2% in HBO group, 93.9% in non-HBO group	MBLs: 0.6 ± 0.6 mm in HBO-, 0.7 ± 0.7 mm in non-HBO group	Adjuvant hyperbaric oxygen therapy does not influence implant survival or peri-implant MBL in radiated mandibular jaw bone. There is no statistically significant difference for postoperative complications and patient satisfaction
Esposito and Worthington, 2013, Systematic review [75]	–	–	–	–	–	Despite the limited amount of clinical research available, it appears that HBO therapy in irradiated patients requiring dental implants may not offer any appreciable clinical benefits. There is a definite need for more RCTs to ascertain the effectiveness of HBO in irradiated patients requiring dental implants
Chambrone et al., 2013, Systematic review [76]	–	–	1689 in irradiated jaws	The mean SR of 15 studies ranged from 46.3 to 98.0%	–	The risk of implant failure increases significantly in irradiated patients (RR: 2.74) and in maxillary sites (RR: 5.96). HBO therapy does not reduce the risk of implant failure

HBO, hyperbaric oxygen; RR, risk ratio; RCT, randomized controlled trial; MBL, marginal bone loss.

Table 15. The effect of hyperbaric oxygen (HBO) on reducing the risk of DI failure in irradiated patients.

2.13. Immunosuppressive conditions

Immunosuppressive disabilities encompass several disorders and conditions including RDs, autoimmune skin diseases (scleroderma, pemphigus, burning mouth syndrome etc.), organ transplantation, and immunosuppressive drug usage [2, 77, 78].

Since a good immune response is necessary for wound healing, immunocompromised conditions have been commonly assumed as a contraindication for DI placement [31]. In animal studies, it is showed that immunosuppressive drugs reduce osteoblast's proliferation and impair implant osseointegration [79, 80]. Furthermore, immunocompromised condition may present additional risks for blood borne infections [28]. Therefore, installation of DIs in patients under long-term immunosuppressive treatment should be elucidated with additional measures [81].

2.13.1. Organ transplantation

Bone healing is negatively affected by immunosuppressive medications. There are reports of case series and clinical studies that show successful treatments of DIs in patients who underwent organ transplants (**Table 16**). Reviewers stated that DIs could be a valid treatment providing that the appropriate surgical procedures and hygienic conditions are ensured [28, 78]. Modification of the immunosuppressive medication could lead a significantly lower toxicity [78].

As a conclusion, it is apparent that DI is not contraindicated for the patients who had organ transplants. However, it is suggested that the patients' medical condition should be investigated with the relevant physician before DI surgery, and the surgery should also be conducted under prophylactic medication in order to reduce the risk of blood-borne infections [28, 31].

2.13.2. HIV-positive patients

Acquired immune deficiency syndrome (AIDS) is a condition that is caused by the infection of the human immunodeficiency virus (HIV). HIV-infected individuals may have compromised oral health because of having HIV-associated gingivitis and periodontitis etc. [85] that yield an additional impairment of the general health.

Recently, HIV-infection is regarded as a chronic disease rather than a terminal disease owing to the therapeutic regimen of highly active antiretroviral therapy (HAART) that includes combinations of diverse antiretroviral medications. This regimen, however, is associated with many adverse effects including bone disorders, osteopenia, osteonecrosis, and osteoporosis [86, 87]. Hence, there is a need for identifying the predictability of dental implant therapy in patients with HIV-infection.

According to the clinical studies available (**Table 17**), clinical outcomes regarding the peri-implant pathology are conflicting. There may be a tendency for peri-implant infections due to the immunocompromised condition. However, HIV infection does not seem to increase the failure in the short or long term. So DI could be regarded as an eligible treatment for improving quality of life in the HIV-positive patients.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Gu and Yu, 2011, Case series [82]	3 years	13	45	100%	MBL is 1.30 mm	DI treatment can be offered to liver transplant patients who are stable under long-term immunosuppression. Stable liver function and general condition should be affirmed though overall examination and consultation
Gu et al., 2011, Case report [83] (only abstract available)	5 years	1	11	–	–	A stable osseointegration with moderate vertical bone loss is achieved
Montebugnoli et al., 2012, Prospective [84]	3 months	20 (10 have organ transplant, the other 10 are in control group)	32 (20 in transplanted, 12 in control group)	–	MBL is 0.21 mm for transplanted, 0.32 mm is for control group	The bone response around submerged DI in immunocompromised organ transplant patients does not differ from that observed in control patients
Montebugnoli et al., 2015, Prospective [81]	1 year	13 organ transplanted (11 hearts, two livers, and 13 control subjects)	29 in transplanted, 28 in healthy control subjects	–	For transplanted and control subjects, MBLs are 0.17 and 0.20 mm, PDs are 0.06 and 0.11 mm	It seems that bone and periodontal response and microbiological status around submerged DI in immunocompromised organ-transplanted patients do not differ 1 year after loading from those observed in healthy control patients
Mean/total of values/subjects	1–5 years	37 patients had organ-transplant	105 implants	100%	0.19 mm for 1st year 1.30 mm at 3rd year	SR outcome is scarce. MBL seems acceptable More studies needed

MBL, marginal bone loss; DI, dental implant; SR, survival rate; PD, pocket depth.

Table 16. Studies that indicate dental implant outcomes in patients who received organ transplant.

2.14. Psychiatric disorders

Patients with neurologic disorders or other disabilities such as cerebral palsy, mental retardation, epilepsy, Down syndrome, Rett's syndrome, Asperger syndrome, Prader-Willi syndrome, fragile X chromosome, dystrophia myotonica, autism, and schizophrenia cause many problems during implant treatment and prosthetic maintenance [93]. Epilepsy impairs the oral condition of patients due to nausea-induced vomiting, mechanical trauma caused by seizures, and antiepileptic drugs-associated oral complications such as gingival overgrowth, xerostomia, and yeast infections [94, 95]. Likewise, most widely used antidepressant drugs, selective serotonin reuptake inhibitors (SSRIs), affect not only the nervous system but also peripheral tissues

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Stevenson et al., 2007, Prospective [88]	6 months	20 HIV+, and 9 HIV− edentulous adults	40 in HIV+, 18 in HIV− subjects	100% for both groups	–	No difference in short-term clinical outcome is found between the HIV+ and the HIV− subjects
Oliveira et al., 2011, Pilot study [89]	1 year	40 (11 PI-based HAART, 14 NNRTI-based HAART without PI, 15 control group of who had HIV−)	60 (20 in each groups)	100% for all groups	0.49 mm in PI-HAART group, 0.47 mm in NNRTI-HAART and 0.55 mm in control	The placement of DI in HIV+ patients is a reasonable treatment, regardless of CD4+ cell count, viral load levels, and type of antiretroviral therapy. Longer follow-ups are necessary to ascertain the success
Neves et al., 2016, Retrospective [2]	7.3 years of mean	5 HIV+	ND	60% (patient based)	60% (patient-based peri-implant pathology rate)	AIDS is not risk factor for neither higher implant failure nor peri-implant pathology (>4 mm pocket depth with BoP or MBL). However, these rates are high when compared mean failure rates of population
Gherlone et al., 2016, Prospective [90, 91]	1 year	66 HIV+	190	92.1% on implant basis (a, b)	MBL is 1.19 mm, peri-implantitis prevalence is 5.2% on implant basis (a, b)	Despite higher incidence of peri-implant infections in the first 6 months (a), DI is a suitable treatment with a slightly worse results (a, b) regardless of CD4+ cell count (b). HIV+ heavy smokers (>10 cig/day) demonstrated increased risk of early failure, peri-implantitis, pus, and pain (b)
Gay-Escoda et al., 2016, Retrospective case series [92]	6.5 years of mean	9 HIV+	57	98.3%	Success rate: 68.4%. Patient- and implant-based rates of peri-implant mucositis: 22.2%–10.5%, peri-implantitis: 44.4%–45.6%	Though there is a high prevalence of peri-implant diseases, DI in HIV+ patients seem to provide satisfactory clinical results
Mean/total of values/subjects	Up to 7.3 years	125 HIV+ patients	347 (in 4 out of 5 studies)	Approx. 90% SR	0.83 mm MBL in 1st year. 50% of peri-implant pathology rate for mean follow-up of 7 years	SR is acceptable. Mean MBL outcomes are scarce and conflicting. Peri-implant pathology incidences seem higher as compared to the healthy population

HAART, highly active anti-retroviral therapy; PI, protease inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; MBL, marginal bone loss; BoP, bleeding on probing; SR, survival rate; resp, respectively.

Table 17. Studies that indicate dental implant outcomes in HIV-infected patients.

Author, year, study design	Follow-up	No. of patients	No. of implants	SR of implant	Peri-implant pathology	Conclusion
Cune et al., 2009, Retrospective [95]	16 years	61 patients with epilepsy, additional motor and/or intellectual impairments	134	97.6%	72% of implants were considered having inadequate level of hygiene PD is 2 mm	Although adequate plaque control is not feasible in those patients, MBLs remained stable and implant loss is rare
Ekfeldt et al., 2013, Prospective [93]	10 years	22 patients with different neurologic disabilities	70	85.8%	Peri-mucositis: 14 implants in 10 patients (PD ≥ 4 mm). Peri-implantitis: 4 implants in 3 patients (bone loss ≥ 3 threads)	DI is a valid option in patients with ND, although maintenance often requires the management of more complications compared with healthy patients
Wu et al., 2014, Retrospective cohort [98]	3–67 months	490 total number of SSRI-users and nonusers	916 (94 in users, 822 in nonusers)	88.4% for users, 95.4% for nonusers	–	SSRI is associated with increased failure risk of osseointegrated implants, which might suggest a careful surgical treatment planning for SSRI users

ND, neurologic disabilities; SSRI, selective serotonin reuptake inhibitor; PD, probing depth; MBL, marginal bone loss; SR, survival rate.

Table 18. Studies that indicate dental implant outcomes in patients with psychiatric disorders.

including bones because of having serotonin receptors [96]. Therefore, SSRI blocks on bone cells have been reported to affect bone formation negatively [97].

Since bone metabolism and oral conditions have an influence on the osseointegration of DI, neuropsychiatric disabilities and the drugs used are considerable issues for DI treatment. Clinical research related to the effect of psychiatric disorders on DI success is limited. It seems that this kind of disorders do not cause higher failures or peri-implant pathology (**Table 18**). On the other hand, SSRIs might increase DI failure rate as presented in a cohort study with a large number of subjects. Further studies are required to ascertain the association between antidepressant drugs and DI failure.

3. Conclusion

Implant survival in the elderly population, osteoporosis (OP) and HIV infection seem to be similar with the healthy population. CVDs or diabetes may present a small risk. RT seems to have the worst effect on DI success with an average SR of 83%. Some of the other compromised conditions such as alcoholism, bleeding disorders, thyroid disorders, hepatitis, RDs, organ transplantation, and HBO therapy should be investigated with additional clinical data to reveal objective conclusions regarding DIs.

Results with regard to peri-implantitis or peri-implant conditions are insufficient and even conflicting for majority of the compromising systemic aspects. Future studies should be designed for indicating peri-implant tissue health and maintenance in compromised patients.

It must be taken into account that follow-up of the patients in a professional oral maintenance regimen after implant placement reduces the implant failure rate by 80% [12]. Thus, it can be stated that controlling the systemic diseases before the implant therapy and proper establishment of the medical conditions are more important than the presence of a compromise alone.

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