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 |
Regarding the MBL, smoking seems to have a destructive 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].

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

| 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 | 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) | SR is 90% for long-term period | 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.
| 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 |
| Author, year, study design | Follow-up | No. of patients | No. of implants | SR of implant | Peri-implant pathology | Conclusion |
|---------------------------|-----------|----------------|----------------|---------------|----------------------|------------|
| Busenlechner et al., 2014, Retrospective [9] | 8 years | 1726 smoker | ND (1347 total) | 97.5% (6 failed out of 246 implant) | Smoking increases the failure rate by 3-fold | Smoking is risk factors for MBL (OR: 8.9) |
| Tran et al., 2016, Retrospective chart review [12] | 10 years | 215 smoker | (272 total) | 97.5% for smokers overall (SR is 97%) | 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 | ND | Smoking is not associated with higher risk of implant failure and peri-implant pathology (>4 mm pocket depth) | Smoking is risk factors for MBL (OR: 8.9) |
| Neves et al., 2016, Retrospective [2] | 7.3 years | 476 smoker | ND | 85.1% for patients of mean age | Smoking increases the failure rate by 2.6-fold | Smoking has an influence on both mesial and distal bone loss (p = 0.037) |
| 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) | 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 | Smoking is risk factors for MBL (OR: 8.9) |
| Clementini et al., 2014, Systematic review and meta-analysis [14] | >1 year | 478 smoker and 1207 nonsmoker | ND | ND | Smoking increases the failure rate by 2.6-fold | Smoking has an influence on both mesial and distal bone loss (p = 0.037) |

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

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

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

Table 4. Studies that report peri-implant health condition in patients with diabetes mellitus.
| 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 | 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 | – |
| Alsaadi et al., 2008, Retrospective [21] | 2 years | 9 | 33 | 100% | – |
| Busenlechner et al., 2014, Retrospective [9] | 8 years | 185 (4.3% out of 4316 total) | ND | 95.1% for diabetes (overall 97%) | – |
| Neves et al., 2016, Retrospective [2] | 7.3 years (mean) | 56 diabetic | ND | 92.9% (patient based SR) | 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% | – |
| Shi et al., 2016 Meta-analysis [41] (abstract available) | ND | 252 | 587 | ND | – |
| 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 | – | – | – | 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.
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].
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 |
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 |
|---------------------------|-----------|----------------|----------------|--------------|------------------------|------------|
| 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 |

Table 10. Studies that indicate dental implant outcomes in patients with bone diseases.
In conclusion, BF does 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 BF [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 |
|---------------------------|-----------|----------------|----------------|---------------|------------------------|------------|
| Alsaadi et al., 2008, Retrospective [21] | 2 years | 6 patients with RD | 28 | 100% | – | RA does not seem predominant player for late implant loss |
| Krennmaier 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.
| Author, year, study design | Follow-up | No. of patients | No. of implants | SR of implant pathology | 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 OBP’s 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, 66.7 and 100% in BF users, 95.5 | Ranged between | – | There is not enough evidence that BFs have a negative impact upon implant SR Further, prospective studies |
Mean/total of values/subjects 1–10 years 1238

Mean/total of values/subjects 1–10 years 1238

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] | 2006 | 22 patients received RT | 15 in irradiated patients | 80% | ND | Late implant failure is influenced by the local factor of “implant location,” and the systemic factor of “radiotherapy.” There is a correlation between head and neck radiation and increased failure rate (RR = 2.73). Implant loss in irradiated patients is higher than in nonirradiated patients (p < 0.001). |
| Alsaadi et al., 2008, Retrospective [21] | 2 years | 2 patients received RT | 15 in irradiated patients | ND | ND | RT is affected significantly the late implant loss (OR: 3.32). |
| Carr, 2012, Retrospective case series [69] | 2 years | ND (142 total) | ND (1512 total) | ND | ND | Late implant failure is influenced by the local factor of “implant location,” and the systemic factor of “radiotherapy.” There is a correlation between head and neck radiation and increased failure rate (RR = 2.73). Implant loss in irradiated patients is higher than in nonirradiated patients (p < 0.001). |
| Mancha, 2012, Retrospective [70] | 2012 | 30 RT-group, 20 control (non-RT treated oral cancer group) | 318 in RT-group, 206 in control group | 91.5% for irradiated, 99.5% for nonirradiated | ND | Late implant failure is influenced by the local factor of “implant location,” and the systemic factor of “radiotherapy.” There is a correlation between head and neck radiation and increased failure rate (RR = 2.73). Implant loss in irradiated patients is higher than in nonirradiated patients (p < 0.001). |
| Korfage et al., 2014, Retrospective [71] | 14 years | 164 patients with oral cancer (also 91% of them are smoker, 65 patients are nonsmoker) | 654 implants in irradiated (61 patients) and 654 implants in nonirradiated group | 91.5% for irradiated, 99.5% for nonirradiated | ND | Late implant failure is influenced by the local factor of “implant location,” and the systemic factor of “radiotherapy.” There is a correlation between head and neck radiation and increased failure rate (RR = 2.73). Implant loss in irradiated patients is higher than in nonirradiated patients (p < 0.001). |
| Rana et al., 2016, Retrospective [72] | 5 years | 46 patients with oral cancer | 62 implants had lost | 67% | (2 implants had lost) | Late implant failure is influenced by the local factor of “implant location,” and the systemic factor of “radiotherapy.” There is a correlation between head and neck radiation and increased failure rate (RR = 2.73). Implant loss in irradiated patients is higher than in nonirradiated patients (p < 0.001). |
| Nooh, 2013, Systematic Review [68] | 1-20 years | 944 patients with oral cancer | 3775 implants in irradiated patients (in 4 out of 6 available studies) | 88.9% (for 357 implants) | ND | Late implant failure is influenced by the local factor of “implant location,” and the systemic factor of “radiotherapy.” There is a correlation between head and neck radiation and increased failure rate (RR = 2.73). Implant loss in irradiated patients is higher than in nonirradiated patients (p < 0.001). |

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.
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− subjects, 18 in HIV+ | 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 group) | 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%, periimplantitis: 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/subj | 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.
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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