Chronic Diseases and Implants – A Review of the Status Quo

Frank Halling

Dr.med. Dr. med. dent. Frank Halling practices as an oral maxillofacial surgeon in Fulda and also works as a hospital consultant. He has been an ITI Fellow since 2006 and has been lecturing at the University of Marburg since 2010. His focus is on dental pharmacology, dental medicine and the Internet as well as diagnosis and treatment of skin tumors. He is the author of almost 60 original publications and in 2008 published his book "Zahnärztliche Pharmakologie".

ABSTRACT

Implant dentistry has become a standard component of the therapeutic range available to dental medicine. Demographic changes have led to the increasing use of implants in older and comorbid patients. How successful implant solutions are in chronically ill patients is a question that has therefore become more central. The volume of data available is fairly limited. There are hardly any conclusive studies with substantial patient groups. One approach to evaluating a patient's general condition that has proven useful is the classification system based on the ASA. Implants should only be considered in patients whose general condition is stable. Morbidity forecasts assume a clear increase in cardiovascular diseases as well as those associated with dementia. Diabetes mellitus is also predicted to stabilize at a relatively high level. While cardiac disease and well controlled diabetes are not contraindicated for implants, untreated or unstable diabetes can have a negative effect on the early stages of osseointegration. The main problems in regard to neuropsychiatric diseases or those with associated dementia often stem from the medication (e.g. dry mouth). Osteoporosis is the most frequently diagnosed bone disease in older people but it has relatively little impact on the survival rate of implants. The treatment of osteoporosis with oral bisphosphonates seems to have no negative impact on implant survival. For rheumatic disorders and mucosal diseases, in the main only case studies and smaller studies are available and the results are very heterogeneous. In general, however, prophylactic antibiotics are recommended for immunocompromised patients. When treating patients who suffer from one or more chronic underlying conditions, the clinician must engage in a continuous process of weighing up the advantages of the prosthetic gain in function that is aimed for with implants against possible complications.

Key words: Implant survival, chronic diseases, comorbidity, risk factors, treatment outcomes

Disease	Increase by 2030	Increase by 2050
High blood pressure	9%	2%
Diabetes	22%	22%
All types of cancer	26%	27%
Stroke	37%	62%
Heart attack	42%	75%
Dementia	53%	113%

Table 1: Forecast of the increase in selected diseases in Germany between 2009 and 2050 (Beske et al. 2009)

INTRODUCTION

Implant therapy using optimized treatment techniques and materials is part of the standard range of dento-surgical treatment options. Implant dentistry is associated with well documented, good long-term results and is regarded as a safe method of treatment (Behrens et al. 2004, Buser et al. 2012). Although the indications for dental implants have expanded significantly since they were first introduced, there are still localized and general medical risk factors that need to be taken into consideration during planning and treatment. In addition to technical issues, biological factors play a central role in implant failure. While smoking and aggressive periodontitis as part of a case history are no longer likely to be questioned as risk factors for peri-implantitis (Paquette et al. 2006, Mombelli et al. 2012), studies relating to the interpretation of general medical risk factors for implant treatment are significantly more heterogeneous.

HIGH-RISK PATIENTS IN THE DENTAL SURGERY

In implant dentistry, high-risk patients are those with whom strict adherence to standard protocols does not lead to the hoped-for results and the level of complications and failures is higher than average (Renouard & Rangert 2006). Which general medical risks to patients must dentists who work with implants take into consideration today? According to figures supplied by the Robert Koch Institut (RKI), 41.1% of women and 48.6% of men in Germany who are between 45 and 64 years old suffer from at least one chronic disease. In the next age group with those who are 65 years and over, this figure increases to 53.7% for women and 59.2% for men (RKI 2012).

According to a morbidity forecast, by 2050 high to very high increases are expected for selected health issues in Germany – in particular cardiovascular disease and diseases associated with dementia (Beske et al. 2009) (Tab. 1).

Given the current demographic changes, a significant increase in older and comorbid patients can be expected in the future. Comorbidity refers to the concomitant presence of several diseases or health issues in a single individual (Van der Akker et al. 1998). It is closely associated with advanced age and chronic diseases. In Germany, more than 50% of people over 65 years are classified as comorbid (Kohler & Ziese 2004). This figure is also reflected in international data (Radfar & Suresh 2007).

Within the foreseeable future, therefore, increasing numbers of older and comorbid individuals will be calling on not only medical but also dental services. In implant dentistry in particular, a comprehensive medical picture (illnesses and medication) (Besimo 2007) is necessary to meet the individual needs of the patient and carry out the necessary interdisciplinary treatment.

GENERAL RISK FACTORS

Systematic overviews dealing with the implications of medical risk factors in implant treatment are still relatively rare (Moy et al. 2005, Bornstein et al. 2009, Schiegnitz & Kämmerer 2012, Mombelli et al. 2012, Diz et al. 2013, Renvert et al. 2014). Bornstein et al. (2009) state that there is a low level of

Classification	Definition
ASA I	Patients are considered to be normal and healthy
ASA II	Patients have mild to moderate systemic disease
ASA III	Patients have severe systemic disease that limits activity, but is not incapacitating
ASA IV	Patients have severe systemic disease that limits activity and is a constant threat to life
ASA V	Patients are moribund and are not expected to survive more than 24 hours with or without an operation
ASA VI	Clinically dead patients being maintained for harvesting of organs

Table 2: ASA Physical status classification system for dental patient care (mod. after Fehrenbach & Weiner 2009)

evidence for relative and absolute contraindications to implant therapy in connection with systemic diseases. The criteria of evidence level 1 are not met by any studies, those of evidence level 2 by very few and those of evidence level 3 by only a number of studies (AHRQ 1992).

A differentiation needs to be made between patients who should not be operated on due to their poor general health and patients suffering from chronic systemic diseases or taking medication who can be operated on but represent a higher risk in terms of implant survival.

The ASA classification has proved useful when determining the general health status of a patient (Tab. 2)

Implants can be placed in patients who fall into ASA categories I and II without any problem. Patients who fall into ASA category III require intensive care and normally need to be hospitalized in order to avoid any potentially harmful consequences of placing implants or related secondary disorders (Nkenke et al. 2007). More than 25% of patients in dental practices who are over 65 years fall into ASA III and IV categories and as such present a high risk profile (Smeets et al. 1998). Patients in ASA categories IV to VI should not undergo implant surgery. In general, when dealing with patients who are at risk, an eye should be kept on the treatment of the underlying condition and implants only undertaken if the patient's general condition is stable (Nkenke et al. 2007).

There is less controversial discussion attached to the influence of a patient's age and gender. Apart from Moy and associates (Moy et al. 2005), who saw the risk of implant loss double in patients between 60 and 79 years old in comparison with younger patients, numerous other authors could not confirm a higher risk related to advanced age and/or gender (Mc Dermott et al. 2003, Merk 2007, Renvert et al. 2013). While generally speaking, there is little risk associated with implants for patients with systemic diseases (Chuang et al. 2002), this does not always apply to individual diseases.

SYSTEMIC DISEASE AS A RISK FACTOR WHEN PLACING IMPLANTS

Cardiovascular disease
The link between cardiovascular disease and implant survival has rarely been studied to date. In a study by Khadivi and associates (Khadivi et al. 1999), no significant difference was found between those with and without heart disease. Later studies confirm this result (Moy et al. 2005, Merk 2007, Alsaadi et al. 2008). However, in a retrospective analysis of 270 patients with peri-implant disease, Renvert's working group found that those patients with a cardiovascular indication had an 8.7-fold higher risk of peri-implantitis than the healthy control group. Nonetheless, in general cardiac disease does not represent a contraindication for implants (Diz et al. 2013).

Dementia and neuropsychiatric diseases
For this spectrum of diseases in association with implants, there are only individual reports with an evidence level of 4 (Bornstein et al. 2009). However, in the future a clear increase in the number of patients suffering from dementia must be reckoned with (Beske et al. 2009). An implant success rate of 85% has been recorded for case reports of patients with Parkinson's disease (Packer et al. 2009).

It is clear that before an operation the patient must supply a full medical history along with medication. If there is any question of dementia, it is essential to contact the patient's neurologist and, where appropriate, close family members in order to avoid any errors when selecting patients (Feijoo et al. 2012).

An additional problem is posed by the medication prescribed for neuropsychiatric diseases. Many psychotropic drugs can significantly amplify the effects of adrenaline during the operation and can lead to quite severe dry mouth, particularly when prescribed in combination with other drugs (Halling 2013). The degree of hyposalivation must be evaluated before implant surgery in order to assess the degree of vulnerability of the mucosa (Payne et al. 1997).

Osteoporosis
The most frequently diagnosed bone disease among the elderly is osteoporosis. The clinical picture of osteoporosis represents an increasing problem worldwide and has been classified by the World Health Organisation (WHO) as one of the 10 most economically significant widespread diseases (WHO 2003). It is estimated that over 200 million people worldwide have osteoporosis. The prevalence of osteoporosis is continuing to escalate with the increasingly elderly population (Reginster & Burlet 2006).

In 2009, 24% of women and 6% of men in Germany were known to be suffering from osteoporosis, which corresponds to a total of 6.3 million people. The number of people diagnosed each year is estimated at 885,000 (Hadji et al. 2013) Osteoporosis is a systemic disease of the skeleton characterized by reduced bone mass and microarchitectural deterioration of bone tissue, resulting in

fragile bones. Bone density or T-scores are a major criterion in the diagnosis of osteoporosis. According to the WHO, a diagnosis of osteoporosis can be made if the results for bone density are at least 2.5 standard deviations (SD) below the normal value for a healthy young person (T-score ≤–2.5) (WHO 1994). Bone density in osteopenia lies between –1 and –2.5 SD. 95% of all diagnosed cases of osteoporosis refer to primary osteoporosis that, by definition, is not the result of another disease.

There is no correlation between systemic bone density, mandibular bone density, bone quality and implant loss (Slagter et al. 2008). However, Ruskin recommends allowing 1 to 2 months longer than "normal" for postoperative implant healing (Ruskin 2007) as primary stability has been reduced (Schiegnitz & Kämmerer 2012). In a cross-sectional study with 203 patients and 967 implants, Dvorak and associates (Dvorak et al. 2012) found that osteoporosis (47 women) or osteopenia (16 women) did not significantly influence the survival of the implant. In the cohort study carried out by Moy and associates (Moy et al. 1995), of the 1,140 enrolled patients, the 161 women undergoing hormone substitute therapy had an approximately 2.5-fold higher risk of losing their implant. A recently published meta-analysis that covers four studies on osteoporosis found no increased risk of implant loss in the presence of osteoporosis (Chen et al. 2013).

Overall it appears that a clinical impression of the jaw supplemented by a CT or DVT is more telling when estimating the risk of implant loss than measuring bone density (Bornstein et al. 2009, Holahan et al. 2011). The data available on the effectiveness of dental implants in the presence of osteoporosis are at level 3a (case-control studies) (Bornstein et al. 2009).

In the treatment of osteoporosis, the anti-fracture efficacy of approved first-line bisphosphonates, which are mostly orally prescribed, has been proven in randomized controlled clinical trials. However, with more extensive and prolonged clinical use of bisphosphonates, the occurrence of rare, but serious, adverse events like osteonecrosis of the jaw (BRONJ) have been reported. On average, patients take oral bisphosphonates for 4.6 years (and a minimum of three years) before developing BRONJ (Zavras 2011). But the prevalence of BRONJ in patients taking oral bisphosphonates is very low, ranging from 0.07 to 0.10% (Lo et al. 2010). In a retrospective review with more than 211 women taking oral bisphosphonates who received 347 implants, the success rate (98.7%) was consistent with standard implant success rates (Famili et al. 2011). In a review and meta-analysis with 4,562 dental implants (1,090 dental implants in cases with oral and intravenous bisphosphonate therapy and 3,472 in controls) there was not enough evidence that bisphosphonates have a negative impact on implant survival (Ata-Ali et al. 2014). On the other hand, complications have been noted in patients treated with bisphosphonates. As a consequence, adequate informed consent based on detailed explanations, in particular on the possible risk of implant loss, bony necrosis or poor outcome from sinus lift, should be obtained (Diz et al. 2013). Based on the current literature, a history of oral or intravenous BP use is not an absolute contraindication for dental implant placement, but well-controlled studies with higher strength of evidence and larger population sizes are urgently needed to assess this topic more comprehensively.

Diabetes

Some 382 million people worldwide, or 8.3% of adults, are estimated to have diabetes. About 80% live in low- and middle-income countries. If these trends continue, by 2035 some 592 million people, or one adult in 10, will suffer from diabetes (IDF Diabetes Atlas 2013).

A clear increase in the prevalence of diabetes in Germany has also been observed. Within 14 years, the percentage of diabetics as part of the overall population rose from 5.8 to 7.2% (RKI 2012) (Fig. 1). The risk of becoming diabetic increases considerably with age and is estimated at 15% for the over-60s and 20% for the over-70s (IDF Diabetes Atlas 2013). Measurement of HbA_{1c} values has proved itself a reliable approach to controlling diabetes. HbA_{1c}, also known as glycohemoglobin (GHb), is the red blood cell pigment (hemoglobin) to which glucose is attached. It provides information on blood sugar levels of the previous eight weeks (average age of erythrocytes).

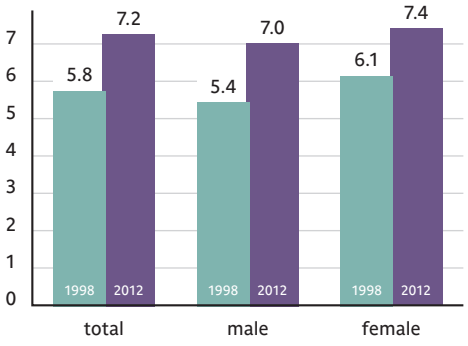

Fig. 1: Prevalence of diabetes in Germany 1998 and 2012 (modified after RKI 2012)

As a lifestyle disease that is increasing in all industrialized countries, a good number of studies on diabetes and implant treatment have been carried out and a higher frequency of early implant loss has been recorded for diabetics (Bornstein et al. 2009). However, while the proportion of implants placed in diabetics that are lost is relatively high, the proportion of implants lost overall is relatively low (Bornstein et al. 2009).

A systematic search of the literature that encompassed 18 studies up to 2009 showed that poorly controlled diabetes had a negative influence on osseointegration (Javed & Romanos 2009). A different overview of the literature found 17 studies in which the rate of implant failure for patients with diabetes was between 0 and 14.3%, which meant that a general contraindication for implants could not be assumed (Oates & Huynh-Ba 2012). It can be said, however, that the results for patients with well-controlled diabetes (blood sugar and HbA_{1c} values within the normal range) are comparable to those of healthy individuals (de Morais et al. 2009, Javed & Romanos 2009).

Ongoing consultation with the patient's doctor (diabetes specialist) is recommended (Schiegnitz & Kämmerer 2012, Marchand et al. 2012) as is a course of antibiotics (Amoxicillin or Clindamycin) to prevent the development of infection during the primary healing phase (Al-Nawas & Stein 2010).

No statistically supported conclusions can be drawn due to the heterogeneous nature of the patient groups and the different methods used to evaluate the data. In the majority of the studies, the diabetics displayed good blood glucose values during the implant treatment period. The largest study that investigates the early and late loss of implants was carried out by Moy and associates (Moy et al. 2005). The patient group was made up of 48 diabetics and 1,092 non-diabetics. The relative risk of losing an implant here was calculated as 2.75-fold higher for diabetics than non-diabetics. The highest evidence level (2b) is found in the study carried out by Accursi (Accursi 2000) in which no increased risk of implant loss in diabetics could be proven. Morris and associates (Morris et al. 2000) studied more than 650 patients with type 2 diabetes and were able to establish an implant loss rate that was only 1% higher than that of healthy patients. However, it does appear that an HbA_{1c} value of more than 8% has a negative impact on early, post-operative implant stability and the length of the entire healing period. (Oates et al. 2009) (Fig. 2).

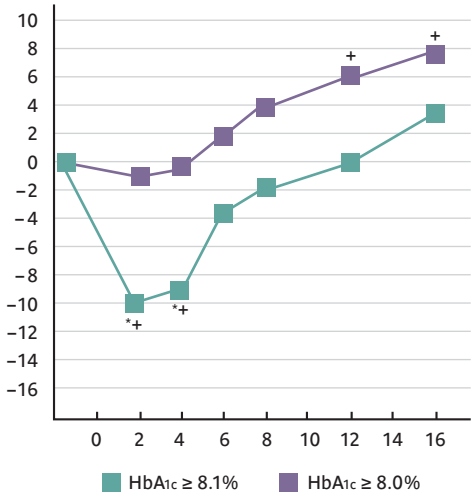

Fig. 2: Implant stability monitored over first four months after placement with high (>8.1%) (green) and low HbA_{1c} values (<8.0%) (blue) (modified after Oates et al. 2009)

Fig. 3: Advanced degeneration of the finger joints caused by rheumatoid arthritis

An animal study delivered similar results whereby untreated diabetes was shown to have a negative impact on early osseointegration of dental implants (Schlegel et al. 2013). However, other authors have pointed out that good chewing function is linked to good glycemic control (Oates & Huynh-Ba 2012). It is likely that the greatest improvements resulting from implant therapy will be felt by those patients whose chewing function has been severely compromised and who have difficulty in getting their diabetes under control (Oates & Huynh-Ba 2012).

Rheumatic and immunologic diseases

Only very few case studies are available that look at the link between implants and rheumatoid arthritis, the latter of which is found in around 1% of the population. Diagnosis is based largely on the clinical findings ("the hands represent the calling card of the rheumatoid sufferer" (Fig. 3). Many authors regard this disease as an absolute contraindication for dental implants (Cacaci et al. 2006). Others authors advise taking particular care in the case of connective tissue disease (e.g. rheumatoid nodules) (Krenamaier et al. 2011). For patients undergoing long-term glucocorticoid therapy of >10 mg/day or with recurrent stomatitis accompanying methotrexate therapy, complications in wound healing are particularly problematic (Fischer-Betz & Schneider 2012).

Crohn's disease tends to be regarded as a critical factor. In addition to possible lesions of the oral mucosa, use of steroids is accompanied by problems (Schiegnitz & Kämmerer 2012). In a large long-term study that observed almost 7,000 implants, an almost 8-fold rate of early implant loss was recorded (Alsaadi et al. 2007). However, in a prospective follow-up study by the same group, 11 out of 12 implants in patients with Crohn's disease osseointegrated successfully (Alsaadi et al. 2008). This means that the presence of Crohn's disease can only be regarded as a relative contraindication for implants.

In a follow-up study with 40 test subjects and 59 dental implants, a higher level of peri-implant bone loss was not recorded for HIV patients than for healthy subjects, regardless of the type of antiviral therapy level of viral load (Oliveira et al. 2011).

In general, however, strict anti-infective prophylactic measures should be taken when treating immune-compromised patients (Diz et al. 2012).

Mucosal diseases

Studies on implant loss associated with autoimmune diseases like scleroderma, ectodermal dysplasia and oral lichen planus are limited to case studies and therefore demonstrate level 4 evidence (Bornstein et al. 2009).

Scleroderma is a group of rare diseases that involve the hardening and tightening of the skin and connective tissues. Only seven case reports involving scleroderma with up to two patients could be found in the literature. From the present results, it appears that implants can successfully be placed and maintained (Oczakir et al. 2005).

Ectodermal dysplasias (ED) are a group of disorders in which two or more ectodermally derived structures – skin, sweat glands, hair, nails, teeth and mucus membranes – develop abnormally. Dental implants are often the treatment of choice in patients with ED and hypodontia. No randomized controlled or case-controlled studies were found (evidence level 4). The survival and success rates in the upper maxilla are

significantly lower than in the mandible (Bornstein et al 2009). In a survey the percentage for success of implant treatment ranged from 35.7–100% (Candel-Marti et al. 2011).

Implants placed in ED patients younger than 18 years have a higher risk of failure (Yap & Klineberg 2009).

Oral lichen planus (OLP) is a chronic inflammatory T-cell-mediated autoimmune disease that affects the mucus membrane of the oral cavity. Corticosteroids are the most commonly used group of drugs for the treatment of OLP (Lavanya et al. 2014). In a literature review based on eight studies between 1980 and 2011 with 41 OLP patients and 135 implants, after a mean follow-up of 56 months the survival rate of implants was 94.8%. The authors say that the benefits and negative effects of using implants in people with OLP require thorough evaluation in properly designed randomized, controlled studies (Petruzzi et al. 2012). The results of two small studies with 16 and 18 patients with OLP show that the implant survival rate in OLP patients does not differ from the success rate among the general population. In both studies, however, the proportion of patients with peri-implant mucositis and peri-implantitis was higher in the OLP groups than in the controls (Hernández et al. 2012; López-Jornet et al. 2014). The effect of glucocorticoids on implant healing remains unclear. In animal models, reduction in bone turnover and bone-to-implant contact was observed (Fu et al. 2012). In summary, OLP is not an absolute contraindication for implants, but they should be placed only if mucosal symptoms are in the remission phase (Petruzzi et al).

Combination of risk factors

While diseases like hypertension, diabetes or occlusive arterial disease do not represent a general contraindication for implant treatment, the combination of serious systemic diseases should be regarded as a further risk factor. However, a south Korean retrospective study involving 35 geriatric patients who were under regular medical observation and were being adequately treated with medication showed no significant link between peri-implant bone resorption and the presence or deficiency related to systemic disease after an average loading period of 33 months (Lee et al. 2010).

SUMMARY

With the changes in the demographic structure of our society, it is becoming increasingly necessary to treat patients suffering from various diseases. However the data available that evaluates the degree of risk for dental implant failure to patients who are already suffering from a disease(s) is still largely incomplete and confusing. There is a lack of studies made up of large groups of patients where the disease and medication criteria have been clearly defined and a similar lack of prospective longitudinal studies. This can only be achieved through multicenter studies as the necessary number of patients cannot otherwise be found. Given the complexity of this area in which patients are often comorbid with an accompanying polypharmacy, meaningful studies are likely to remain the exception for a while.

In general, when treating patients who are at risk clinicians must weigh up the prosthetic gain in function potentially available through implant treatment against possible complications. This process should be communicated to the patient in the form of informed consent following provision of all the relevant information that also includes alternatives to implant treatment (Grötz et al. 2013). Where the implant option is chosen, it is recommended that the surgical procedure and perioperative medication are managed so that any additional risks to the patient can be avoided as far as possible.

REFERENCES

Accursi, G. E. (2000) Treatment outcomes with osseointegrated Branemark implants in diabetic patients: a retrospective study [MSc Thesis], Toronto: Toronto University Press.

Agency for Health Care Policy and Research (1992) AHCPR Publication 92-0032: 100–107.

Al-Nawas, B. & Stein, K. (2010) Indikation einer präoperativen antibiotischen Prophylaxe bei Insertion enossaler Implantate – ein systematisches Review. *Zeitschrift für Zahnärztliche Implantologie* **26:** 22–33.

Alsaadi, G., Quirynen, M., Komarek, A. & van Steenberghe, D. (2007) Impact of local and systemic factors on the incidence of oral implant failures, up to abutment connection. *Journal of Clinical Periodontology* **34:** 610–617.

Alsaadi, G., Quirynen, M., Komarek, A. & van Steenberghe, D. (2008) Impact of local and systemic factors on the incidence of late oral implant loss. *Clinical Oral Implants Research* **19:** 670–676.

Ata-Ali, J., Ata-Ali, F., Peñarrocha-Oltra, D. & Galindo-Moreno, P. (2014) What is the impact of bisphosphonate therapy upon dental implant survival? A systematic review and meta-analysis. *Clinical Oral Implants Research* [doi: 10.1111/clr.12526. Epub ahead of print].

Behrens, E., Kolenda, U., Terheyden, H. & Wiltfang, J. (2004) Long term results with the ITI-system. *Implantologie* **2:** 133–147.

Besimo, E. (2007) Polymorbidität und Polypharmakotherapie im Alter – Eine interdisziplinäre Herausforderung. *ZWR – Das Deutsche Zahnärzteblatt* **116:** 286–291.

Beske F., Katalinic, A., Peters, E. & Pritzkuleit, R. (2009) Morbiditätsprognose 2050. Ausgewählte Krankheiten für Deutschland, Brandenburg und Schleswig-Holstein. Bd. 114. Kiel: Schriftenreihe/Fritz Beske Institut für Gesundheits-System-Forschung.

Bornstein, M. M., Cionca, N. & Mombelli, A. (2009) Systemic conditions and treatments as risks for implant therapy. *International Journal of Maxillofacial Implants* **24 Suppl:** 28–38.

Buser, D., Janner, S. F., Wittneben, J. G., Bragger, U., Ramseier, C. A. & Salvi, G. E. (2012) 10-year survival and success rates of 511 titanium implants with a sandblasted and acid-etched surface: a retrospective study in 303 partially edentulous patients. *Clinical Implant Dentistry and Related Research* **14:** 839–851.

Cacaci, C., Neugebauer, J., Schlegel, A. & Seidel, F. (2006) Checklisten der Zahnmedizin: Orale Implantologie, Stuttgart – New York: Thieme.

Candel-Marti, M.E., Ata-Ali, J., Peñarrocha-Oltra, D., Peñarrocha-Diago, M. & Bagán, J.V. (2011) Dental implants in patients with oral mucosal alterations: An update. *Medicina Oral Patologia Oral y Cirugia Bucal* **16:** e787–793.

Chen, H., Liu, N., Xu, X., Qu, X. & Lu, E. (2013) Smoking, radiotherapy, diabetes and osteoporosis as risk factors for dental implant failure: a meta-analysis. *PLOS ONE* **8:** e71955.

Chuang, S. K., Wie, L. J., Douglass, C. W. & Dodson, T. B. (2002) Risk factors for dental implant failure: a strategy for the analysis of clustered failure-time observations. *Journal of Dental Research* **81:** 572–577.

De Morais, J. A., Trindade-Suedam, I. K., Pepato, M. T., Marcantonio E. Jr., Wenzel, A. & Scaf, G. (2009) Effect of diabetes mellitus and insulin therapy on bone density around osseointegrated dental implants: a digital subtraction radiography study in rats. *Clinical Oral Implants Research* **20:** 796–801.

Diz, P., Scully, C. & Sanz, M. J. (2013) Dental implants in the medically compromised patient. *Journal of Dentistry* **41:** 195–206.

Dvorak, G., Arnhart, C., Heuberer, S., Huber C. D., Watzek, G. & Gruber, R. (2011) Peri-implantitis and late implant failures in postmenopausal women: a cross sectional study. *Journal of Clinical Periodontology* **38:** 950–95

Famili, P., Quigley, S. &, Mosher, T. (2011) Survival of dental implants among post-menopausal female dental school patients taking oral bisphosphonates: a retrospective study. *Compendium of Continuing Education in Dentistry* **32:** e106–109.

Fehrenbach, M. & Weiner, J. (2009) Saunders Review of Dental Hygiene. 2nd Ed. Oxford: Elsevier.

Feijoo, J. F., Limineres, J., Diniz, M., Del Llano, A., Seoane, J. & Diz, P. (2012) Osseointegrated dental implants in patients with intellectual disability: a pilot study. *Disability and Rehabilitation* **34:** 2025–2030.

Fischer-Betz, R. & Schneider, M. (2012) Rheumatologie. In: Wagner, W. & Fischereder, M. (eds.) Innere Medizin für Zahnmediziner. 2. Aufl. Stuttgart – New York: Thieme.

Fu, J.H., Bashutski, J.D., Al-Hezaimi, K. & Wang, H. L. (2012) Statins, glucocorticoids, and nonsteroidal anti-inflammatory drugs: their influence on implant healing. *Implant Dentistry* **21:** 362–367.

Grötz, K. A., Al-Nawas, B. & Terheyden, H. (2013) Implantate und Bisphosphonat-Therapie. *Implantologie* **21:** 53–59.

Hadji, P., Klein, S., Gothe, H., Häussler, B., Kless, T., Schmidt, T., Steinle, T., Verheyen, F. & Linder, R. (2013) The epidemiology of osteoporosis – Bone Evaluation Study (BEST): an analysis of routine health insurance data. *Deutsches Ärzteblatt International* **110:** 52–57.

Halling, F. (2013) Zahnärztlich relevante Neben- und Wechselwirkungen der meistverordneten Arzneimittel in Deutschland. *Deutsche Zahnärztliche Zeitschrift* **68:** 669–676.

Hernandez, G., Lopez-Pintor, R. M., Arriba, L., Torres, J. & de Vincente, J. C. (2012) Implant treatment in patients with oral lichen planus: a prospective-controlled study. *Clinical Oral Implants Research* **23:** 728–732.

Holahan, C. M., Wiens, J. L., Weaver, A., Assad, D. & Koka, S. (2011) Relationship between systemic bone mineral density and local bone quality as effectors of dental implant survival. *Clinical Implant Dentistry and Related Research* **13:** 29–33.

International Diabetes Federation (2013) Diabetes Atlas. 6th edition. (http://www.idf.org/sites/default/files/EN_6E_Atlas_Full_0.pdf)

Javed, F. & Romanos, G. E. (2009) Impact of diabetes mellitus and glycemic control on the osseointegration of dental implants: a systematic literature review. *Journal of Periodontology* **80:** 1719–1730.

Khadivi, V., Anderson, J. & Zarb, G. A. (1999) Cardiovascular disease and treatment outcomes with osseointegration surgery. *The Journal of Prosthetic Dentistry* **81:** 533–536.

Kohler, M., Ziese, T. (2004) Telefonischer Gesundheitssurvey des Robert-Koch-Institutes zu chronischen Krankheiten und ihren Bedingungen. Berlin: Robert Koch-Institut.

Krennmaier G., Seemann, R. & Piehslinger E. (2010) Dental implants in patients with rheumatoid arthritis: clinical outcome and peri-implant findings. *Journal of Clinical Periodontology* **37:** 928–936.

Lavanya, N., Jayanthi, P., Umadevi, K. R. & Ranganathan, K. (2014) Oral lichen planus: An update on pathogenesis and treatment. *Quintessence International* **45:** 599–603.

Lee, H. J., Kim, Y. K., Park, J. K., Kim, S. G., Kim, M. J. & Yun, P. Y. (2010) Short-term clinical retrospective study in geriatric patients older than 70 years. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* **110:** 442–446.

Lo, J. C., O'Ryan, F. S., Gordon, N. P., Yang, J., Hui, R. L., Martin, D., Hutchinson, M., Lathon, P. V., Sanchez, G., Silver, P., Chandra, M., McCloskey, C. A., Staffa, J. A., Willy, M., Selby, J. V. & Go, A. S. & Predicting Risk of Osteonecrosis of the Jaw with Oral Bisphosphonate Exposure (PROBE) Investigators (2010) Prevalence of osteonecrosis of the jaw in patients with oral bisphosphonate exposure. *Journal of Oral and Maxillofacial Surgery* **68:** 24–253.

López-Jornet, P., Camacho-Alonso, F. & Sánchez-Siles, M. (2014) Dental implants in patients with oral lichen planus: a cross-sectional study. *Clinical Implant Dentistry and Related Research* **16:** 107–115.

Marchand, F., Raskin, A., Dionnes-Hornes, A., Barry, T., Dubois, N., Valéro, R. & Vialettes, B. (2012) Dental implants and diabetes: conditions for success. *Diabetes & Metabolism* **38:** 14–19.

McDermott, N. E., Chung, S. K., Woo, V. V. & Dodson, T. B. (2003): Complications of dental implants: identification, frequency, and associated risk factors. *International Journal of Oral & Maxillofacial Implants* **18:** 848–855.

Merk, M. (2007) Retrospektive Untersuchung zum Implantaterfolg bei Risikopatienten unter Berücksichtigung von patienten-, implantat- und restaurationsabhängigen Einflussfaktoren. Medizinische Dissertation, Gießen.

Mombelli, A., Müller, N. & Cionca, N. (2012) The epidemiology of peri-implantitis. *Clinical Oral Implants Research* **23 Suppl:** 67–76.

Morris, H.F., Ochi, S. & Winkler, S. (2000) Implant survival in patients with type 2 diabetes: Placement to 36 months. *Annals of Periodontology* **5:** 157–165.

Moy, P. K., Medina D., Shetty, V. & Aghaloo. T. L. (2005) Dental implant failure rates and associated risk factors. *International Journal of Oral and Maxillofacial Implants* **20:** 569–577.

Nkenke, E., Vairaktaris, E. & Neukam, F. W. (2007) Systemerkrankungen und andere Einflussfaktoren auf den Erfolg implantologischer Versorgungen. In: Neukam, F. W., Wichmann, M. & Wiltfang, J. (eds.) Zahnärztliche Implantologie unter schwierigen Umständen. Stuttgart – New York: Thieme.

Oates, T. W., Dowell, S., Robinson, M. & McMahan, C. A. (2009) Glycemic control and implant stabilization in type 2 diabetes mellitus. *Journal of Dental Research* **88:** 367–371.

Oates, T. W. & Huynh-Ba, G. (2012) Diabetes Effects on Dental Implant Survival. *Forum Implantologicum* **8:** 78–87.

Oczakir, C., Balmer, S. & Mericske-Stern, R. (2005) Implant-prosthodontic treatment for special care patients: a case series study. *The International Journal of Prosthodontics* **18:** 383–389.

Oliveira, M. A., Gallotini, M., Pallos, D., Maluf, P. S., Jablonka, F. & Ortega, J. L. (2011) The success of endosseous implants in human immunodeficiency virus-positive patients receiving antiretroviral therapy: a pilot study. *The Journal of the American Dental Association* **142:** 1010–1016.

Packer, M., Nikitin, V., Coward, T., Davis, D. M. & Fiske, J. (2009) The potential benefits of dental implants on the oral health quality of life of people with Parkinson's disease. *Gerodontology* **26:** 11–18.

Paquette, D. W., Brodala, N. & Williams, R. C. (2006) Risk factors for endosseous dental implant failure. *Dental Clinics of North America* **50:** 361–374.

Payne, A. G., Lownie, J. F. & Van der Linden, W. F. (1997) Implant-supported prostheses in patients with Sjögren's syndrome: a clinical report on three patients. *International Journal of Oral and Maxillofacial Implants* **12:** 679–685.

Petruzzi, M., De Benedittis, M., Cortelazzi, R., Milillo, L., Lucchese, A., Serpico, R & Grassi, F. R. (2012) Implant rehabilitation in patients with oral lichen planus: an overview. *Clinical Oral Investigations* **16:** 1347–1352.

Radfar, I. & Suresh, L. (2007) Medical profile of a dental school patient population. *Journal of Dental Education* **71:** 682–686.

Reginster, J. Y. & Burlet, N. (2006) Osteoporosis: a still increasing prevalence. *Bone* **38 (Suppl 1):** 4–9.

Renouard, F. & Rangert, B. (2006) Risikofaktoren in der Implantologie, Berlin: Quintessenz.

Renvert, S., Aghazadeh, A., Hallström, H. & Persson, G. R. (2014) Factors related to peri-implantitis – a prospective study. *Clinical Oral Implants Research* **25:** 522–529.

Robert-Koch-Institut (2012) Daten und Fakten: Ergebnisse der Studie – Gesundheit in Deutschland aktuell, Berlin.

Ruskin, J. D. (2007) Medical risk factors – Myth and reality. *Forum Implantologicum* **3:** 114–119.

Schiegnitz, E. & Kämmerer P. W. (2012) Systemische Erkrankungen als Risiko für die Implantattherapie – Eine Übersicht. *Quintessenz* **63:** 191–197.

Schlegel, K. A., Prechtl, C., Möst, T., Seidl, C., Lutz, R. & von Wilmowsky, C. (2013) Osseointegration of SLActive implants in diabetic pigs. *Clinical Oral Implants Research* **24:** 128–134.

Slagter, K. W., Raghoebar, G. M. & Vissink, A. (2008) Osteoporosis and edentulous jaws. *The International Journal of Prosthodontics* **21:** 19–26.

Smeets, E. C., de Jong, K. J. & Abraham-Inpijn, L. (1998) Detecting the medically compromised patient in dentistry by means of the medical-related history. A survey of 29,424 patients in The Netherlands. *Preventive Medicine* **27:** 116–120.

Van der Akker, M., Buntinx, F., Metsemakers, J. F., Roos, S. & Knottnerus, J. A. (1998) Multimorbidity in general practice: prevalence, incidence, and determinants of co-occuring chronic and recurrent diseases. *Journal of Clinical Epidemiology* **51:** 367–375.

World Health Organisation (1994) Assessment of fracture risk and its implication to screening for postmenopausal osteoporosis: *World Health Organization Technical Report Series* **843,** Geneva.

World Health Organization (2003) Prevention and management of osteoporosis. *World Health Organization Technical Report Series* **921:** 1–164.

Yap, A.K. & Klineberg, I. (2009) Dental implants in patients with ectodermal dysplasia and tooth agenesis: a critical review of the literature. *International Journal of Prosthodontics* **22:** 268–276.

Zavras, A. I. (2011) The impact of bisphosphonates on oral health: lessons from the past and opportunities for the future. *Annals of the New York Academy of Sciences* **1218:** 55–61.