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Outcomes of Dental Implants in Osteoporotic Patients. A Literature Review

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Abstract

Purpose: This article reviews available data on the outcome of dental implants in osteoporotic patients.
Materials and Methods: A search was performed in PubMed and completed in July 2007. The keywords "dental AND implants AND osteoporosis," "dental AND implants AND age," "dental AND implants AND gender," and "dental AND implants AND bone AND quality," with no limitations for language or year of publication, resulted in 82, 598, 94, and 541 articles, respectively. After abstract scanning (in case of doubt the article was read), 39 nonreview articles studying dental implant outcomes in osteoporotic/osteopenic subjects remained for our review. The bibliographies of the 39 articles were also inspected, but no additional studies were identified.
Results: Thirteen of 16 animal studies found lower osseointegration rates in osteoporotic/osteopenic bone than in normal bone. Six in nine clinical reports mention success. Eight of 12 studies in humans support the applicability of dental implants in osteoporotic patients.
Conclusions: There are no data to contraindicate the use of dental implants in osteoporotic patients; however, a proper adjustment of the surgical technique and a longer healing period may be considered in order to achieve osseointegration. Data on the use of biphosphonates in osteoporotic patients and implant outcomes are very limited, and no conclusions can be drawn. In addition, large prospective studies investigating the long-term success of dental implants in osteoporotic individuals are required.

Dental implants constitute a well-documented treatment modality.[1-3] Osteoporosis is the most common human metabolic bone disease.[4] The influence of this disease on the jawbone is still a matter of controversy. The outcome of dental implants in patients with osteoporosis in the jaws or in other skeletal sites will be the subject of this article.

Definition of osteoporosis

Osteoporosis has been defined as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with consequent increase in bone fragility and susceptibility to fracture.[5]

According to the World Health Organization (WHO), subjects with a T-score value 2.5 standard deviations (SDs) or more below the mean bone mineral density (BMD) value of the young (20 to 29 years old) sex-matched reference population at the total hip, femoral neck, or lumbar spine are classed as osteoporotic.[6] Osteoporosis is divided into osteoporosis with pathologic fracture, without pathologic fracture, and osteoporosis caused by other diseases (multiple myelomatosis, endocrine disorders, etc.). When a fragility fracture is present, the condition is defined as "established osteoporosis."[7]

Subjects with a T-score value 1 to 2.5 SDs below the mean BMD value of the young sex-matched reference population in the prementioned skeletal sites are classed as osteopenic.[6]

Bone mineral content (BMC) is the amount of mineral in the specific site scanned, and when divided by the area measured, it can be used to derive a value for BMD[8] (mg/cm^2). When quantitative computed tomography (QCT) is used, BMD is not an areal but a volumetric density measurement (mg/cm^3).[9]

Epidemiology of osteoporosis

Osteoporosis occurs in about one-third of the Western female population above the age of 65 years.[10] Currently, it is

estimated that over 200 million people worldwide suffer from this disease.[11] Because the distribution of values for the BMD in the young healthy population is Gaussian, the incidence of osteoporosis increases exponentially after the age of 50 years.[12]

According to others, at some point in their lives, 40% of women[13-15] or 50% of women over the age of 50[16] and up to 29% of men[17] may sustain an osteoporotic fracture.

A higher prevalence of fragility fractures has been described in white populations,[18] especially in non-Hispanic Caucasians;[19] lower rates have been found among black populations.[18] In Europe, the Scandinavian countries have the highest prevalence of fragility fractures.[20]

Pathophysiology of osteoporosis

Sex-hormone deficiency seems to be an important causal factor of primary osteoporosis in both men and women. Estrogen deficiency in women causes bone loss both through the loss of the direct action of estrogen on bone cells (that restrain bone turnover) and through the loss of the action of estrogen on the intestine and kidney (that maintain extraskeletal calcium fluxes).[21] It leads to increased numbers of bone multicellular units and to uncoupling of bone formation and bone resorption.[22]

Men exhibit only a slow phase of bone loss during which increased levels of sex-hormone-binding globulin (SHBG) bind sex steroids in an inactive complex.[23]

Cancellous bone is much more richly vascularized by osseous vascular complexes that pass between the less dense trabeculae. This arrangement produces a much higher surface-to-volume ratio to bone extracellular fluids. Therefore, cancellous bone responds more quickly to metabolic alterations and for this reason, skeletal sites such as vertebral bodies, the forearm, and hip are more susceptible to processes that increase bone resorption, such as osteoporosis.[24] Similarly, it can be expected that any osteoporosis influence should be greater in the maxilla rather than in the mandible, because of the presence of a higher percentage of trabecular bone in the former.[25]

Osteoporosis risk factors[4,8,26-29] are presented in Table 1.

Table 1 Osteoporosis risk factors

- Female sex
- Age
- Asian or white ethnic origin
- Genetic disorders
- 1st-degree relative with low trauma fracture
- Thin habitus
- Deficiency states:
  - Calcium
  - Magnesium
  - Vitamin D
- Diseases:
  - Amyloidosis
  - Chronic metabolic acidosis
  - Chronic obstructive pulmonary disease
  - Cystic fibrosis
  - Depression
  - Emphysema
  - End-stage renal disease
  - Endocrine disorders:
    - Acromegaly
    - Adisson's disease
    - Cushing's syndrome
    - Diabetes mellitus
    - Hyperparathyroidism
    - Thyrotoxicosis
  - Hypogonodal states:
    - Androgen insensitivity
    - Anorexia nervosa/bulimia
    - Athletic amenorrhea
    - Hyperprolactinaimia
    - Panhypopituitarism
    - Premature menopause
  - Gastrointestinal diseases
  - Hematological diseases
  - Idiopathic hypercalciuria
  - Idiopathic scoliosis
  - Multiple sclerosis
  - Neuromuscular disorders
  - Post-transplant bone disease
  - Rheumatologic diseases
  - Sarcoidosis
  - Stroke
- Drugs:
  - Anticoagulants
  - Anticonvulsants
  - Antiepileptics
  - Cyclosporines
  - Cytotoxic drugs
  - Excessive thyroxine dose
  - Glucocorticoids
  - Gonadotropin-releasing hormone agonists
  - Lithium
  - Tacrolimus
- Immobilization
- Cigarette smoking
- Alcoholism
- Parenteral nutrition

Systemic complications of osteoporosis

There is no evidence that bone loss itself causes any symptoms. Progressive bone loss has therefore been called "the silent thief."[16] Fractures among the elderly may occur after a moderate trauma or even spontaneously. The most common fractures associated with osteoporosis occur at the hip, spine, and wrist.[16,30]

Dental implants and osteoporosis

Osteoporosis in other skeletal sites seems to be associated with a decrease of BMD in the jaw. The authors agree that the correlation is not strong enough to be used for proper predictions in the jaw.[31] In addition, a majority of relevant studies suggest that postmenopausal osteoporosis may be important for the progression of bone loss in periodontitis.[22] This may reduce bone quantity at implantation sites. Finally, a correlation of periodontitis with peri-implantitis has been suggested,[32] and therefore a question arises concerning peri-implantitis in osteoporotic patients.

Materials and methods

A search was performed in PubMed and completed in July 2007. The main keywords of the search were "dental AND implants AND osteoporosis." The search yielded 82 articles. No limitations were set for language or year of publication. The inclusion criteria were nonreview articles dealing with the possible relation between osteoporosis and dental implants. After scanning abstracts, 38 articles, including 9 clinical reports and 18 animal and 11 human studies, remained for our review.

To identify additional studies that were not returned in the first search even though they study the possible relation between dental implants outcome and osteoporosis, three more keywords were used:

(1) "dental AND implants AND age"→ 598 articles
(2) "dental AND implants AND gender"→ 94 articles
(3) "dental AND implants AND bone AND quality"→ 541 articles.

Inclusion and exclusion criteria remained the same, and the studies' abstracts were scanned (in cases of doubt the article was read), but only one that had not been included in

our first search directly referred to the osteoporosis condition. In other words, the use of the last three keywords added one study directly addressing the question of osteoporosis effect on dental implants outcome. Finally, 39 articles were included in the results of the present review; however, the rest of the second group studies were not totally excluded from our article. We reconsidered the second group articles, excluding this time not only reviews but also clinical reports and animal studies. We are focusing now on the final conclusions of the already sufficiently studied age, gender, and bone-quality effect on dental implants outcome. The reason is that the strong relation of the above three parameters with osteoporosis offers important indirect information suiting well to our discussion.

The bibliographies of the 39 reviewed articles were also inspected, but no additional studies were identified.

Results

Thirteen of 16 animal studies found lower osseointegration rates in osteopenic/osteoporotic bone than in normal bone.[33-45] It is suggested that there is a biphasic effect of female gonodal hormone deficiency that may temporarily interfere in the early implant-tissue integration process, and which may be associated with a failure to upregulate a select set of bone extracellular matrix genes.[43] It is also suggested that osseointegration in osteoporotic animals is 50% slower than that of normal experiment animals.[38,43] Only three[46-48] out of 16 animal studies found no difference (Table 2).

Three animal studies (two of them are not included in Table 2, because they did not compare healthy to osteoporotic animals but only treated to untreated osteoporotic animals) addressed the question of whether therapies used in osteoporotic animals affect osseointegration. Two of them suggested that estrogen replacement therapy may promote bone healing around titanium implants in osteoporotic bone.[40,49] The third study supported that local administration of growth hormone at the point of surgery could enhance osteoid synthesis and mineralization around titanium sheets in an osteoporotic animal.[50]

Six in nine clinical reports mention success,[51-56] even after immediate loading[54] of dental implants in osteoporotic patients. Two of the three[57-59] clinical reports that mention failure of dental implants either just hypothesize the presence of osteoporosis[58] or refer to mandible fractures.[59]

Twelve studies in humans directly address the question of systemic osteoporosis effect on dental implants outcome[60-71] (Table 3). Eight of the studies[60-67] reveal a rather optimistic opinion concerning the applicability of dental implants in osteoporotic patients. Hormone replacement therapy (HRT) may not be related to significantly increased implant success,[62,68] although previously mentioned animal studies implied the opposite. It is suggested that simple visual assessment of local bone quality has a moderately sized relationship to implant failure.[61] Only four of 12 studies relate osteoporosis to increased failure rates of dental implants,[68-71] especially in the maxilla.[68] But one of these three studies found statistically insignificant results.[68]

Discussion

The following parameters have to be discussed in our attempt to sufficiently analyze the present subject:

(1) WHO definition of osteoporosis,
(2) animal studies deficiencies,
(3) human studies deficiencies,
(4) indirect information from studies on dental implants and age, gender, and jawbone quality, and
(5) implication of biphosphonate therapy in dental implants outcomes.

WHO definition of osteoporosis

The WHO criteria are aimed at providing a quantitative definition that would separate individuals having the disease, even if no osteoporotic fracture had occurred yet, from those at risk of becoming osteoporotic, and those who are still normal. Since BMD is continuously distributed in the population, and the risk of fracture is also continuous, in the absence of fracture, there is no absolute criterion that can be made to delineate an individual with the disease from one without. For this reason, there is an overlap between BMD in populations with and without fracture.[72] The estimation of fracture risk by BMD measurements is similar to the assessment of the risk of stroke by blood pressure readings. Despite the decision of a cutoff threshold value that separates individuals with recognized high risk for osteoporotic fracture or stroke from the rest, there is no threshold of BMD/blood pressure that discriminates absolutely between those who will or will not have a clinical event.[8] BMD is one of the main, but not the only, factor determining the risk of fracture.[72] It has been shown that the loss of connectivity within the network of trabecular bone is independent from BMD risk factor for fractures.[73] Additionally, bone geometry features such as bone size, the distribution of bone mass around its bending axis (moments of inertia), and some derivative functions, such as the hip axis length, affect bone strength and fracture risk.[74]

BMD measures at various sites have given discordant results.[72] So, individuals may be deemed osteoporotic at one specific site and not at another. The WHO criteria for the diagnosis of osteoporosis were defined for DXA (dual X-ray absorptiometry) of the forearm, spine, and hip, and selected at a level that would identify as osteoporotic 30% of the population of postmenopausal women. The definition did not originally intend to be applied to other patient groups, or to BMD measurements made by different methods and at other skeletal sites.[74,75] This is important when considering the impact of systemic osteoporosis in the jawbone.

The normative data against which BMD comparisons are most often made have been determined for Caucasian men and women, and do not necessarily apply to other ethnic groups.

Although BMD is clearly related to body weight, routine clinical bone mass assessments are not weight adjusted.[74]

Animal studies deficiencies

It must be underlined that in 14 of the 16 prementioned animal studies implants were not placed in the jaws.[33-45,48] They were inserted in the tibia[33-39,42-45,48] (11 studies) or the

Table 2 Animal studies reviewed

Study	Animal model	Nr. of animals	Postimplantation period	OP-like conditions	Results	Type of examination
Keller et al, 2004[42]	Rabbit	4 groups of 10	4 weeks	By daily intramuscular injections of glucocorticoids	Altered and compromised ECM expression in all animals with OP-like conditions, reduced bone-implant interface when OP-like conditions were present prior to the establishment of osseointegration, no significant differences in pull-out strength	Histologic, mechanical property testing
Cho et al, 2004[36]	Rats	5 groups of 7	12 weeks	OVE	Osseointegration achieved, surrounding bone stabilized	Histologic and histomorphometric analysis
Okamura et al, 2004[48]	Rats	4 groups of 5	1 month	OVE	High turnover situation is more favorable for implantation than low-turnover one	Biochemical, histological, and histometrical analysis
Narai and Nagahata, 2003[40]	Rats	25	1 month	OVE	Reduced removal torque in OP animals compared to healthy or alendronate-administered OP animals	Removal torque, histologic, histometric evaluation
Duarte et al, 2003[33]	Rats	15 OVE, 15 sham-OVE	60 days	OVE	No significant differences in cortical bone but lower bone-implant contact in cancellous regions of OP bone	Histometric analysis, biochemical serum analysis
Fini et al, 2002[35]	Rats, sheep	9 OVE and 9 sham-OVE rats, 3 OVE and 3 sham-OVE sheep	Rats: 8 weeks Sheep: 12 weeks	OVE	Delay of peri-implant bone formation and maturation in OP animals	Histomorphometric examination, bone-implant interface microhardness
Ozawa et al, 2002[43]	Rats	28 OVE, 28 sham surgery	2 and 4 weeks	OVE	Delay of osseointegration in OVE rats, differences diminished at 4 weeks postimplantation	Histomorphometric analysis, biomechanical push-in test, RT-PCR
Jung et al, 2001[39]	Rabbit	14 OVE, 13 sham surgery	12 weeks	OVE	Lower bone volume but no statistically significant lower bone-to-metal contact in OVE versus sham-operated rabbits	Histomorphometric analysis, removal torque, osteoblast culturing
Pan et al, 2000[41]	Rats	18 OVE and 18 sham-OVE 168 days postimplantation	28, 84, 168 days post-OVE or post-sham-OVE	OVE	Significant decrease in the bone volume around the implant and implant-bone contact in the cancellous bone area in OVE compared to sham-operated rats	Histologic and histomorphometric measurements
Lugero et al, 2000[37]	Rabbits	8 controls and 12 OP	8 weeks	OVE	Less bone formation in OP cases, improved bone formation with screw-type implants in cases and controls	Histomorphometry
Yamazaki et al, 1999[45]	Rats	30 test and 30 controls	7 to 56 days	OVE	Lower rate of bone contact and relative bone mass around the implant in cancellous bone of OVE rats	Histologic and histomorphometric examination
Fujimoto et al, 1998[47]	Rabbit	6 steroid-treated and 6 controls	3 months	Prednizolone treatment	Steroid administration effects less osseointegration in the mandibles than in the skeletal bone	Removal torque of implants in the mandible and the tibia and microdensitometry measurements in the left femur

Continued

Table 2 Continued

Study	Animal model	Nr. of animals	Postimplantation period	OP-like conditions	Results	Type of examination
Nasu et al, 1998[46]	Rats	2 groups of 6 test animals and 6 controls	7 to 42 days	Ca-deficient diet	No differences in osseointegration between cases and controls	Microradiographs and autoradiographs
Mori et al, 1997[38]	Rabbit	2 groups of 12 animals each and 12 controls	2, 4, 8, or 12 weeks	OVE or OVE + low-Ca diet	Osseointegration is achieved in OP animals, but a longer healing period is needed	Histologic and microradiographic examination of the bone-implant interface in the tibia
Martin et al, 1988[44]	Beagle dogs	5 OVE, 5 sham-OVE	2 months	OVE	OVE caused no difference in the amount of ingrowth of bone, significant increase in the amount of fibrous connective tissue	Mechanical tests, histological study
Hayashi et al, 1994[34]	Rats	3 models	24 weeks	OVE, OVE + neurectomy	Significant decrease of affinity index bone-implant in OP-like cases	Histological study

OVE = ovariectomy/ovariectomised; ECM = extra cellular matrix; HRT = hormone replacement therapy; OP = osteoporosis/osteoporotic; BMC% = BMD percentage of age-matched (describes the mean value matched for age and sex and is normally 100%); B = biphosphonates; PTV = Periotest values.

femur[35,40,43] (three studies). Only two studies[46,47] tested dental implants in the mandible of experiment animals and, interestingly enough, they both found no significant difference of osseointegration rate between osteoporotic/osteopenic animals and controls. Particularly, Fujimoto et al[47] found that rabbits' systemic osteoporosis-like condition had less effect on osseointegration of titanium implants in the mandible than in skeletal bone; however, this study refers to steroid-induced osteoporosis, and its pathogenetic mechanisms are different from those of postmenopausal osteoporosis.[22]

Besides the already mentioned implantation site, there are several other important factors involved in the final results of these studies:

(a) *Animal model:* The rat was used in $10^{33\text{-}36,40,41,43,45,46,48}$ of 16 animal studies; however, it may not provide the best model for the analogous condition in humans because of the failure to achieve true skeletal maturity and the normal inhibition of intracortical remodeling.[76] On the contrary, the rabbit, used in five studies,[37-39,42,47] achieves skeletal maturity shortly after reaching sexual development at approximately six months and shows significant intracortical remodeling.[77] Regarding dogs, used in one study,[44] data are controversial. Some studies,[78] but not all,[79-83] have shown insignificant bone loss in dogs after cessation of ovarian function. Last, the sheep, used in one study,[35] is considered a good animal model, although seasonal fluctuations of bone mass and biochemical markers must be addressed as a potential variable when studying osteoporosis.[76,84]

(b) *Method used for the creation of osteoporosis-like condition*: In $13^{33\text{-}41,43\text{-}45,48}$ of the 16 animal studies, ovariectomy is used for the creation of osteoporosis-like conditions; however, according to Mori et al, ovariectomy did not result in adequate reduction of BMD in rabbits unless it was combined with a low-Ca diet.[38] Two studies were based on corticosteroid-induced osteoporosis[42,47] and one in calcium-deficient diet.[46] In addition, there is a variety of experiment animal ages, diets, and intervening time between ovariectomy and implant surgery.

(c) *Evaluation of the obtained level of osteopenia/osteoporosis*: As already mentioned, a variety of protocols have been used for the induction of osteoporosis. In addition, bone changes in ovariectomized rats are considered as osteopenia rather than osteoporosis.[84] Despite these two facts, $10^{33,35,36,39,41\text{-}43,45\text{-}47}$ of the 16 studies do not mention any assessment of BMD prior to implantation so that the level of the provoked osteopenia/osteoporosis could be clarified.

(d) *Osseointegration assessment criteria*: There are a variety of measurements used for the assessment of osseointegration. Some of them (mechanical test values) evaluate osseointegration indirectly and may be affected by other parameters such as implant fixation mainly in cortical bone,[40] implant surface, length, width, composition, shape, and healing period.[47] Keller et al found a statistically significant decrease in implant-bone contact in osteoporotic rabbits compared to controls, although interfacial strength was not affected.[42]

(e) *Postimplantation observation period:* Postimplantation observation period varies from 7 days to 168 days in the rat model, from 2 weeks to 3 months in the rabbit model, 12 weeks for the sheep model, and 2 months for beagle dogs. The relatively short observation period is one of the shortcomings of these studies. Additionally, dental implants in clinical practice are differently loaded from animal models. Thus, short-term animal studies offer no information concerning the long-term response of the osteoporotic bone to the presence of functionally loaded dental implants.

Table 3 Human studies reviewed

Study	Patients	OP patients	Sites with diagnosed OP	BMD measurement	Implant receiving jaw	Nr. of implants in the OP group	Nr. of implants in the control group	Bone quality assessment	Experimental period	Osseointegration assessment	Results
Alsaadi et al, 2007[71]	1212 females, 792 males				Mandible, Maxilla		6946 implants totally in OP + non-OP		Up to abutment connection	Intraoral radiograpghy, PTV ≥5, subjective signs of pain or infection that required implant removal	Osteoporosis significantly related to early implant failures
Amorim et al, 2006[64]	39 women/48 to 70 years old	19	Lumbar spine, femoral neck	DXA	Mandible	39	43	Panoramic X-rays, histomorphometric, bone biopsy	9 months	Clinical and X-ray examination	No association
Jeffcoat, 2006[63]	25 postmenopausal women receiving B. + 25 postmenopausal women without B.	50				102	108		3 years	Clinical and X-ray examination	Success: 99.2% without, 100% with oral biphosphonates
Smolka et al, 2006[67]	10 females + 5 males, 18 to 68 years old, mean age 52 years, patients, only 5 in 1-year follow-up	9 females	Generalized osteoporosis	Bone densitometry	8 Mandibles, 8 maxillas			CT scanning	Maximum 1 year	CT scanning for grafts bone density measurements	Generalized osteoporosis did not increase the resorption rate of calvarial transplants
Moy et al, 2005[70]	1140 patients 12 to 94 years, 59.4% females, 161 on PMHRT, 304 on no PMHRT, median age = 58 years				Mandible, maxilla				Retrospective cohort study, 1982–2003	Implant survival	Lower success rate for postmenopausal women on HRT
van Steenberghe et al, 2002[65]	399, 15 to 80, mean age 50, SD ± 14					2		Clinical and panoramic examination, CT scanning when needed	Up to the abutment connection		No increased percentage of early failures in OP

Continued.

Table 3 Continued

Study	Patients	OP patients	Sites with diagnosed OP	BMD measurement	Implant receiving jaw	Nr. of implants in the OP group	Nr. of implants in the control group	Bone quality assessment	Experimental period	Osseointe-gration assessment	Results
Friberg et al, 2001[60]	11 females + 2 males, 55 to 79 years, mean age 68 years	13	Lumbar spine, hip	DXA	Mandible, maxilla	70	No control group	Clinical and X-rays examination	6 months to 11 years, mean 3.3 years	Clinical and X-ray examination	Maxilla: 97%, mandible: 97.3%success
von Wowern et al, 2001[66]	22 patients, 18 postmenopausal women, 54 to 78 years, mean age 65 years	7 women with OP in the mandible,8 with OP in the forearm	Forearm, mandible	Dual-photon scanner for BMC in the jaws	Mandibles	7 × 2 and 8 × 2	No control group	Clinical and X-rays examination	5 years	Clinical and X-ray examination	Load-related bone formation minimizing mandibular BMC loss
August et al, 2001[68]	No treatment for OP, Maxilla: 78, 36 cases, 60, 41, 60 controls. Mandible:90, 39 cases, 54, 18, 50 controls (mean ages: 66.3, 61.7, 36, 34.5, 64.2)				Mandible, maxilla	Maxilla: 302, 111. Mandible: 268, 130	Maxilla: 112, 64, 172. Mandible: 101, 32, 121		Maximum 5 years	Stability at stage II uncovering surgery by manual torque and X-ray	Estrogen deficiency may be a risk factor for dental implant failure in the maxilla
Becker et al, 2000[61]	49 cases, 49 controls, (19 males + 30 females in each group) 44 to 85 years	7 controls and 10 cases already diagnosed OP	Proximal and distal radius and ulna	pDEXA at the distal and proximal radius and ulna	Mandible, maxilla	184	180	Visual assessment of local bone	Average 3 years and 10 months	Implant survival	No association
Minsk and Polson, 1998[62]	116 (25 on HRT + 91 without HRT) women, older than 50 years				Mandible, maxilla					Implant survival	HRT may not improve implants success
Blomqvist et al, 1996[69]	11 (7 females + 4 males) cases, 11 controls, 46 to 75, mean age 59 years			Single-photon gamma absorptiom-etry of forearm	Maxilla, + bone grafting	74	71	Osteometry, hemato-logic, urinary tests	14 to 58 months, mean of 30 months	Implant survival	Significantly different BMD% in successful and failure cases

OVE = ovariectomy/ovariectomised; ECM = extra cellular matrix; HRT = hormone replacement therapy; OP = osteoporosis/osteoporotic; BMC% = BMD percentage of age-matched (describes the mean value matched for age and sex and is normally 100%); B. = biphosphonates; PTV = Periotest values.

Human studies deficiencies

Various study design characteristics perplex the comparison of the existing human studies and limit their contribution to the clarification of dental implant outcomes in osteoporotic patients. A quick presentation of limiting factors follows.

In a total of 12 studies in humans, six retrospective[61,62,65,69-71] and six prospective,[60,63,64,66-68] control groups are not included in three,[60,62,66] implants are not divided according to site of implantation in three of them,[62,63,67] and osteoporosis is not diagnosed in any skeletal site in four studies.[62,68-70] It is interesting that three of the last four studies are the ones that mention osteoporosis as a risk factor for dental implant failure.

None of the studies stratified patients for the number of postmenopausal years. One study presented relative information that controls had nine fewer postmenopausal years than osteoporotic patients.[69]

In addition, sample size was usually small. Ten studies had 0 to 19 osteoporotic patients,[60-62,64-70] one study did not clarify the number,[71] and only one study[63] included 50 osteoporotic women. Follow-up periods were usually short. One study followed patients up to stage II uncovering surgery,[68] and two to the abutment connection.[65,71] Only two studies had a mean follow-up period of five or more years.[66,70] As expected, the initially small sample size is furthermore reduced in the long-term evaluation.

Success criterion of osseointegration is another factor of major importance. Five of the 12 studies refer to implant survival as the only success criteria.[61,62,65,69,70]

Osteoporosis is a site-specific disease. There is a tendency to support that jawbone is also affected in osteoporotic patients.[20,31] Still, jawbone is not one of the main skeletal sites affected by osteoporosis. The fact that some studies examined osseointegration of dental implants in osteoporotic patients without clarifying the existence of osteoporosis in the jaws[60-62,65,68-70] and the severity of the existing osteopenia/osteoporosis,[63] or having already proved that osteoporosis has not affected implantation sites of the certain subjects,[64,67] maintains confusion.

After having discussed the limiting factors of the available human studies, it is now obvious that the ideal study about dental implants in osteoporotic patients is not among them. Two main issues of research existed.

The first one was whether osseointegration may be obtained in osteoporotic patients. A majority of studies appear positive. According to Friberg et al, implant placement in patients in whom the average bone density showed osteoporosis in both lumbar spine and hip as well as poor local bone texture may be successful over a period of many years (mean follow-up period 3 years and 4 months, ranging from 6 months to 11 years).[60] The mean healing periods were extended to 8.5 months in the maxilla and 4.5 months in the mandible. Extending the healing period by 50% agrees with prementioned animal study results.[38,43]

The second issue is the long-term results of dental implants in osteoporotic patients. In this case, a better study design may be recognized in the study of von Wowern and Gotfredsen,[66] mainly because of the estimation of mandibular osteoporosis by mandibular BMC measures at baseline, just after attachment insertion, and at 2- and 5-year visits. In addition, this study has the longest follow-up period, long-term edentulous patients, all implants placed in both mandibular canine regions, and clinical and radiographic assessment of dental implants. Unfortunately, there is no control group, and only seven women out of 22 patients showed mandibular osteoporosis at the start of trial. No implant failures were observed. BMC measures at implantation sites showed a load-related, positive bone remodeling that minimizes or in some cases counteracts age-related changes in bone remodeling processes. Simultaneously, a significantly larger bone height loss occurred in women with mandibular osteoporosis and dental implants than in the remaining women with dental implants after the 5-year follow-up (not earlier), despite the high level of oral hygiene and the prementioned positive functional stimulus.

Therefore, further research on the long-term outcomes of dental implants in patients with osteoporosis in the jawbone is needed. Larger sample sizes are required to sufficiently document the relationship between dental implant outcomes and osteoporosis, especially since the severity of osteoporosis may influence the strength of the studied relationship. Clear evidence that osteoporosis has affected the jawbone of tested patients is of major importance. Finally, to our knowledge, there are no studies dealing with the previously mentioned question of periimplantitis in osteoporotic patients.

Dental implants and age, gender, and jawbone quality

The analysis of existing data about the impact of age and sex on dental implant success may offer indirect information about the outcome of dental implants in osteoporotic patients. This is because age and gender are risk factors for osteoporosis. If osteoporosis was a risk factor for dental implant osseointegration, then relevant studies might have found a positive relationship between aging and gender and implant failure. There is a general consensus that there is no impact of age or gender on implant failure.[25,60,64,68-69,85-119] Some studies[120-125] found even better results for women than men. Others found higher bone loss for the first year[108] or lower initial stability[126,127] in the female population, but these facts were not followed by increased long-term failure rates.[126] Some articles more or less clearly support the opposite without sufficient documentation.[68,128-133] These results support the opinion that osteoporosis is not a contraindication to dental implants, despite the fact that several confounding factors are involved in these studies. Site-specific factors have a greater impact on dental implant outcome than age and gender.[90] There is a positive, although rough, estimation of long-term[91] dental implants outcome in osteoporotic patients.

The osteoporotic bone is characterized as type IV according to the Lekholm and Zarb classification,[134] that is, soft bone. Soft bone, not necessarily osteoporotic, has been related to low success rates of dental implants in some studies, because of its reduced potential to offer initial implant stability.[63,86,135-145] On the contrary, other studies did not find such differences.[99,100,146-162]

Bone quality is a significant factor, but not the only one determining result. Implant design,[138,141,144,158,163,174] length,[163,165] surface characteristics,[138,151-153,155,158,159,164-177] surgical technique,[154,163,165,178-179] prosthodontic rehabilitation,[148,165,180] and patient hygiene[148,164] are some of the factors involved. Smedberg et al[181] reported 100% implant success in type 3 or 4 quality combined with type A, B, or C bone quantity in maxillary overdentures followed for two years, in comparison to 77% for implants in type 3 or 4 bone quality combined with type D or E bone quantity.

Friberg et al,[182] studying the frequency of early and late failures of Branemark System implants, related this outcome to differences in the surgical protocol, as well as to various patient and implant characteristics. Regarding jawbone quality, type 4 showed the highest failure rate in maxilla (40.4%) and type 1 in the mandible (13%). After proper adjustment of the surgical technique (omitting the threading procedure, using wide diameter implants in standard diameter bone sites, and extending the healing period in low-density bone), type 2 bone showed a failure rate of 4.7%, and type 4 a failure rate of 2.8%. It can be concluded that proper adjustment of the surgical preparation is a major factor in the determination of dental implant outcome.

Biphosphonate therapy

Biphosphonate drugs are used as an alternative of HRT for the prevention and treatment of osteoporosis. The long-term application of these drugs may induce osteonecrosis of the jaws (ONJ), due to decreased osteoclast numbers and activity resulting in decreased bone resorption. Although the precipitating event that produces this complication may be spontaneous, biphosphonate therapy is considered a contraindication to implants;[183-187] however, it is recognized that oral biphosphonates are a low-risk group versus the high-risk intravenous biphosphonates[63,183] used in cancer therapy. This was confirmed by Jeffcoat's[63] recent randomized, placebo-controlled study; however, the two- to three-year follow-up period of this study is not sufficient to determine the long-term effects of long half-life biphosphonates. Data on the use of biphosphonates in osteoporotic patients and implant outcomes are very limited. Therefore, no conclusions can be drawn.

Practical measures aimed at the improvement of dental implant outcomes in osteoporotic patients

In cases of treatment with dental implants, osteoporotic patients may be candidates for surgical techniques used to overcome the disadvantages of reduced bone quantity and deteriorated bone quality.[89,146,153,188-200]

The detailed analysis of such techniques is beyond the scope of this article, because they are not a special treatment for osteoporotic patients. Briefly we are mentioning the following:

Reduced bone quantity may be an indication for:

(1) A reduction of number of implants. According to Branemark et al,[198] a reduced jawbone volume was the major reason for limiting the number of implants to four in mandibles and maxillae of fully edentulous patients. It is interesting that although a tendency existed for an increased failure rate in patients with four implants, the survival rate for both implants and prostheses at the end of the 10-year observation period was the same with the six implants-per-jaw-patients group.
(2) Bone augmentation techniques.[195-197]
(3) Osteotome sinus floor elevation.[195]
(4) Zygomatic implants.[199]

Poor bone quality is considered a relative problem because of the lack of primary implant stability. The following have been proposed:

(1) A longer healing period. This seems to be needed if osteoporosis is exhibited in the jawbone. There are no studies to give the exact time needed, but a healing period 50% longer than normal has proved sufficient.[60] There are studies supporting immediate and early loading in soft bone;[146,153] nevertheless, the conservative approach is at present considered safer.
(2) The relation between the last used drill and the diameter of the implant chosen may be altered, which means that a smaller drill or an implant with larger than normal diameter may be used.[88,190-194]
(3) The osteotome technique, which may improve bone density around the implant, since the implant is placed without drilling.[195]
(4) Root-shaped implants.[192]
(5) Penetration in cortical layers to a higher extent;[45] however, regarding bicortical implant anchorage, the available data are controversial.[200]

Conclusion

There are no data to contraindicate the use of dental implants in osteoporotic patients; however, a proper adjustment of the surgical technique and a longer healing period may be considered in order to achieve osseointegration. Data on the use of biphosphonates in osteoporotic patients and implant outcomes are very limited, and no conclusions can be drawn. In addition, large prospective studies investigating the long-term success of dental implants in osteoporotic individuals are required.

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