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The fate of marginal bone around axial vs. tilted implants: A systematic review

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Aims: The use of tilted implants has recently gained popularity as a feasible option for the treatment of edentulous jaws by means of implant-supported rehabilitations without recurring to grafting procedures. The aim of this review was to compare the crestal bone level change around axially placed vs. tilted implants supporting fixed prosthetic reconstructions for the rehabilitation of partially and fully edentulous jaws, after at least 1 year of function.

Materials and methods: An electronic search of databases plus a hand search on the most relevant journals up to January 2014 was performed. The articles were selected using specific inclusion criteria, independent of the study design. Data on marginal bone loss and implant survival were extracted from included articles and statistically analysed to investigate the effect of implant tilting, location, prosthesis type, loading mode and study design. The difference in crestal bone level change around axial vs. tilted implants was analysed using meta-analysis.

Results: The literature search yielded 758 articles. A first screening based on titles and abstracts identified 62 eligible studies. After a full-text review, 19 articles (14 prospective and five retrospective studies) were selected for analysis. A total of 670 patients have been rehabilitated with 716 prostheses (415 in the maxilla, 301 in the mandible), supported by a total of 1494 axial and 1338 tilted implants. Peri-implant crestal bone loss after 1 year of function ranged from 0.43 to 1.13 mm for axial implants and from 0.34 to 1.14 mm for tilted implants. In spite of a trend for a lower bone loss around axial implants with respect to tilted ones at 12 months, as well as after 3 or more years of function, no significant difference could be found ($P = 0.09$ and $P = 0.30$, respectively). The location (maxilla vs. mandible), the loading mode (immediate vs. delayed), the restoration type (full vs. partial prosthesis) and the study design (prospective vs. retrospective) had no significant effect on marginal bone loss. Forty-six implants (18 axial and 28 tilted) failed in 38 patients within the first year of function. All failures except five occurred in the maxilla. After 12 months of loading, the survival rate of implants placed in the maxilla (97.4%) was significantly lower as compared to the mandible (99.6%). No prosthesis failure was reported.

Conclusions: Tilting of the implants does not induce significant alteration in crestal bone level change as compared to conventional axial placement after 1 year of function. The trend seems to be unchanged over time even though the amount of long-term data is still scarce. The use of tilted implants to support fixed partial and full-arch prostheses for the rehabilitation of edentulous jaws can be considered a predictable technique, with an excellent prognosis in the short and mid-term. Further long-term trials, possibly randomised, are needed to determine the efficacy of this surgical approach and the remodelling pattern of marginal bone in the long term.

Conflict-of-interest statement: *The authors declare that they have no conflict of interest.*

Introduction

After tooth loss the alveolar ridge undergoes progressive atrophy, which may become severe over time, especially for totally edentulous jaws. A number of prosthetic treatment alternatives are available to address this situation, such as complete dentures, implant-retained removable reconstructions, fixed implant-supported prostheses[1]. The latter represent today a common and well-accepted treatment for the rehabilitation of partial and completely edentulous jaws. They offer an established long-term predictability as well as a higher level of satisfaction for the patient in terms of aesthetics, phonetics and functionality, as compared to removable prostheses[2-4].

Most patients wearing complete dentures complain about progressive loss of stability during phonetics and mastication, and request a fixed rehabilitation. However, the rehabilitation of severely atrophic jaws using implant-supported prosthesis is often challenging because of the poor quality and quantity of residual jawbone, especially in patients with long term edentulism.

For example, progressive bone loss in the posterior mandible may lead to superficialisation of the alveolar nerve, which may cause pain to denture wearers during mastication. Bone augmentation procedures might represent a solution for facilitating implant placement in the posterior mandible, but these types of intervention are poorly accepted by patients. With regard to the maxilla, its rehabilitation with osseointegrated implants is often associated with several problems. In many cases, sufficient alveolar crest volume is found in the anterior region, while in the premolar and molar region, severe bone resorption can occur as a consequence of tooth loss.

The presence of the maxillary sinus and a limited ridge dimension must also be considered when placing implants in this region[5-6]. During past decades, various alternative surgical procedures have been adopted to place implants in the posterior atrophic maxilla; one of them is the maxillary sinus augmentation procedure, with either lateral or transcrestal approach. In spite of the excellent outcomes of this procedure, it is associated with several possible complications like morbidity at the donor site, sinusitis, fistulae, loss of the graft or the implants, and osteomyelitis[7-11]. Grafting procedures are generally demanding for both clinicians and patients and are often associated with increased surgical risks and financial cost as well. Another therapeutic option in case of limited available bone is represented by the use of implants of reduced length[12-13]. However, in the posterior maxilla, a minimum ridge height of 6 to 7 mm should be present for a safe placement of implants shorter than 8 mm. On the other hand, in the case of extremely atrophic posterior mandible, the use of short implants is to be carefully considered because of the risk of violating the alveolar nerve.

The combined use of axially placed and tilted implants represents another possible alternative for the treatment of edentulous jaws, which has been extensively documented in the recent years[14-19]. Implant inclination may be carefully planned by the surgeon in order to avoid damage to important anatomical structures. At the same time, the adoption of longer implants and a proper insertion axis may allow engagement of as much cortical bone as possible, favouring the achievement of adequate primary stability of the implants[20]. This may allow for immediate rehabilitation in many cases. Furthermore, increasing the inter-implant distance and reducing cantilever length, an optimal load distribution may be achieved. Several computational studies suggested possible biomechanical advantages of implant tilting in full-arch restorations[21-23]. On the other hand, unfavourable loading direction could in theory induce greater bone resorption around tilted implants as compared to axially placed ones, as suggested by other *in vitro* studies that reported accentuated stresses around non-axially placed implant necks[24-25].

Excellent clinical results of rehabilitations supported by a combination of axial and tilted implants have been reported, with high implant survival and prosthesis success rates, and a high level of satisfaction for the patients, in spite of a relatively high incidence of biomechanical complications (from 15.6%[26] to 27%[15] of cases). The latter could be generally managed at chairside[16-19].

What still remains to be studied is the stability of the peri-implant hard and soft tissues around tilted and axially placed implants over time. According to previous systematic reviews, while excellent implant survival rates were always emphasised by most studies, the crestal bone level change around tilted implants has not been systematically reported[16-18].

The primary aim of this systematic review was to evaluate the fate of marginal bone around tilted versus axial implants supporting partial and complete rehabilitations, after at least 1 year of function. Further aims were to investigate if a relationship exists between marginal bone change and the survival rate of axial and tilted implants over time and if factors like the arch (maxilla vs. mandible) the type of prosthesis (partial vs. complete) or the loading timing (immediate vs. delayed) could affect marginal bone changes.

Materials and methods

Search methods

An electronic search was performed on the following databases: MEDLINE; Embase; and the Cochrane Central Register of Controlled Trials (CENTRAL). The last search was performed on 15 January, 2014. The search terms used were: 'dental implant*'; 'oral implant*'; 'tilted implant*'; 'angled implant*'; 'angulated implant*'; 'offset implant*'; 'upright implant*'; 'straight implant*'; 'axial implant*'; 'edentulous patient*'; 'edentulous mandible'; 'edentulous maxilla'; 'All-on-four'; 'All-on-4', 'All-on-six'; and 'All-on-6'. They were used alone or in combination using Boolean operators OR and AND. Furthermore, a hand search of issues from 2000 up to the last issue available on 15 January, 2014, including the 'Early view' (or equivalent) section was undertaken on the following journals: *Clinical Implant Dentistry and Related Research; Clinical Oral Implants Research; Implant Dentistry; European Journal of Oral Implantology; International Journal of Oral and Maxillofacial Surgery; International Journal of Prosthodontics; Journal of Implantology; Journal of Oral and Maxillofacial Surgery; Journal of Periodontology; Journal of Prosthetic Dentistry; The International Journal of Oral and Maxillofacial Implants;* and *The International Journal of Periodontics and Restorative Dentistry*. The reference list of the retrieved reviews and of the included studies was also searched for possible additional eligible studies not identified by the electronic search.

Inclusion criteria

The search was limited to clinical studies involving human subjects. Restrictions were not placed regarding the language. Both prospective and retrospective studies were included. Further inclusion criteria were: a minimum of 10 partially edentulous or completely edentulous patients rehabilitated with partial or complete fixed prosthesis supported by both axially placed and tilted implants; a minimum follow-up duration of 1 year; bone loss around tilted and axial implants clearly reported; survival rate for tilted and axial implants clearly indicated or calculable from data provided; and implants placed in a pristine jawbone without additional grafting.

Publications that did not meet the above inclusion criteria and those that were not dealing with original clinical cases (e.g. reviews, technical reports) were excluded. Multiple publications of the same pool of patients were also excluded from the database. When papers from the same group of authors, with very similar databases of patients, materials, methods and outcomes were identified, the authors were contacted for clarifying if the pool of patients was indeed the same. In case of multiple publications relative to consecutive phases of the same study, only the most recent data (those with the longer follow-up) were considered.

Selection of the studies

Two reviewers (MDF and VC) independently screened the titles and the abstracts of the articles initially retrieved through the electronic search. The reviewers were previously calibrated by assessing a sample of 20 articles. The concordance between reviewers was assessed by means of the Cohen's Kappa coefficient. In case of disagreement, a joint decision was taken by discussion. The full texts of all studies of possible relevance were independently assessed by the same two reviewers to check if they met all inclusion criteria. For articles excluded at this stage, the reason for exclusion was noted.

Data extraction

Data were extracted by two reviewers independently (MDF and VC). Cases of disagreement were subject to joint evaluation until an agreement was reached. The following variables were extracted from each included study: study design; sample size; patient gender and age; proportion of smokers; total number of implants; number, type and location of the prostheses; follow-up duration; number of tilted and upright implants; degree of tilting; number of failed implants and details (time after loading, location; reason for failure); number of patients experiencing implant failure; prosthesis success rate; marginal bone level change around tilted and upright implants; occurrence and type of complications.

The following methodological parameters were also recorded: for randomised studies (if any), the random sequence generation method and allocation concealment; for all studies: clear definition of inclusion and exclusion criteria; clear definition of outcomes assessment and success criteria; number of surgeons involved; completeness of the outcome data reported; recall rate (it was assumed adequate if dropout <20%); explanation for dropouts/withdrawal (when applicable); sample size (it was assumed adequate if >20 patients were treated); and length of follow-up period (it was assumed adequate if the mean duration was ≥3 years). Details on the methods adopted for crestal bone level change evaluation were also noted, such as: type of radiographs and standardisation (periapical radiographs (PA) with an individual holder; PA without individual holder, panoramic radiographs); blinding or independency of evaluators. The methodological quality of the selected studies was evaluated independently and in duplicate by two reviewers (MDF and VC) according to the above methodological parameters. All the criteria were assessed as adequate, unclear, or inadequate. The authors of the included studies were contacted for providing clarifications or missing information as needed. Studies were considered at low risk of bias if more than 2/3 of the nine parameters were judged as adequate.

Statistical analysis

In order to make comparisons between studies with different follow-up duration, the statistics were made considering the 1-year data for all studies. Studies reporting longer follow-ups were considered separately. The data extracted from each included study were imported in the software RevMan (Review Manager [RevMan] Version 5.2, 2012; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) for meta-analysis. For marginal bone loss evaluation the mean value and standard deviation of crestal bone level change and the number of tilted and axial implants available for analysis in each study were used. A random effect model was chosen. The estimates of the bone level change around axial and tilted implants were expressed as mean difference (mm) together with 95% confidence intervals (CI). The statistical evaluation was conducted considering the implant as the analysis unit. The contribution of each article to the primary outcome was weighted based on the sample size and standard deviation. Subgroup analysis was performed taking into account location (maxilla or mandible), angulation (tilted or axial), loading timing (immediate or delayed), study design (prospective or retrospective) and restoration type (partial or complete prosthesis).

Regarding implant survival, the estimates of the effects of an intervention were expressed as odds ratio (OR) together with 95% confidence intervals. The statistical evaluation was conducted considering both the implant and the patient as the analysis unit. Comparison among studies was performed by meta-analysis. ORs were combined using a fixed-effects model (Mantel-Haenszel method). Pearson's chi-square analysis was used to investigate the effect of implant location, angulation, loading timing, study design and restoration type on implant survival at 1-year follow-up. $P = 0.05$ was considered as the significance level.

Results

The flowchart summarising the screening process is presented in Fig 1. The last electronic search was performed on 15 January, 2014. The electronic search yielded a total of 758 articles. No additional article was found by the hand search. After a first screening of the titles and abstracts, 62 articles were selected, which reported results of clinical studies in which edentulous patients have been rehabilitated using prostheses supported by axial and tilted implants[14,15,20,26-84]. The Cohen's kappa coefficient was 0.92, indicating excellent agreement between reviewers.

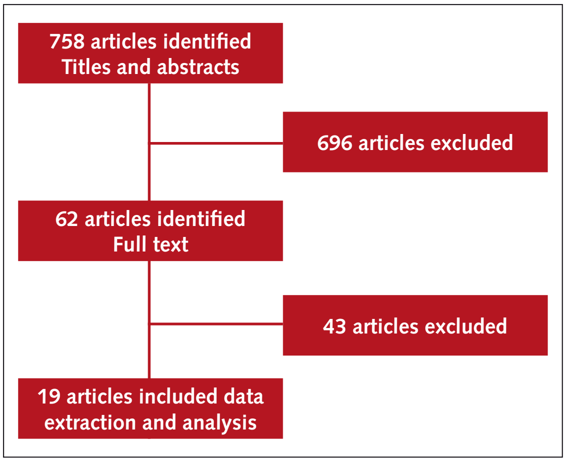


Fig 1 Flowchart of the study selection process.

After examining the full text of the 62 articles, 43 of them were excluded from the review (Table 1). Of the 19 remaining articles, 14 reported the results of prospective studies[27,29,37,38,40,43,44,56,59,60,63,69,71,76] and five of retrospective studies[20,31,32,42,72]. No randomised clinical study was identified. Table 2 reports the most relevant characteristics of the included studies. The main outcomes of these studies are described in Table 3. Of the 19 included studies, 11 have been performed in Italy[37,38,40,43,44,56,59,63,69,71,76], two in Spain[20,42], and one each in Austria[31], Belgium[27], China[29], Germany[60], Portugal[32], and Sweden[72]. All studies were conducted at universities or specialist dental clinics.

A total number of 2993 implants, of which 112 (3.74%) had a machined surface, were originally inserted in 670 patients rehabilitated with 91 partial and 625 complete fixed prostheses (415 in the maxilla, 301 in the mandible). Of the placed implants, 1494 were axial and 1338 tilted. These 2832 implants were submitted to statistical analysis regarding implant survival. Other implants were not considered because they were inserted in unusual regions and/or could not be regarded as axial nor as tilted (e.g. in the study by Peñarrocha et al[42] in the same patients in which axial and tilted implants were placed, 55 implants were pterigomaxillary or zygomatic or placed in the frontomaxillary region, and in the study by Malò et al[32] there were 83 trans-sinus implants). A total of 1576 maxillary (904 axial, 742 tilted) and 1171 mandibular implants (590 axial, 581 tilted) was considered for the analysis on marginal bone level change.

Table 1 Excluded studies and reasons for exclusion.

Excluded studies	Reason for exclusion
Balshi et al, 2013[28]	No details on marginal bone loss
Francetti et al, 2013[30]	No details on marginal bone loss
Tabrizi et al, 2013[33]	No axial implants, only tilted ones
Testori et al, 2013[34]	No details on marginal bone loss; grafting
Agnini et al, 2012[35]	No details on bone loss; inadequate report of failures
Cavalli et al, 2012[36]	Inadequate report of bone loss
Galindo et al, 2012[39]	Inadequate report of bone loss
Malò et al, 2012[41]	Inadequate report of bone loss
Acocella et al, 2011[45]	Inadequate report of bone loss
Butura et al, 2011[46]	Inadequate report of bone loss
Butura et al, 2011[47]	No details on marginal bone loss
Butura et al, 2011[48]	Redundant publication (Butura et al, 2011[47])
De Vico et al, 2011[50]	Redundant publication (Pozzi et al, 2012[43])
Franchini et al, 2011[51]	Too few tilted implants (not in all patients)
Graves et al, 2011[52]	Technical article; no details on marginal bone loss
Graves et al, 2011[53]	Redundant publication (Graves et al, 2011[52])
Kawasaki et al, 2011[54]	Inadequate report of failures and bone loss
Parel et al, 201155	Inadequate report of failures and bone loss
Agliardi et al, 2010[26]	Redundant publication (Agliardi et al, 2010[56])
Alves et al, 2010[57]	No details on marginal bone loss
Balleri et al, 2010[58]	Peculiar clinical procedure; no details on marginal
Corbella et al, 2011[49]	No details of implants and failures, no bone loss report
Peñarrocha et al, 2010[61]	Redundant publication (Peñarrocha et al, 2012[42])
Pomares et al, 2010[62]	Inadequate report of bone loss
Fortin et al, 2009[64]	No bone loss report
Pancko et al, 2009[65]	No axial implants, no bone loss report
Agliardi et al, 2008[66]	Redundant publication
Bilhan et al, 2008[67]	Case report (1 patient)
Francetti et al, 2008[68]	Redundant publication (Francetti et al, 2012[38])
Testori et al, 2008[70]	Redundant publication (Capelli, 2007[71])
Malò et al, 2007[73]	Inadequate report of bone loss
Rosén and Gynther, 2007[74]	Inadequate report of bone loss
Malò et al, 2006[78]	Inadequate report of bone loss
Krennmair et al, 2005[77]	Inadequate report of bone loss
Malò et al, 2005[78]	Inadequate report, few hollow cylinder tilted implants
Karoussis et al, 2004[79]	Inadequate report of bone loss
Malò et al, 2003[15]	Inadequate report on patients & bone loss
Aparicio et al, 2002[80]	Inadequate report of bone loss
Fortin et al, 2002[81]	Inadequate report of bone loss
Krekmanov et al, 2000[14]	Inadequate report of bone loss
Krekmanov et al, 2000[82]	Inadequate report and partially redundant (Krekmanov et al, 2000[14])
Mattsson et al, 2000[83]	Inadequate report of bone loss

Table 2 Characteristics of the included studies.

Articles	Study Type	Setting	No. of patients	% Men/ women	Mean age (range)	Smokers	Total No. of implants	No. maxillary prostheses (implants)	No. mandibular prostheses (implants)	Type of restoration	Follow-up duration, months (range)
Browaeys et al, 2014[27]	P	University	20	30% / 70%	55 (35–74)	NR	80	9 (36)	11 (44)	Full-arch	36
Di et al, 2013[29]	P	University	69	54% / 46%	56.7 (37–74)	NR	344	38 (152)	48 (192)	Full-arch	33.7 (12–56)
Krennmair et al, 201331	R	University	38	39% / 61%	67.1 (NR)	18%	152	-	38 (152)	Full-arch	66.5 (5–7 yrs)
Malò et al, 2013[32]	R	Private Centre	70	41% / 59%	54 (35–81)	27%	280	70 (280)	-	Full-arch	36
Crespi et al, 2012[37]	P	University	36	39% / 61%	54.6 (41–81)	39%	176	24 (96)	20 (80)	Full-arch	36
Francetti et al, 2012[38]	P	University	47	53% / 47%	53 (44–63)	32%	196	16 (64)	33 (132)	Full-arch	36 max. 60 mand.
Grandi et al, 2012[40]	P	1 Private 2 Univ. centres	47	47% / 53%	62 (52–78)	23%	188	-	47 (188)	Full-arch	18
Peñarrocha et al, 2012[42]	R	University	18	33% / 67%	NR (35–69)	39%	117	18 (62)*	-	Full-arch	39.2 (12–84)
Pozzi et al, 2012[43]	P	University	27	56% / 44%	54 (38–77)	NR	81	37(81)	-	FPD	43.3 (36–54)
Weinstein et al, 2012[44]	P	University	20	40% / 60%	60.8 (44–77)	20%	80	-	20 (80)	Full-arch	30.1 (20–48)
Agliardi et al, 2010[56]	P	Private Centre	24	42% / 58%	56.4 (42–73)	25%	96	-	24 (96)	Full-arch	26.8 (14–42)
Degidi et al, 2010[59]	P	Private Centre	30	53% / 47%	58.1 (NR)	NR	210	30 (210)	-	Full-arch**	36
Hinze et al, 2010[60]	P	Private Centre	37	49% / 51%	64.6 (39–84)	30%	148	19 (76)	18 (72)	Full-arch	12
Agliardi et al, 2009[63]	P	University	20	55% / 45%	57 (44–68)	35%	120	20 (120)	-	Full-arch	27.2 (18–42)
Tealdo et al, 2008[69]	P	University	21	52% / 48%	58 (NR)	NR	111	21 (111)	-	Full-arch	20 (13–28)
Capelli et al, 2007[71]	P	University	65	34% / 66%	59.2 (28–83)	15%	342	41 (246)	24 (96)	Full-arch	55 (33–82)
Koutouzis and Wennstrom, 2007[72]	R	University	38	53% / 47%	59.5 (NR)	26%	111	24 (40)	18 (39)	FPD	60
Calandriello and Tomatis, 2005[76]	P	Private Centre	18	39% / 61%	64 (51–76)	heavy smokers excluded	60	19 (60)	-	12 FPD 7 full-arch	12
Aparicio et al, 2001[20]	R	University	25	40% / 60%	59 (M) 49 (F)	24%	101	29 (101)	-	29 FPD	37 (21–87)

P = prospective; R = retrospective; NR = not reported; * only tilted (n = 30) and conventionally placed axial implants (n = 32) were considered; **the implants were all splinted by a welded bar.

Table 3 Main outcomes of the included studies.

Articles	Inserted implants (failures)		PSR	Location of failed implants	12 m bone loss, mm (no. of implants)		>12 m bone loss, mm (no. of implants)		Complications reported
	axial	tilted			axial	tilted	axial	tilted	
Browaeys et al, 2014[27]	40	40	100%	–	1.13 ± 0.71 (n = 32)	1.14 ± 1.,14 (n = 32)	1.55 ± 0.73 (n = 32)	1.67 ± 1.22 (n = 32)	
Di et al, 2013[29]	172	172	100%	11 maxilla (1 ax, 10 tilt), 2 mandible (1 ax 1 tilted)	0.7 ± 0.2 (n = 148)	0.8 ± 0.4 (n = 148)			3 abutment screw loosened, 5 artificial teeth separated from the acrylic resin base. Fracture near the implant metal coping in 3 provisional restorations.
Krennmair et al, 2013[31]	76	76	100%	–	–	–	1.17 ± 0.26 (n = 76)	1.24 ± 0.32 (n = 76)	256 in total (described in details in a table).
Malò et al, 2013[32]	140(1)	57(1)*	100%	Maxilla	0.62 ± 0.35 (n = 114/135)	0.89 ± 0.54 (n = 47/55)	1.15 ± 0.51 (n = 88/123)	1.06±0.71 (n = 40/50)	Mechanical complications in 36 patients (28 prosthetic screw loosening, 8 prosthesis fracture); Biological complications in 26 patients/30 implants: bone resorption and BoP (11), fistulae (2), excessive bone loss (2).
Crespi et al, 2012[37]	88	88 (3)	100%	1 maxilla 2 mandible	Maxilla: 1.02 ± 0.35 (n = 48)	Maxilla: 1.05 ± 0.29 (n = 47)	Maxilla: 1.08 ± 0.4 (n = 48; 24m) 1.10 ± 0.45 (n = 48; 36m)	Maxilla: 1.07 ± 0.46 (n = 47; 24 m) 1.11 ± 0.32 (n = 47; 36 m)	1 case of mucositis around 1 axial implant.
					Mandible: 1.04 ± 0.30 (n = 40)	Mandible: 1.05 ± 0.32 (n = 38)	Mandible: 1.04 ± 0.35 (n = 40; 24 m) 1.06 ± 0.41 (n = 40; 36 m)	Mandible: 1.09 ± 0.29 (n = 38; 24 m) 1.12 ± 0.35 (n = 38; 36 m)	
Francetti et al, 2012[38]	98	98	100%	–	Maxilla: 0.40 ± 0.27 (n = 32)	Maxilla: 0.32 ± 0.28 (n = 32)	Maxilla: 0.44 ± 0.37 (n = 32; 24 m) 0.85 ± 0.74 (n = 14; 36 m)	Maxilla: 0.63 ± 0.38 (n = 32; 24 m) 0.85 ± 0.34 (n = 14; 36 m)	Light hypoaesthesia on the left side of the lower lip after surgery, resolved after 6 months (1 patient); fracture of the acrylic prosthesis (7 patients); 3 axial implants showed peri-implantitis after 3 y (3 mm bone loss).
					Mandible: 0.57 ± 0.42 (n = 66)	Mandible: 0.48 ± 0.23 (n = 66)	Mandible: 0.90 ± 0.49 (n = 64; 24 m) 0.92 ± 0.43 (n = 54; 36 m) 0.51 ± 0.17 (n = 24; 60 m)	Mandible: 0.67 ± 0.38 (n = 64; 24 m) 0.69 ± 0.52 (n = 54; 36 m) 0.39 ± 0.18 (n = 24; 60 m)	
Grandi et al, 2012[40]	94	94	100%	–	0.57 ± 0.13 (n = 94)	0.60 ± 0.16 (n = 94)	0.68 ± 0.14 (n = 94; 18 m)	0.68 ± 0.14 (n = 94; 18 m)	Three patients had a fracture of the provisional restoration, but all of the definitive prostheses remained stable throughout the study period without any complications.
Peñarrocha et al, 2012[42]	32 (2)	30 (1)	100%	3 maxilla	0,52 ± 0,10 (n = 32)	0,76 ± 0.06 (n = 30)	–	–	NR

Table 3 *(cont.)* Main outcomes of the included studies.

Articles	Inserted implants (failures)		PSR	Location of failed implants	12 m bone loss, mm (no. of implants)		>12 m bone loss, mm (no. of implants)		Complications reported
	axial	tilted			axial	tilted	axial	tilted	
Pozzi et al, 2012[43]	39 (1)	42 (2)	100%	3 maxilla (1 patient)	0.48 ± 0.3 (n = 38)	Ant: 0.6 ± 0.38 (n = 14) Post: 0.62 ± 0.37 (n = 26)	0.5 ± 0.3 (n = 38. 36m)	Ant: 0.7 ± 0.38 (n = 14; 36 m) Post: 0.7 ± 0.2 (n = 26; 36 m)	No biological or mechanical complications occurred during the entire follow-up period.
Weinstein et al, 2012[44]	40	40	100%	–	0.6 ± 0.3 (n = 36)	0.7± 0.4 (n = 36)	–	–	NR
Agliardi et al, 2010[56]	48	48	100%	–	0.9 ± 0.4 (n = 42)	0.8 ± 0.5 (n = 42)	–	–	No complication during surgical and prosthetic procedures.
Degidi et al, 2010[59]	90 (1)	120	100%	maxilla	0.60 ± 0.11 (n = 89)	0.63 ± 0.24 (n = 120)	0.92 ± 0.89 (n = 89; 36 m)	1.03 ± 0.87 (n = 120; 36 m)	Three implants had serious biologic complication (peri-implantitis).
Hinze et al, 2010[60]	74 (3)	74 (4)	100%	Tilted: 3 maxilla 1 mandible Axial: 3 maxilla	0.82 ± 0.31 (n = 71)	0.76 ± 0.49 (n = 70)	–	–	4 fractures of provisional prostheses. One fracture of definitive prosthesis. Loss of the screw access hole restoration in 9.5% of the cases. Occlusal screw loosening in 6% of cases. Extensive bruising in 2 patients.
Agliardi et al, 2009[63]	40	80	100%	–	0.8 ± 0.4 (n = 30)	0.9 ± 0.5 (n = 60)	–	–	No complications occurred during surgical and prosthetic procedures.
Tealdo et al, 2008[69]	64 (3)	47 (5)	100%	maxilla	Mesial: 0.62 (n = 61); Distal 0.86 (n = 61)	Mesial 0.92 (n = 42); Distal 1.04 (n = 42)	–	–	No loose abutment screws nor reported fractures of prosthesis frameworks.
Capelli et al, 2007[71]	189 (2)	117 (1)	100%	maxilla	Maxilla: 0.95 ± 0.44 (n = 84); Mandible: 0.82 ± 0.64 (n = 32)	Maxilla: 0.88 ± 0.59 (n = 42); Mandible: 0.75 ± 0.55 (n = 32)	–	–	Two more implants failures (1 axial and 1 tilted in maxilla) were recorded during the second year of function.
Koutouzis and Wennstrom, 2007[72]	36	33	100%	–	–	–	0.4 ± 0.94 (n = 36; 60 m)	0.5 ± 0.95 (n = 33; 60 m)	Three implant fractures, three cases with crown-screw loosening and three cases with minor porcelain fractures.
Calandriello and Tomatis, 2005[76]	33 (1)	27 (1)	100%	maxilla	0.82 ± 0.86 (n = 32)	0.34 ± 0.76 (n = 26)	–	–	One fracture of the acrylic bridge that probably lead to implant failure.
Aparicio et al, 2001[20]	59 (2)	42	100%	maxilla	0.43 ± 0.45 (n = 53)	0.57 ± 0.50 (n = 40)	0.92 ± 0.55 (n = 12; 60 m)	1.21 ± 0.68 (n = 12; 60 m)	28 mechanical incidents in 16 prostheses (55.2%). 18 retightening of the abutment screw in 14 prostheses, gold screw retightening in five prostheses. Fracture of the abutment screws and of the occlusal material was in two prostheses.

* in adjunct, 83 trans-sinus tilted implants were placed; NR = not reported.

Study or subgroup	axial			tilted				Mean difference		Mean difference
	Mean (mm)	SD (mm)	Total	Mean (mm)	SD (mm)	Total	Weight	IV, Random, 95% CI (mm)	Year	IV, Random, 95% CI (mm)
Aparicio et al, 2001[20]	0.43	0.45	57	0.57	0.5	42	5.0%	-0.14 [-0.33, 0.05]	2001	
Calandriello et al, 2005[76]	0.82	0.86	35	0.34	0.76	26	2.0%	0.48 [0.07, 0.89]	2005	
Capelli et al, 2007[71]	0.91	0.58	116	0.81	0.57	74	5.5%	0.10 [-0.07, 0.27]	2007	
Tealdo et al, 2008[69]	0.74	0.5	61	0.98	0.5	42	4.8%	-0.24 [-0.44, -0.04]	2008	
Agliardi et al, 2009[63]	0.8	0.4	30	0.9	0.5	60	5.0%	-0.10 [-0.29, 0.09]	2009	
Hinze et al, 2010[60]	0.82	0.31	71	0.76	0.49	70	6.3%	0.06 [-0.08, 0.20]	2010	
Degidi et al, 2010[59]	0.6	0.11	89	0.63	0.24	120	8.3%	-0.03 [-0.08, 0.02]	2010	
Agliardi et al, 2010[56]	0.9	0.4	42	0.8	0.5	42	4.9%	0.10 [-0.09, 0.29]	2010	
Pozzi et al, 2012[43]	0.48	0.3	38	0.61	0.38	40	5.9%	-0.13 [-0.28, 0.02]	2012	
Crespi et al, 2012[37]	1.03	0.33	88	1.05	0.31	85	7.3%	-0.02 [-0.12, 0.08]	2012	
Grandi et al, 2012[40]	0.57	0.13	94	0.6	0.16	94	8.4%	-0.03 [-0.07, 0.01]	2012	
Weinstein et al, 2012[44]	0.6	0.3	36	0.7	0.4	36	5.6%	-0.10 [-0.26, 0.06]	2012	
Peñarrocha et al, 2012[42]	0.52	0.1	32	0.76	0.06	30	8.4%	-0.24 [-0.28, -0.20]	2012	
Francetti et al, 2012[38]	0.51	0.37	98	0.43	0.25	98	7.5%	0.08 [-0.01, 0.17]	2012	
Di et al, 2013[29]	0.7	0.2	148	0.8	0.4	148	7.9%	-0.10 [-0.17, -0.03]	2013	
Malo et al, 2013[32]	0.62	0.35	114	0.89	0.54	47	5.5%	-0.27 [-0.44, -0.10]	2013	
Browaeys et al, 2014[27]	1.13	0.71	32	1.14	1.14	32	1.6%	-0.01 [-0.48, 0.46]	2014	
Total (95% CI)			**1181**			**1086**	**100.0%**	**-0.06 [-0.12, 0.01]**		

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 110.31$, df = 16 ($P < 0.00001$); $I^2 = 85\%$
Test for overall effect: Z = 1.72 ($P = 0.09$)

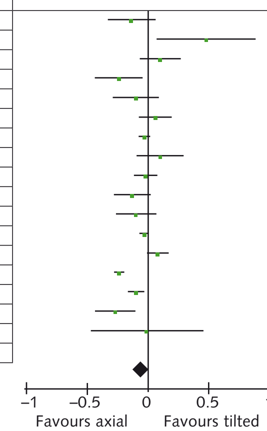


Fig 2 Forest plot of the mean differences in marginal bone level change between axial and tilted implants in the included studies at 12-months follow-up.

Study or subgroup	axial			tilted				Mean difference		Mean difference
	Mean (mm)	SD (mm)	Total	Mean (mm)	SD (mm)	Total	Weight	IV, Random, 95% CI (mm)	Year	IV, Random, 95% CI (mm)
Aparicio et al, 2001[20]	0.92	0.55	13	1.21	0.68	12	3.5%	-0.29 [-0.78, 0.20]	2001	
Koutouzis & Wennstrom, 2007[72]	0.4	0.94	36	0.5	0.95	33	4.0%	-0.10 [-0.55, 0.35]	2007	
Degidi et al, 2010[59]	0.92	0.89	89	1.03	0.87	120	9.6%	-0.11 [-0.35, 0.13]	2010	
Crespi et al, 2012[37]	1.08	0.43	88	1.115	0.33	85	17.5%	-0.03 [-0.15, 0.08]	2012	
Pozzi et al, 2012[43]	0.5	0.3	94	0.7	0.3	94	19.5%	-0.20 [-0.29, -0.11]	2012	
Francetti et al, 2012[38]	0.91	0.49	68	0.72	0.48	68	14.0%	0.19 [0.03, 0.35]	2012	
Malo et al, 2013[32]	1.15	0.51	88	1.06	0.71	40	9.5%	0.09 [-0.15, 0.33]	2013	
Krennmair et al, 2013[31]	1.17	0.26	76	1.24	0.32	76	19.0%	-0.07 [-0.16, 0.02]	2013	
Browaeys et al, 2014[27]	1.55	0.73	32	1.67	1.22	32	3.4%	-0.12 [-0.61, 0.37]	2014	
Total (95% CI)			**1181**			**1086**	**100.0%**	**-0.06 [-0.12, 0.01]**		

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 21.36$, df = 8 ($P < 0.006$); $I^2 = 63\%$
Test for overall effect: Z = 1.04 ($P = 0.30$)

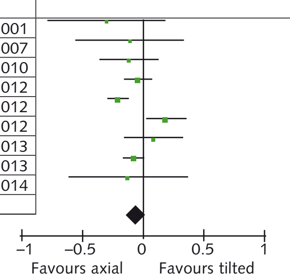


Fig 3 Forest plot of the mean differences in marginal bone level change between axial and tilted implants in the six included studies reporting data of at least 36-months follow-up.

Crestal bone level change

One-year follow-up (seventeen studies)

The results of the random effects meta-analysis for marginal bone level change around axial vs. tilted implants at 12 months are presented in Fig 2. Two studies provided results at 5 years only[31,72], therefore they were not included in this meta-analysis. The comparison between axial and tilted implants across the 17 studies (Fig 2) showed considerable statistical heterogeneity ($I^2 = 0.85\%$, $P < 0.001$). No significant difference was found ($P = 0.09$), with a slight discrepancy in favour of the axially placed implants (mean difference in bone loss -0.06 mm (95% C.I.: -0.12, 0.01)). Only one study reported significantly lower bone loss for tilted implants as compared to axial ones[76]. A sensitivity analysis was also performed by excluding such a study, but the result did not substantially change, though slight significance was achieved ($P = 0.04$, mean difference in bone loss -0.07 mm (95% C.I.: -0.13, 0.00)), confirming the robustness of the analysis.

At least 36-months follow-up (nine studies)

Nine studies evaluated marginal bone level change around axial and tilted implants after at least 36 months of loading[20,27,31,32,37,38,43,59,72]. The meta-analysis relative to these studies is shown in Fig 3. Again, a trend for lower marginal bone level change in favour of the axial implants was found (-0.05 mm, 95% C.I.: -0.15, 0.05) but did not achieve significance ($P = 0.30$).

Prosthesis type (sixteen studies)

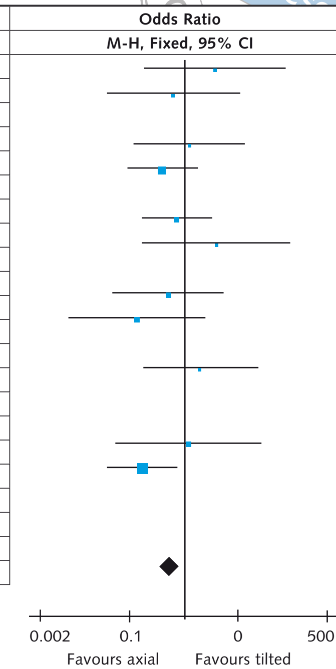
When separating the data according to the prosthesis type, a significant difference in marginal bone loss in favour of axial implants was found for fixed partial prostheses ($P = 0.03$, mean difference -0.13 mm, 95% C.I.: -0.25, -0.02) but not for full-arch fixed prostheses ($P = 0.09$, mean difference -0.06 mm, 95% C.I.: -0.13, 0.01). The study by Calandriello and Tomatis[76] was not considered because the bone loss data for full-arch and partial prostheses

Fig 4 Forest plot of the differences in implant survival between axial and tilted implants in the included studies at 12-months follow-up.

Study or subgroup	axial		tilted			Odds Ratio	
	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year
Aparicio et al, 2001[20]	2	57	0	42	1.8%	3.83 [0.18, 81.87]	2001
Calandriello et al, 2005[76]	1	25	1	16	3.8%	0.63 [0.04, 10.76]	2005
Koutouzis & Wennstrom, 2007[72]	0	36	0	33		Not estimable	2007
Capelli et al, 2007[71]	2	162	1	103	3.9%	1.27 [0.11, 14.24]	2007
Tealdo et al, 2008[69]	3	61	5	42	18.3%	0.38 [0.09, 1.70]	2008
Agliardi et al, 2009[63]	0	40	0	80		Not estimable	2009
Hinze et al, 2010[60]	3	71	4	70	12.5%	0.73 [0.16, 3.38]	2010
Degidi et al, 2010[59]	1	88	0	119	1.4%	4.10 [0.16, 101.77]	2010
Agliardi et al, 2010[56]	0	24	0	24		Not estimable	2010
Pozzi et al, 2012[43]	1	38	2	40	6.2%	0.51 [0.04, 5.91]	2012
Crespi et al, 2012[37]	0	88	3	85	11.5%	0.13 [0.01, 2.62]	2012
Francetti et al, 2012[38]	0	98	0	98		Not estimable	2012
Peñarrocha et al, 2012[42]	2	30	1	29	3.1%	2.00 [0.17, 23.34]	2012
Grandi et al, 2012[40]	0	94	0	94		Not estimable	2012
Weinstein et al, 2012[44]	0	40	0	40		Not estimable	2012
Malo et al, 2013[32]	1	135	0	55	2.3%	1.24 [0.05, 30.85]	2013
Di et al, 2013[29]	2	172	11	172	35.3%	0.17 [0.04, 0.79]	2013
Krennmair et al, 2013[31]	0	76	0	76		Not estimable	2013
Browaeys et al, 2014[27]	0	40	0	40		Not estimable	2014
Total (95% CI)		1375		1258	100.0%	0.56 [0.31, 1.00]	
Total events	18		28				
Total (95% CI)			**1181**		**100.0%**	**-0.06 [-0.12, 0.01]**	

Heterogeneity: Chi² = 8.28, df = 10 (*P* = 0.60); I² = 0%

Test for overall effect: Z = 1.97 (*P* = 0.05)



were not reported separately. The study by Krennmair et al[31] and Koutouzis et al[72] provided bone loss data on fixed partial dentures relative only to 5-year follow-up, so they were excluded from this subgroup analysis.

Implant location (fifteen studies)

When considering the data from the maxilla and from the mandible separately, no significant difference was found in marginal bone loss between axial and tilted implants at 12-months follow-up in both jaws. For maxillary implants the mean difference in bone loss was -0.08 mm, 95% C.I.: -0.17, 0.01 ($P = 0.09$) and for the mandibular implants it was 0.00 mm, 95% C.I.: -0.06, 0.05 ($P = 0.96$). The studies by Hinze et al[60], Di et al[29] and Browaeys et al[27] were not considered because the bone loss data of axial and tilted implants relative to maxilla and mandible were not reported separately. Conversely, the study by Koutouzis et al[72] reported separately the bone loss data for maxilla and mandible, but only 5-year data were provided.

Study design (eighteen studies)

When separating the studies according to the study design, no significant difference in bone loss around axial and tilted implants was found at 12-months follow-up in 14 prospective studies[27,29,37,38,40,43,44,56,59,60,63,69,71,76] ($P = 0.32$, mean difference -0.02 mm, 95% C.I.: -0.07, 0.02), while significant difference in favour of axial implants was found in three retrospective studies[20,32,42] ($P < 0.001$, mean difference -0.24 mm, 95% C.I.: -0.28, -0.20). Again, the retrospective studies by Krennmair et al[31] and Koutouzis et al[72] were not considered because they only reported 5-year data.

Loading timing (eighteen studies)

A similar result was found when considering the studies separately according to loading timing. In fact, 14 of the 15 immediate loading studies were the same prospective studies considered above. Only one study adopting immediate loading protocol had a retrospective design[32]. Two studies in which conventional delayed loading procedure was adopted[20,42] showed significant difference in bone loss in favour of axial implants ($P < 0.001$, mean difference -0.24 mm, 95% C.I.: -0.28, -0.19). The overall sample size of implants rehabilitated according to a delayed loading protocol was consistently lower than immediately loaded implants (n = 161 and 2106, respectively).

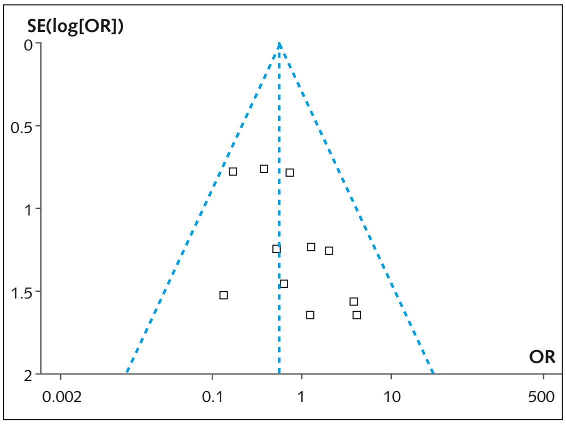


Fig 5 Funnel plot of the studies reporting implant survival for axial and tilted implants at 12-months follow-up, showing homogeneity among studies.

Implant survival

A total number of 46 implants (1.54%) failed in 38 patients (6.58%) during the first year of function. The reasons for failure were: mobility/lack of osseointegration (n = 31); mobility and pain (n = 2); pain (n = 3); while for 10 implants (22%) no reason was reported. Two maxillary implants (one axial and one tilted) failed in two patients later than 1 year, after 15 and 18 months of function[71] and another maxillary tilted implant failed after 23 months in another patient[32]. Of the implants that failed within 12 months, 18 were axial and 28 tilted and all but five implants (one axial and four tilted) were placed in the maxilla. Two of the failed implants (one axial and one tilted, both in maxilla) had a machined surface[76]. One-year implant survival was 97.4% and 99.6% for the maxilla and the mandible, respectively. No prosthesis failure was reported in any of the evaluated studies. Consequently, no further analysis was performed at prosthesis level.

The results of the fixed effects meta-analysis for implant survival at 1 year is presented in Fig 4. Considering the outcome of tilted versus axial implants in both jaws, slightly statistically significant difference in favour of axial implants (OR = 0.56, 95% CI: 0.31, 1.00, $P = 0.05$) and no heterogeneity was found (Fig 5). In this analysis, a single recent study had a consistent influence on such result, as its weight was more than one-third (35.3%) of the overall studies[29]. Sensitivity analysis performed excluding this study showed no significant difference in implant survival between axial and tilted implants ($P = 0.43$).

Table 4 Results of the comparisons of implant survival at 12-months follow-up for axial and tilted implants according to loading time and location.

	P value (chi square)	Tilted vs. axial			
		Tilted ISR%	Axial ISR%	Tilted N.	Axial N.
Total	0.481	97.9%	98.8%	1338	1494
Delayed	0.849	99.4%	98.1%	181	213
Immediate	0.225	97.7%	98.9%	1157	1281
Maxilla total	0.545	96.8%	98.1%	742	904
Maxilla delayed	0.860	98.9%	96.5%	90	113
Maxilla immediate	0.266	96.5%	98.4%	652	791
Mandible total	0.763	99.3%	99.8%	581	590
Mandible delayed	1.000	100.0%	100.0%	91	100
Mandible immediate	0.771	99.2%	99.8%	490	490
	P value (chi square)	Maxilla vs. mandible			
		Maxilla ISR%	Mandible ISR%	Maxilla total	Mandible total
Total	<0.001*	97.4%	99.6%	1576	1171
Tilted	0.037*	96.8%	99.3%	742	581
Axial	0.003*	98.1%	99.8%	904	590

* = significant difference.

Table 4 reports the results of the comparisons of implant survival between axial and tilted implants according to the arch and the loading mode, as well as comparisons between survival rates of maxillary and mandibular implants. Implants placed in the mandible (independent of the inclination) displayed a significantly better survival rate after 12 months as compared to maxillary ones ($P < 0.001$). This trend was confirmed when the analysis was performed separately for tilted ($P = 0.037$) and axial implants ($P = 0.003$). When performing the analysis at patient level, no significant difference in implant survival rate was found according to the loading mode ($P = 1.00$), while a significant difference was found according to the arch, with patients rehabilitated in the mandible experiencing significantly fewer implant failures than patients treated with maxillary prostheses ($P = 0.01$).

As most of the failed implants were located in the maxilla, a further meta-analysis was conducted on 14 studies that reported 1-year treatment out-

	Study design	No. of surgeons	Definition of selection criteria	Definition of outcome assessment	RX examination method	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Sample size	Follow-up length	
Agliardi et al, 2009	+	+	+	+	+	+	+	+	−	L
Agliardi et al, 2010	+	+	+	+	−	?	+	+	−	H
Aparicio et al, 2001	−	−	+	+	−	?	+	+	+	H
Browaeys et al. 2014	+	+	+	+	−	+	+	+	+	L
Calandriello et al, 2005	+	−	+	+	+	+	+	−	−	H
Capelli et al, 2007	+	−	+	−	+	+	−	+	+	H
Crespi et al, 2012	+	?	+	+	−	−	+	+	+	H
Degidi et al, 2010	+	+	+	+	+	?	+	+	+	L
Di et al, 2013	+	−	+	+	−	?	+	+	−	H
Francetti et al, 2012	+	−	+	+	+	+	+	+	+	L
Grandi et al, 2012	+	−	+	+	+	+	+	+		L
Hinze et al, 2010	+	−	+	+	−	?	+	+		H
Koutouzis et al, 2007	−	−	+	+	+	+	+	+	+	L
Krennmair 2013	−	?	+	+	?	−	+	+	+	H
Malo et al, 2013	−	?	+	+	?	−	+	+	+	H
Peñearrocha et al, 2012	−	+	+	+	+	?	+	−	+	H
Pozzi et al, 2012	+	?	+	+	+	+	+	+	+	L
Tealdo et al, 2008	+	?		+	+	+	+	+	−	H
Weinstein et al, 2012	+	+	+	+	−	+	+	+	−	L

Fig 6 Risk of bias summary: review authors' judgements about each risk of bias item for each included study (H = high risk of bias; L = low risk of bias).

comes for the maxilla (in total 870 axial and 716 tilted implants). Again, significant difference favouring axial implants (OR = 0.45, 95% CI: 0.24, 0.83, *P* = 0.01) and no heterogeneity was found.

The 1-year implant survival rate was at 97.2% and 97.8% for maxillary complete rehabilitations supported by 4 implants according to the all-on-four concept (total n. implants = 704) or supported by 5 to 7 implants (n = 777 implants), respectively. The difference was not significant (*P* = 0.96).

Complications

The most common complications described in the included studies were fracture of the temporary acrylic prosthesis and screw loosening (Table 3). No significant relationship with the arch was found for such mechanical complications. A few authors reported wear patterns in the opposing dentition[41]. Most of patients that experienced fracture of the prosthetic reconstruction orloosening of the prosthetic screw displayed parafunctions like bruxism[41,43] or had a short face morphotype with powerful mastication muscles[46,48].

Other outcome variables

In studies that assessed parameters related to oral hygiene level, plaque and bleeding scores progressively decreased over the first year of function[38,44,56,59,60,63]. Two studies with longer follow-up reported substantial maintenance of plaque and bleeding scores up to 5 years[31,38]. Finally, all studies that evaluated patient satisfaction by means of questionnaires or interviews reported extremely positive feedback of patients regarding function, phonetics and aesthetics after 1 year of loading[32,38,44,56,63].

Quality assessment/risk of bias of the included studies

According to the criteria established in this review, eleven studies[20,29,31,32,37,42,56,60,69,71,76] were considered to have a high potential risk of bias and eight[27,38,40,43,44,59,63,72] having a low risk (Fig 6). Of the five retrospective studies, only the study by Koutouzis et al[72] was considered at low risk of bias. The most critical parameter was the number of surgeons involved, which was not declared in five studies[31,32,37,43,69] and was greater than one in another seven studies[20,29,38,40,60,71,76]. One of them declared that surgeries have been performed by a "surgical team"[69]. The bone loss assessment method in six studies was based on non standardised periapical radiographs [20,27,31,32,40,76], and in three studies it was performed using only panoramic radiographs[29,37,60]. Finally, eight studies reported a mean follow-up shorter than 3 years (see Table 2).

■ Discussion

The aim of this review was to determine the trend of marginal bone loss around axial and tilted implants supporting partial and full-arch rehabilitations, after at least 1 year of function. For this reason, some studies with a large sample size and/or long term follow-up that reported details on the survival/success of axial and tilted implants, but not on crestal bone level changes around axial and tilted implants have been excluded from the present review. A different situation was represented by the study by Agnini et al, which correctly reported the results of bone loss evaluation separately for tilted and axially placed implants for the maxilla and mandible, up to 5 years of function[35]. However, it had to be excluded, because not all patients received tilted implants and the bone loss data of those patients treated with both tilted and axial implants could not be separated from the overall data.

The level of evidence of the included studies was rather poor because no randomised clinical trials neither comparative prospective trials were found. The included studies were mostly prospective single cohort or multicentre studies. The study quality assessment showed that more than half of the studies were at high risk of bias. Among the parameters that were considered to potentially affect the reliability of the study outcomes was the procedure for radiographically evaluating the peri-implant bone loss. Since the main aim of the present review was to assess changes in peri-implant bone level around tilted and axial implants, particular emphasis was dedicated to parameters related to such outcome. In fact, the quality of the radiographic method adopted might potentially affect the accuracy of the measurements. Of the 19 included studies only eight (42%) adopted a standardised paralleling technique based on periapical radiographs taken with an individual film holder, while others used non standardised periapical radiographs (five studies) or panoramic radiographs (three studies). Two studies used panoramic radiographs and, when possible, periapical films, but did not specify the relative proportion of both techniques[44,63]. Standardised periapical radiographs should be adopted whenever possible because they have a better accuracy than panoramic radiographs, estimated within a range of 0.2 mm from actual values[85]. In adjunct to a low resolution, panoramic radiographs may cause image distortion rate averaging up to 25%[86]. However, it has to be acknowledged that in cases of extremely atrophic jaws in patients with a shallow vestibule, it might be practically very difficult to take periapical radiographs. Furthermore, in nine studies the radiographic evaluation was reported to be performed by a non-independent/not blinded evaluator or was not specified[20,29,31,32,37,42,56,59,60]. Therefore, the non systematic use of a standardised technique aiming at obtaining a precise and reproducible bone loss measurement poses an experimental limitation and suggests that the results of the present review should be cautiously interpreted.

The meta-analyses comparing axial versus tilted implants were performed at implant level. In fact, since all patients received both axial and tilted implants and no individual data was provided, it was not feasible to present results at patient level. The analysis took into account different factors. Considering the overall studies, peri-implant bone loss at 1 year of function did not show significant difference between axial and tilted implants, although there was a trend in favour of the axially placed implants. Only the study of Calandriello and Tomatis, which also included partial prostheses, was discordant with such a trend[76]. In that study, lower bone loss values for tilted implants were recorded, as compared to axial ones. The authors suggested that this could be related to the position of the implant neck relative to the bone crest: mesially, the neck was in a supracrestal position, while distally it was positioned subcrestally, resulting in a favourable soft tissue seal[76]. It should be considered that in the study by Calandriello and Tomatis[76], partial and complete restorations were analysed together, even though a different performance could be expected, given the biomechanical differences between complete and partial prosthetic rehabilitations. However, after performing a sensitivity analysis by excluding this specific study, the result did not substantially change, suggesting that the weight of this study was negligible, and highlighting the robustness of the meta-analysis.

In all the included studies, limited peri-implant bone loss was observed over a follow-up period of 1 year, the greatest value reported averaging 1.13 mm and 1.14 mm around axial and tilted implants, respectively[27]. In the nine studies reporting peri-implant bone loss after 3 or more years of function, a similar trend was observed, that is an overall limited bone loss around axial and tilted implants, with the latter presenting slightly higher (but not significant) bone loss values (Fig 3). The subgroup analysis showed that such a trend was unaffected by the arch and the prosthesis type, and a significant difference was achieved in the delayed loading studies but not in the immediate loading ones. However, one should consider that the sample size of delayed loading studies is very small respect to the immediate loading cases, preventing any comparison.

The results of the present review are slightly discordant with another recent meta-analysis on a similar topic[18]. That review found that marginal bone loss was lower (though not significantly) around tilted as compared to axial implants at 12 months, while the trend reversed in favour of the axial implants in studies with follow-up greater than 1 year. Our review adopted similar inclusion criteria but since we could count upon a more extended database of studies, a greater number of patients could be included. In fact most of the recent studies report a slight difference in bone loss in favour of axial implants at 12 months[29,31,40,42-44]. This trend is maintained in studies with a longer follow-up, this result being similar to that found in the review by Monje et al[18]. However, it must be acknowledged that, significant or not, the order of magnitude of the mean difference in marginal bone loss between axial and tilted implants (0.05 mm in the Monje et al review[18] and 0.06 mm in the present one at 12-months follow-up) can be considered clinically irrelevant.

In theory, the stress received by tilted implants under functional loading is higher than axially placed implants, which should result in greater marginal bone loss. Studies based on finite element analysis showed higher stress around a tilted implant neck[24,25]. The compressive stress can be up to five times higher around tilted implants when the load is applied vertically[24]. Furthermore, tensile stresses were shown to peak on the opposite side of the inclination[87], posing tilted implants in a situation of nonhomogeneous stress pattern[88]. *In vivo* animal studies showed that both cortical and trabecular bone remodelling is greater around non-axially placed implants under loading[89-90]. Nevertheless the present meta-analysis, like the previously published ones, did not support the hypothesis of greater bone loss around tilted implants.

The use of posterior tilting of the implants presents some biomechanical advantages as compared to the configuration based fairly axial position for all implants[22-23]. This could be due to several reasons. For example, tilting of the implants may allow using longer implants that may engage greater quantity of residual bone, which is beneficial to implant stability. In the majority of studies on tilted implants, length ranged from at least 10 mm up to 20 mm[20]. When increasing implant length, a more even distribution of stress around implants is achieved as shown by a number of computer-simulated studies[91-94]. Further important means for reducing stress around tilted implant necks are splinting into a fixed suprastructure and shortening of the distal cantilever, both producing favourable biomechanical situations[21,95-96]. These features were observed in most of the prosthetic configurations of the included studies. In all studies, tilted implants were splinted in both partial and full-arch reconstructions. The distalisation of the implant platform reduces the moments of force, improving the load distribution[22-23,78,97]. Recent finite element studies support the hypothesis that reduction of the cantilever length in a full-arch prosthesis, achieved by tilting of the distal implants, allows for a more widespread distribution of the occlusal forces under loading and consequently for a reduction of the stresses at the implant neck[23,95-96,98]. The findings of such computer-simulated studies may partially explain the favourable crestal bone level changes observed around tilted implants.

One limitation to the widespread use of tilted implants is the relative difficulty in the placement of the fixtures that must be inserted with a precise angulation, so as to engage as much cortical bone as possible. The latter is essential for achieving adequate primary implant stability, which is a prerequisite in case an immediate implant loading protocol is adopted, as in the majority of the studies included in the present review. However, in recent years, the placement of tilted implants has become easier due to the introduction of computer-guided implant planning and the widespread use of customised surgical mask.

The survival of tilted vs. axial implants was not the primary aim of the present review. Therefore the failure analysis performed on the studies included according to the specific criteria of this review is under-representative of the published evidence regarding tilted vs. axial implant survival. Nevertheless, the results of the present analysis are in line with those of other recent reviews that addressed this topic in a more comprehensive way[16-19].

In this review, slight statistically significant difference in implant survival at 12-months follow-up was observed, favouring axial over tilted implants (Fig 4), although, similar to what was discussed for marginal bone loss, such difference cannot be considered clinically relevant, being less than 1%. Regarding implant survival, a fair homogeneity was found among studies, as shown by the funnel plot in Fig 5. Due to the absence of randomised clinical studies, definitive conclusions cannot be drawn on the efficacy of rehabilitations supported by a combination of axial and tilted implants. However, based on the available included studies, the present review suggests that the prognosis of such a therapeutic approach is excellent, as only 1.54% of the implants was lost during the first year of loading, and only three failures were recorded thereafter.

From the implant failure analysis, some trends can be observed. Regarding the comparison between axial and tilted implants, the meta-analysis performed on the overall studies provided borderline significance ($P = 0.05$, Fig 4) in favour of the axial implants. However, such meta-analysis was strongly affected by a single study[29] in which 2 axial and 11 tilted implants failed (that is 40% of the overall failed tilted implants). Since the author of that study attributed most failures to the early cases in which there was scarce acquaintance with the all-on-four technique, we repeated the meta-analysis after excluding that study. Such sensitivity analysis displayed no significant difference in survival rate between axial and tilted implants ($P = 0.43$). The latter more closely reflects the standard clinical outcomes of most clinical studies included in the review as well as the results of all the subgroup analyses. In fact, when considering subgroups, no effect could be attributed to loading temporisation, to the arch or to a combination or both. In other words, as shown in Table 4, there was no significant difference in failure rate between axial and tilted implants when the immediate and the delayed loading cases were evaluated separately, though the latter was not significantly different between implants placed in the maxilla and those placed in the mandible.

The technical difficulty of placing angulated implants in the maxilla for surgeons not accustomed to such a technique has been claimed by some authors as a factor contributing to implant failure[29]. As a consequence, for achieving optimal outcomes when dealing with tilted implants, a learning curve is recommended and guided surgery might help in the early approaches.

The improvement in oral hygiene parameters frequently reported in some studies on tilted implants might reflect the easy maintenance of this type of rehabilitations, in which there is a relatively wide distance between fixtures. Another factor that might be accounted for such a good compliance is the high level of satisfaction correlated with this treatment, as reported by patients[45-46,49] in a few studies.

The most frequent complication reported by the included studies was the fracture of the acrylic prosthesis. One of the reasons addressed for such inconvenience was the progressive shift from a soft diet to a diet including hard food, as well as the wear of the resin due to repeated cycles of deglutition and mastication[38,44,63]. Furthermore, some authors pointed out that most fractures of the prosthesis occurred close to the temporary abutments of the anterior implants, which can be considered a relatively weak point[26,38,68]. In the study by Tealdo and co-workers, the provisional and definitive prostheses were made of cast metal (palladium-alloy) frameworks[69]. Metal reinforced frameworks, as suggested by these authors, are significantly stronger than all-acrylic resin frameworks since they provide increased rigidity, and could represent a solution for reducing the incidence of such complication.

The current review presents some limitations, which deserve to be discussed. First of all, the follow-up duration for most studies is in the short-medium range (Table 2). As a matter of fact, the introduction of tilted implants for supporting prosthetic rehabilitations is a relatively recent technique, which started to spread among clinicians during the past 10 years with the advent of the so-called "All-on-four" technique[15]. Studies evaluating the performance of tilted implants with a follow-up longer than 5 years are quite scarce[30,32,38,98]. Only one study on the all-on-four technique with a follow-up range of 10 years has been published to date but did not provide specific information about marginal bone loss around axial and tilted implants[98]. Besides, different implant-supported prosthetic designs, which differ regarding the total number of implants as well as the number and angulation of tilted implants were considered all together, thus neglecting any possible different performance. It should also be taken into account that the minimum angulation required to define an implant as tilted has not yet been established. Some studies arbitrarily defined a threshold of 15 degrees of inclination respect to the occlusa plane[20,80]. In the included studies, the inclination of the distal fixtures in the full-arch rehabilitations ranged from about 25 to 35 degrees for the mandible and from 25 to 45 degrees for the maxilla, respective to the occlusal plane. Only in the study by Calandriello and Tomatis was a higher inclination reported (45 to 75 degrees relative to the occlusal plane)[76]. In some studies, the angulation was standardised, while in most cases of extreme atrophy it was individually chosen according to the available bone[44,63,76]. Most of the studies were performed in private practice settings by experienced surgeons, and some report that multiple operators performed the surgeries. Though the latter might introduce a source of variability undermining the internal validity of the single studies, the relative homogeneity in outcomes suggests that the external validity of the results of this review is rather high, provided that the surgical operators are adequately skilled. The most consistent limitation, however, is represented by the low level of evidence for publications on this topic to date. This review, in fact, was based only on retrospective and single-cohort prospective studies (except for Capelli et al[71] and Grandi et al[40] that were multicentric prospective studies), which provided indications on the prognosis of the technique mostly in the short-medium term.

Conclusion

This review demonstrated that the tilting of implants does not induce significant alteration in crestal bone level change as compared to conventional axial placement after 1 year of function, and this trend apparently maintains up to 5 years of function. Due to the lack of evidence, no conclusion can be drawn regarding the fate of marginal bone around axial vs. tilted implants in the long term.

In rehabilitations supported by tilted and axial implants, there is a higher risk of implant failure in the maxilla as compared to the mandible, although no significant difference in bone loss was found around implants placed in the maxillary as compared to the mandible, independent of implant inclination. In the maxilla, the all-on-four concept is as successful as rehabilitations supported by five or more implants.

In order to determine the efficacy of tilted implants as an alternative to grafting techniques or to the use of short implants or other treatment options for the rehabilitation of edentulous atrophic jaws, randomised clinical trials with large sample size and long-term follow-up are urgently needed. The impact on the quality of life for the patients of these two alternative techniques cannot be ignored.

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