Marginal Bone Loss Around Dental Implants Inserted with Static Computer Assistance in Healed Sites: A Systematic Review and Meta-analysis

Jeison B. Carbajal Mejía, DDS[1]/Kazumichi Wakabayashi, DDS, PhD[2]/
Tamaki Nakano, DDS, PhD[3]/Hirofumi Yatani, DDS, PhD[4]

Purpose: *The radiologic outcomes of implants placed using static computer-guided surgery have not yet been systematically investigated. The purpose of this study was to evaluate the marginal bone loss (MBL) around dental implants inserted with static computer assistance in healed sites.* ***Materials and Methods:*** *An electronic search of publications in English from three databases (from 2000 to March 2015), including PubMed, Web of Science, and Cochrane Oral Health Group Trials Register, and a hand search of peer-reviewed journals for relevant articles were performed. Only clinical human studies, either randomized or nonrandomized, with at least 10 cases and a minimum follow-up time of 12 months, reporting on MBL were included.* ***Results:*** *The search strategy resulted in 18 publications, with 2,675 implants inserted with static computer assistance in healed sites. The pooled mean MBL at 1-year follow-up was 1.06 mm (95% CI: 0.83 to 1.30 mm; heterogeneity: random-effects model, I^2 = 99.38%; $P < .01$). Moreover, when considering studies with a 3-year follow-up only (n = 5; 748 implants), the pooled MBL was 1.48 mm (95% CI: 0.81 to 2.15 mm; heterogeneity: random-effects model, I^2 = 99%; $P < .01$).* ***Conclusion:*** *Within the limitations of this review, the MBL around dental implants placed in healed sites with computer-guided surgery seems to be a well-functioning one-stage alternative to extended two-stage conventional procedures if patients are appropriately selected and an appropriate width of bone is available for implant placement. However, current evidence is limited by the quality of available studies and the lack of comparative long-term clinical trials.* Int J Oral Maxillofac Implants 2016;31:761–775. doi: 10.11607/jomi.4727

Keywords: *bone loss, dental implants, flapless, guided surgery, immediate loading, stereolithography*

Over the past decades, technical and scientific advances in diagnostic and therapeutic methods in the biomedical field have produced substantial progress. In implantology, the introduction of cone beam computed tomography (CBCT), three-dimensional (3D) planning software, computer-aided manufacturing (CAM), and rapid prototyping (RP) have contributed to the development of guided surgery techniques.[1,2] Now, such a technology allows a "computer-aided" insertion of implants to their planned position, thus limiting the elevation of flaps and enabling the immediate loading of the inserted implants.

Initially, the introduction of computerized tomography (CT) into the medical field by Hounsfield[3] in the early 1970s was a breakthrough; however, this fell short because it was basically for diagnostic purposes, and it was not until 1993 that CT images began to be used in combination with virtual planning software[1,4,5] (Simplant, Materialise Dental) and later with CAM surgical guides for real dental implant placement.[6,7] Today, computer-guided implant surgery can be classified as dynamic, when the navigation device uses an optical tracking system, or static when using a surgical template fabricated by either stereolithography (rapid prototyping) or mechanical positioning devices that convert the virtual template into an actual one by executing computer transformation algorithms on a cast.[8]

Guided-implant surgery can be especially useful in cases with critical bone volume or anatomy where ideal implant placement is mandatory. Moreover, the use of this technique reduces the surgical intervention time, limits the elevation of flaps, avoids bone grafting

[1]PhD Candidate, Department of Fixed Prosthodontics, Osaka University Graduate School of Dentistry, Osaka, Japan.
[2]Associate Professor, Department of Fixed Prosthodontics, Osaka University Graduate School of Dentistry, Osaka, Japan.
[3]Associate Professor, Department of Fixed Prosthodontics, Osaka University Graduate School of Dentistry, Osaka, Japan.
[4]Professor and Head, Department of Fixed Prosthodontics, Osaka University Graduate School of Dentistry, Osaka, Japan.

Correspondence to: Dr Jeison Carbajal, Department of Fixed Prosthodontics, Osaka University Graduate School of Dentistry, 1-8 Yamadaoka, Suita, Osaka 565-0871, Japan. Email: carbajalds@gmail.com

procedures, reduces bacteremia, enables immediate loading, reduces surgical morbidity, and makes it easier for patients to understand the proposed procedures.[9,10] However, the introduction of this relatively new, sophisticated technique raises important questions about the long-term impact on success in implant dentistry.

One essential factor for the long-term success of dental implants is the peri-implant bone tissue. Even though there is no consensus regarding the definition of success in implantology,[11] the achievement and maintenance of osseointegration are recognized as crucial factors; therefore, the determination of marginal bone loss (MBL) is highly relevant, as it provides information to determine the peri-implant health status. Unfortunately, there is a lack of information regarding the changes in the crestal bone after placing implants with guided surgery.

Moreover, a recent study demonstrated that the classic drilling technique for implant osteotomy had less of a negative influence on immediate cell viability than guided surgery.[12] Such results are hypothesized to be related to the deficient irrigation that the use of guided surgery implies. In this regard, studies conducted independently by Bulloch et al[13] and Jeong et al[14] concluded that using surgical drill guides does not cause an increase in bone temperature greater than that seen with standard sequential drilling with or without a surgical guide. In contrast, Misir et al[15] evaluated the amount of heat generated in bone by two implant drill systems with and without using surgical drill guides at depths of 3, 6, and 9 mm. They suggested that preparing an implant site using surgical drill guides generates heat more than classical implant site preparation regardless of the irrigation type. Also, dos Santos et al[16] reported that guided surgery generates a higher bone temperature than classic drilling, and even though neither technique generated critical necrosis-inducing temperatures, its long-term effect on the peri-implant bone remains unknown.

With this background, the purpose of the present systematic review was to evaluate the MBL around dental implants inserted with static computer assistance in healed sites.

MATERIALS AND METHODS

Focused Question

The focused question in this systematic review was framed following the PRISMA statement[17] suggestions. It was elaborated as, "what is the marginal bone loss around dental implants inserted with static computer assistance in healed sites?":

- **P**articipants: Patients of any age receiving implants in healed sites.
- **I**ntervention: The insertion of dental implants with static computer guidance.
- **C**omparison: No comparison with other therapeutic modalities was made.
- **O**utcome: Peri-implant crestal bone level change (in millimeters).

Search Strategy

A search of three electronic databases, namely, PubMed, Web of Science, and Cochrane Oral Health Group Trials Register, for relevant articles published in the English language from January 1, 2000 to March 31, 2015 was performed. The search strategy included the combination of keywords using Boolean operators (OR, AND). The following terms were used in the search strategy:

- PubMed: (dental implant OR oral implant [all fields]) AND (three dimensional planning OR computer guided surgery OR computer aided surgery OR 3D navigation [all fields])
- Web of Science: (dental implant OR oral implant [topic]) AND (three dimensional planning OR computer guided surgery OR computer aided surgery OR 3D navigation [topic])
- Cochrane Library (Oral Health Group Trials Register): (dental implant OR oral implant) AND (3D navigation OR computer guided surgery OR computer aided surgery OR three dimensional planning)

Additionally, a manual search was performed in dental implant–related journals, including *The International Journal of Oral & Maxillofacial Implants, Clinical Implant Dentistry and Related Research, Journal of Oral Implantology, Clinical Oral Implants Research, Implant Dentistry, European Journal of Oral Implantology, Journal of Oral and Maxillofacial Surgery, British Journal of Oral and Maxillofacial Surgery, International Journal of Oral and Maxillofacial Surgery, Journal of Clinical Periodontology, Journal of Periodontology, International Journal of Periodontics and Restorative Dentistry, Journal of Prosthetic Dentistry, International Journal of Prosthodontics, Quintessence International,* and *International Journal of Computerized Dentistry*. Moreover, the reference list of relevant review articles on the subject was used to retrieve additional studies.

Inclusion Criteria

The following criteria had to be met for inclusion: *(1)* publication in peer-reviewed journals; *(2)* full text written in the English language; *(3)* clinical human studies (either randomized or nonrandomized); *(4)* static computer-guided implant insertion through virtual

3D planning based on CT/CBCT imaging; *(5)* minimum period of follow-up of 12 months; *(6)* implants placed in healed sites; *(7)* studies reporting on marginal bone loss around osseointegrated implants.

Exclusion Criteria

For this review, only articles regarding static computer-assisted implant surgery performed after virtual 3D planning based on CT/CBCT scans were considered. Hence, studies using real-time navigation systems (dynamic), guides fabricated based on CT/CBCT imaging but without the assistance of 3D navigation software, and bidimensional radiographic guides were not considered. Additional exclusion criteria were studies with zygomatic or pterygoid implants, studies with mini-implants for orthodontic reasons, studies reporting implants placed in reconstructed arches or requiring bone grafting, animal studies, in vitro studies, letters to the editor, case reports, cases series with less than 10 participants, technical reports, and review papers, although the bibliography of review studies was used to identify and to retrieve potential additional information.

Study Selection and Data Collection Process

Search results were imported as text files into EndNote Basic (Thomson Reuters) bibliographic manager software, and duplicates were identified and deleted. Then, titles and abstracts of the search-identified studies that fulfilled the eligibility criteria were individually assessed, and full texts of all eligible studies were downloaded. Any disagreement in the determination of eligibility was resolved by consensus.

Once the studies were selected for the final analysis, whenever available, data regarding the following parameters were retrieved by one reviewer (J.C.): study group, year of publication, study design, number of patients, patients' age, number of smokers, type of edentulism, follow-up, number of implants, number of failed implants, implant survival rate, implant dimensions, implant healing period/loading, grafting procedures, mean marginal bone loss, implant system, type of guide production, flap elevation, arches receiving implants (maxilla and/or mandible), type of prosthetic rehabilitation, opposing dentition, and prosthesis survival rate. If needed, authors of the potentially included papers were contacted via email to gather missing data. Two reviewers (H.Y. and K.W.) double-checked the extracted data, and if any disagreement arose, this was resolved by discussion.

Quality Assessment

The methodologic quality of the studies was evaluated with the Newcastle-Ottawa scale (NOS).[18] This scale assesses study quality by evaluating three domains: selection (four items), comparability (two items), and outcome for cohort studies (exposure for case-control studies, three items). According to this quality scale, a maximum of nine stars/points can be given to a study, and this score represents the highest quality, where six or more points was considered of high quality.

Data Synthesis and Meta-analysis

Meta-analysis was carried out using OpenMeta[Analyst] software (Agency for Healthcare Research and Quality) and Review Manager (version 5.3.3, The Nordic Cochrane Centre, The Cochrane Collaboration). This study aimed to combine the included investigations taking the MBL mean value and standard deviation as effect size. Therefore, the weighted mean difference and 95% confidence interval (CI) were calculated for the MBL. Statistical homogeneity among studies was determined using the Cochran Q-test and its associated P value, and the I^2 statistic. Data heterogeneity was considered when the P value was less than .1, and the I^2 statistic became increasingly higher. The I^2 statistic ranges from 0% to 100%, with 25% corresponding to low heterogeneity, 50% to moderate, and 75% to high. Where statistically significant ($P < .10$) heterogeneity was detected, a random-effects model was used to assess the treatment effects. Moreover, forest plots were produced to graphically represent the difference in outcomes when placing implants with computer assistance. Descriptive summaries of included studies were entered into tables, and a qualitative synthesis of the evidence was planned as well.

RESULTS

Literature Search

The study selection process is summarized in Fig 1. The initial electronic search strategy yielded 1,563 papers. One hundred nineteen articles were identified in more than one electronic search strategy (duplicates) and eliminated. The subsequent search at the title level exhibited 93 titles out of the remaining 1,444, and further screening at the abstract level identified 34 articles for full-text reading. After thoroughly screening the full-text reports, 20 studies were excluded because they did not meet the inclusion criteria. However, hand searching of the reference lists of selected studies yielded four additional papers. The reasons for exclusion are presented in Table 1.[19–37] Finally, a total of 18 studies published between 2005 and 2015 fulfilled the inclusion criteria applied in this systematic review.

Features of the Included Studies

Study Design and Patient Features

Detailed data of the 18 included studies are listed in Tables 2a and 2b.[38–55] Two RCTs,[43,54] 13 prospective studies,[38,40,42,44–51,53,55] and three retrospective analyses[39,41,52] were included in the meta-analysis. Four

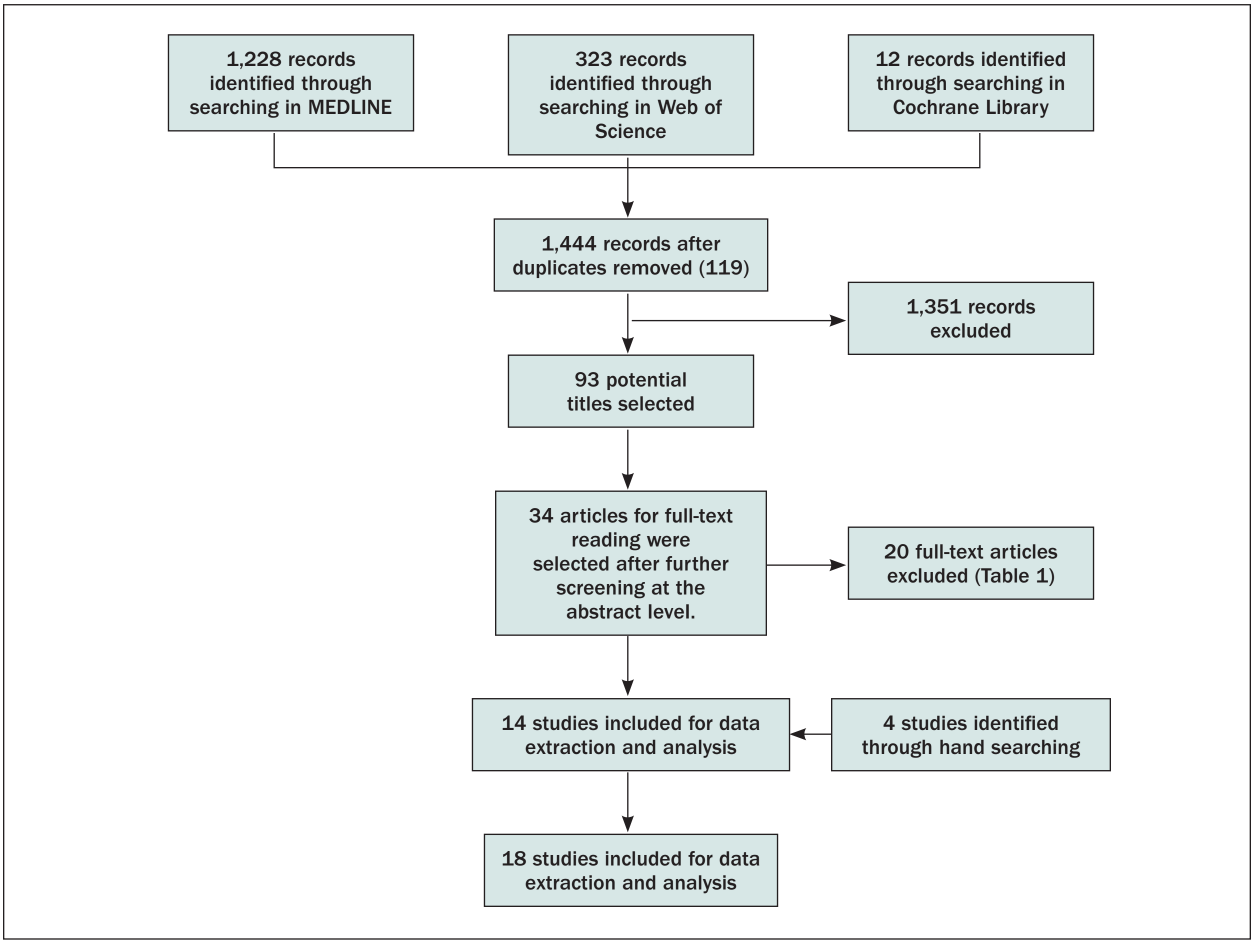

Fig 1 Flowchart of the study selection.

Table 1 Summary of the Excluded Articles

Reason for Exclusion	References
Unclear data and/or lack of parameters to evaluate bone loss	Pomares et al (2010)[19] Galindo et al (2012)[20] Tahmaseb et al (2012)[21] Schnitman et al (2015)[22]
Reconstructed arches	Meloni et al (2012)[23]
Follow-up less than 12 months	Ozan et al (2007)[24] Nickenig et al (2010)[25] Katsoulis et al (2012)[26]
Data for the same population reported in a later study or part of another study	Malo et al (2007)[27] Danza et al (2010)[28]
Implants placed in fresh extraction sockets	Meloni et al (2013)[29] Meloni et al (2013)[30]
Data for computer-guided implant placement in healed sites could not be separated from fresh extraction sockets	Danza et al (2011)[31] Danza et al (2011)[32] Meloni et al (2013)[33] Pozzi et al (2014)[34]
Systematic review	Voulgarakis et al (2014)[35] Chrcanovic et al (2014)[36] Tahmaseb et al (2014)[2] Moraschini et al (2015)[37]

studies were multicenter.[38,40,49,53] All studies reporting the outcome of interest had at least 12 months of follow-up. Two studies had a maximum follow-up of up to 5 years.[39,51] From the studies with available data of patients' age, two articles[49,52] did not inform about it but the age range was obtained after contacting the authors. The total number of patients ranged from 14 to 52. Fifteen studies[38–51,55] reported the mean age of study participants, which was from 51.8 to 71.9 years (age range, 20 to 92 years). Some patients in 12 studies[38–41,44,45,47,49,51,53–55] were smokers (range, 5 to 13), while three studies[43,46,50] did not mention it. One study reported the inclusion of patients previously diagnosed with and successfully treated for generalized chronic periodontitis before placing dental implants.[44]

Placement Site and Implant-Related Characteristics

A total of 2,675 implants were placed under static computer guidance in healed sites, with 61 failures (2.28%). Diameters and lengths ranged from 3.3 to 5 mm and 7 to 18 mm (except for one 5.5-mm implant[46]), respectively. The number of implants per study ranged from 36 to 314. Eleven studies[38–41,45,48–51,54,55] included only complete edentulous arches, and four studies[42–44,46] included only partially edentulous patients. Moreover, six studies[38,40,41,43,46,55] included implants placed only in maxillary arches, whereas another three studies[42,47,48] had implants exclusively in the mandible. In nine studies,[39,44,45,49–54] implants were placed in both the maxillary and mandibular arches.

From the 11 studies reporting on implants placed exclusively in completely edentulous arches, a total of 1,620 implants were inserted with 36 failures (2.22%), and 351 implants were inserted in exclusively partially edentulous arches (four studies), with 10 failures (2.84%). Furthermore, of the six studies evaluating implants inserted only in maxillae, a total of 652 dental implants were placed (12 failures, 1.84%), and for the mandible only (three studies), 357 implants were inserted (21 failures, 5.88%).

Surgical Technique

All implants were placed into healed sites without any bone grafting procedure. Regarding flap raising, two publications[44,54] reported the elevation of a full-thickness flap prior to static surgical guide positioning, whereas 14 studies did not raise any. Two studies[46,52] raised a miniflap at the discretion of the surgeon to preserve or enhance the surrounding soft tissue. Eleven studies[41,44,46–53,55] reported the implant insertion torque, which ranged from 30 to 50 Ncm except for Yamada et al,[55] who reported values ranging from 10 to 70 Ncm (mean, 57.7 Ncm). Four guided surgery systems were used in the included studies, namely, NobelGuide (Nobel Biocare),[38–41,45,46,48–53,55] Materialise (Materialise NV),[42,43,54] Implant 3D (Med3D),[44] and Facilitate (Dentsply Implants).[47,54] The most used system was NobelGuide (13 studies) followed by Materialise (3 studies), Facilitate (2 studies), and Implant 3D (1 study). Seventeen studies had their surgical guides fabricated by means of stereolithography, and only one study[44] converted the virtual template to an actual one by executing computer transformation algorithms on a cast.

Loading Protocols and Restoration Characteristics

All implants were immediately loaded in 13 studies,[38–41,43–46,48–51,55] 3 studies[47,52,53] reported loading the implants either immediately or after 2 to 4 months, and 2 studies[42,54] had 2 to 4 months of healing time before implant loading in all cases. Only four studies[43,46,48,55] provided information about the opposing dentition. Analysis of prosthetic procedures showed that seven studies[38–40,45,46,48,49] used immediate prosthesis, whereas seven studies used immediate-loading provisionals in all cases.[41,43,44,47,50,51,55] Definitive prostheses were placed 2 to 7 months after surgery.

Ten studies[38–41,45,48–51,55] evaluated patients receiving only fixed full-arch implant-supported prostheses, while three studies[42,43,46] included patients who received implants rehabilitated exclusively with fixed partial prostheses. Vercruyssen et al[54] rehabilitated all cases with either fixed full-arch implant-supported prostheses (n = 20) or implant-retained overdentures (n = 28). For the 10 studies assessing implants rehabilitated with only full-arch implant-supported prostheses, a total of 1,308 dental implants were placed with 36 failures (2.75%), whereas for the three studies rehabilitated exclusively with fixed partial prostheses, a total of 261 implants were inserted with 6 failures (2.29%).

Other Features

Study outcomes were assessed by clinical visual examination,[38–55] periapical radiographs,[38,40–52,54,55] panoramic radiographs,[39,45,49,53] probing,[43,45,48,53,54] and/or patient satisfaction questionnaires.[38,49,54,55] When evaluating bone level changes, either the implant shoulder[38,40–44,46–54] or an implant thread[39,45,55] was used as a reference point in relation to the alveolar bone crest.

Quality Assessment

In total, 16 studies were of high quality, and 2 were of moderate quality.[45,53] The scores are summarized in Table 3. The average score for the quality assessment of included studies was 6.61.

Quantitative Synthesis

The assessment of 18 studies included a total of 2,675 implants. The lowest and highest mean marginal bone loss was 0.32 mm and 2.05 mm, respectively, at the 1-year follow-up. The pooled MBL was 1.06 mm (95% CI: 0.83 to 1.30 mm; heterogeneity: random-effects model, $I^2 = 99.38\%$; $P < .01$; Fig 2). Moreover, when considering studies with a 3-year follow-up only (n = 5; 748 implants), the lowest and highest mean MBL was 0.60 mm and 1.90 mm, respectively, whereas the pooled MBL was 1.48 mm (95% CI: 0.81 to 2.15 mm; heterogeneity: random-effects model, $I^2 = 99\%$; $P < .01$; Fig 3).

The outcome was also classified in subgroups according to the type of edentulism: *(1)* completely edentulous patients and *(2)* partially edentulous patients. The pooled results showed an increase of the MBL when placing implants in completely edentulous patients (Fig 4): *(1)* mean MBL = 1.20 mm (95% CI: 0.93 to 1.48 mm; heterogeneity: random-effects model, $I^2 = 99.31\%$; $P = .00$) and *(2)* mean MBL = 0.81 mm (95% CI: 0.53 to 1.09 mm; heterogeneity: random-effects

Table 2a Features of the Included Studies

Study	Study design	Patients (n)	Patient age range (mean) (y)	Smokers included (n)	Edentulism
Van Steenberghe et al (2005)[38]	Prospective (multicenter)	27	34–89 (63)	5	Complete
Sanna et al (2007)[39]	Retrospective (unicenter)	26	38–74 (56)	13	Complete
Johansson et al (2009)[40]	Prospective (multicenter)	52	37–85 (72)	5	Complete
Meloni et al (2010)[41]	Retrospective (unicenter)	15	40–70 (52)	5	Complete
Nikzad et al (2010)[42]	Prospective (unicenter)	16	42–66 (51.9)	0	Partial
Van de Velde et al (2010)[43]	RCT (unicenter)	14	39–75 (55.7)	NM	Partial
Horwitz et al (2012)[44]	Prospective (unicenter)	18	34–69 (54)	5	Partial
Komiyama et al (2012)[45]	Prospective (unicenter)	29	44–92 (71.9)	3	Complete
Pozzi et al (2012)[46]	Prospective (unicenter)	27	38–77 (54.2)	NM	Partial
D'Haese et al (2013)[47]	Prospective (unicenter)	26	20–81 (51.8)	9	Partial (n = 13) Complete (n = 13)
Landazuri-Del Barrio et al (2013)[48]	Prospective (unicenter)	16	49–73 (59)	0	Complete
Marra et al (2013)[49]	Prospective (multicenter)	30	NM (61.9)	5	Complete
Browaeys et al (2014)[50]	Prospective (unicenter)	20	35–74 (55)	NM	Complete
Lopes et al (2014)[51]	Prospective (unicenter)	23	34–70 (55.4)[a]	2	Complete
Schnitman et al (2014)[52]	Retrospective (unicenter)	27	25–81 (NM)	0	Partial; complete
Vasak et al (2014)[53]	Prospective (multicenter)	30	31–80 (NM)	4	Partial; complete
Vercruyssen et al (2014)[54]	RCT (unicenter)	48	31–78 (NM)	6	Complete
Yamada et al (2015)[55]	Prospective (unicenter)	48	34–74 (56)	13	Complete

[a]Data obtained after contacting the author.

Table 2b Features of the Included Studies

Study	Marginal bone loss (mean ± SD) in mm	Guided surgery system	Drill guide production
Van Steenberghe et al[38]	1.15 ± 1.05	Nobel Biocare	Stereolithography
Sanna et al[39]	Overall: 0.95 ± 1.25 (1 y) S: 1.1 ± 1.4; NS: 0.8 ± 1.1 Overall: 1.20 ± 1.40 (2 y) S: 1.6 ± 1.6; NS: 0.8 ± 1.2 Overall: 1.60 ± 1.35 (3 y) S: 2.0 ± 1.6; NS: 1.2 ± 1.1 Overall: 1.95 ± 1.30 (4 y) S: 2.6 ±1.6; NS: 1.3 ± 1.0	Nobel Biocare	Stereolithography
Johansson et al[40]	1.3 ± 1.28	Nobel Biocare	Stereolithography
Meloni et al[41]	1.66 ± 0.20 (1 y); 1.81 ± 0.18 (1.5 y)	Nobel Biocare	Stereolithography
Nikzad et al[42]	0.55 ± 0.15	Materialise	Stereolithography
Van de Velde et al[43]	2.05 ± 0.46 (1 y); 1.95 ± 0.93 (1.5 y)	Materialise	Stereolithography
Horwitz et al[44]	0.65 ± 0.5	Implant 3D	Laboratory

Follow-up	Placed/failed implants (n)	Implant survival rate	Implant dimensions (width/length in mm)	Healing period/loading	Bone grafting
1 y	184/0 (Nobel Biocare)	100%	3.75–4.0/7–15	Immediate	No
5 y	183/9 (Nobel Biocare)	95%	3.75–5/8.5–15	Immediate	No
1 y	312/2 (Nobel Biocare)	99%	3.75–4.0/10–15	Immediate	No
1.5 y	90/2 (Nobel Biocare)	98%	4.3–5/10–13	Immediate	No
1 y	57/2 (Different manufacturers)	97%	3.3–5/8–15	2–4 mo	No
1.5 y	36/1 (Straumann)	97%	4.1–4.8/8–12	Immediate	No
1 y	50/4 (MIS implants)	92%	3.75–5/10–13	Immediate	No
1 y	165/3 (Nobel Biocare)	98%	NM	Immediate	No
3 y	81/3 (Nobel Biocare)	96%	3.5–5/5.5–18	Immediate	No
1 y	114/13 (Astra Tech)	89%	NM/8–15	Immediate (n = 13); 3 mo (n = 13)	No
1 y	64/6 (Nobel Biocare)	91%	4.0/10–15	Immediate	No
3 y	312/7 (Nobel Biocare)	98%	3.3–4/8.5–18	Immediate	No
3 y	80/0 (Nobel Biocare)	100%	3.75–4.0/10–15	Immediate	No
5 y	92/3 (Nobel Biocare)	97%	4/8.5–18	Immediate	No
1 y	100/0 (Nobel Biocare)	100%	3.5–4/8.5–18	Immediate (48 implants); 3–4 mo (52 implants)	No
1 y	163/2 (Nobel Biocare)	99%	3.5–5/8–16	Immediate (n = 17); 2–3 mo (n = 13)	No
1 y	314/0 (Astra Tech)	100%	3.5–4/8–15	3–4 mo	No
1 y	278/4 (Nobel Biocare)	99%	3.3–5/8.5–18	Immediate	No

Flap elevation	Region/Prosthetic rehabilitation/ opposing dentition	Prosthesis survival rate	Observations
No	Maxilla/FAP/NM	100%	Three patients smoked more than 10 cigarettes/day. One patient was withdrawn after 9 months because the fixed prosthesis was replaced for a removable one, yet the 1-year follow-up showed stable implants.
No	Maxilla, mandible/FAP/NM	NM	The smoking group was defined as smoking more than 10 cigarettes/day. Nine implants were lost (8 of them in smokers). Panoramic radiographs were used.
No	Maxilla/FAP/NM	96%	75 radiographs were not regarded as readable. More than 2 mm of marginal resorption was noted in 19% of the implants. Two patients dropped out.
No	Maxilla/FAP/NM	NM	Two patients smoked more than 10 cigarettes/day. One surgical guide was fractured during the operation.
No	Mandible/FPP/NM	100%	All failed implants belonged to one patient. Implants from different manufacturers were inserted (Zimmer Dental, Straumann, Astratech, and Easy Implant).
No	Maxilla/FPP/natural teeth, tooth- or implant-supported FPP	100%	Heavy smokers (> 10 cigarettes/day) were excluded. Six patients had bone augmentation procedures at least 6 months before implant surgery. Two patients were withdrawn (one needed bone grafting during implant placement and the other died for different reasons).
Yes	Maxilla, mandible/SC (n = 5), FPP (n = 45)/NM	NM	This study included patients previously diagnosed with and treated for generalized chronic periodontitis. The four failed implants were in two smokers.

Table 2b (cont) Features of the Included Studies

Study	Marginal bone loss (mean ± SD) in mm	Guided surgery system	Drill guide production
Komiyama et al[45]	1.2 ± 1.4	Nobel Biocare	Stereolithography
Pozzi et al[46]	0.57 ± 0.3 (1 y); 0.60 ± 0.3 (3 y)	Nobel Biocare	Stereolithography
D'Haese et al[47]	Overall: 0.47 ± 0.94; NS: 0.36 ± 0.89; S: 0.62 ± 1.05 E: 0.44 ± 1.41; PE: 0.42 ± 0.95	Dentsply Implants	Stereolithography
Landazuri-Del Barrio et al[48]	0.83 ± 0.14	Nobel Biocare	Stereolithography
Marra et al[49]	1.2 ± 0.7 (1 y); 1.9 ± 1.3 (3 y)	Nobel Biocare	Stereolithography
Browaeys et al[50]	1.13 ± 0.94 (1 y); 1.61 ± 1.4 (3 y)	Nobel Biocare	Stereolithography
Lopes et al[51]	1.7 ± 1.4 (1 y); 1.7 ± 0.9) (3 y) 1.9 ± 1.1 (5 y)	Nobel Biocare	Stereolithography
Schnitman et al[52]	1.46 ± 0.83	Nobel Biocare	Stereolithography
Vasak et al[53]	1.44 ± 1.35	Nobel Biocare	Stereolithography
Vercruyssen et al[54]	0.61 ± 0.86	Materialise (n = 24); Dentsply Implants (n = 24)	Stereolithography
Yamada et al[55]	0.32 ± 0.43	Nobel Biocare	Stereolithography

NM = not mentioned; SC = single crown; FAP = full-arch prosthesis; FPP = fixed partial prosthesis; S = smokers; NS = nonsmokers;

model, I^2 = 98.63%; *P* = .00). Also, when studies evaluated implants placed with static computer assistance in a defined group of smokers, there was a statistically significant effect of smoking on the magnitude of MBL (mean difference: 0.48 mm, 95% CI: 0.20 to 0.77 mm; *P* = .0009; heterogeneity: *P* = .26; I^2 = 25%, random-effects model; Fig 5).

DISCUSSION

Summary of Main Results

The present systematic review was conducted approaching the following question: what is the marginal bone loss around dental implants inserted with static computer assistance in healed sites? The results showed a mean MBL of 1.06 mm (SD = 0.12 mm) for dental implants placed with static computer assistance at the 1–year follow–up period and 1.48 mm (SD = 0.34 mm) after 3 years. This observation has important clinical implications, as the progression and amount of MBL are important data for the diagnosis

Flap elevation	Region/Prosthetic rehabilitation/ opposing dentition	Prosthesis survival rate	Observations
No	Maxilla, mandible/FAP/NM	100%	Three cases (patients with CPOD) were excluded because the assessment protocol could not be followed. Panoramic and intraoral radiographs were used. Only 136 (n = 68 implants) intraoral radiographs of 324 sites were available. MBL of more than 1.5 mm or 2.0 mm was observed in 42% and 27% of the sites, respectively.
No/ Miniflap	Maxilla/FPP/natural teeth or implant-supported FPP	100%	Heavy smokers (> 10 cigarettes/day) were excluded. 42 implants were tilted (25.57–34.79 degrees). Three implants failed in the same patient.
No	Mandible/FPP (n = 13) FAP (n = 13)/NM	81%	Thirteen implants were lost (12 in smokers). Five immediately loaded fixed dental prostheses had to be modified or removed in the first 12 months because of underlying implant failures.
No	Mandible/FAP/Removable complete denture	NM	A radiographic misfit was observed in 13 of 16 patients. Therefore, an extra laboratory procedure was necessary to allow perfect positioning of the prosthesis.
No	Maxilla, mandible/FAP/NM	100%	Panoramic and intraoral radiographs were used. Six patients were heavy bruxers.
No	Maxilla, mandible/FAP/NM	100%	There was a 20% radiographic dropout (n = 19 implants). At the end of the third year, 30% of the implants had already lost more than 1.9 mm. Forty implants were titled (20–40 degrees).
No	Maxilla,mandible/FAP/NM	100%	Two patients were heavy smokers (one of whom was a controlled HIV-positive patient). Two subjects dropped out. 30% of the patients experienced fracture of the definitive prosthesis.
No/ Miniflap	Maxilla, mandible/FPP; FAP; SC; Overdenture/NM	100%	Seventy-three (91.3%) of 80 implants had readable radiographs.
No	Maxilla, mandible/FPP (n = 21); FAP (n = 15); SC (n = 8)/NM	97%	38% of the implants did not have a readable radiograph. Panoramic radiographs were used. Implant failure was due to the lack of primary stability.
Yes (n = 24); No (n = 24)	Maxilla, mandible/FAP (n = 20); Overdentures (n = 28)/NM	NM	Two patients had an acute abscess formation and suppuration before loading, and three were diagnosed with peri-implantitis. They were treated with resective surgery and antibiotics. Four of them were smokers, and one had history of bruxism. One subject dropped out.
No	Maxilla/FAP/natural teeth, tooth- or implant-supported FPP, removable denture	100%	Four implants were lost in two smokers (two implants each) due to the lack of osseointegration before delivering the definitive prostheses.

E = edentulous; PE = partially edentulous; COPD = chronic obstructive pulmonary disease.

of peri-implant health. However, there is still no consensus regarding the ideal MBL expected around dental implants under function and its progression over time,[11] although a certain physiologic amount of dimensional bone loss will surely happen. In accordance with success criteria defined by Albrektsson and Isidor,[56] implant treatment can be considered successful if the peri-implant bone loss within the first year after loading is 1.5 mm or less and if, during the following years, bone loss of no more than 0.2 mm per year occurs. The results of this systematic review showed that the mean MBL around implants placed with computer guidance meets this success criteria.

Also, the outcome of interest was classified in subgroups according to the type of edentulism. The mean MBL in completely edentulous patients was 1.20 mm (SD = 0.14 mm), whereas partially edentulous patients showed a mean MBL of 0.81 mm (SD = 0.14 mm) during a follow-up of 1 to 3 years. The difference found when pooling data based on the type of edentulism (0.39 mm) is hypothesized to be related mainly to the effect of the extent of the restoration (full-arch, partial/single tooth prosthesis). With regard to this, similar values were found for the conventional technique. For instance, Gholami et al[57] reported a nonsignificant 0.40-mm difference in the MBL between implant-supported

Table 3 Quality Assessment of the Studies by the Newcastle-Ottawa Scale

	Selection				Comparability		Outcome			
					Comparability of cohorts					
Study	Representative of the exposed cohort	Selection of external control	Ascertainment of exposure	Outcome of interest not present at the start of the study	Main factor	Additional factor	Assessment of outcomes	Sufficient follow-up time[a]	Adequacy of follow-up	Total (9/9)
Van Steenberghe et al[50]	*	0	*	*	*	0	*	*	*	7/9
Sanna et al[51]	0	*	*	*	*	0	*	*	*	7/9
Johansson et al[52]	*	0	*	*	*	0	*	*	0	6/9
Meloni et al[53]	*	0	*	*	*	0	*	*	*	7/9
Nikzad et al[54]	*	0	*	*	*	*	*	*	*	7/9
Van de Velde et al[55]	*	*	*	*	*	0	*	*	*	8/9
Horwitz et al[56]	0	0	*	*	*	0	*	*	*	6/9
Komiyama et al[57]	0	0	*	*	*	0	*	*	0	5/9
Pozzi et al[58]	*	0	*	*	*	0	*	*	*	7/9
D'Haese et al[59]	0	*	*	*	*	0	*	*	*	7/9
Landazuri-Del Barrio et al[60]	*	0	*	*	*	*	*	*	*	8/9
Marra et al[61]	0	0	*	*	*	0	*	*	*	6/9
Browaeys et al[62]	0	*	*	*	*	0	*	*	0	6/9
Lopes et al[63]	0	0	*	*	*	0	*	*	*	6/9
Schnitman et al[64]	0	0	*	*	*	*	*	*	0	6/9
Vasak et al[65]	0	0	*	*	*	0	*	*	0	5/9
Vercruyssen et al[66]	*	*	*	*	*	0	*	*	*	8/9
Yamada et al[67]	*	0	*	*	*	0	*	*	*	7/9

[a]One year of follow-up was chosen to be enough for the outcome "marginal bone loss" to occur.[56]

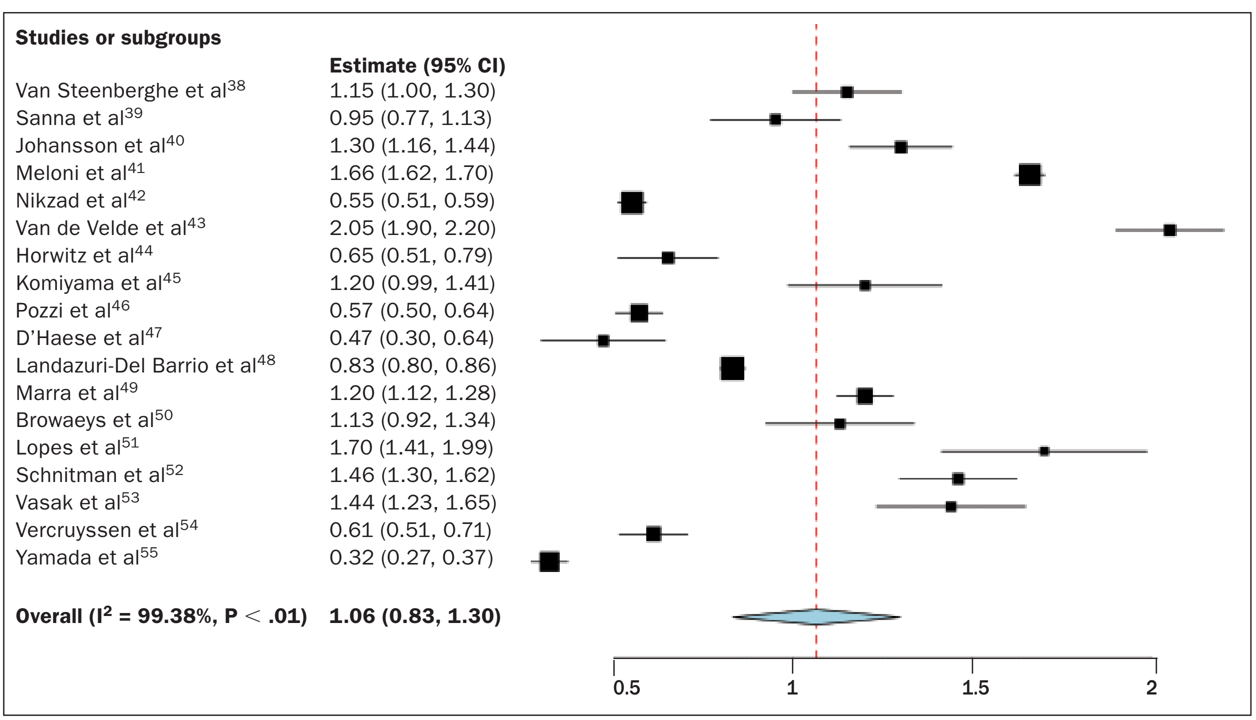

Fig 2 Forest plot for the event "marginal bone loss" at 1-year follow-up.

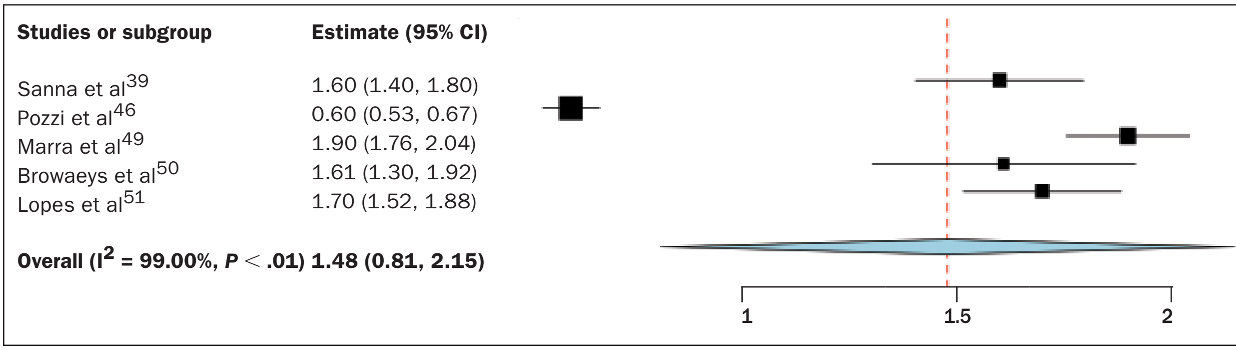

Fig 3 Forest plot for the event "marginal bone loss" at 3-year follow-up.

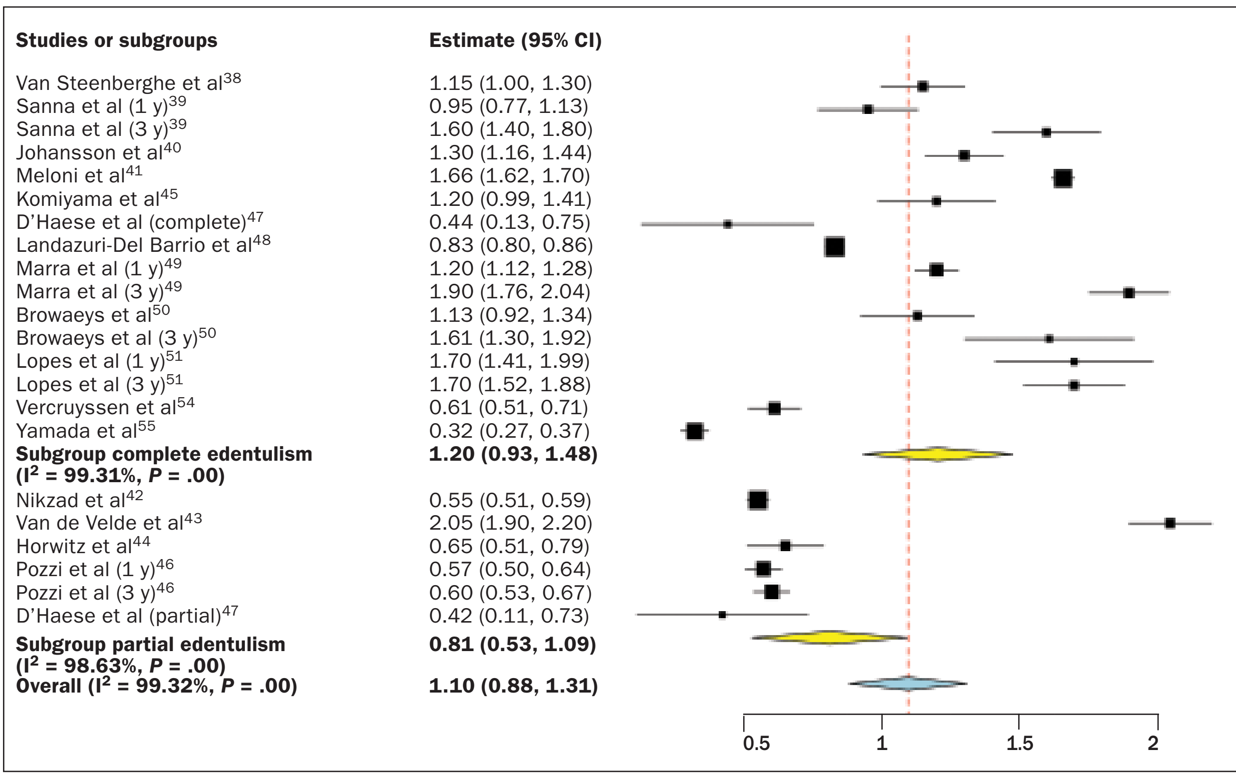

Fig 4 Forest plot for the event "marginal bone loss" when studies were pooled based on the type of edentulism.

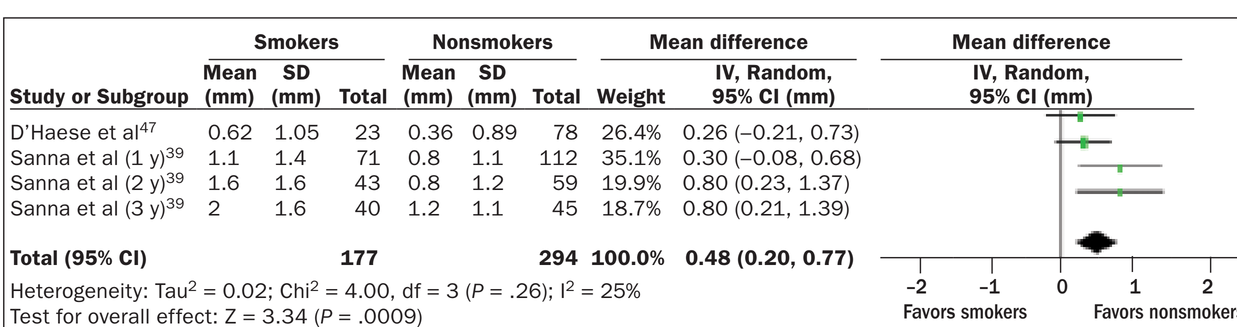

Fig 5 Forest plot of comparison of computer-guided implants placed in smokers versus computer-guided implants placed in nonsmokers for the event "marginal bone loss."

reconstructions in edentulous and partially dentate patients after a minimum of 5 years of loading. Also, in a recently published meta-analysis, Firme et al[58] found a 0.32-mm difference between single fixed prostheses and multiple-unit screw-retained prostheses.

Another factor evaluated for the outcome "MBL" was "smoking." The analysis of the two studies[39,47] reporting on the MBL in a group of smokers showed a statistically significant effect of smoking on the magnitude of MBL around implants placed with static computer assistance ($P = .0009$). This observation is in accordance with previous works showing that smokers have a higher risk of implant failure, peri-implantitis, and MBL than nonsmokers.[59–62] Also, most of the complications or failed implants occurred in smokers.[39,44,47,54,55] Therefore, smoking should also be considered as a risk factor for MBL when placing implants with computer guidance, yet there is insufficient evidence to draw robust conclusions.

On the other hand, there is some concern that heat-induced necrosis can occur during the guided flapless drilling,[13–16] because the sleeves limit direct irrigation from the active point of the drill (external irrigation). In addition, it was demonstrated that the classic drilling procedure is more favorable to cell viability than guided surgery.[12] As a result, one would argue that static computer-guided surgery might lead to more crestal bone loss over time, but the findings of the present review indicate that mean MBL values for computer-guided surgery are comparable to extended two-stage conventional procedures. It is worth mentioning, however, that in this review, three studies observed a mean MBL of more than 2 mm at the 1-year follow-up (Johansson et al[40] in 19% of all implants, Komiyama et al[45] in 27%, and Lopes et al[51] in 15.6%). The presence of "pressure-like-ulcers"[45] was suggested as a possible cause of MBL, although all studies speculated that such bone loss might be an intrinsic trait of the computer-guided technique.

Overall Completeness and Applicability of Evidence

Unlike two-stage conventional procedures, static computer-guided surgery offers the possibility of not raising a mucoperiosteal flap. Previous studies have shown that precluding the elevation of a flap may reduce the surgical trauma, the time spent during the operation, and patient's morbidity (eg, postoperative bacteremia, discomfort, swelling, and pain).[9,10,63] As a result, this approach has gained interest because some investigations also showed that raising a flap leads to bone resorption.[64–66] In contrast, it is noteworthy to address two studies that performed flap elevation in the present review. First, Horwitz et al[44] carried out a study in patients previously diagnosed with and treated for generalized chronic periodontitis, and after the 1-year follow-up, the mean MBL was 0.65 mm (SD = 0.5 mm). In spite of raising a flap and the previous history of periodontal disease, the annual mean MBL was less than 1.5 mm. Second, Vercruyssen et al[54] conducted a RCT to compare guided surgery with conventional implant placement. The computer-guided group was subdivided into mucosa-supported guides (without flap elevation) and bone-supported guides (with flap elevation), and after the 1-year follow-up, no significant differences were found between the flapless and the flap group (mean MBL= 0.61 mm, SD = 0.86 mm). Moreover, three recent systematic reviews[36,67,68] concluded that MBL of flapless interventions were comparable with the flap surgery approach, so it is prudent not to draw conclusions, as the influence of raising a flap on MBL remains unclear.

Another feature of computer-guided surgery is the possibility of immediate/early loading of implants. Immediate implant loading protocols have been proposed to reduce the time interval between implant surgery and the delivery of the prosthetic restoration with the objective of improving patient comfort and satisfaction.[69–72] In the present review, except for two studies,[42,54] all implants were immediately/early-loaded, and the difference found between the mean MBL after a 1-year and 3-year follow-up was 0.42 mm. This observation is in line with some recent studies evaluating the relationship between immediate loading and MBL.[73–75] For instance, Agliardi et al[73] evaluated the clinical and radiographic outcomes of immediate full-arch fixed maxillary prostheses supported by two axial and four tilted implants after 3 years of loading. For the variable marginal bone level change, the difference between the mean MBL after a 1-year and 3-year follow-up was 0.48 mm (axial implants) and 0.58 mm (tilted implants). Similarly, despite methodologic differences, Calandriello et al[74] found a clinically irrelevant difference of 0.31 mm and De Bruyn et al[75] of 0.36 mm, all favoring immediate loading. Furthermore, Xu et al[76] found that immediate and early loading of dental implants after flapless placement did not differ in terms of survival rate and MBL.

From all the aforementioned studies, the MBL around implants placed with computer assistance seems to be comparable with the conventional two-stage technique. However, the extrapolation of the results of this review to ordinary clinical practice should be made with caution, as the inclusion criteria of the majority of the included trials were strict, and only patients known to be ideal candidates for static computer-guided implant surgery were recruited. Also, experienced clinicians performed most of the surgeries in university hospitals, and it is important to bear in mind that in those trials with less experienced operators, some patients experienced a crestal bone loss of more than 2 mm at the 1-year follow-up.[40,45]

Quality of the Evidence

Peri-implant MBL is influenced by many factors, including surgical technique,[65] tissue thickness,[77] implant design,[78] implant positioning,[79] and the presence of a microgap[80] at the implant-abutment interface,[81] all of which may have affected the outcome of interest and not just the fact that implants were inserted with static computer assistance, so as mentioned before, the significance of the results should not be overstated because of its limitations.

On the other hand, when nonrandomized studies are included in systematic reviews and meta-analyses, potential biases are likely to be greater compared with studies including only RCTs; therefore, results should always be interpreted with caution.[82] Since static computer-guided implant placement is a relatively new technique, there is a lack of well-controlled long-term clinical trials; thus, narrowing the inclusion criteria increases homogeneity among studies, but it also excludes significant data.[83] In fact, in the present review, only two studies were RCTs, and from the remaining 16 studies, 13 were prospective studies, and 3 retrospective analyses; therefore, adding more information from observational studies may aid in clinical reasoning and establish a more solid foundation for causal inferences.[83] Having considered this, all included studies were evaluated using the Newcastle-Ottawa scale, and the mean score of all included papers was 6.61 from a maximum of 9 points, and according to this scale, 6 or more points was considered of high quality.

Presence and Impact of Potential Biases

In the present systematic review, five studies[40,45,50,52,53] had a radiographic dropout, as some films were regarded as "not readable." Also, only panoramic radiographs were used to measure MBL in two studies,[39,53] which might have made interpretation difficult, especially when examining the anterior region of the arches, although no significant differences of marginal bone level measurements between standardized intraoral and panoramic radiographs had been demonstrated.[84,85] Another potential source of bias in the review process could be the fact that only papers written in the English language were included.

Agreement with Previous Reviews

To the best of the authors' knowledge from indexed literature, the present study is the first to present a more comprehensive and detailed analysis of the MBL expected when placing computer-guided dental implants. It is noteworthy that Moraschini et al[37] partially addressed this issue in a recently published systematic review, but they included only eight studies and combined data without differentiating according to the follow-up time.

CONCLUSIONS

Within the limitations of this systematic review and meta-analytic approach to the literature, a moderate level of evidence indicates that the MBL around implants placed with static computer guidance in healed sites is not different from the criteria established for the standard technique during a follow-up of 1 to 3 years. Future well-controlled longitudinal comparative research is needed to draw robust conclusions and refine this technique.

ACKNOWLEDGMENTS

The authors deny any conflicts of interest related to this study. This study was not supported by any grant.

REFERENCES

1. Azari A, Nikzad S. Computer-assisted implantology: Historical background and potential outcomes-a review. Int J Med Robot 2008;4:95–104.
2. Tahmaseb A, Wismeijer D, Coucke W, Derksen W. Computer technology applications in surgical implant dentistry: A systematic review. Int J Oral Maxillofac Implants 2014;29:25–42.
3. Hounsfield GN. Computerized transverse axial scanning (tomography). 1. Description of system. Br J Radiol 1973;46:1016–1022.
4. Sethi A. Precise site location for implants using CT scans: A technical note. Int J Oral Maxillofac Implants 1993;8:433–438.
5. Verstreken K, Van Cleynenbreugel J, Marchal G, et al. Computer-assisted planning of oral implant surgery: A three-dimensional approach. Int J Oral Maxillofac Implants 1996;11:806–810.
6. Fortin T, Champleboux G, Lormée J, Coudert JL. Precise dental implant placement in bone using surgical guides in conjunction with medical imaging techniques. J Oral Implantol 2000;26:300–333.
7. Tardieu PB, Vrielinck L, Escolano E. Computer-assisted implant placement. A case report: Treatment of the mandible. Int J Oral Maxillofac Implants 2003;18:599–604.
8. Vercruyssen M, Fortin T, Widmann G, Jacobs R, Quirynen M. Different techniques of static/dynamic guided implant surgery: Modalities and indications. Periodontol 2000 2014;66:214–227.
9. D'haese J, Van De Velde T, Komiyama A, Hultin M, De Bruyn H. Accuracy and complications using computer-designed stereolithographic surgical guides for oral rehabilitation by means of dental implants: A review of the literature. Clin Implant Dent Relat Res 2012;14:321–335.
10. Arısan V, Bölükbaşı N, Öksüz L. Computer-assisted flapless implant placement reduces the incidence of surgery-related bacteremia. Clin Oral Investig 2013;17:1985–1993.
11. Papaspyridakos P, Chen CJ, Singh M, Weber HP, Gallucci GO. Success criteria in implant dentistry: A systematic review. J Dent Res 2012;91:242–248.
12. dos Santos PL, Queiroz TP, Margonar R, et al. Guided implant surgery: What is the influence of this new technique on bone cell viability? J Oral Maxillofac Surg 2013;71:505–512.

13. Bulloch SE, Olsen RG, Bulloch B. Comparison of heat generation between internally guided (cannulated) single drill and traditional sequential drilling with and without a drill guide for dental implants. Int J Oral Maxillofac Implants 2012;27:1456–1460.
14. Jeong SM, Yoo JH, Fang Y, Choi BH, Son JS, Oh JH. The effect of guided flapless implant procedure on heat generation from implant drilling. J Craniomaxillofac Surg 2014;42:725–729.
15. Misir AF, Sumer M, Yenisey M, Ergioglu E. Effect of surgical drill guide on heat generated from implant drilling. J Oral Maxillofac Surg 2009;67:2663–2668.
16. dos Santos PL, Queiroz TP, Margonar R, et al. Evaluation of bone heating, drill deformation, and drill roughness after implant osteotomy: Guided surgery and classic drilling procedure. Int J Oral Maxillofac Implants 2014;29:51–58.
17. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. Ann Intern Med 2009;151:W65–W94.
18. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 27 March 2015.
19. Pomares C. A retrospective study of edentulous patients rehabilitated according to the "all-on-four" or the "all-on-six" immediate function concept using flapless computer-guided implant surgery. Eur J Oral Implantol 2010;3:155–163.
20. Galindo DF, Butura CC. Immediately loaded mandibular fixed implant prostheses using the all-on-four protocol: A report of 183 consecutively treated patients with 1 year of function in definitive prostheses. Int J Oral Maxillofac Implants 2012;27:628–633.
21. Tahmaseb A, De Clerck R, Aartman I, Wismeijer D. Digital protocol for reference-based guided surgery and immediate loading: A prospective clinical study. Int J Oral Maxillofac Implants 2012;27:1258–1270.
22. Schnitman PA, Hayashi C. Papilla formation in response to computer assisted implant surgery and immediate restoration. J Oral Implantol 2015;41:459–466.
23. Meloni SM, De Riu G, Pisano M, Massarelli O, Tullio A. Computer assisted dental rehabilitation in free flaps reconstructed jaws: One year follow-up of a prospective clinical study. Br J Oral Maxillofac Surg 2012;50:726–731.
24. Ozan O, Turkyilmaz I, Yilmaz B. A preliminary report of patients treated with early loaded implants using computerized tomography-guided surgical stents: Flapless versus conventional flapped surgery. J Oral Rehabil 2007;34:835–840.
25. Nickenig HJ, Wichmann M, Schlegel KA, Nkenke E, Eitner S. Radiographic evaluation of marginal bone levels during healing period, adjacent to parallel-screw cylinder implants inserted in the posterior zone of the jaws, placed with flapless surgery. Clin Oral Implants Res 2010;21:1386–1393.
26. Katsoulis J, Avrampou M, Spycher C, Stipic M, Enkling N, Mericske-Stern R. Comparison of implant stability by means of resonance frequency analysis for flapless and conventionally inserted implants. Clin Implant Dent Relat Res 2012;14:915–923.
27. Malo P, de Araujo Nobre M, Lopes A. The use of computer-guided flapless implant surgery and four implants placed in immediate function to support a fixed denture: Preliminary results after a mean follow-up period of thirteen months. J Prosthet Dent 2007;97:S26–S34.
28. Danza M, Carinci F. Flapless surgery and immediately loaded implants: A retrospective comparison between implantation with and without computer-assisted planned surgical stent. Stomatologija 2010;12:35–41.
29. Meloni SM, De Riu G, Pisano M, et al. Computer-assisted implant surgery and immediate loading in edentulous ridges with dental fresh extraction sockets. Two years results of a prospective case series study. Eur Rev Med Pharmacol Sci 2013;17:2968–2973.
30. Meloni SM, De Riu G, Pisano M, Tullio A. Full arch restoration with computer-assisted implant surgery and immediate loading in edentulous ridges with dental fresh extraction sockets. One year results of 10 consecutively treated patients: Guided implant surgery and extraction sockets. J Maxillofac Oral Surg 2013;12:321–325.
31. Danza M, Grecchi F, Zollino I, Casadio C, Carinci F. Spiral implants bearing full-arch rehabilitation: Analysis of clinical outcome. J Oral Implantol 2011;37:447–455.
32. Danza M, Zollino I, Carinci F. Comparison between implants inserted with and without computer planning and custom model coordination. J Craniofac Surg 2009;20:1086–1092.
33. Meloni SM, De Riu G, Pisano M, et al. Implant restoration of edentulous jaws with 3D software planning, guided surgery, immediate loading, and CAD-CAM full arch frameworks. Int J Dent 2013;683423. doi:10.1155/2013/683423.
34. Pozzi A, Tallarico M, Marchetti M, Scarfò B, Esposito M. Computer-guided versus free-hand placement of immediately loaded dental implants: 1-year post-loading results of a multicentre randomised controlled trial. Eur J Oral Implantol 2014;7:229–242.
35. Voulgarakis A, Strub JR, Att W. Outcomes of implants placed with three different flapless surgical procedures: A systematic review. Int J Oral Maxillofac Surg 2014;43:476–486.
36. Chrcanovic BR, Albrektsson T, Wennerberg A. Flapless versus conventional flapped dental implant surgery: A meta-analysis. PLoS One 2014;9:e100624.
37. Moraschini V, Velloso G, Luz D, Barboza EP. Implant survival rates, marginal bone level changes, and complications in full-mouth rehabilitation with flapless computer-guided surgery: A systematic review and meta-analysis. Int J Oral Maxillofac Surg 2015;44:892–901.
38. van Steenberghe D, Glauser R, Blombäck U, et al. A computed tomographic scan-derived customized surgical template and fixed prosthesis for flapless surgery and immediate loading of implants in fully edentulous maxillae: A prospective multicenter study. Clin Implant Dent Relat Res 2005;7:S111–S120.
39. Sanna AM, Molly L, van Steenberghe D. Immediately loaded CAD-CAM manufactured fixed complete dentures using flapless implant placement procedures: A cohort study of consecutive patients. J Prosthet Dent 2007;97:331–339.
40. Johansson B, Friberg B, Nilson H. Digitally planned, immediately loaded dental implants with prefabricated prostheses in the reconstruction of edentulous maxillae: A 1-year prospective, multicenter study. Clin Implant Dent Relat Res 2009;11:194–200.
41. Meloni SM, De Riu G, Pisano M, Cattina G, Tullio A. Implant treatment software planning and guided flapless surgery with immediate provisional prosthesis delivery in the fully edentulous maxilla. A retrospective analysis of 15 consecutively treated patients. Eur J Oral Implantol 2010;3:245–251.
42. Nikzad S, Azari A. Custom-made radiographic template, computed tomography, and computer-assisted flapless surgery for treatment planning in partial edentulous patients: A prospective 12-month study. J Oral Maxillofac Surg 2010;68:1353–1359.
43. Van de Velde T, Sennerby L, De Bruyn H. The clinical and radiographic outcome of implants placed in the posterior maxilla with a guided flapless approach and immediately restored with a provisional rehabilitation: A randomized clinical trial. Clin Oral Implants Res 2010;21:1223–1233.
44. Horwitz J, Levin L, Gabay E, Zuabi O, Machtei EE. Immediate restoration of delayed placement of dental implants in patients with treated periodontal disease: 1-year results. Int J Oral Maxillofac Implants 2012;27:1569–1575.
45. Komiyama A, Hultin M, Näsström K, Benchimol D, Klinge B. Soft tissue conditions and marginal bone changes around immediately loaded implants inserted in edentate jaws following computer guided treatment planning and flapless surgery: A ≥ 1-year clinical follow-up study. Clin Implant Dent Relat Res 2012;14:157–169.
46. Pozzi A, Sannino G, Barlattani A. Minimally invasive treatment of the atrophic posterior maxilla: A proof-of-concept prospective study with a follow-up of between 36 and 54 months. J Prosthet Dent 2012;108:286–297.
47. D'haese J, Vervaeke S, Verbanck N, De Bruyn H. Clinical and radiographic outcome of implants placed using stereolithographic guided surgery: A prospective monocenter study. Int J Oral Maxillofac Implants 2013;28:205–215.
48. Landázuri-Del Barrio RA, Cosyn J, De Paula WN, De Bruyn H, Marcantonio E Jr. A prospective study on implants installed with flapless-guided surgery using the all-on-four concept in the mandible. Clin Oral Implants Res 2013;24:428–433.

49. Marra R, Acocella A, Rispoli A, Sacco R, Ganz SD, Blasi A. Full-mouth rehabilitation with immediate loading of implants inserted with computer-guided flap-less surgery: A 3-year multicenter clinical evaluation with oral health impact profile. Implant Dent 2013;22:444–452.
50. Browaeys H, Dierens M, Ruyffelaert C, Matthijs C, De Bruyn H, Vandeweghe S. Ongoing crestal bone loss around implants subjected to computer-guided flapless surgery and immediate loading using the All-on-4 concept. Clin Implant Dent Relat Res 2015;17:831–843.
51. Lopes A, Maló P, de Araújo Nobre M, Sanchez-Fernández E. The NobelGuide All-on-4 treatment concept for rehabilitation of edentulous jaws: A prospective report on medium- and long-term outcomes. Clin Implant Dent Relat Res 2015;17:e406–e416.
52. Schnitman PA, Hayashi C, Han RK. Why guided when freehand is easier, quicker, and less costly? J Oral Implantol 2014;40:670–678.
53. Vasak C, Kohal RJ, Lettner S, Rohner D, Zechner W. Clinical and radiological evaluation of a template-guided (NobelGuide) treatment concept. Clin Oral Implants Res 2014;25:116–123.
54. Vercruyssen M, van de Wiele G, Teughels W, Naert I, Jacobs R, Quirynen M. Implant-and patient-centred outcomes of guided surgery, a 1-year follow-up: An RCT comparing guided surgery with conventional implant placement. J Clin Periodontol 2014;41:1154–1160.
55. Yamada J, Kori H, Tsukiyama Y, Matsushita Y, Kamo M, Koyano K. Immediate loading of complete-arch fixed prostheses for edentulous maxillae after flapless guided implant placement: A 1-year prospective clinical study. Int J Oral Maxillofac Implants 2015;30:184–193.
56. Albrektsson T, Isidor F. Consensus report of session I. In: Mejía NP, Karring TS (eds). Proceedings of the 1st European Workshop on Periodontology. London: Quintessence, 1994:365–369.
57. Gholami H, Mericske-Stern R, Kessler-Liechti G, Katsoulis J. Radiographic bone level changes of implant-supported restorations in edentulous and partially dentate patients: 5-year results. Int J Oral Maxillofac Implants 2014;29:898–904.
58. Firme CT, Vettore MV, Melo M, Vidigal GM Jr. Peri-implant bone loss around single and multiple prostheses: Systematic review and meta-analysis. Int J Oral Maxillofac Implants 2014;29:79–87.
59. Chrcanovic BR, Albrektsson T, Wennerberg A. Smoking and dental implants: A systematic review and meta-analysis. J Dent 2015;43:487–498.
60. Wallace RH. The relationship between cigarette smoking and dental implant failure. Eur J Prosthodont Restor Dent 2000;8:103–106.
61. DeLuca S, Habsha E, Zarb GA. The effect of smoking on osseointegrated dental implants. Part I: Implant survival. Int J Prosthodont 2006;19:491–498.
62. Klokkevold PR, Han TJ. How do smoking, diabetes, and periodontitis affect outcomes of implant treatment? Int J Oral Maxillofac Implants 2007;22:S173–S202.
63. Arisan V, Karabuda CZ, Ozdemir T. Implant surgery using bone- and mucosa-supported stereolithographic guides in totally edentulous jaws: Surgical and post-operative outcomes of computer-aided vs. standard techniques. Clin Oral Implants Res 2010;21:980–988.
64. Job S, Bhat V, Naidu EM. In vivo evaluation of crestal bone heights following implant placement with 'flapless' and 'with-flap' techniques in sites of immediately loaded implants. Indian J Dent Res 2008;19:320–325.
65. Sunitha RV, Sapthagiri E. Flapless implant surgery: A 2-year follow-up study of 40 implants. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:e237–e243.
66. Tsoukaki M, Kalpidis CD, Sakellari D, Tsalikis L, Mikrogiorgis G, Konstantinidis A. Clinical, radiographic, microbiological, and immunological outcomes of flapped vs. flapless dental implants: A prospective randomized controlled clinical trial. Clin Oral Implants Res 2013;24:969–976.
67. Lin GH, Chan HL, Bashutski JD, Oh TJ, Wang HL. The effect of flapless surgery on implant survival and marginal bone level: A systematic review and meta-analysis. J Periodontol 2014;85:e91–e103.
68. Vohra F, Al-Kheraif AA, Almas K, Javed F. Comparison of crestal bone loss around dental implants placed in healed sites using flapped and flapless techniques: A systematic review. J Periodontol 2015;86:185–191.
69. Brånemark PI, Engstrand P, Ohrnell LO, et al. Brånemark Novum: A new treatment concept for rehabilitation of the edentulous mandible. Preliminary results from a prospective clinical follow-up study. Clin Implant Dent Relat Res 1999;1:2–16.
70. Engstrand P, Gröndahl K, Ohrnell LO, Nilsson P, Nannmark U, Brånemark PI. Prospective follow-up study of 95 patients with edentulous mandibles treated according to the Brånemark Novum concept. Clin Implant Dent Relat Res 2003;5:3–10.
71. Rocci A, Martignoni M, Gottlow J. Immediate loading in the maxilla using flapless surgery, implants placed in predetermined positions, and prefabricated provisional restorations: A retrospective 3-year clinical study. Clin Implant Dent Relat Res 2003;5:S29–S36.
72. Barndt P, Zhang H, Liu F. Immediate loading: From biology to biomechanics. Report of the committee on research in fixed prosthodontics of the American Academy of Fixed Prosthodontics. J Prosthet Dent 2015;113:96–107.
73. Agliardi EL, Pozzi A, Stappert CF, Benzi R, Romeo D, Gherlone E. Immediate fixed rehabilitation of the edentulous maxilla: A prospective clinical and radiological study after 3 years of loading. Clin Implant Dent Relat Res 2014;16:292–302.
74. Calandriello R, Tomatis M. Immediate occlusal loading of single lower molars using Brånemark System Wide Platform TiUnite implants: A 5-year follow-up report of a prospective clinical multicenter study. Clin Implant Dent Relat Res 2011;13:311–318.
75. De Bruyn H, Van de Velde T, Collaert B. Immediate functional loading of TiOblast dental implants in full-arch edentulous mandibles: A 3-year prospective study. Clin Oral Implants Res 2008;19:717–723.
76. Xu L, Wang X, Zhang Q, Yang W, Zhu W, Zhao K. Immediate versus early loading of flapless placed dental implants: A systematic review. J Prosthet Dent 2014;112:760–769.
77. Puisys A, Linkevicius T. The influence of mucosal tissue thickening on crestal bone stability around bone-level implants. A prospective controlled clinical trial. Clin Oral Implants Res 2015;26:123–129.
78. Shin YK, Han CH, Heo SJ, Kim S, Chun HJ. Radiographic evaluation of marginal bone level around implants with different neck designs after 1 year. Int J Oral Maxillofac Implants 2006;21:789–794.
79. Caneva M, Salata LA, de Souza SS, Baffone G, Lang NP, Botticelli D. Influence of implant positioning in extraction sockets on osseointegration: Histomorphometric analyses in dogs. Clin Oral Implants Res 2010;21:43–49.
80. Dias EC, Bisognin ED, Harari ND, et al. Evaluation of implant-abutment microgap and bacterial leakage in five external-hex implant systems: An in vitro study. Int J Oral Maxillofac Implants 2012;27:346–351.
81. Broggini N, McManus LM, Hermann JS, et al. Persistent acute inflammation at the implant-abutment interface. J Dent Res 2003;82:232–237.
82. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. (updated March 2011). The Cochrane Collaboration. Available at: http://www.cochrane-handbook.org. Accessed 6 March 2015.
83. Shrier I, Boivin JF, Steele RJ, et al. Should meta-analyses of interventions include observational studies in addition to randomized controlled trials? A critical examination of underlying principles. Am J Epidemiol 2007;166:1203–1209.
84. De Smet E, Jacobs R, Gijbels F, Naert I. The accuracy and reliability of radiographic methods for the assessment of marginal bone level around oral implants. Dentomaxillofac Radiol 2002;31:176–181.
85. Zechner W, Watzak G, Gahleitner A, Busenlechner D, Tepper G, Watzek G. Rotational panoramic versus intraoral rectangular radiographs for evaluation of peri-implant bone loss in the anterior atrophic mandible. Int J Oral Maxillofac Implants 2003;18:873–878.