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Clinical effects of conventional and underprepared drilling preparation of the implant site based on bone density: A systematic review and meta-regression

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Abstract

Purpose: There is no clinical consensus to determine the right balance between underpreparation and marginal bone level changes. The purpose of this systematic review and meta-regression was to investigate the influence of the type of drilling preparation of the implant site in relation to the bone mineral density on the clinical success, expressed in terms of the MBL and implant failure rate.

Study Selection: A thorough search was performed using the digital databases MEDLINE PubMed, EMBASE, and Cochrane Central Register of Controlled Trials by entering research lines or various combinations of free words. The main keywords used were "dental implants", "bone density", and "torque".

Results: The mean bone resorption in the conventional preparation group was -0.43 (± 0.28) mm, whereas it was -0.80 (± 0.37) mm in the underprepared group. For the D1/D2/D3 bone group, the slope was significantly different from zero and linearity; the D4 bone group slope was not significantly different from zero and was almost parallel, although it was significantly different from linearity. The box and whiskers plot shows that the MBL in underprepared sites tended to be significantly higher with a higher variation than that in conventionally prepared sites.

Conclusions: Within its limits, our meta-regression analysis showed that MBL is influenced by the type of drilling preparation and bone mineral density. In particular, a lower MBL was observed in the D1 bone with conventional preparation than with underpreparation. Moreover, a greater implant-to-osteotomy site mismatch was positively associated with greater MBLs in the bone densities of D1/D2/D3.

Keywords: Bone drilling, Bone density, Conventional preparation, Undersized preparation, Oral implantology

1. Introduction

Currently, one of the most important challenges in dental implant surgery is the optimization of techniques to obtain a high grade of stability. This is a key factor for survival and long-term predictability, especially in immediate loading procedures [1]. Implant stability can be classified as primary and secondary, which represent the mechanical retention of the bone at the time of implant insertion and the formation of biologically stable bone around the fixture, respectively [2,3].

A commonly used surgical protocol to obtain increased primary stability consists of under-dimensioning the preparation of the site, especially in the case of low-density bone. With this technique, also called underpreparation or underized drilling, an implant is inserted in a substantially smaller osteotomy than its diameter, and is typically obtained by skipping the use of the last drill from the drilling protocol. This leads to an immediate direct contact of the implant surface with the bone, which promotes primary stability, and is clinically perceived as insertion torque (ITQ) [4]. The initial bone-to-implant contact then undergoes a major change during the healing period and while functioning. The increased lateral compression induced by underpreparation might affect the local microcirculation and bone cellular responses, leading to bone compression necrosis [5]. A review by Insua et al. [6] clarified the bases of bone metabolism during implant healing and the processes that can lead to peri-implant bone loss. The review consistently demonstrated, from a cel-

lular and histological point of view, how the value of ITQ could be omitted, especially in cases with thick bone cortex. Furthermore, to avoid microfractures of the cortical bone resulting from a high value of ITQ, tap drilling is advisable. Therefore, the authors recommend that a customized drilling protocol based on the bone characteristics should be advocated.

At the beginning of the implantology era, very few customized preparation protocols existed in accordance with bone density. This was mainly due to the standardization of the loading protocols and the overlap and simplicity of the implant shapes.

As implants with different macro-designs were introduced and immediate loading protocols became a common procedure, the preparation protocols have become extremely varied. In fact, while each implant company has its own surgical site preparation protocol according to the implant shape and diameter, this is not exhaustive and standardizable in all cases because the clinical conditions of individual patients always differ [7].

Animal studies [8,9] have observed an increased predictability of implant treatment when the insertion resulted in an insertion torque ≥ 32 Ncm; however, there are conflicting opinions in literature on the limits of this value [10]. A high insertion torque (greater than 50 or 70 Ncm) has been shown to lead to the formation of microfractures, damage to microcirculation leading to bone necrosis especially in cortical or bicortical bones, alterations to the prosthetic connection, and changes in the surface roughness and microtopography of implants [5,11,12]. Another animal study noticed that implants inserted in underprepared sites with high ITQ (> 100 Ncm) induced considerable bone remodeling, circumferential to the implant [13]. Moreover, a recent clinical study observed that implants inserted with high-grade ITQ had greater marginal bone loss [14]. Conversely, some studies have shown that a high ITQ (≥ 50 Ncm) can lead to an increase in the survival rate compared to moderate torques [15]. Therefore, there is no consensus regarding the amount of insertion torque or optimal drilling protocol necessary to improve the clinical performance of implants in a certain bone density.

The purpose of this systematic review and meta-regression was to investigate the influence of the type of drilling preparation of the implant site, in relation to bone mineral density, on clinical success, as expressed by the marginal bone level (MBL) and implant failure rate. Therefore, conventional drilling protocols and underpreparation were compared.

2. Material and Method

The present review was conducted following the PRISMA guidelines (http://www.prisma-statement.org/) and its recent updates [16]. The review protocol was successfully submitted to the PROSPERO register (ID CRD42021268847), and the main question was formulated according to the PICOT format as presented below:

Patients (P): Patients undergoing implant surgery at healed sites without bone grafting procedures.

Intervention (I): Surgical protocols including drilling preparation with a different implant-to-osteotomy site mismatch, that is, the difference between the diameter of the implant neck and the diameter of the last drill used. This was considered when an additional drill was used for cortical preparation.

Comparison (C): A comparison was made between different bone densities by considering the following groups: hard bone (D1), medium bone (D2-D3), soft bone (D4), and cortical bone (D123).

Outcome (O): MBL (mm); if the value was not related to one of the groups listed above, the study was excluded. When studies involved more than one study group, only those groups that met the eligibility criteria of this review were considered. Implant failure was considered as a secondary outcome.

Time (T): From implant placement to a maximum of 15 months of follow-up

2.1. Focused questions

1) How is bone density related to the implant-to-osteotomy site mismatch and the MBL around the implant?
2) Which implant-to-osteotomy site mismatch produces the lowest MBL? Does it agree with the lowest failure rate?

2.2. Eligibility criteria

The following study characteristics were considered for this review:

- Randomized clinical trials (RCTs), non-randomized clinical trials, and retrospective cohort studies evaluating the outcomes of implant treatment in at least 10 patients (at least five patients per group).
- Studies in which implant surgery was performed only in healed sites that did not require bone augmentation or grafting.
- Studies specifying the drill sequence of the implant preparation or stating that the manufacturer's instructions should be followed in their protocol; if the drilling sequence was not retrievable, the study was excluded.
- Studies evaluating the MBL strictly between implant placement and up to 15 months.
- Only studies reporting MBL values (with standard deviation) stratified by bone density or with at least 95% of the implants placed in one of the bone density groups listed above were considered. In the latter case, it was assumed that all data belonged to the most represented bone density group.

2.3. Search strategy

A literature search was carried out using electronic databases (MEDLINE [PubMed], EMBASE, Cochrane Central Register of Controlled Trials), with an ad hoc search string: ((((((("Dental Implants"[Mesh]) OR "Immediate Dental Implant Loading"[Mesh]) OR "Dental Implants, Single-Tooth"[Mesh] OR "Dental Restoration Failure"[Mesh]) AND "Bone Density"[Mesh]) OR "Torque"[Mesh]) OR "Dental Restoration Failure"[Mesh]) AND "Alveolar Bone Loss"[Mesh].

For the Scopus database, the research line was adapted as follows: ("Dental Implants" OR "Dental Restoration Failure" AND "Bone Density" OR "Torque" AND "Alveolar Bone Loss") AND NOT INDEX (Medline). The research was implemented with a free search by entering different combinations of the following words: bone density, surgical implant protocol, surgical implant preparation, conventional preparation, underpreparation, MBL, implant failure, implant success, bone compression, and bone damage.

The last electronic search was conducted on September 20, 2021. A manual search was also performed in the following journals: British Dental Journal, British Journal of Oral and Maxillofacial Surgery, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Clinical Oral Investigations, European Journal of Oral Implantology, European Journal of Oral Sciences, Implant Dentistry, International Journal of Oral and Maxillofacial Implants, International Journal of Oral and Maxillofacial Surgery, International Journal of Periodontics and Restorative Dentistry, Journal of Clinical Periodontology, Journal of Dental Research, Journal of Dentistry, Journal of Maxillofacial and Oral Surgery, Journal of Oral and Maxillofacial Surgery, Journal of Periodontal Research, Journal of Periodontology, and Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology.

Backward citation search was conducted on the reference list of all identified clinical studies and relevant systematic reviews. Online registries providing information about the in-progress clinical trials were checked (https://clinicaltrials.gov; https://www.centerwatch.com; https://www.clinicalconnection.com). Only articles published in English were considered, and no date restrictions were imposed.

2.4. Study selection

The selection process was independently performed by two authors (DA and MDF). The first stage focused on examining the title and abstract; therein, a list of eligible studies was identified. The full text of all the eligible studies were reviewed to assess if the inclusion criteria were met.

Subsequently, the two authors compared the lists of the selected articles, and any discrepancies were discussed with a third author (LC) until a consensus decision was reached.

Interrater reliability (IRR) was assessed to estimate the concordance of the authors in the selection process and exclusion criteria codes. IRR was measured through Cohen's k coefficient and the result was interpreted in the following manner: ≤ 0, indicated no agreement; 0.01–0.20, none to slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; and 0.81–1.00, almost perfect agreement. A score of ≥ 80% was considered as an adequate result to satisfy the IRR.

2.5. Data collection

Data extraction was performed thoroughly. Information regarding the general characteristics of the study (such as the year, study design, number of patients, pre- or postoperative antibiotic administration, and number and position of implants) were retrieved and entered into a worksheet for subsequent analysis. A second table was set up to extract data for the meta-regression, in which the following information were collected: types of implant, implant diameters, collar characteristics, sequences of the surgical drill, number of implants per bone density (implants placed in D2 and D3 density were considered as a single category "medium bone density"), and MBL specific to the category of bone density listed above. If the bone loss was not divided by bone density, 95% of the implants belonged to category D123 (cortical bone) or D4 (no cortical bone) and the MBL was correlated to one or the other category.

The underpreparation coefficient was calculated by subtracting the diameter of the implant neck of the last drill used at the cortical level, and evaluating the mismatch. The drill sequence that was either recommended by the manufacturer or that specified within the surgical procedures described by the included studies, was considered. Regarding the manufacturer's specifications, the largest drill recommended at the cortical level was always used to assess the implant-to-osteotomy site mismatch. When data were not entirely accessible, the corresponding authors were contacted for clarification or further data. Four authors (Dr. C. Makary, Dr. M. Stocchero, Dr. A. Cucchi, and Dr. B. Pommer) provided the necessary information.

2.6. Risk of bias

The Joanna Briggs Institute (JBI) critical appraisal tools were adopted to assess the risk of including methodological or analysis errors. These tools allow us to evaluate different types of studies together. The appropriate checklist was used for each type of study (https://jbi.global/critical-appraisal-tools). Two authors (DA and MDF) performed the bias risk assessment independently and disagreements were resolved by consulting with a third author (LC). The domains evaluated in RCT studies were: fairness in the assignment (domain 1) and allocation (domain 2) of patients to control or treatment groups, similarity of study groups at the baseline that may result in selection bias (domain 3), blinding of patients (domain 4), those delivering treatment (domain 5) and outcome assessors (domain 6), fairness between the groups regarding treatment or care received (domain 7), completeness of follow-up information and reasons for withdrawal by the trial group (domain 8) and the presence of intention-to-treat (ITT) analysis (domain 9), reliability of the measuring instrument (domain 10) and reliability of the comparison method by excluding confounding factors (domain 11), appropriateness of statistical analysis (domain 12) and trial design (domain 13). The domain assessing the blindness of the operator performing the surgery (domain 5) has been removed as it was impossible for the operator to be unaware of the type of preparation he was performing. For non-randomized or retrospective studies, JBI critical appraisal tools checklist for cohort studies was applied. In this checklist, 11 domains are listed: fairness in the assignment (domain 1) and allocation (domain 2), exposure measured with a valid and reliable method (domain 3), identification (domain 4) and appropriate addressing (domain 5) of confounding factors, if patients/groups were free of the outcome at baseline (domain 6), reliability of instruments measuring the outcome (domain 7), appropriate duration of follow-up (domain 8), adequate description of follow-up (domain 9), suitable strategies to address incomplete follow-up (domain 10), and appropriateness of the statistical strategy (domain 11). Each domain was scored as "yes" (adequate), "no" (inadequate), "unclear," or "not applicable." Studies were stratified as: low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were judged adequate or one was judged unclear; moderate risk of bias (plausible bias that raises some doubt about the results) if two to four criteria were considered unclear or one was inadequate; or high risk of bias (plausible bias that seriously weakens confidence in the results) if more than one criteria was judged inadequate or more than four criteria was judged unclear.

2.7. Data analysis

The primary outcome for the present study was MBL, and the independent variable was implant-to-osteotomy site mismatch. To understand if there was a relationship between MBL and mismatch, meta-regression analyses were performed by aggregating data extracted from the included studies. Summary data for the continuous variables are expressed as mean value and standard deviation.
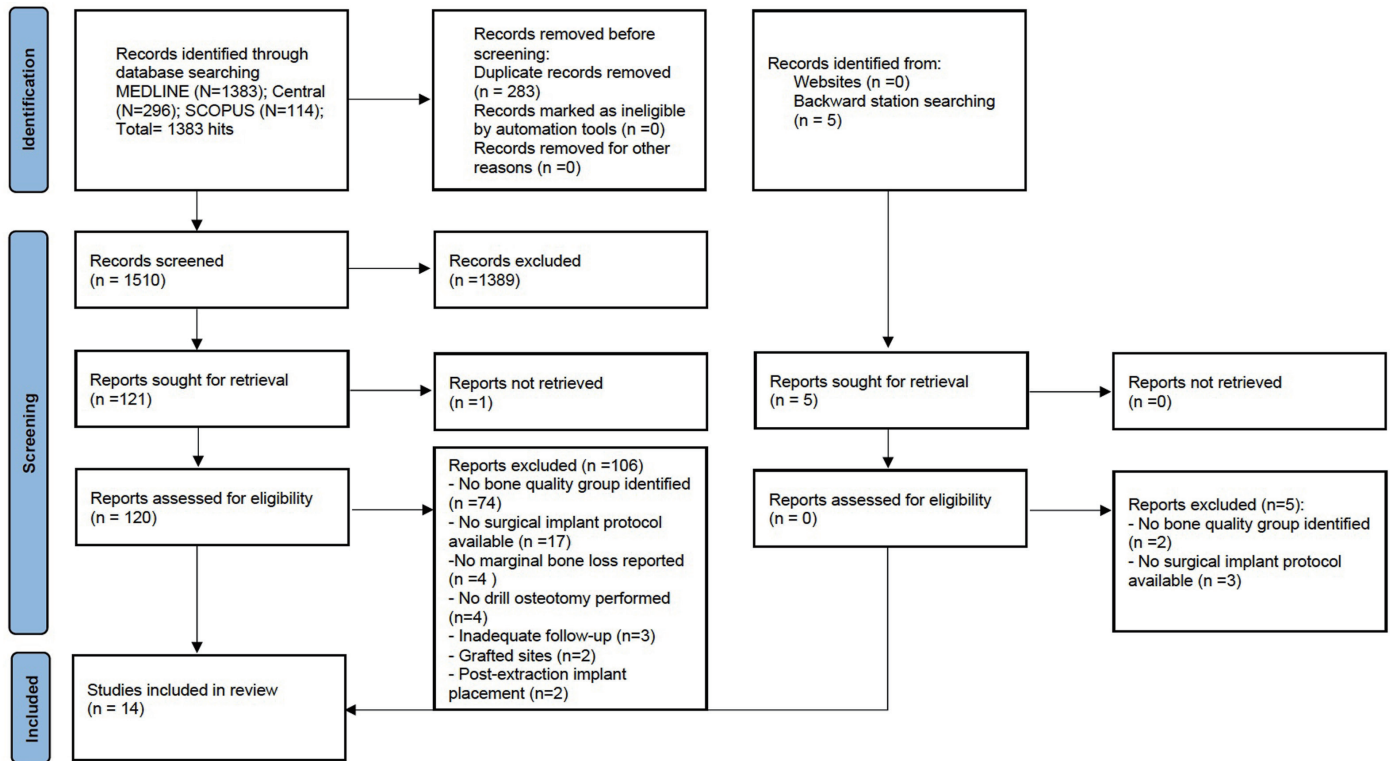
Fig. 1. Flow chart illustrating the screening process for the selection of articles

In the first analysis, the data were divided according to bone density, by combining data from D1, D2, and D3 groups, versus the D4 group. This was done because the cortical bone in the first three groups always contributes to primary implant stability, whereas in D4, the cortical bone is sometimes absent, and implant stability at placement is usually achieved by underpreparing the implant site. Another reason for this aggregation was to avoid excessive data fragmentation. As the original data were seldom available, the mean values from each study contributing to this analysis were used for both MBL and mismatch. The sample size (n) for each study was taken into consideration by repeating the mean values n times. To determine whether there was a significant difference between the regressions, the slopes were compared with best-fit analysis using GraphPad Prism software (Version 5.1, GraphPad Software Ltd., La Jolla, CA, USA).

In the second analysis, the data were divided according to the type of preparation (conventional vs. underpreparation). Mismatches equal to or greater than -0.20 mm were considered for the "conventional preparation" group, all others belonged to the "underpreparation" group. This threshold was derived from implant manufacturers' manuals or surgical guides such as Nobel Active and Nobel Speedy Manuals, Nobel Biocare, AnyRidge Manual, Megagem, Basic Information SLA, Straumann, Surgical and Restorative Manual, and JDentalCare. Linear regression analysis correlating MBL and mismatch was performed and the two regressions were compared as described above. In addition, the distribution of mean MBL of the conventional preparation and underpreparation groups was graphically represented using box and whiskers plot, and compared with the unpaired Student's t-test. The between-group difference in the overall implant survival was assessed using Pearson's chi-square test.

A probability value of P=0.05 was considered the significance threshold.

3. Results

Fourteen eligible studies [17-30] were included for meta-regression analysis. The IRR score from Cohen's k statistic at the full text article selection stage was 0.83 (83%), suggesting substantial agreement between the reviewers. The primary reason for exclusion was the impossibility of identifying a bone category with a corresponding MBL, as most studies provided a mean value for all bone densities; the second reason was the inability to retrieve the insertion protocol for outdated or unavailable implant lines. Further details of the data selection and collection process can be found in the flow-chart (**Fig. 1**).

The studies were categorized into six randomized control trials, seven clinical trials and one retrospective study. In the entire sample, the average age was 52 years, and women had higher participation. The administration of antibiotics was as follows: three studies did not report information, five employed preoperative and postoperative administration, three only preoperative, and three only postoperative administration. Thus, the majority of studies used at least preoperative prophylaxis. The full details of the included studies are presented in **Tables 1 and 2**.

3.1. Risk of Bias

Figures 2a and 2b show the risk of bias assessment for the RCTs and cohort studies, respectively. In total, six studies were assessed as having a moderate risk and eight as having a low risk of introducing

bias in the systematic review. In RCTs, information on ITT analysis and blinding of outcome assessors is often unclear and not reported. In cohort studies, the risk of bias was low, but two studies reported deficiencies in the description of the initial population and incompleteness of the inclusion and exclusion criteria. The overall risk of bias in the systematic review was considered moderate.

3.2. Qualitative Analysis and Meta-regression

The number of implants placed in the D123 and D4 groups were 1609 and 150, respectively. Considering the dichotomy by type of preparation, 484 implants belonged to the conventional preparation group and 1275 to the underpreparation group. The mean follow-up was 10.6 (± 2.6) months, which was suitable to investigate the early MBL. The mean bone resorption in the conventional preparation group was -0.43 (± 0.28) mm, whereas it was -0.80 (± 0.37) mm in the underpreparation group. Regarding bone density, the lowest marginal resorption occurred in the D1 subgroup and averaged -0.31 (± 0.22) mm (n = 51 implants).

A total of 38 implant failures were reported. The implant survival rate was 96.9% in the conventional preparation group and 98.2% in the underpreparation group; the difference was not significant (P = 0.095).

Figure 3 shows the trend of bone loss based on implant-to-osteotomy site mismatch in the two groups: implants placed in D1, D2, and D3 bone densities (D123) and implants placed in D4. The slopes of D123 and D4 groups was 0.71 (± 0.01) and 0.03 (± 0.04), respectively. For the D123 group, the slope was significantly different from zero and linearity (P < 0.0001 for both, determination coefficient $r^2 = 0.50$), whereas D4 was not significantly different from 0, and therefore almost parallel (P = 0.40, $r^2 = 0.005$), but was significantly different from linearity (P < 0.0001). Because the slopes differed substantially, it was not possible to test whether the intercepts differed significantly. Similar results emerged from the analysis of the conventional preparation vs. underpreparation groups (**Fig. 4**), with the trend in conventional preparation group almost parallel to zero (P = 0.16, $r^2 = 0.003$) and significantly different from zero in the underprepared group (P < 0.0001, $r^2 = 0.59$). Again, the difference between the slopes was extremely significant (P < 0.0001). The box and whisker plot in **Figure 5** shows that MBL in underprepared sites tends to be significantly higher (P < 0.0001) and to have a higher variation than in conventionally prepared sites.

4. Discussion

The purpose of this meta-regression was to determine which drilling preparation technique of the implant site could be more favorable for bone healing at different bone densities. In particular, considerable attention was paid to the MBL in relation to the mismatch between osteotomy and implant neck in the cortical and cancellous bones when conventional drilling or underpreparation was performed.

In this review, comparative studies that analyzed the osteotomy preparation protocols, implant body diameter, and qualitative assessment of the bone and MBL at different time points, were included. However, due to the lack of research necessary to conduct a meta-analysis, factors regarding the implant connection, abutment, material of the prosthesis, and crown-to-implant rate were not considered. Data on prosthetic load, type of healing (submerged or not),

and surface treatments were also collected as relevant confounding factors. Therefore, the purpose of the review was to examine the noninfectious aspects concerning the outcome of MBL.

As previously demonstrated in the literature, together with surgical trauma, MBL can also be affected by the biologic width reestablishment following prosthetic restoration [31].

However, because these biological processes occur subsequent to each other, early MBL (within the first 6 months) may be presumed to be mostly due to surgical trauma following site osteotomy and implant insertion [32]. This is the reason why the attention of the present study focused on short-term MBL.

Early MBL is thought to be a noninfectious reaction of the bone to surgical trauma [33].

Many studies have histologically demonstrated that implant insertion could cause overheating or excessive compression of the cortical bone with the formation of microfractures in early MBL [34,35]. Microfractures and overheating of the cortical bone are complications that can occur when placing an implant in an underprepared osteotomy [18,36]. Therefore, many studies have attempted to correlate the outcomes of MBL, implant survival, and success rate with primary stability calculated using the insertion torque (ITQ) [37].

ITQ represents the measurement of rotational resistance of the implant on the bone at the time of insertion [38]. Achieving optimal primary stability is essential for osseointegration. For this purpose, underpreparation of the implant site is often indicated in low-density bone (D3-D4) [36,39].

An insertion torque between 25 and 45 Ncm is recommended to prevent micromovements that can lead to fibrous encapsulation due to micromovements of the implant [40]. Unfortunately, it may be difficult to achieve this range in low-density bone (D3-D4). In such cases, underpreparation of the implant site is often indicated. However, this approach has become increasingly popular because of its short-term positive effect on the osseointegration process [41]. In fact, from a clinical perspective, it creates a wide mismatch between the implant body and osteotomy.

Some studies have pointed out that ITQ cannot be considered an absolute method for calculating primary stability, as it can also change depending on the design of the implant. From a theoretical perspective, ITQ can be divided into cutting torque influenced by the shape of the threads and compression torque influenced by the friction of the implant body on the bone [42,43].

As the coronal compression component of an implant is the most critical risk to the cortical bone, ITQ was not taken into consideration [44]. In particular, the diameter of the implant body, coronally without threads, was related to the diameter of the osteotomy to underline the risks of underpreparing the cortical bone. This conclusion was prompted by the need to enhance the friction component of the implant as opposed to the cutting component. The frictional component in contact with the cortical bone, which has a low modulus of elasticity, can lead to overheating of the bone and can subsequently lead to necrosis at temperatures above 47°C [45]. Furthermore, the excessively stressed cortical component can develop microfractures, resulting in bone necrosis with delayed healing or fibrointegration [46,47].

Table 1. Characteristics of the included study

Author Year	Type of study	Follow-up (month)	Antibiotics	Subject treated	Purpose of the study	implant	Implant position (maxilla/mandible)	Type of implant	Bone quality assessment
Makary 2019[17]	CT	12	Postoperative	14	Correlation implant type and implant stability	52	27/25	Anyridge (MegaGen, Gyeongbuk, South Korea).	Lekholm and Zarb
Toia 2017[18]	Retrospective study	5	Both	87	Bone responses to different implant-to-osteotomy mismatch	181	57/131	OsseoSpeed EV (Astra Tech Implant System)	Lekholm and Zarb
Hingsammer 2017[19]	CT	12	Both	30	The influence of the Crown-to-Implant Ratio and patient-parameters on early MBL	74	29/45	NobelSpeedy Groovy Shorty (Nobel Biocare)	Misch
De Santis 2016[20]	CT	6	Both	62	To achive highest primary stability	144	NR	NobelActive, Nobel TiUnite (Nobel Biocare)	Lekholm and Zarb
Cannizzaro 2015[21]	RCT	6	Preoperative	50	Bone responses to high (>80 Ncm) or medium (25 to 35 Ncm) insertion torque	100	38/62	NanoTite NT tapered (Biomet 3i)	Trisi
Rossi 2014[22]	CT	12	Postoperative	40	Clinical and radiographic outcomes of early loading of 6-mm implants	82	14/28	SLActive (Straumann)	Lekholm and Zarb
Arnhart 2012[23]	RCT	12	NR	177	Influence of different tapered design after immediate loading	325	103/222	NobelActive int, NobelActive ex, Nobel Replace (Nobel Biocare)	Lekholm and Zarb
Grandi 2012[24]	RCT	12	Both	30	To compare success rates of immediately and early loaded implants in partially edentulous patients	161	41/120	JDEvolution (JDentalCare)	Lekholm and Zarb
Shayesteh 2011[25]	RCT	12	Postoperative	15	To assess the bone loss in implants that were placed by the osteotome compared with the conventional drilling technique	23	maxilla	SLA (Straumann)	Lekholm and Zarb
Karabuda 2010[26]	RCT	15	Preoperative	22	Influence of different implant design	96	60/36	SLA and modSLA (Straumann)	Lekholm and Zarb
Park 2009[27]	RCT	12	NR	56	Influence of different implant design	75	mandible	Standar Plus (Straumann) and Ostemm TSII	Lekholm and Zarb
Johansson 2009[28]	CT	12	Both	52	Influence of different implant design	312	maxilla	TiUnite RP (Nobel Biocare)	Lekholm and Zarb
Fischer 2008[29]	CT	12	Preoperative	28	The aim was also to correlate implant stability with implant diameter bone quality, and marginal bone loss	53	maxilla	Replace Select TiUnite (Nobel Biocare)	Lekholm and Zarb
Rocci 2003[30]	CT	12	NR	46	The aim of the present study was to evaluate an immediate-loading treatment protocol	97	maxilla	Bränemark System Mk IV implants (Nobel Biocare)	Lekholm and Zarb

The table presents the relevant data collected from the included studies.
CT= Non-Randomized Clinical Trial, RCT= Randomized Clinical Trials, NR= Not Reported.

Table 2. Qualitative Result

Author Year	Gender (M/F)	Age (mean±SD /or range)	Type of Surgical Preparation	Failure Rate	D1 ITOM	MBL D1	N D1	D2-3 ITOM	MBL D2-3	N D2-3	D4 ITOM	MBL D4	N D4
Makary 2019[17]	4/8	52.3 ± 13.7	C/U	0%	0.3	-0.2(0.27)	16	-0.7	-0.11(0.11)	23	-1.1	-0.33(0.14)	7
Toia 2017[18]	76/75	60.8 ± 13.3	U	0%	-0.3			-0.3	-0.10(0.16)	18	-0.3	-0.19(0.16)	4
			C	0%	0	-0.41(0.54)	4	0	-0.12(0.13	32	0	-0.47(0.1)	2
			U	0%	-0.15	-0.09(0.09)	2	-0.15	-0.17(0.13)	6	-0.15	-0.18	1
			C	0%	0	-0.09(0.20)	11	0	-0.08(0.15)	52	0	-0.21(0.21)	2
Hingsammer 2017[19]	NR	52 ± 11.9	U	2.7%	-0.7	-0.66(0.72)	15	-0.9	-0.6(0.77)	38	-1.3	-0.65(0.68)	21
De Santis 2016[20]	27/35	57 (32 to 74)	U	1.4%				-0.3	-0.68(0.65)	35	-0.6	-0.73(0.46)	109
Cannizzaro 2015[21]	24/26	38.8 (18 to 71)	C	14%	-0.1		32	-0.1	D123 -0.26(0.35)	68	-0.1		
Rossi 2014[22]	13/22	51	U	5%	-0.6		7	-0.6	D123 -0.55(0.8)	31			
Arnhart 2012[23]	85/92	48.7 ± 13.7	U	4.3%	-0.3		16	-0.7	D123 -0.95(1.37)	98	-1.4		.
			C	3.7%	0.4		2	-0.16	-0.64(0.97)	76	-0.4		
			C	3.4%	0		14	0	D123 -0.64(0.17)	108	0		
Grandi 2012[24]	29/31	53 (41 to 65)	U	0%	0		5	-0.4	D123 -0.44(0.01)	156			.
Shayesteh 2011[25]			U	0%				-0.6	-0.34(0.21)	23			.
Karabuda 2010[26]	7/15	46.68 (24 to 58)	U	2.1%				-0.6	-0.44(0.09)	96			
Park 2009[27]	32/21	47.84 ± 11.70	U	1.5%			8	-0.6	-1.08(0.46)	24			
			U				7	-0.4	-0.79(0.42)	32			
Johansson 2009[28]	21/31	72 (37 to 85)	U	0.6%	-0.8		126	-1.2	D123 -1,3(1.28)	183			
Fischer 2008[29]	7/9	65 (52 to 81)	C	1.9%	0		1	0	-1.1(1.0)	49			
Rocci 2003[30]	20/26	51 (24 to 77)	U	9%				-0.9	D123 -1(1.1)	97			.

The table presents the numerical data on which the metaregression plots are based.
ITOM=implant-to-osteotomy mismatch, M=male, F=female, N=number, U=underprepared, C=conventional preparation.
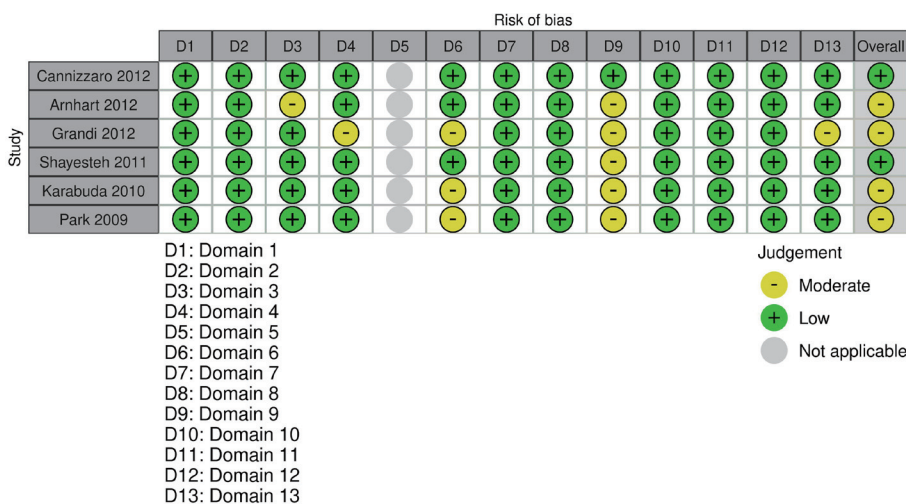
Risk of bias

Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	Overall
Cannizzaro 2012	+	+	+	+		+	+	+	+	+	+	+	+	+
Arnhart 2012	+	+	-	+		+	+	+	-	+	+	+	+	-
Grandi 2012	+	+	+	-		-	+	+	-	+	+	+	-	-
Shayesteh 2011	+	+	+	+		+	+	+	-	+	+	+	+	+
Karabuda 2010	+	+	+	+		-	+	+	-	+	+	+	+	-
Park 2009	+	+	+	+		-	+	+	-	+	+	+	+	-

D1: Domain 1
D2: Domain 2
D3: Domain 3
D4: Domain 4
D5: Domain 5
D6: Domain 6
D7: Domain 7
D8: Domain 8
D9: Domain 9
D10: Domain 10
D11: Domain 11
D12: Domain 12
D13: Domain 13

Judgement
- Moderate
+ Low
Not applicable

Fig. 2a. Risk of bias for RCT studies included in the present review

The implant cutting capacity is therefore a relevant factor, which may impact the dynamics of osseointegration [48]. The combination of osteotomy preparation and implant design features, namely implant body, thread shape, depth, and pitch, produces different spaces between the bone and the implant surface, and different responses are expected [49]. The cutting features at the apex and at the thread crest allow the implant to scrape the osteotomy walls, reducing the magnitude of compression. In fact, the thread cutting edge creates a mating thread that removes the bone, while bone debris is collected in chip cavities. Implant threads, besides providing

Fig. 2b. Risk of bias for cohort studies included in the present review

initial stability, can influence the secondary stability by enlarging the implant surface area and minimizing the peak stresses, which in turn generate bone microcracks [50].

From a biological point of view, the presence of microcracks in the cortical bone due to underdimensioned drilling protocols may affect the intracellular and extracellular flow of signals between osteocytes and cells of the osteocyte line [35,51-53]. This can also increase cytokines, resulting in a reduction of the signal. These phenomena are associated with an increase in osteocyte apoptosis and an increased release of receptor activator of nuclear factor-kappa B (RANKL) with osteoclastogenesis and bone resorption [51,52].

From a biomechanical point of view, the trabecular bone is porous and heterogeneous. Contrarily, the cortical bone is dense and homogeneous. Cortical bone has a higher mineralized component with a ratio of bone volume (BV) to total volume (TV) equal to 100%. Conversely, the trabecular bone has an estimated ratio between 50% and 70%. A study by Aghvami et al. [54] showed that temperatures above 47°C lead to apoptosis of osteocytes, and the heterogeneity of the trabecular bone positively affects heat dissipation. When the BV/TV ratio doubled from 50% to 100%, a thermally affected zone greater than 850 μm was obtained with the same osteotomy. This results in a greater risk of "death zones" in the cortical bone than in the trabecular bone. Overheating of the bone compromises the regenerative capacity of the tissue and consequently reduces its mechanical properties leading to early implant failure [53].

An *in vivo* study in sheep by Stocchero et al. [34] further showed that cortical overheating during implant insertion was a determining factor for bone healing. The study results demonstrated that a higher temperature (approximately 8°C compared to 4°C of the con-

ventionally prepared site) is present in an underprepared site during implant placement, resulting in a smaller amount of peri-implant bone after healing. Therefore, the authors recommend utilizing irrigation during implant insertion at low speed, using self-tapping implants, and preparing the implant site in relation to the density of the bone present.

An RCT by Markovic et al. [55] showed that both osteocompaction and drilling are safe procedures for implant insertion in the posterior maxilla. The results also demonstrated a higher temperature at the time of implant installation in the sites prepared with osteotomes than in those prepared with drilling. No significantly higher temperatures were found in implant sites with cortical thicker than 1 mm (3.37 ± 1.63°C for cortical thinner than 1 mm vs. 2.40 ± 1.06°C for cortical thicker than 1 mm). However, the limitations of this research are represented by the absence of MBL values, although the implant success at 6 months was 100%.

In this meta-regression analysis, bone preparations in D1/D2/D3 (D123) were merged because in these densities, there is a cortical with BV/TV equal to 100%. From a mechanical and thermal point of view, cortical bone has a similar healing pattern in D123 for the coronal portion of the osteotomy. D4 bone, being mainly trabecular, heterogeneous, and with a BV/TV ratio of 50–70%, was compared to D123 [56].

The results of the present analysis demonstrated a significant trend for lower MBL at sites where conventional preparation was performed compared to underpreparation. Moreover, in the underpreparation group, there is a trend for MBL to increase when the mismatch increases, while in conventionally prepared sites there is no significant effect of mismatch on MBL. Moreover, a greater mismatch
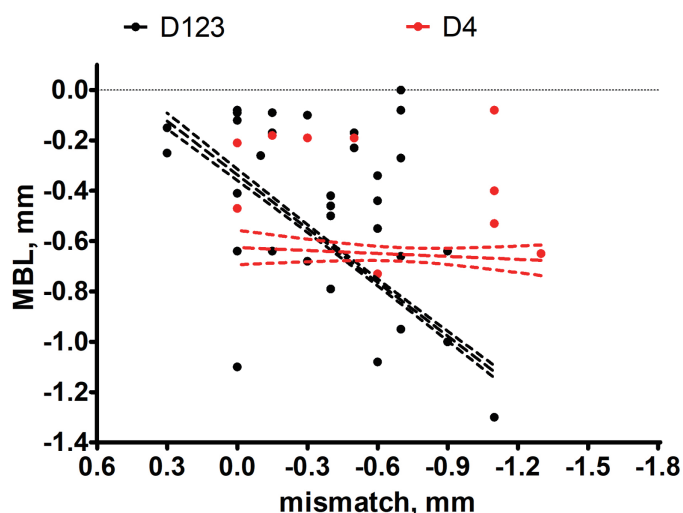
Fig. 3. Regression model describing the correlation between implant neck-to-osteotomy site mismatch and MBL in the two groups: implants placed in bone density D123 and D4 groups. MBL: Marginal Bone Level; mismatch: implant-to-osteotomy site mismatch.
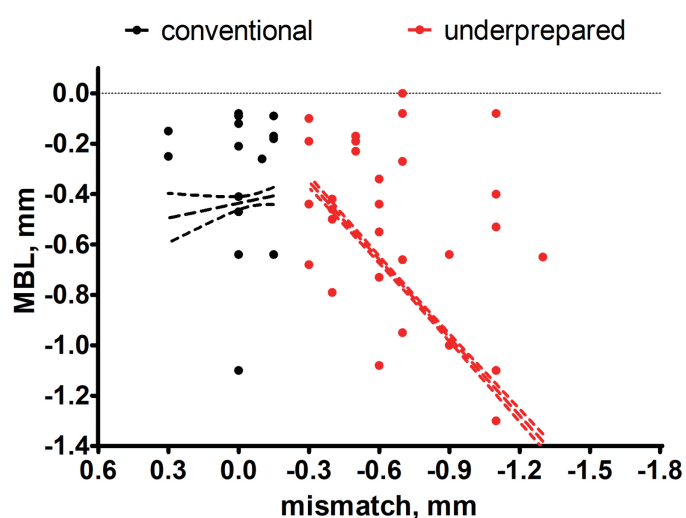

Fig. 4. Regression model describing the correlation between implant-to-osteotomy site mismatch and marginal bone level in the conventional preparation vs. underpreparation groups

was a predictive factor for a higher MBL in the D123 bone group than in the D4 group. In the latter group, MBL is not expected to change when the implant-to-osteotomy site mismatch varies. Conversely, in D123 bone, MBL tends to increase when the mismatch increases. If the overall slopes were identical, there is less than a 0.01% chance of randomly choosing data points with slopes this different. It can be concluded that the differences between the slopes are extremely significant. In the D4 group, an underdimensioned preparation of at least 0.2 mm appears to be necessary; however, when we perform relevant underpreparation (-1.2 mm), the MBL increased by just 0.1 mm. Of course, the overall D4 sample size was not very large because, to adhere strictly to the eligibility criteria, we had to exclude studies that placed implants in soft bone but classified them as D3 combined with D4. Despite this, the work of Thor et al. [57] agrees with the trend displayed in the regression plot (**Fig. 3**), reporting an MBL of -0.44 (0.79) mm with an implant-to-osteotomy site mismatch of -0.30 mm.

Interestingly, the success rate of implants placed with conventional preparation is higher than with underprepared osteotomy (98.2% vs. 96.9%). The difference was not statistically significant, perhaps due to the small sample size or the small number of studies included in the revision. Considering that most implant failures occur in the first year, it can be concluded that the obtained data agree with those of other reviews, even with longer follow-ups [58,59].

Although this study was the first to analyze the relationship between osteotomy, bone density, and implant diameter with meta-regression, there were some limitations due to the design of the clinical trials. To fully understand the behavior of the two different types of osteotomies in relation to bone density, it would be desirable to conduct RCTs that include the thickness values of the prepared cortical bone, the final diameter of the osteotomies of the cortical and trabecular bones separately, the diameter of the implant inserted in the various levels (apex, middle, and coronal), bone density, outcomes of early MBL, and success rate. In addition, pending further analysis, the type of healing (submerged or not submerged) could influence the early level of the bone, as reported by Troiano et al.
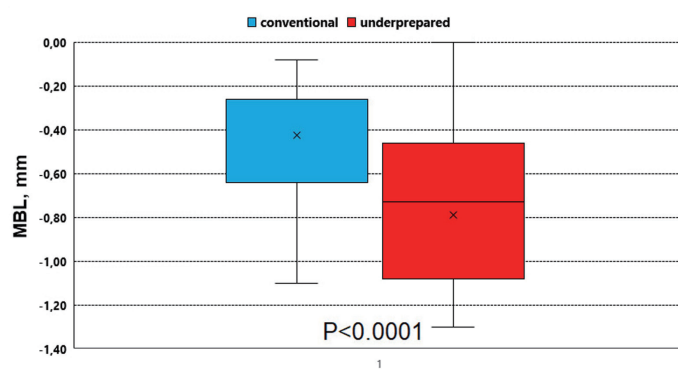

Fig. 5. The box and whiskers plot for marginal bone level in conventional and underpreparation groups

[1]; however, the effect size was small (approximately 0.16 mm). Standardized procedures can certainly facilitate comparison. Nevertheless, regarding the impact of implant placement and loading time, it was concluded that prosthetic loading does not affect the MBL in implants placed in healed sites [60]. One limitation of the present review is that the primary aim of the studies from which the data were extracted and compared was different from that of this review. We reorganized the data from the included studies according to our purpose. This indicates that the comparisons performed in most of the original studies did not match those performed in this review. This might have caused some inhomogeneities in the groups created for the analyses, forcing us to aggregate the data from different bone density groups. This also makes it challenging to determine whether the sample size of our analysis was adequate because tools such as trial sequential analysis, developed for post-hoc power analysis of RCT-based systematic reviews, could not be applied to this review. Furthermore, the difficulties in obtaining the MBL for each bone density, which causes a non-large sample group, could have influenced the overall result. It would be helpful to obtain more detailed and comprehensive data on site preparation, MBL separated by more in-

depth bone density information, and the difference in implant macro geometry.

Although the results of this review are clinically relevant, very few studies have specifically investigated this topic. Therefore, we believe that there is a prospect for future research, and randomized studies are needed to further explore and potentially confirm the findings presented herein.

5. Conclusions

The present meta-regression showed that the MBL is influenced by the type of drilling preparation and bone density in the first year. In particular, a lower MBL was observed in D1 bone with conventional preparations than that observed with underpreparation. Moreover, a greater implant-to-osteotomy site mismatch was positively associated with a greater MBL in D1, D2, and D3 bone densities. Finally, no differences in implant failure rates were noted between conventional and underprepared drilling in all bone types.

Based on these results, practitioners should carefully select the drilling sequence based on bone density to achieve optimal primary stability preserve the crestal-bone morphology.

To better understand the implications of these results, future studies could address the relationship between the mismatch of osteotomy and implant diameter at different bone densities.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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