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Piezoelectric bone surgery for implant site preparation compared with conventional drilling techniques: a systematic review, meta-analysis and trial sequential analysis

KEY WORDS

implant site preparation, implant stability, piezosurgery, trial sequential analysis

ABSTRACT

Purpose: To evaluate whether the use of piezoelectric bone surgery (PBS) for implant site preparation reduces surgical time, improves implant stability, preserves marginal bone level and improves the survival rate of oral implants compared with conventional drilling techniques.

Materials and methods: This meta-analysis followed the PRISMA (preferred reporting items for systematic review and meta-analysis) guidelines and was registered in the PROSPERO (international prospective register of systematic reviews) database (CRD42019142749). The PubMed, Embase, Scopus and Open Grey databases were screened for articles published from 1 January 1990 to 31 December 2018. The selection criteria included randomised controlled trials (RCTs) and case-control studies (CCTs) comparing the PBS with conventional rotary instruments for implant site preparation, and reporting any of the selected clinical outcomes (surgical time, implant stability, marginal bone variations and implant failure rate) for both groups. The risk of bias assessment was performed using the Cochrane Collaboration tool for RCTs and the Newcastle-Ottawa scale (NOS) for CCTs. A meta-analysis was performed, and the power of the meta-analytic findings was assessed by trial sequential analysis (TSA).

Results: Eight RCTs and one CCT met the inclusion criteria and were included in the review. The meta-analysis and the TSA showed moderate evidence suggesting that the PBS prolongs surgery duration and improves secondary stability 12 weeks after implant placement compared with conventional drilling techniques. Insufficient data are available in literature to assess if the PBS reduces marginal bone loss and/or improves the implant survival rate compared with conventional drilling techniques.

Conclusions: Adequately powered randomised clinical trials are needed to confirm the PBS positive effect on the secondary stability and to draw conclusions about the influence of PBS on marginal bone stability and implant survival.

Conflict of interest statement: *The authors report no conflicts of interest related to this study. The present study received no external funding.*

Introduction

The successful osseointegration of dental implants is characterised by the establishment of direct bone-to-implant contact without interposition of non-osseous or connective tissue[1,2]. This phenomenon is influenced by the combined effects of implant characteristics (macro- and micro-geometry, biocompatibility) and the implant site preparation technique[3-6]. Implant bed preparation is fundamental to achieve the ideal compromise between mechanical and biological features, providing adequate interlocking between implant and surrounding bone until primary stability is replaced by biological stability. This is a prerequisite for osseointegration, since detrimental micro-movements during the early healing period can lead to fibrous encapsulation and primary implant failure[7,8]. Although undersized implant osteotomies have proven to enhance primary stability[9], the biological consequences of this method have not been fully elucidated[10]. Some studies suggest that a high insertion torque may cause excessive peri-implant bone compression, resulting in extensive bone remodelling during the healing period[11,12]. Other studies, however, reported no difference in marginal bone levels or implant failure rates when placing implants using a high insertion torque[13,14]. In fact, early bone healing around implants is influenced by numerous variables, including patient-related factors (individual healing response, systemic disease and/or medication, smoking, bone density and alveolar crest width) and surgical trauma related to site preparation (bone overheating, cortical compression and damage to trabecular micro-architecture)[6,15-23].

Alternative techniques have been introduced to overcome the limitations of conventional drilling for implant site preparation, including osteotomes, erbium-doped yttrium aluminium garnet (Er:YAG) laser, osseodensification burs and piezoelectric devices[24]. Piezoelectric bone surgery (PBS) has been proposed in this field to improve surgical control, safety and the bone healing response. Piezoelectric devices modulate the ultrasonic vibration of an active tip and present three main advantages: precise and controllable cutting, selective action on mineralised tissues, and improved intra-operatory visibility due to cavitation of a cooling saline solution[25-28]. Furthermore, PBS enhances the bone healing response in the early postsurgical phase by promoting angiogenesis[29], reducing inflammation and promoting a faster release of bone morphogenetic proteins[30-32].

Numerous clinical studies and recent systematic reviews have already investigated the influence of ultrasonic site preparation on the clinical outcomes of implant therapy[24,33-37]. However, a quantification of the statistical reliability of results in the cumulative meta-analysis, adjusting significance levels for sparse data and repetitive testing on accumulating data, is needed. Hence, the aim of the present systematic review, meta-analysis and trial sequential analysis, was to analyse the clinical outcomes of implant therapy (implant stability, marginal bone loss [MBL], surgical time and implant survival rate), comparing the PBS with conventional drilling for implant site preparation. The present meta-analysis was conducted with strict inclusion criteria for the study selection (only prospective studies with a control group), and statistical reliability of data in the meta-analysis, were quantified by means of a trial sequential analysis (taking into consideration type 1 and 2 errors).

Materials and methods

Protocol and search strategy

The present systematic review is in accordance with the PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines[38], and was registered in PROSPERO (international prospective register of systematic reviews) (www.crd.york.ac.uk/PROSPERO), with the registration number: CRD42019142749.

Focus question

The PICO (Patient, Intervention, Comparison and Outcome) question this review aimed to answer was: "Does the PBS for implant site preparation, compared with conventional drilling techniques,

reduce surgical time, improve implant stability, preserve marginal bone level and improve the survival rate of oral implants?".

- Population: patients requiring dental implants
- Intervention: PBS for implant site preparation
- Comparison: conventional drilling for implant site preparation
- Outcomes: surgical time, implant stability, MBL, implant failure.

Information sources

An extensive electronic search was conducted by two independent reviewers (G.S. and F.B.), who screened in duplicate the PubMed, Embase, Scopus and Open Grey databases from 1 January 1990 to the latest entry, on 31 December 2018. No language restriction was applied to limit the selection bias.

Search

The search in the selected electronic databases was performed using the following algorithms:

- PubMed: (piezosurgery OR piezo* OR ultrasonic* OR rotary instrument* OR conventional drill* OR twist drill*) AND (implant site preparation OR implant osteotomy);
- Embase: ((piezosurgery:ti OR piezo$:ti OR ultrasonic$:ti OR 'rota$ intrument$':ti OR 'conventional drill$':ti OR 'twist drill$':ti) AND 'implant site preparation':ti OR 'implant osteotomy':ti OR 'implant stability':ti) AND [1990-2018]/py;
- Scopus: (piezosurgery OR piezo$ OR ultrasonic$ OR rotary OR drill$ AND implant AND site AND preparation OR implant AND osteotomy OR implant AND stability);
- Open Grey: (piezosurgery OR piezoelectric surgery OR ultrasonic surgery OR rotary instruments OR twist drill OR implant site preparation OR implant osteotomy OR sinus floor elevation OR sinus augmentation OR sinus graft$).

Furthermore, the references cited in all selected papers and in previously published systematic reviews on this topic[24,33-37] were checked for additional studies. The last five years (2014 to 2018) of pertinent dental journals (Implant Dentistry, Clinical Oral Implants Research, Clinical Implant Dentistry and Related Research, The International Journal of Oral and Maxillofacial Implants, The International Journal of Periodontics and Restorative Dentistry, Journal of Clinical Periodontology, British Journal of Oral and Maxillofacial Surgery, Journal of Cranio-Maxillofacial Surgery, Journal of Oral Implantology, and the Journal of Periodontology) were hand searched to identify any potentially relevant papers.

Selection of studies

Two blinded independent reviewers (C.S. and G.T.) performed, in duplicate, the study eligibility assessment. The intraexaminer reliability of the study selection process was assessed using the Cohen's kappa (κ) test, assuming a threshold value of 0.61[39]. Conflicts were resolved by discussing each article until a consensus was reached. Attempts to contact corresponding authors of the included studies were made to retrieve any missing information or to clarify specific items.

Types of studies

The present systematic review includes only prospective studies conducted on human subjects. Both reviews and studies of lower quality within the hierarchy of scientific evidence (such as expert opinions, letters, case reports, case series and retrospective studies) were excluded.

The studies were evaluated for selection according to the following criteria:

- Inclusion criteria: randomised controlled trials (RCTs) and case-control studies (CCTs) comparing the PBS with conventional rotary instruments for implant site preparation and reporting any of the selected clinical outcomes (surgical time, implant stability, marginal bone variations and implant failure rate) for both groups.
- Exclusion criteria: meta-analyses, systematic and narrative reviews, retrospective studies,

case series, case reports, ex vivo, in vitro and animal studies, were excluded. Studies without control group or dealing with extra-maxillary implants or not providing sufficient data, were also excluded.

Sequential search strategy

Following the initial literature search, all articles were screened to eliminate irrelevant publications, in vitro and animal studies, case reports, case series, retrospective studies and review articles. The studies were screened further based on the relevance of data reported in the abstracts. Finally, the full texts of the selected papers were examined to confirm the study eligibility, following the inclusion and exclusion criteria.

Data extraction

Two reviewers (G.S. and C.S.), using pre-defined forms independently, extracted the following information from the selected studies:

1. Study characteristics: title, authors' names, corresponding author nationality, language of publication, year of publication, journal name and impact factor (IF) in the year of publication, source of funding, study design, Ethics Committee/Institutional Review Board approval number, method of randomisation, duration of follow-up, allocation concealment, and blinding (participants, investigators and outcome examiners).
2. Participants: demographic characteristics, health condition of participants, smoking status, number of participants in test and control groups, number and reasons for dropouts.
3. Interventions: the PBS for implant site preparation (type of piezoelectric device, implant brand, number of implants and timing of prosthetic loading).
4. Comparison: conventional drilling for implant site preparation (implant brand, number of implants and timing of prosthetic loading).
5. Outcomes: surgical time, implant stability measured with resonance frequency analysis (RFA), marginal bone level variation and implant failure.

Attempts to contact authors of the included studies were made to retrieve any missing information or clarification of specific items.

Assessment of risk of bias in individual studies

Two reviewers (A.R. and G.T.) independently assessed the risk of bias in the selected RCTs using the Cochrane Collaboration tool for risk of bias assessment[40]. The analysis was based on the evaluation of six items (random sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias). The studies were then classified into: (a) studies with low risk of bias when all criteria were met; (b) studies with unclear risk of bias when one or more criteria were partially met; or (c) studies with high risk of bias when one or more criteria were not met.

The risk of bias of the included CCTs was independently assessed by two reviewers (A.R. and G.T.) using the Newcastle-Ottawa Quality Assessment Scale (NOS)[41]. NOS was developed for risk of bias and method quality assessment of case-control and cohort studies. NOS for CCTs contains eight items grouped into three categories: selection, comparability, and exposure. NOS is scored using a star system, with a maximum total of nine stars. Studies scoring eight to nine stars were categorised as 'high quality', six to seven stars as 'moderate quality' and zero to five stars as 'low quality'.

If the Cochrane Collaboration tool and/or NOS scores were different between the two examiners, they were discussed until a consensus was obtained. If a consensus could not be obtained, a third independent examiner (C.S.) evaluated the articles for the final quality control, and a consensus was obtained.

Assessment of risk of bias across studies

Heterogeneity was assessed using the χ^2-based Q-statistic method with a significant P value < 0.05. However, due to the relative insensitivity of the Q statistic[42], an I^2 index was also reported with values $\geq 50\%$ considered to be associated to

the substantial heterogeneity of the studies[43]. In particular, the I^2 index describes the percentage of total variation across studies due to heterogeneity rather than chance.

Data synthesis

The implant stability variation, MBL and surgical procedure duration were meta-analysed, the mean difference (MD) computed between test and control groups, and the dichotomous outcome implant failure was pooled by calculating the risk ratio (RR) and its 95% confidence interval (CI). A fixed- or a random-effect model was used based on the presence of heterogeneity (calculated as above-mentioned). In the meta-analysis both crossover and parallel studies were pooled assuming absence of the carry-over effect between different interventions performed on the same patient. The overall effects were compared using the inverse of variance test, setting $P < 0.05$ as the threshold of statistical significance. The pooled analysis and heterogeneity were calculated using the Review Manager software (version 5.2.6, Cochrane Collaboration). In addition, a trial sequential analysis (TSA) (Trial Sequential Analysis v0.9 β, Copenhagen Trial Unit, Copenhagen, Denmark) was performed to adjust the results for the presence of type 1 and 2 statistical errors and to analyse the power of the available evidence. Specifically, a type 1 error of 5% and a power of 80% (type 2 error = 80%) were set to calculate trial sequential monitoring boundaries, futility boundaries and the required information size (RIS). A 'model variance-based' approach was performed for the heterogeneity correction, whilst data for the MD, RR and their variance were extracted from the meta-analysis results. A graphical evaluation was performed to analyse whether the *Z*-curve (showing the treatment effect) crossed either monitoring or futility boundaries and to obtain the RIS threshold.

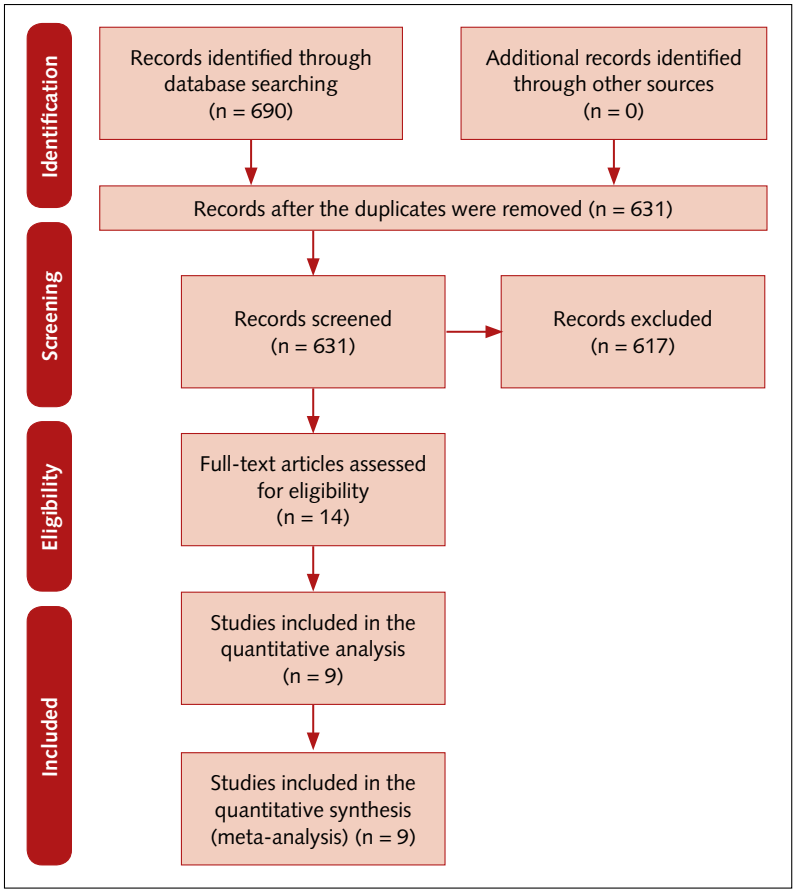


Fig 1 Flowchart of the search process.

Results

Description of studies

A total of 690 articles (in English, Chinese, French, German, Italian, Spanish and Russian) resulted from the initial search (206 from PubMed, 343 from Embase, 96 from Scopus, 45 from Open Grey and none from other sources). After removing duplicates, 631 titles were examined and 617 were excluded after reviewing abstracts (Cohen's κ test for inter-reviewer agreement = 0.87). Fourteen articles were downloaded in full text[44-57] and nine studies[46,48-52,54-56], matching the inclusion and exclusion criteria, were included in the final analysis (Cohen's κ test for inter-reviewer agreement = 1). Results from the electronic and manual searches are summarised in Figure 1. The list of excluded studies[44,45,47,53,57] and reasons for exclusion are described in Table 1. Of the nine included studies, three were RCTs

Table 1 Reasons for the exclusion of individual studies

Reference	Reason for exclusion
Danza et al (2009)[44]	Used a different surgical technique
Di Alberti et al (2010)[45]	Did not report data on the outcomes of this review
Vercellotti et al (2014)[47]	No control group
Fugito Junior et al (2018)[53]	In vitro study
Gürkan et al (2019)[57]	Same population of another included study[50]

with split-mouth design[48,50,56], five were RCTs with crossover design[46,49,52,54,55] and one was a CCT[51]. Four studies were partially supported by private companies[46,50,51,55] and by university grants[50], one study was self-funded[56], whilst no information about funding was present in the other four articles[48,49,52,54]. All included studies were approved by the Ethics Committee/

Table 2 Characteristics of the individual studies

Characteristics		Reference			
		Stacchi et al (2013)[46]	da Silva Neto et al (2014)[48]	Canullo et al (2014)[49]	Peker Tekdal et al (2016)[50]
Study characteristics	Study design	RCT (crossover)	RCT (split-mouth)	RCT (crossover)	RCT (split-mouth)
	Country	Italy	Brazil	Italy	Turkey
	Journal (IF)	Clinical Implant Dentistry and Related Research (3.821)	British Journal of Oral and Maxillofacial Surgery (1.133)	Clinical Oral Implants Research (3.123)	Clinical Oral Implants Research (3.464)
	Funding	Private companies (partial)	No information	No information	Private company (partial) and University grant
	Evaluated patients/ implants	20/39	30/68	15/29	14/38
	PBS	20	34	15	19
	Drills	19	34	14	19
	Gender (M/F)	12/8	6/24	6/9	4/10
	Mean age (range) in years	59.7 (41–81)	(20–60)	57.3 (32–76)	50.0 (31–64)
	Implant brand	Biomet 3i Nanotite	Neodent	Sweden & Martina	Biodenta
	Test group preparation technique	Ultrasonic	Ultrasonic	Drills/Ultrasonic finalisation	Ultrasonic
	Piezoelectric device	Piezosurgery 3, Mectron, Italy	Piezosonic, Driller, Brazil	Piezon Master, EMS, Switzerland	Piezon Master, EMS, Switzerland
ISQ at baseline	PBS	70.5 ± 5.8	77.5 ± 4.6	67.3 ± 7.1	NR
	Drills	72.2 ± 5.8	69.1 ± 6.1	67.9 ± 7.5	NR
ISQ follow-ups	PBS	69.4 ± 5.2 (4 wk) 70.1 ± 3.6 (8 wk) 71.0 ± 2.9 (12 wk)	77.0 ± 4.2 (12 wk) 79.1 ± 3.1 (21 wk)	70.8 ± 7.2 (8 wk) 75.7 ± 5.2 (12 wk)	NR
	Drills	66.1 ± 6.7 (4 wk) 67.3 ± 6.2 (8 wk) 69.2 ± 5.5 (12 wk)	70.7 ± 5.7 (12 wk) 71.7 ± 4.5 (21 wk)	67.7 ± 5.2 (8 wk) 73.3 ± 4.6 (12 wk)	NR
	Timing of prosthetic loading	5 mo	5 mo	3 mo	NR (after 6 mo)
MBL (mm)	PBS	NR	NR	0.74 ± 0.3 (15 mo)	0.15 ± 0.2 (6 mo)
	Drills	NR	NR	0.78 ± 0.3 (15 mo)	0.22 ± 0.3 (6 mo)
Surgery duration (min)	PBS	7.20 ± 1.3	NR	NR	9.0 ± 1.8
	Drills	6.00 ± 1.8	NR	NR	5.0 ± 1.4
Implant failure rate (%)	PBS	0	0	0	5
	Drills	5	0	6.7	5

CCT, case-control studies; F, female; IF, impact factor; ISQ, implant stability quotient; M, male; MBL, marginal bone loss; min, minutes; mo, months; NR, not reported; PBS, piezoelectric bone surgery; RCT, randomised clinical trial; wk, weeks.

Institutional Review Board. The characteristics of the included studies are listed in Table 2.

Patient characteristics

The sample size in single studies ranged from a minimum of 10[51] to a maximum of 50[56] patients. The total number of treated patients was 235 (102 females, 67 males and 66 not specified). Two studies[51,52] did not report gender distribution, and one study[54] reported incorrect gender distribution data (26 patients: 16 females and 12 males). The age ranged from 19[54] to 81[46] years old. One study[51] did not report the age of patients.

Patients were enrolled in individual studies according to the following criteria:

	Reference				
	Makary et al (2017)[51]	Soheilifar et al (2018)[52]	Alattar et al (2018)[54]	Stacchi et al (2018)[55]	Scarano et al 2018[56]
CCT	RCT (crossover)	RCT (crossover)	RCT (crossover)	RCT (crossover)	RCT (split-mouth)
Lebanon	Iran	Iraq	Italy	Italy	
Implant Dentistry (1.107)	Journal of Long-Term Effects of Medical Implants (–)	Journal of Craniofacial Surgery (0.772)	Biomed Research International (2.583)	Materials (2.467)	
Private company	No information	No information	Private company (partial)	Self-funded	
10/21	30/60	26/54	40/80	50/50	
11	30	26	20	25	
10	30	28	20	25	
NR	NR	12/16 (wrong data)	18/22	21/29	
NR	(20–70)	48.0 (19–66)	60.1 (39–79)	52.0 (41–63)	
Tekka	SIC	Dentium	Sweden & Martina	Isomed	
Ultrasonic	Ultrasonic	Drills/Ultrasonic finalisation	Ultrasonic	Ultrasonic	
NR	Variosurg, NSK, Japan	Piezosurgery 3, Mectron, Italy	Piezosurgery Touch, Mectron, Italy	Surgysonic, Esacrom, Italy	
74.9 ± 10.8	66.6 ± 1.4	79.1 ± 9.7	NR	NR	
74.2 ± 6.4	67.6 ± 2.6	80.2 ± 8.1	NR	NR	
78.4 ± 8.1 (4 wk)	70.1 ± 1.5 (12 wk) 69.3 ± 1.6 (21 wk)	71.0 ± 9.7 (8 wk) 78.3 ± 5.6 (16 wk)	NR	NR	
75.3 ± 6.0 (4 wk)	67.8 ± 1.7 (12 wk) 68.3 ± 2.0 (21 wk)	71.6 ± 12.3 (8 wk) 80.1 ± 12.4 (16 wk)	NR	NR	
10 wk	5 mo	4 mo	Immediate loading	3 mo	
NR	NR	NR	1.39 ± 1.0 (6 mo) 1.92 ± 1.1 (1 yr) 1.95 ± 1.0 (2 yr)	0.036 ± 0.001 (3 mo – wrong data)	
NR	NR	NR	1.42 ± 1.2 (6 mo) 2.14 ± 1.5 (1 yr) 2.22 ± 1.0 (2 yr)	0.03 ± 0.001 (3 mo – wrong data)	
NR	NR	4.13 ± 2.1	6.59 ± 2.9	10.5 ± 3.1	
NR	NR	2.75 ± 1.3	5.08 ± 2.5	2.5 ± 0.3	
0	0	0	4.2	4	
0	0	3.6	4.2	4	

Inclusion criteria

- healthy patients[48,51,54];
- at least 6 months of healing after dental extraction[46,48,49,52,54,55];
- both implant sites inserted in similar bone quality[52,55];
- no grafted areas[46,48,49,54];
- the peak insertion torque was between 35 and 60 Ncm[55];
- patients were totally[56] or partially[50,56] edentulous;
- patients did not wear removable prosthesis[46,52].

Exclusion criteria

- presence of relevant medical conditions[49,51,54,56];
- history of systemic disease contraindicating surgical treatment[46,52,55];
- systemic disease or use of medication potentially impairing surgery and bone healing dynamics[50,52];
- history of radiotherapy in head and neck region[46,52,55,56];
- uncontrolled diabetes[46,48,52,55,56];
- immunosuppressed or immunocompromised[55];
- hypertension[48];
- osteoporosis[48];
- treated or under treatment with intravenous aminobisphosphonates[46,49,52,55];
- smokers[48,50,56];
- heavy smokers (> 10 cigarettes/day)[46,49,52];
- pregnant or lactating women[49];
- substance abusers, psychiatric problems or unrealistic expectations[46,52,55];
- sites with acute infection[49,50,54];
- active periodontitis and/or poor oral hygiene and motivation[46,48,49,50,52,54,55,56];
- bruxism[48];
- insufficient bone volume for implant insertion without augmentation procedures[46,48,49,50,52,54,55];
- insufficient mesiodistal crestal space to properly insert two adjacent implants[46,48,52];
- at least 2 mm buccal keratinised mucosa width and 3 mm mucosa thickness[50].

Clinical procedures

The PBS was used for implant site preparation in the test group and conventional drilling was used in the control group in all included studies. The implant beds were prepared in adjacent[46,49], bilateral[48,50,56] or in both adjacent and bilateral[52,54,55] sites. One study[51] did not report the location of implant placement. Submerged healing of implants was adopted in four studies (with a duration of: 4 weeks[51], 8 weeks[54] and 12 weeks[48,56]), non-submerged healing was adopted in four studies[46,49,50,52] and immediate loading was adopted in one study[55]. In one study[49], the implants were left submerged for 8 weeks when the implant stability quotient (ISQ) at baseline was < 60. Antibiotic prophylaxis was used in five studies[46,48-50,52], postoperative antibiotics were prescribed in six trials[48,49,51,52,55,56], and one study did not report relevant information[54]. Prostheses were delivered at different time points after implant insertion; implants were immediately loaded in one study[55] and after 10[51], 12[49,56], 16[54], 20[46,48,52] and 24[50] weeks of healing in the other trials.

Risk of bias in the individual studies

Three studies[46,49,55] were judged to be at low risk of bias after the authors of two of these studies[46,49] provided additional information, which had not been reported in the articles. One study[50] was judged to be at unclear risk of bias, and four studies[48,52,54,56] were judged to be at high risk of bias (Table 3). One CCT[51] was categorised as a low-quality study based on the NOS evaluation (Table 4).

Surgical time

Five studies recorded the operative time necessary for implant site preparation in both test and control groups[46,50,54,55,56]. The MD between the two procedures was 3.21 minutes, significantly favouring the control group (95% CI = 0.93 to 5.49; $P = 0.006$; Fig 2). Heterogeneity was present among the five included studies ($I^2 = 96\%$; df = 4; $P < 0.00001$; $\chi^2 = 105.71$), therefore, a

Table 3 Risk of bias among individual studies (randomised clinical trials [RCTs])

Reference	Random sequence generation	Allocation concealment	Blinding of outcome assessment*	Incomplete outcome data	Selective reporting	Other bias
Stacchi et al (2013)[46]	Low risk; reported as "computer generated table, which was prepared using a balanced, randomly permuted block approach"	Low risk; authors replied "opaque numbered sealed envelopes"	Low risk; reported as "a blinded operator recorded in triplicate ISQ values"	Low risk; all data presented	Low risk; all outcomes seem to be reported	None detected
da Silva Neto et al (2014)[48]	High risk; no information in the article	High risk; no information in the article	High risk; no information in the article	Low risk; all data presented	Low risk; all outcomes were reported	None detected
Canullo et al (2014)[49]	Low risk; reported as "computer generated randomization tables"	Low risk; authors replied "opaque numbered sealed envelopes"	Low risk; reported as "data collection was made by a blinded single trained clinician, different from the surgeon"	Low risk; all data presented	Low risk; all outcomes were reported	None detected
Peker Tekdal et al (2016)[50]	Low risk; reported as "toss of a coin at the beginning of the surgery session by an independent examiner"	Unclear risk; insufficient information in the article	Low risk; reported as "by a calibrated examiner who was masked to the groups"	Low risk; the exclusion of one patient was not likely to have influenced the outcomes	Low risk; all outcomes were reported	None detected
Soheilifar et al (2018)[52]	High risk; no information in the article	High risk; no information in the article	Low risk; reported as "an investigator blinded to treatment groups analyzed implant stability"	Low risk; all data presented	Low risk; all outcomes were reported	None detected
Alattar et al (2018)[54]	Low risk; reported as "randomization was achieved by a permuted block approach"	High risk; no information in the article	High risk; no information in the article	Low risk; all data presented	Low risk; all outcomes were reported	None detected
Stacchi et al (2018)[55]	Low risk; reported as "a table was prepared by using a web-based software with a balanced, randomly permuted block approach"	Low risk; reported as "the randomization codes were enclosed in numbered, sealed, opaque envelopes which were opened by a clinical assistant after flap elevation"	Low risk; reported as "marginal bone level was assessed using a measuring software by a single blinded and calibrated examiner"	Low risk; all data presented	Low risk; all outcomes were reported	None detected
Scarano et al (2018)[56]	Low risk; reported as "a computer-generated table, which was prepared using a balanced, randomly permuted implant site approach"	High risk; no information in the article	High risk; no information in the article	Low risk; all data presented	Low risk; all outcomes were reported	None detected

The Cochrane Collaboration tool for risk of bias assessment was used to evaluate the RCTs.
*The risk of bias for not blinded operators performing treatment was not judged as a significant risk of bias.

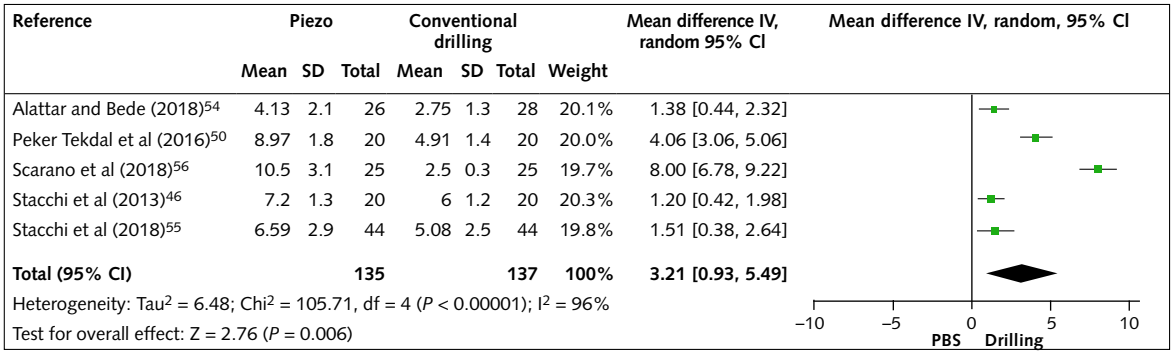
random-effect model was used. A TSA confirmed these findings as shown by the *Z*-curve, crossing the lower trial sequential monitoring boundary. In addition, the power was close to the RIS threshold (299 implants would have been the required sample for a power of 80% versus 272 implants that were included in this meta-analysis), showing a moderate power of evidence (Fig 3).

Table 4 Risk of bias among individual studies (case-control studies [CCT])

Reference	Selection				Comparability	Exposure			
	1	2	3	4	1	1	2	3	Total
Makary et al (2017)[51]			*	*		*	*	*	5

The Newcastle-Ottawa Quality Assessment Scale (NOS) was used to evaluate CCTs.

Fig 2 Duration of surgery.



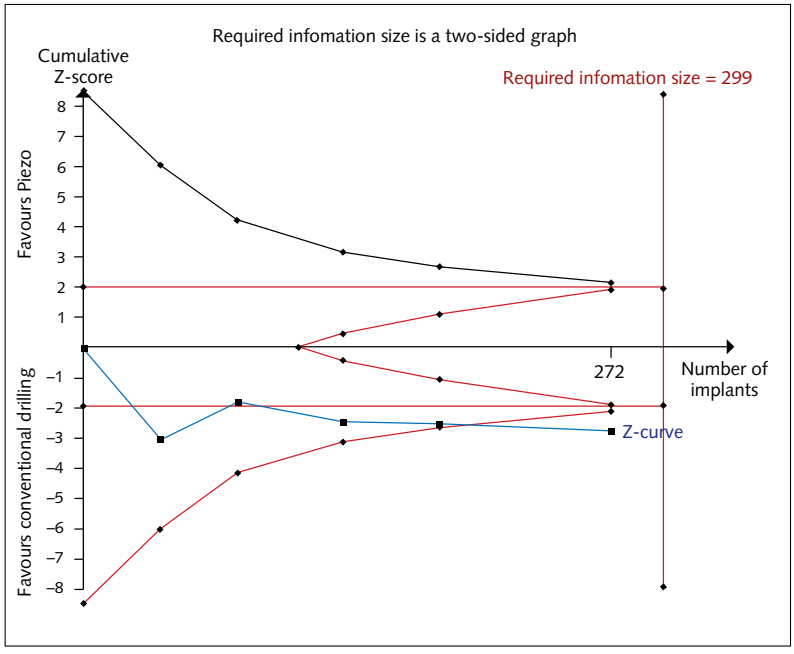


Fig 3 Trial sequential analysis (TSA) for the duration of the surgery.

Implant stability

The implant stability was assessed using RFA at baseline and at different time points in six studies[46,48,49,51,52,54]. Two studies[46,51] recorded ISQ values 4 weeks after implant placement, three studies[46,49,54] after 8 weeks, and four studies after 12 weeks[46,48,49,52].

The meta-analysis revealed no significant difference in terms of primary stability (ISQ at baseline) between test and control groups (MD = 0.93; 95% CI = –3.02 to 4.87; $P = 0.64$; Fig 4). Heterogeneity was noted across studies ($I^2 = 89\%$; df = 5; $P < 0.00001$; $\chi^2 = 45.53$), and therefore, a random-effect model was used.

The stability pattern was then meta-analysed at the 4-, 8- and 12-week follow-ups to evaluate the secondary stability trend. The ISQ values were significantly higher in the test than in the control group at each time point. The 4- and 8-week analyses gave similar results, with higher stability of the PBS group (4-week analysis: MD = 3.25; 95% CI = 0.08 to 6.41; $P = 0.04$; Fig 5) (8-week analysis: MD = 2.18; 95% CI = 0.05 to 4.32; $P = 0.05$; Fig 6). No heterogeneity among studies was noted at both time points (4-week: $I^2 = 0\%$, df = 1, $P = 0.96$, $\chi^2 = 0.00$; and 8-week: $I^2 = 0\%$, df = 2, $P = 0.60$, $\chi^2 = 1.02$), and therefore, fixed-effect models were used. The TSA confirmed these results, even if a more powered information size was required to draw conclusions at both 4- and 8-week follow-ups (61 implants included at the 4-week follow-up versus 237 implants that would have been necessary for a power of 80%; 120 implants included at the 8-week follow-up versus 471 implants that would have been necessary for a power of 80%; Figs 7 and 8).

Reference	Piezo			Conventional drilling				Mean difference IV, random, 95% CI
	Mean	SD	Total	Mean	SD	Total	Weight	
Alattar and Bede (2018)[54]	79.1	9.7	26	80.1	8.2	28	15.8%	–1.00 [–5.81, 3.81]
Canullo et al (2014)[49]	67.3	7.1	15	67.9	7.5	15	15.2%	–0.60 [–5.83, 4.63]
da Silva Neto et al (2014)[48]	77.5	4.6	34	69.1	6.1	34	19.0%	8.40 [5.83, 10.97]
Makary et al (2017)[51]	74.9	10.8	11	74.2	6.4	10	11.8%	0.70 [–6.81, 8.21]
Soheilifar et al (2018)[52]	66.6	1.4	30	67.6	2.6	30	20.4%	–1.00 [–2.06, 0.06]
Stacchi et al (2013)[46]	70.5	5.8	20	72.2	5.8	20	17.7%	–1.70 [–5.29, 1.89]
Total (95% CI)			**136**			**137**	**100%**	**0.93 [–3.02, 4.87]**
Heterogeneity: Tau² = 19.57; Chi² = 45.53, df = 5 (*P* < 0.00001); I² = 89%								
Test for overall effect: Z = 0.46 (*P* = 0.64)								

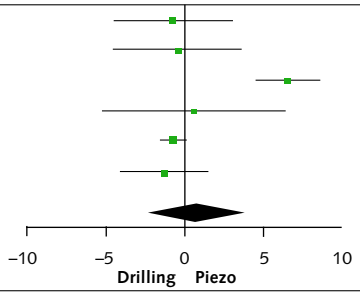


Fig 4 Implant stability quotient (ISQ) at baseline.

Reference	Piezo			Conventional drilling				Mean difference IV, fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total	Weight	
Makary et al (2017)[51]	78.4	8.1	11	75.3	6	10	27.3%	3.10 [–2.96, 9.16]
Stacchi et al (2013)[46]	69.4	5.2	20	66.1	6.7	20	72.7%	3.30 [–0.42, 7.02]
Total (95% CI)			**31**			**30**	**100%**	**3.25 [0.08, 6.41]**
Heterogeneity: Chi² = 0.00, df = 1 (*P* = 0.96); I² = 0%								
Test for overall effect: Z = 2.01 (*P* = 0.04)								

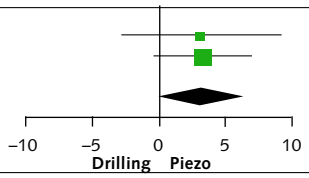


Fig 5 Implant stability quotient (ISQ) at the 4-week follow-up.

Reference	Piezo			Conventional drilling				Mean difference IV, fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total	Weight	
Alattar and Bede (2018)[54]	71	9.1	26	71.6	12.3	26	13.2%	–0.60 [–6.48, 5.28]
Canullo et al (2014)[49]	70.1	3.6	15	67.7	5.2	14	42.4%	2.40 [–0.88, 5.68]
Stacchi et al (2013)[4]	70.1	3.6	20	67.3	6.2	19	44.4%	2.80 [–0.40, 6.00]
Total (95% CI)			**61**			**59**	**100%**	**2.18 [0.05, 4.32]**
Heterogeneity: Chi² = 1.02, df = 2 (*P* = 0.60); I² = 0%								
Test for overall effect: Z = 2.00 (*P* = 0.05)								

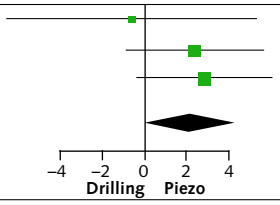


Fig 6 Implant stability quotient (ISQ) at the 8-week follow-up.

At the 12-week follow-up, the MD between the test and control groups was 3.23 ISQ units (95% CI = 1.25 to 5.21; *P* = 0.001; Fig 9). Heterogeneity among studies was noted ($I^2 = 69\%$; df = 3; *P* = 0.02; $\chi^2 = 9.74$), and therefore, a random-effect model was used. The TSA confirmed these findings as shown by the *Z*-curve crossing the lower trial sequential monitoring boundary. The statistical power was close to the RIS threshold (306 implants would have been the required sample for a power of 80% versus 196 implants included in this meta-analysis), showing a moderate power of evidence (Fig 10).

Marginal bone loss (MBL)

The MBL around implants was measured at baseline and at different time points in four

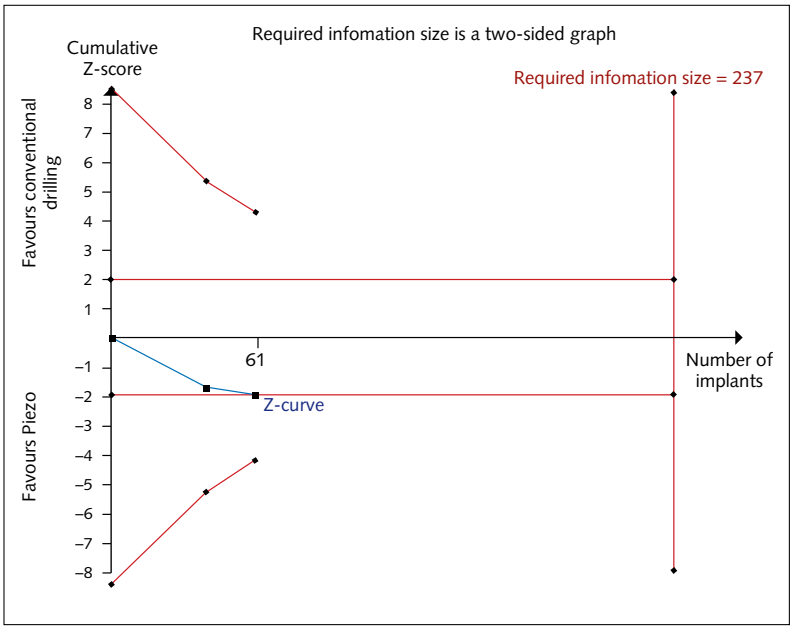


Fig 7 Trial sequential analysis (TSA) for implant stability at the 4-week follow-up.

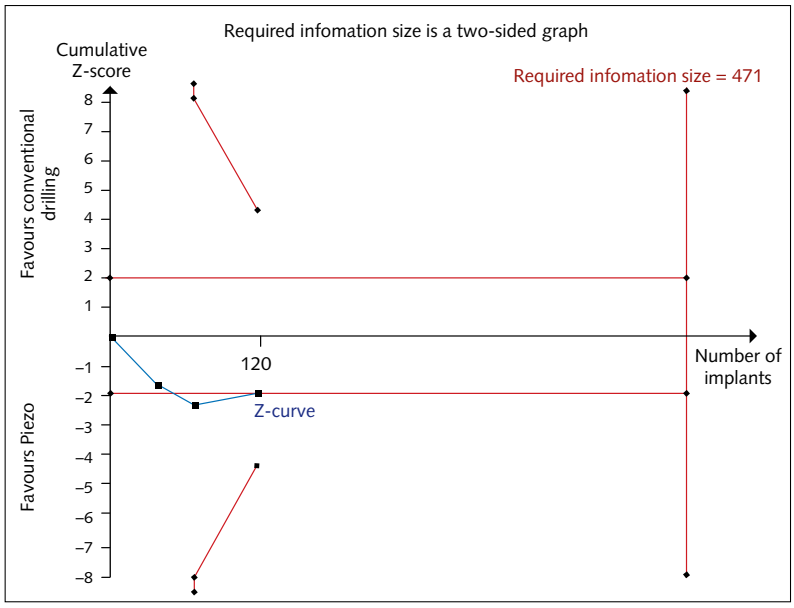


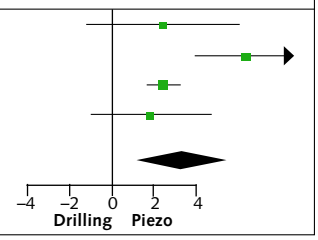
Fig 8 Trial sequential analysis (TSA) for implant stability at the 8-week follow-up.

studies[49,50,55,56]. One study[56] recorded the MBL 3 months after implant placement, two studies[50,55] after 6 months, one trial[55] after 12 and 24 months and one study[49] after 15 months. After contacting the authors, the MBL measurements in the study by Scarano et al[56] were excluded from the final analysis due to an error of data reported in the article.

In terms of MBL, the meta-analysis found no significant differences between test and control groups, both at the 6-month follow-up (MD = –0.07; 95% CI = –0.22 to 0.09; *P* = 0.40; Fig 11) and at the 12- to 15-month follow-up (MD = –0.06; 95% CI = –0.27 to 0.14; *P* = 0.55; Fig 11). No heterogeneity across studies was found, at either the 6-month follow-up (I^2 = 0%;

Fig 9 Implant stability quotient (ISQ) at the 12-week follow-up.

Reference	Piezo			Drilling				Mean difference IV, random, 95% CI
	Mean	SD	Total	Mean	SD	Total	Weight	
Canullo et al (2014)[49]	75.7	5.2	15	73.3	4.6	14	17.1%	2.40 [–1.17, 5.97]
da Silva Neto et al (2014)[48]	77	4.2	34	70.7	5.7	34	24.8%	6.30 [3.92, 8.68]
Soheilifar et al (2018)[52]	70.2	1.5	30	67.8	1.7	30	36.2%	2.40 [1.59, 3.21]
Stacchi et al (2013)[46]	71	2.9	20	69.2	5.5	19	21.9%	1.80 [–0.98, 4.58]
Total (95% CI)			**99**			**97**	**100.0%**	**3.23 [1.25, 5.21]**
Heterogeneity: Tau² = 2.65; Chi² = 9.74, df = 3 (*P* = 0.02); I² = 69%								
Test for overall effect: Z = 3.20 (*P* = 0.001)								



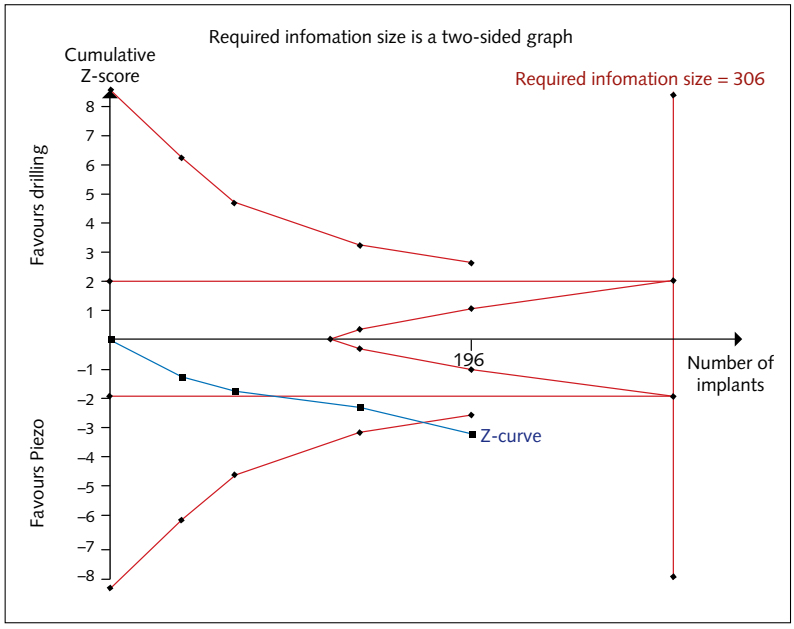


Fig 10 Trial sequential analysis (TSA) for implant stability at the 12-week follow-up.

df = 1; *P* = 0.88; χ^2 = 0.02) or the 12- to 15-month follow-up (I^2 = 0%; df = 1; *P* = 0.57; χ^2 = 0.33). In terms of MBL, no difference between the PBS group and the drilling group was detected at any time point (MD = –0.06; 95% CI = –0.19 to 0.06; *P* = 0.30; Fig 11). No heterogeneity was found (I^2 = 0%; df = 3; *P* = 0.95; χ^2 = 0.35), and therefore, a fixed-effect model was used. No TSA analysis was performed for this specific outcome since the number of included studies was too small for each time-point analysed.

Implant failure

Implant failure was reported in all included studies[46,48-52,54-56] with a follow-up varying from 3[51] to 24[55] months after implant placement. Four implants failed in the PBS group (from a total of

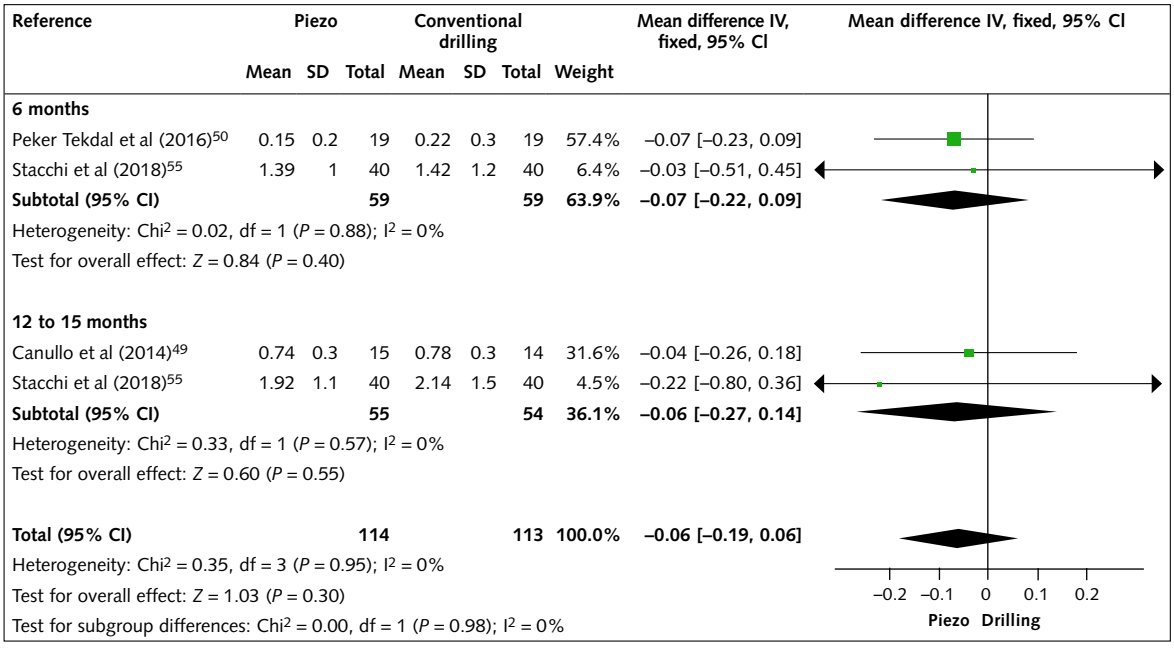


Fig 11 Marginal bone loss (MBL).

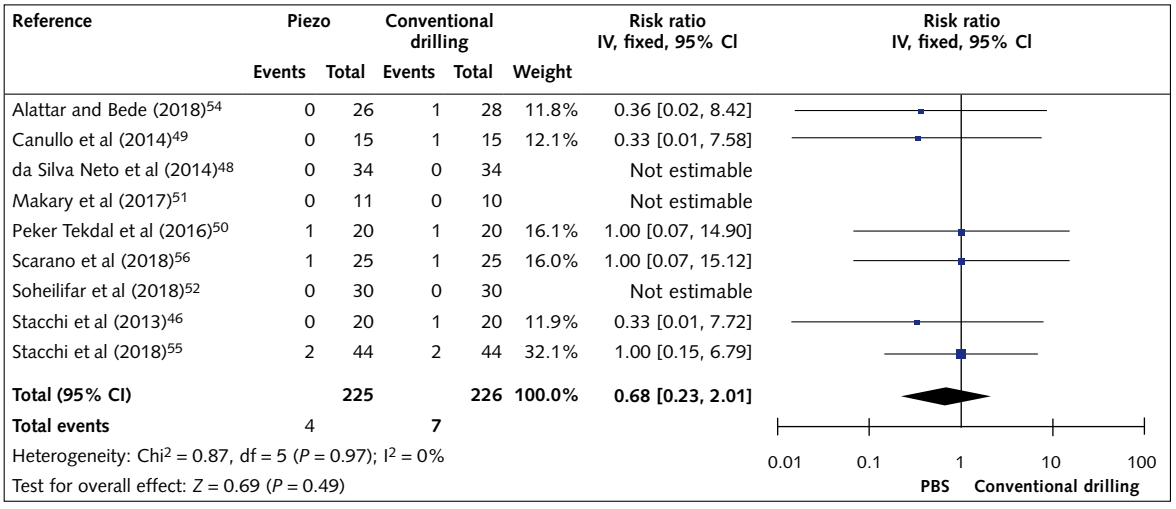


Fig 12 Implant failure.

225 implants) and seven implants failed in the drilling group (from a total of 226 implants). The meta-analysis showed no statistically significant difference in the implant failure rate between the two groups (RR 0.68; 95% CI = 0.23 to 2.01; $P = 0.49$; Fig 12). No evidence of heterogeneity across studies was noted ($I^2 = 0\%$; df = 5; $P = 0.97$; $\chi^2 = 0.87$), and for this reason a fixed-effect model was used. These results were confirmed in the TSA; however, this analysis showed that a much more powered information size (RIS = 4440 implants, compared with 451 implants included in the present meta-analysis) was needed to draw conclusions regarding the magnitude of the treatment effect (Fig 13).

Discussion

Clinical findings

The PBS used to prepare implant osteotomy was first investigated in 2007 and showed promising results in terms of bone healing response in an animal model. The PBS seemed to be more efficient than conventional drilling in promoting early expression of bone morphogenetic proteins

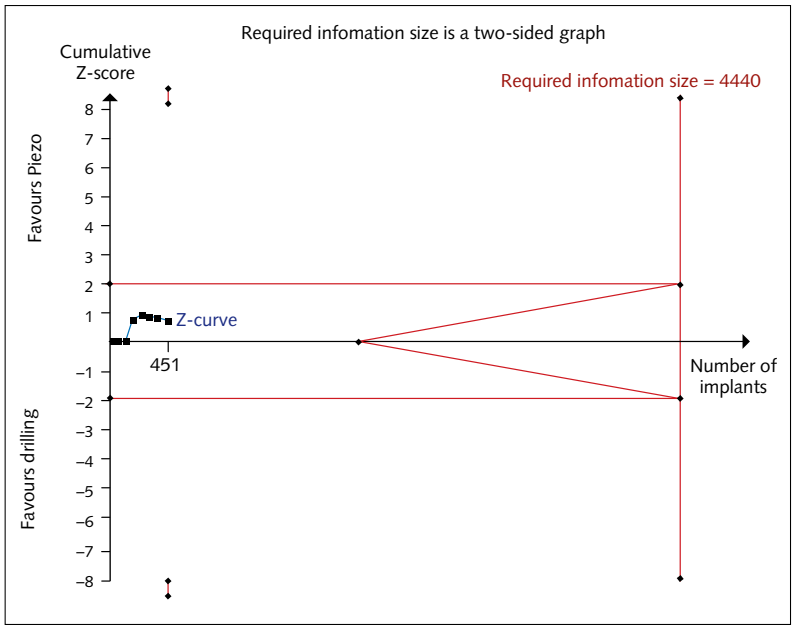


Fig 13 Trial sequential analysis (TSA) for implant failure.

and controlling the inflammatory process[30]. These findings were confirmed later by biomolecular studies demonstrating lower levels of mediators of inflammation, apoptosis and bone resorption[32,50] and greater osteoblastic cell viability[58] in PBS sites compared with drilled sites.

These encouraging biological outcomes, together with the technological characteristics of piezoelectric cutting (micro-vibrations enhancing surgical control and selective action on mineralised tissues), paved the way for the clinical application of ultrasonic implant site preparation. In 2014, Vercellotti et al[47] published a case series analysing the clinical outcomes of 3579 implants inserted using the PBS for up to 3 years. The reported survival rate (97.8%) was comparable to implants inserted with conventional drilling techniques. Nonetheless, further studies with long-term follow-ups, analysing more specific features (e.g. implant stability and MBL), will be required to evaluate advantages and disadvantages of the PBS in this particular clinical application.

The present systematic review, meta-analysis and trial sequential analysis evaluated the available evidence comparing the PBS and conventional drilling techniques with respect to implant stability, MBL, implant failure and duration of surgery.

Implants inserted with both techniques exhibited comparable primary stability, despite the fact that six implant systems with different macro- and micro-geometry were used in the included studies. This finding is in accordance with recent meta-analyses[35-37] and in vitro and ex vivo studies[28,59,60], supporting the hypothesis that the PBS produces precise osteotomies and facilitates good implant adaptation to the recipient bed, even if the ultrasonic tips are not specific to different implant shapes. Moreover, data from the included studies suggests that the PBS improves secondary stability compared with drilling techniques. The ISQ values were significantly higher in the test group at 4-, 8- and, above all, 12 weeks after implant insertion. These outcomes could be explained by the PBS-induced biomolecular modifications described above, which may result in a faster bone healing response. This is in accordance with recent meta-analyses by Atieh[34], Sendyk[36] and García-Moreno[37], whilst Amghar-Maach[35] reported opposite results after meta-analysing the same clinical studies. Finally, it still remains unclear if the MD observed in implant stability between the two techniques (3.23 ISQ points) represented a real clinical advantage.

The MBL was slightly lower in the PBS group than in the drilling group but without statistical significance after 6- and 12- to 15-months of healing. This result is in agreement with Atieh et al[34], the only meta-analysis investigating this specific outcome. It is worth noting that the final analysis on the MBL included only three studies in which multiple confounding factors were present (e.g. different implants, different loading protocols and different population).

Implant failure was an uncommon finding in the present study. Four implants out of 225 were lost in the test group (98.2% survival rate), which is in almost perfect accordance with recent clinical studies[47,61], whilst seven implants, out of 226, failed in the control group (96.9% survival rate). The meta-analysis showed that the difference between the two groups was not significant, confirming the outcomes of previous systematic reviews[34,35]. However, it should be noted that the included studies had a short follow-up period (from 3 to 24 months).

The duration of surgery, as reported by other meta-analyses[34,35], was significantly shorter in the conventional, drilling group. Two studies[49,54] tried to overcome this limitation by using a mixed preparation (starting implant osteotomy with conventional drills and finalising it with ultrasonic tips). One of these studies[49] did not record the duration of the surgery, and in the second study[54] the conventional drilling technique resulted significantly faster than the mixed preparation. Furthermore, it remains unclear if the MD between the two techniques (3.21 minutes) represents a real clinical advantage either for the operator or the patient.

Quality of evidence

Four[48,52,54,56] out of eight RCTs included in the present meta-analysis were judged to be at high risk of bias, one trial[50] was considered at an unclear risk of bias and three studies[46,49,55] at low risk of bias. The only included CCT[51] was judged to be a low-quality study. Trial sequential analysis conducted on implant stability at the 4- and 8-week follow-ups showed that the power of evidence of the present meta-analysis was weak. At these time points the required information size needed to evaluate the magnitude of the treatment effect with a statistical power of 80% would have been 237 and 471 implants, respectively, compared with the 61 and 120 implants included in the present study. The power of evidence of the meta-analysis on implant stability at the 12-week follow-up was moderate, even if some heterogeneity across studies was present. A required sample size of 306 implants would have been necessary for a power of 80%, compared with the 196 implants that were included in the present study.

No TSA analysis was performed for the meta-analysis of marginal bone variation, since the number of included studies was too small.

The meta-analysis of the implant failure rate between the PBS and the conventional drilling had an extremely weak power of evidence. The TSA showed that a sample of 4440 implants would have been necessary for a power of 80%, compared with the 451 implants that were evaluated in the included studies.

Conversely, the TSA of the difference in surgery duration between the two techniques showed a moderate power of evidence, confirming that the ultrasonic preparation was slower than conventional drilling techniques, even if a high heterogeneity was present across studies. For this specific item, the power of the present meta-analysis was close to the required information size threshold (272 included implants versus 299 implants that would have been required for a power of 80%).

Limitations

It should be stated that the strict inclusion criteria adopted in the present meta-analysis increased not only the study homogeneity, but also the risk of excluding significant data[62]. This methodological approach helped to understand the real available evidence on this specific topic and should motivate researchers to design appropriate future clinical trials. Hence, the results reported in the present meta-analysis should be interpreted with caution.

Suggestions for future research

Further randomised controlled trials comparing the PBS with conventional drills for implant site preparation are needed. Future studies should be designed with accurate standardisation of surgical and prosthetic protocols and control of patient-related confounding factors. Standardised methods for implant stability assessment and MBL measurement should be adopted to obtain comparable results. Finally, the incidence of postoperative neurological complications during implant site preparation with the two techniques should also be evaluated.

Conclusions

Based on the results of the present meta-analysis and trial sequential analysis to assess if the PBS for implant site preparation prolonged surgery duration, improved implant stability, reduced MBL and improved the survival rate of dental implants compared with conventional drilling techniques, the following conclusions can be drawn:

- There was moderate evidence suggesting that ultrasonic implant site preparation prolonged the surgery duration compared with conventional drilling techniques;
- There was weak evidence suggesting that ultrasonic implant site preparation improved secondary stability 4 and 8 weeks after implant placement compared with conventional drilling techniques;
- There was moderate evidence suggesting that ultrasonic implant site preparation improved secondary stability 12 weeks after implant placement compared with conventional drilling techniques;
- There was insufficient data to assess if the ultrasonic implant site preparation could reduce the MBL compared with conventional drilling techniques;
- There was insufficient data to assess if the ultrasonic implant site preparation improved the survival rate of dental implants compared with conventional drilling techniques.

Further well-designed, adequately powered randomised clinical trials are necessary to improve the level of evidence on this topic.

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