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Meta-Analysis Pre-Implant Surgery

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Efficacy of the autogenous dentin graft for implant placement: a systematic review and meta-analysis of randomized controlled trials

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Abstract. The aim of this study was to determine whether the autogenous dentin graft (ADG) shows comparable results and similar clinical performance to other graft materials when utilized for implant placement. Four databases were searched, and controlled human studies that applied autogenous dentin for implant surgery, comparing it with other bone grafts, were included. Nine articles met the inclusion criteria, five of which were randomized controlled trials and were included in the meta-analysis. ADG showed equivalent primary and secondary implant stability when compared to Bio-Oss (primary: mean difference -0.74, 95% confidence interval (CI) -3.36 to 1.88, P = 0.58; secondary: mean difference -1.29, 95% CI -5.69 to 3.11, P = 0.57). The standardized mean difference (SMD) of marginal bone loss at 6 months and at the final follow-up (18 months) showed the two grafts to be similar (6 months: SMD -0.26, 95% CI -0.64 to 0.12, P = 0.18; final follow-up: SMD -0.12, 95%CI -0.50 to 0.26, P = 0.53), and survival after immediate implant placement was the same in the two groups: 97.37% and 97.30%, respectively. Incidences of complications with the autogenous dentin particles or blocks were in line with those of Bio-Oss or autogenous bone blocks, respectively. This meta-analysis indicates that the autogenous dentin graft is an effective option for bone augmentation around dental implants, with acceptable implant stability, marginal bone loss, and incidences of complications and failure.

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Dental implants are the preferred choice to replace missing teeth and restore function and aesthetics. However, implant placement becomes challenging in sites where tooth extraction or tooth loss has occurred and the area has been left untreated for a long period of time, as the alveolar bone loses its structure, resulting in a deficient alveolar ridge. It is documented that following tooth loss, ridge resorption is an inevitable outcome, especially during the first 6 months, being more notable in the horizontal dimension and at the buccal aspect of the extraction socket.^{1,2}

To overcome this phenomenon and make implant placement possible, several treatment modalities have been proposed, such as bone augmentation followed by delayed implant placement,³ immediate implant placement in fresh extraction sockets,⁴ and simultaneous implantation with ridge augmentation, using the guided bone regeneration technique (GBR).⁵ All of these procedures require an important step in the treatment sequence, which is bone grafting. This is done by placing a material in the edentulous site to promote bone formation and healing.

Several bone grafts for this purpose are available, among which autogenous bone is considered the gold standard. since it possesses all of the features needed for new bone formation, namely osteoinduction, osteoconduction, and osteogenesis. Although autogenous bone is unique in its qualities, it has major drawbacks that limit its use. To obtain this graft, a second surgical procedure has to be done, which results in donor site morbidity. In addition, the resorption rate of autogenous bone is unpredictable.⁶ Hence, other options for bone augmentation have been introduced to eliminate the additional surgery needed to harvest the graft, such as allografts and xenografts, although they are not able to fully replace the use of autogenous bone in all grafting procedures, as these materials fall short in attaining all of the qualities to be considered optimal. Allografts have a very high cost and xenografts lack osteoinductivity.4,7 Moreover. both grafts may raise concerns regarding their source, which can restrict their clinical application for certain individuals.

A new material has been proposed recently, namely the autogenous dentin graft (ADG). This material has gained attention from researchers and clinicians as the structure of the tooth is very similar to that of bone, there is no risk of disease transmission, and it is relatively inexpensive to obtain.^{8–10}

This material is acquired from extracted teeth that have no signs of infection or peri-apical lesions. The extracted tooth undergoes a process that includes the removal of caries, root canal filling material, and any type of restoration (e.g., composite filling, crown). It is then ground into particles using a grinding machine (e.g., Smart Dentin Grinder), which are then placed in a cleansing solution (most often NaOH with 20% alcohol) to remove organic remnants and bacteria, following which they are washed with phosphate buffered saline.^{3,10} Some studies have reported an additional step - demineralization of the dentin graft with the aim of improving bone ingrowth in the graft particles.²

Recent investigations have shed light on the use of the ADG, evaluating its clinical performance in several bone augmentation procedures. The results have been satisfactory, and the application of this type of graft has shown acceptable clinical outcomes.^{8,10–15} Thus, this systematic review and metaanalysis was performed to confirm whether the ADG provides comparable results to autogenous bone or to other commercially available bone grafts (i.e. Bio-Oss) and shows similar performance when used for implant placement procedures.

Materials and methods

This systematic review and meta-analysis has been registered in the PROS-PERO database (CRD42021289188), and was conducted adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.¹⁶ The aim was to answer the focused question "For patients receiving dental implants (P) in sites augmented with an autogenous dentin graft (I), compared to implants placed in sites augmented with other bone grafts (C), what are the implant stability values, marginal bone loss, and implant survival rates (O)?

The PICO guidelines were followed to develop a suitable review design and select potential studies. The population comprised candidates for implant placement, who needed bone grafting in the implant recipient site. The intervention was bone augmentation using an ADG with immediate (fresh extraction socket)/simultaneous (deficient alveolar ridge) implantation, or followed by delayed implant placement. The comparison was bone augmentation with materials other than an ADG. Outcomes were implant stability and peri-implant marginal bone loss (MBL) (primary outcomes), as well as the incidences of implant-related complications and failure (secondary outcomes).

Search strategy

Four databases were searched in this study: PubMed/MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and Scopus. No limitations were applied in any of the search engines. The combination of keywords used in this search was ("staged implant" OR "delayed implant" OR "implant placement" OR "immediate implantation" OR "ridge augmentation") AND ("tooth roots" OR "tooth graft" OR "whole tooth" OR "autogenous tooth" OR "particulate dentin" OR "dentin particulate" OR "autogenous dentin" OR "demineralized dentin" OR "demineralized dentin matrix" OR "mineralized dentin").

Study selection

Studies fulfilling the following criteria were included: (1) human studies (both prospective and retrospective), (2) a control group of patients who underwent bone grafting using a material other than autogenous dentin, with comparison to (3) a study group of patients who had ADG applied (alone, and not mixed with other bone graft material), in any type of alveolar bone defect (i.e., fresh extraction socket, horizontal/vertical ridge defect, insufficient maxillary sinus floor height) via an immediate or staged bone augmentation, (4) implant placement done in the augmented area, and (5) availability of information directly related to the procedure, i.e., the implant stability quotient (ISQ), peri-implant MBL, and/or complications/failure. Animal and in vitro studies and case reports that only presented successful graft use with no measurements were excluded from this systematic review.

The search process was conducted by two reviewers independently (B.M. and S.J.), navigating the database results on the Rayyan website (Rayyan, Qatar Computing Research Institute, Qatar Foundation).¹⁷ In the case of any disagreement with respect to the inclusion/exclusion of screened studies, this was resolved by discussion or by consulting a third reviewer (A.P.). The study selection ended on August 31, 2022. A manual search was done in the references of the papers that were eligible for full-text assessment, with the aim of identifying additional studies that could be included.

Data extraction

Data compiled from the selected studies were the graft used, type of bone defect, timing of bone augmentation (immediate, staged), type of implant placement, number of implants, follow-up after implant placement, mean MBL and ISQ values, and the incidences of complications and failure. Each element was reported for both the study and the control group.

Risk of bias and level of evidence

The revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess the risk of bias in the randomized/controlled clinical trials included.¹⁸ This tool evaluates five main domains, with the risk of bias in each study judged as 'low', 'some concerns', or 'high'. The RoB 2 Excel tool was implemented to give an idea of the risk of bias in each study, along with critical judgment from the reviewer.

To appraise the risk of bias in the retrospective studies included, the Risk of Bias in Non-randomized Studies - of Interventions (ROBINS-I) tool was utilized,¹⁹ which evaluates three stages (pre-intervention, at intervention, postintervention), divided into seven domains. Each study was judged as having a low risk of bias if all seven domains were low, while it was evaluated as having a moderate or serious risk of bias if at least one domain showed a moderate or serious risk of bias, respectively. The Risk-of-Bias Visualization tool (robvis) was used to illustrate the risk of bias for all included studies.²⁰ The quality of evidence was also evaluated, using the Centre for Evidence-Based Medicine (CEBM) levels of evidence,²¹ with each study given a level from 1 to 5.

Data synthesis and statistical analysis

MBL at two time-intervals (6 months and the final follow-up) and primary and secondary implant stability (ISQ) (all mean and standard deviation values) were extracted from the studies included in the quantitative synthesis. In one study, the mean ISQ values were reported with the range,²² therefore the approximate standard deviation was calculated and used in this meta-analysis.^{23,24} Considering the different methods by which MBL was measured, the continuous data for this outcome were analysed using the standardized

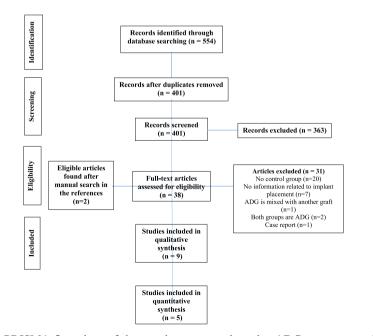


Fig. 1. PRISMA flow chart of the search process and results. ADG, autogenous dentin graft.

mean difference (SMD), with the 95% confidence interval (CI). The ISQ values were analysed using the mean difference (MD), with the 95% CI.

The level of heterogeneity in the selected studies was assessed with the χ^2 test and I^2 statistic. I^2 values of 25%, 50%, and 75% were judged to be low, moderate, and high heterogeneity, respectively.²⁵ Whenever an I^2 value of 50% or higher was noted, the randomeffects model was utilized, in order to reduce the bias resulting from methodological differences between studies. If no evidence of significant heterogeneity was noticed, the fixed-effects model was applied. P-values of < 0.05 indicated a significant difference between groups. Forest plots were generated to illustrate the results of the meta-analysis of the included studies. All data were synthesized using Review Manager version 5.4 (2020; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

Results

Search outcomes and characteristics of the included studies

The database search led to the identification of 554 publications. After the removal of duplicates, as well as screening the titles and abstracts, 38 publications reached the full-text assessment stage. Of these, seven articles were included in this review. Moreover, screening the references of articles that qualified for full-text assessment resulted in two more eligible articles being found. Consequently, nine studies were included in this systematic review.^{3-5,8,22,26-29} Out of these, five randomized controlled trials (RCTs) were included in the meta-analysis. Fig. 1 shows the flowchart of the search process and results.

Table 1 summarizes the characteristics of the included studies. Five studies were RCTs,³ one was a controlled clinical trial (CCT),²⁸ and three were retrospective in their design.^{4,5,29} The articles were published between 2014 and 2021. ADG was implemented to augment several types of fresh bone defect: extraction sockets,3,4,8 insufficient alveolar ridge width,^{5,28} vertical alveolar bone defect,²⁶ and insufficient maxillary sinus floor height.² Bone grafting was immediate in three studies,^{3,4,8} while it was staged in the other studies. Two studies investigated the use of ADG for

1 ype	Study/control		Type of bone defect		Timing of bone augmentation	Type of implant placement	Number of implants Study/control
RCT	Demineralized whole tooth/	whole tooth/	Insufficient height of		Staged	Delayed, 4 months	29/28
Retrospective	B10-Oss Demineralized whole tooth/	whole tooth/	maxillary sinus floor Insufficient height of		Staged	Simultaneous implant placement with	18/16
4	Ŭ		maxillary sinus floor		_	crestal sinus floor augmentation	
RCT	Demineralized whole tooth/ Bio-Oss + SureOSS	whole tooth/ OSS	Insufficient height of maxillary sinus floor		Staged	Simultaneous implant placement with lateral sinus floor augmentation	28/31
RCT	Demineralized whole tooth/ Bio-Oss	whole tooth/	Vertical bone defect		Staged	Delayed, 6 months	21/12
RCT	Demineralized	Demineralized dentin/Bio-Oss	Fresh extraction socket (ridge preservation)		Immediate	Immediate placement	23/22
Retrospective	Demineralized whole tooth	whole tooth/	Fresh extraction socket		Immediate	Immediate placement	15/15
CCT	Tooth roots/au	Tooth roots/autogenous bone	Indee preservation) Insufficient horizontal ridge width		Staged	Delayed, 26 weeks (≈6 months)	13/10
Retrospective	Demineralized whole tooth/ autogenous bone	whole tooth/ ne	Insufficient horizontal ridge width		Staged	Simultaneous implant placement with ridge augmentation	38/41
RCT	Mineralized whole tooth/ Bio-Oss	iole tooth/	Fresh extraction socket (ridge preservation)		Immediate	Delayed, 6 months	34/32
			1.0				Total: 219/207
Follow-up placement	Follow-up after implant placement	Mean MBL (mm) Study/control		Mean ISQ Study/control	Complications Study/control	Failure Study/control	Oxford scale
N/A		N/A	Prim	Primary 64.92/70.59	N/A	N/A	2b
Study: 23.8 months Control: 29.1 month	Study: 23.8 months Control: 29.1 months	$0.07/0.04^{a}$	N/A		No	0/1	2b
2 years		N/A	Seco	Secondary 64.2/69.4	No	No	2b
N/A		N/A	Prim	Primary 72.8/70.0	N/A	N/A	1b
18 months		1.7/1.8 (6 months) 1.0/2.0 (18 months)		Primary 53.6/54.1 Secondary 77.6/78.1	No	1/1	1b
12 months		0.11/0.13 (6 months) 0.38/0.31 (12 months)		1.07.07.1 0.1	No	No	2b
Schwarz et al. ²⁸ 36–47 weeks 2019 (average 41 v months)	36–47 weeks (average 41 weeks, ≈10 months)	N/A			6/2 peri-implant mucositis	sitis No	1b
3 months		1 mm (1 case)/ 0.5 mm (1 case) (Highest values taken months)	at 3	Secondary 73.3/74.7	1/2 wound dehiscence 0/4 inflammation (pus)	No	2b

Table 1. Characteristics of the studies included in this systematic review.

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Study	Follow-up after implant Mean MBL (mm) placement Study/control	Mean MBL (mm) Study/control	Mean ISQ Study/control	Complications Study/control	Failure Study/control	Oxford scale
Santos et al. ³ 2021	18 months	0.10/0.13 (6 months) 0.35/0.42 (18 months)	Primary 77.1/77.0 2/3 peri-implant J Secondary 81.8/80.1 13/15 dehiscence 9/6 haematoma 4/4 membrane ex	2/3 peri-implant mucositis No 13/15 dehiscence 9/6 haematoma 4/4 membrane exposure imm ADo Bio- Bio-	No Cumulative survival following immediate placement: ADG 97.37% Bio-Oss 97.30%	1b
RCT, randomized	CT, randomized clinical trial; CCT, controlled clinical trial.	d clinical trial.				

Table 1. (Continued)

immediate implant placement,^{4,8} four for delayed placement,^{3,22,26,28} and three applied the graft for simultaneous implantation with ridge augmentation and maxillary sinus floor augmentation, respectively.^{5,27,29} The total number of implants placed in the ADG groups was 219, while in the control groups it was 207. The postoperative follow-up period ranged from 3 months to 29 months.

The MBL in the ADG groups ranged from 0.1 mm to 1.9 mm.^{3,8} Primary implant stability in sites grafted with an ADG following immediate implant placement was reported in one study,⁸ with a value of 53.6, while the primary ISQ values following delayed implant placement ranged from 64.92 to 77.1.^{3,22,26} Moreover, secondary implant stability measured by ISQ for the ADG groups ranged from 64.2 to 81.8.3 ⁷ One study compared secondary ISQ between autogenous dentin blocks and autogenous bone blocks, presenting values of 73.3 and 74.7, respectively, and indicating no significant difference between the groups.

Reported complications in the ADG group were peri-implant mucositis,^{3,28} haematoma, membrane exposure,³ and wound dehiscence.^{3,5} One of the two studies on immediate implant placement had two cases of failure, one in each of the groups, ADG and Bio-Oss.⁸ Thus, from the included studies, the cumulative survival rate following immediate implant placement was 97.37% for ADG and 97.30% for Bio-Oss.

Risk of bias

ADG, autogenous dentin graft; ISO, implant stability quotient; MBL, marginal bone loss; N/A, not available. ^aMarginal bone resorption is from native bone (not grafts), since the procedure was sinus floor augmentation.

The RoB 2 tool was applied to six studies (five RCT and one CCT). One was judged to have a low risk of bias³ and four had some concerns, 8,22,26,27

while the study by Schwarz et al.²⁸ had a high risk of bias. The reason for the high risk in the latter study was the high dropout rate (seven out of 30 patients) from the initially recruited cases. Fig. 2 shows the risk of bias in each domain for the included trials.

Regarding the retrospective studies, the study by Wu et al.⁴ showed a moderate risk of bias, while those by Kim et al.²⁹ and Korsch and Peichl⁵ were evaluated as having a serious risk of bias, due to the unclear inclusion of cases and the possibility of selective reporting. Fig. 3 demonstrates the risk of bias in each domain for the retrospective studies.

Results of the meta-analysis: RCTs comparing ADG to Bio-Oss

Primary implant stability (ISQ)

Three studies provided data on primary implant stability of ADG compared to Bio-Oss after delayed implant placement.^{3,22,26} Low heterogeneity was noted ($I^2 = 43\%$); therefore, the fixed-effects model was used. Overall, the meta-analysis of these studies revealed no significant difference in primary implant stability between the groups (MD -0.74, 95% CI -3.36-1.88, P = 0.58) (Fig. 4).

Secondary implant stability (ISQ)

The meta-analysis for this outcome included three studies.^{3,8,27} The measurement of implant stability was performed at 6 months postoperatively in two studies,^{8,27} while it was performed at 2 months in the other.³ The random-effects model was applied, due to the high heterogeneity between studies ($I^2 = 86\%$). No significant

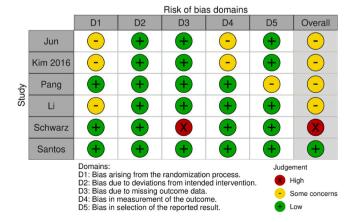


Fig. 2. Risk of bias in each domain for the randomized/controlled clinical trials.

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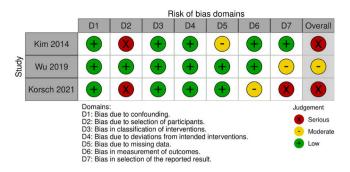


Fig. 3. Risk of bias in each domain for the included retrospective studies.

difference in secondary implant stability was noted between the ADG and Bio-Oss groups (MD -1.29, 95% CI -5.69-3.11, P = 0.57) (Fig. 5).

Marginal bone loss at 6 months

Two studies were included in this analysis.^{3,8} The total number of implants was 56 in the ADG group and 53 in the Bio-Oss group. No heterogeneity was found ($I^2 = 0\%$), and thus the fixed-effects model was applied. The results of the meta-analysis of these studies demonstrated no significant difference in MBL at 6 months between the two groups (SMD -0.26, 95% CI -0.64 to 0.12, P = 0.18) (Fig. 6).

Marginal bone loss at the final follow-up

Two studies were included this analysis.^{3,8} The final follow-up measure-

ments were taken at 18 months postoperatively. The fixed-effects model was used, as no heterogeneity was found ($I^2 = 0\%$). The meta-analysis showed no significant difference in MBL at the final follow-up between the ADG and Bio-Oss groups (SMD -0.12, 95% CI -0.50 to 0.26, P = 0.53) (Fig. 7).

Discussion

This meta-analysis is novel in investigating the autogenous dentin graft in relation to implant placement. Several studies have been conducted on this material, proving its efficacy and applicability for this procedure.^{6,12,30} Therefore, the present study was performed in order to obtain an initial comparison between the ADG and other bone grafts and to establish a base for future studies and investigations.

The ADG was applied in different procedures related to implant placement, which were delayed placement,^{3,22,26,28} immediate placement in the anterior and posterior zones,^{4,8} and simultaneously with defect repair⁵ or sinus floor elevation.^{27,29} The results were acceptable when compared with autogenous bone,²⁸ or with Bio-Oss.^{3,4,8} The cumulative survival rate following immediate implant placement was 97.37% in the ADG group and 97.30% in the Bio-Oss group. Furthermore, no reports of implant failure were mentioned after delayed implantation. However, this high survival of implants placed in ADG-augmented sites cannot be seen as conclusive, since only a few studies were included, and due to the small sample size and the short period of postoperative follow-up in these studies. Nonetheless, it can be stated that, for these limited data, the rate is comparable to those reported in other investigations on implant survival rates.³¹ Moreover, it falls within the same range when comparing it with the survival rates from other reports on the ADG.

Among the most significant complications at the implant site are peri-implant mucositis and peri-implantitis. Peri-implantitis, in particular, compromises the health of the implant and may lead to a high chance of failure, even when treated.³³ One of the aims of the present systematic review was to

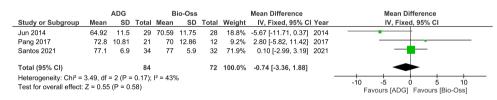


Fig. 4. Forest plot comparing primary implant stability between autogenous dentin graft (ADG) and Bio-Oss.

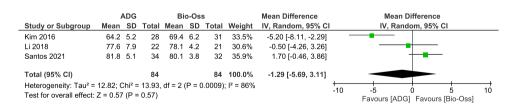


Fig. 5. Forest plot comparing secondary implant stability between autogenous dentin graft (ADG) and Bio-Oss.

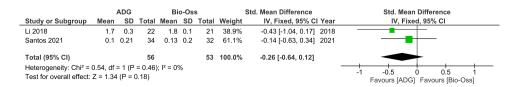


Fig. 6. Forest plot comparing marginal bone loss between autogenous dentin graft (ADG) and Bio-Oss at 6 months.

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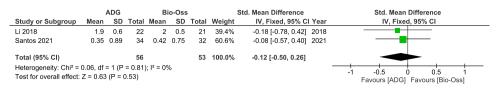


Fig. 7. Forest plot comparing marginal bone loss between autogenous dentin graft (ADG) and Bio-Oss at the final follow-up.

present preliminary data on the performance of the ADG and whether it leads to a higher degree of complications or failure. There was no case of peri-implantitis in any of the studies included. Moreover, the results from the studies comparing the incidence rates of implant-related complications and failure showed no difference between autogenous dentin and other bone grafts (autogenous bone and Bio-Oss), whether this graft was used in block or particulate form,^{3,5,28} indicating that the ADG was safe and effective for use around dental implants and did not lead to an increased risk of complications or failure.

Primary stability is an essential factor that indicates the biomechanical stability of the implant at the time of insertion in the alveolar bone, and therefore successful implant surgery. This is achieved by the mechanical retention of the fixture in the bone.⁴ Hence, a viable grafting material should promote bone formation to provide acceptable primary stability upon implant placement. The results of the meta-analysis revealed no significant difference in primary implant stability between ADG and Bio-Oss. A similar outcome was also noted for the analysis of secondary implant stability. In addition, when the secondary stability of implants placed in sites grafted with ADG blocks was compared to that of sites grafted with autogenous bone blocks, there was also no significant difference.⁵ The stated ISQ values using the ADG were in line with those in other reports using different materials for bone grafting,³⁵ and when several types of implant were placed in sites suitable for implantation without grafting.³⁶ Therefore, it is possible to conclude that the ADG resulted in acceptable implant stability and was not inferior to other bone grafts.

With respect to MBL, studies compared ADG particles and xenografts. Bio-Oss is a commercially available material that is widely used and has been proven to be effective for bone regeneration in several bone augmentation procedures.^{37,38} The outcome of

the meta-analysis on MBL demonstrated no statistically significant difference between the ADG and Bio-Oss at 6 months and at the final follow-up. This indicates that the ADG may be comparable to Bio-Oss in preserving the peri-implant bony structure, as it showed clinical success up to 18 months postoperatively. Moreover, having an MBL of no more than approximately 1-2 mm during the first year is one of the criteria set for implant success.³ Considering the reports from the included studies, it can be observed that they fall within the established range of these criteria, which also confirms that this graft led to a successful implant placement procedure.

It is important to view the results of this systematic review in light of its limitations. A small number of studies were included, and only five of them were included in the meta-analysis due to the lack of sufficient investigations at present. The studies analysed had small sample sizes, with a short period of postoperative follow-up. Moreover, the results of the meta-analysis were derived from studies with different implant placement procedures and/or different follow-up time points, which may reduce the certainty of the results. Hence, the conclusions drawn should be confirmed in future analyses with more homogeneous studies. Additionally, many investigations were excluded due to their lack of a control group, revealing that the literature is still in need of more RCTs with larger sample sizes and longer follow-up periods.

With regards to the autogenous dentin graft, a clear limitation is always present, i.e. the need for a tooth to be extracted in order to process and obtain this material. This may not be an option in several case scenarios. On the other hand, although different types of autogenous dentin graft were included in this systematic review (i.e., mineralized, demineralized, and made from whole tooth or dentin only), it is noteworthy that different conditions and structures of the autogenous dentin graft led to similar clinical outcomes, ^{11,41} and therefore these forms

were considered one in this meta-analysis. Nonetheless, analysing studies with a similar condition and structure of the autogenous dentin when more clinical trials are available would be of a high importance to support the evidence provided by this systematic review.

Ethical approval

Not required.

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Patient consent

Not required.

Competing interests

None.

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