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Autogenous particulated dentin for alveolar ridge preservation. A systematic review

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ABSTRACT

Purpose: This review aimed to investigate the clinical outcomes of autogenous particulated dentin (APD) used for alveolar ridge preservation (ARP), evaluating volume gain, histologic/histomorphometric data, and associated complications.

Material and methods: The review followed PRISMA guidelines and was registered in the International Prospective Register of Systematic Reviews (PROSPERO). An automated search was made in four databases (Medline/Pubmed, Scopus, Web of Science, and Cochrane Library) supplemented by a manual search for relevant clinical articles published before March 10th, 2022. The review included human studies of at least four patients in which extraction and subsequent ARP were performed in a single surgery. Both comparative studies and studies that assessed ARP with APD exclusively were admitted.

The quality of evidence was assessed with the Cochrane bias assessment tool, the Newcastle-Ottawa Quality Assessment Scale, and the Joanna Briggs Institute Critical Appraisal tool.

Results: Eleven studies fulfilled the inclusion criteria and were included for descriptive analysis, with a total of 215 patients, and 337 alveoli preserved by APD, spontaneous healing (blood clot), or other bone substitutes, obtaining comparatively less vertical and horizontal resorption when APD was used.

Conclusions: After dental extraction, autogenous dentin was effective in terms of volume maintenance, showing promising results in histologic/histomorphometric analysis, and a low complication rate. Nevertheless, few comparative studies with comparable parameters have been published and so more research providing long-term data is needed to confirm these findings.

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1. Introduction

Tooth extraction is one of the most widely performed dental procedures. But unless appropriate measures are taken, extraction will lead to unavoidable higher resorption of the alveolar ridge (Araújo et al., 2015), as well as structural and compositional changes in the overlying soft tissue (Tan et al., 2012). The loss of volume during the first three months has been estimated to be approximately 1.67–2.03 mm in height (Thalmair et al., 2013) and 5–7 mm in width within the first 12 months, corresponding to approximately 50 % of the original alveolar bone, this being more pronounced on the buccal than on the lingual aspect of the extraction socket (Thalmair et al., 2013; MacBeth et al., 2017; Fischer et al., 2020, Leblebicioglu et al., 2013). In this way, following dental extraction, alveolar ridge morphology may present a discrepancy in bone height between the lingual and buccal plates (Lang and Zitzmann, 2012), which can jeopardize the aesthetic outcome of any dental treatment involving tooth extraction especially in the anterior zone (Thalmair et al., 2013).

Abbreviations: ARP, Alveolar ridge preservation; GBR, guided bone regeneration; APD, Autogenous particulated dentin

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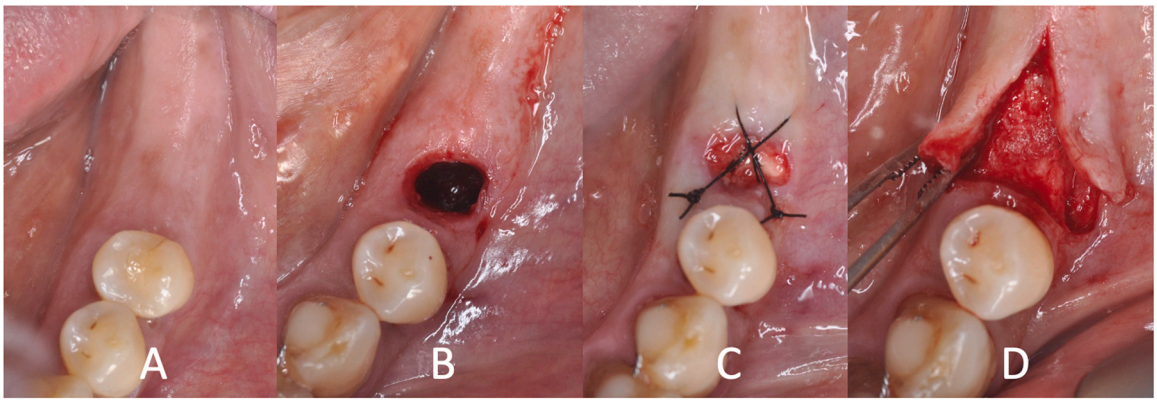

Fig. 1. Alveolar ridge preservation (clinical procedure): (A) Baseline, (B) Extracted tooth, (C) Particulated dentin graft placed in fresh post-extraction socket, (D) Re-entry. Clinical images provided by Dr. Luis Sánchez-Labrador.

In order to minimize or prevent this potential drawback, various surgical techniques have been proposed, including regenerative techniques for socket preservation, soft tissue augmentation procedures (Thoma et al., 2018), immediate implant placement, and even the socket shield technique (Saez-Alcaide et al., 2021). In this context, alveolar ridge preservation (ARP) is defined as any procedure performed at the time of or following an extraction that is designed to minimize external resorption of the ridge and maximize bone formation within the socket, thereby maintaining the existing soft and hard tissue envelope and therefore simplifying further treatment procedures (Figs. 1 and 2, Clinical images provided by Dr. Luis Sánchez-Labrador). It has been observed that 20.8 % of non-preserved alveoli require treatment by an additional bone graft for subsequent implant rehabilitation, in contrast to only 9.9 % of preserved alveoli (Atieh et al., 2015; Cadenas-Vacas et al., 2021). So, given the obvious importance of ARP, different materials have been proposed for these procedures, including autogenous bone, demineralized freeze-dried bone allograft, mineralized freeze-dried bone allograft, deproteinized bovine bone, alloplastic polymers, bioactive glasses and composite ceramic materials (MacBeth et al., 2017; De Risi et al., 2015; Keil et al., 2021). Recently, guided bone regeneration (GBR) with autogenous particulated dentin (APD) has been investigated and has shown good preliminary results in both animal (Gomes et al., 2021; Reis-Filho et al., 2012; Kabir et al., 2017) and human studies (Sánchez-Labrador et al., 2020; Kim et al., 2010, 2016; Pang et al., 2017; Li et al., 2018, Kabir et al., 2015). It has also obtained encouraging results in sinus lifting (Jeong et al., 2011, Jun et al., 2014) and ARP procedures (Del Canto-Diaz et al., 2019; Joshi et al., 2016; Jung et al., 2018).

Autogenous dentin provides a material with ideal physical (density, roughness, homogeneity) and chemical (calcium/phosphate concentration similar to human bone) properties and has been found to stimulate bone tissue formation. Human dentin is composed of 70 % inorganic content with four types of calcium phosphate (hydroxyapatite, tricalcium phosphate, octacalcium phosphate, and amorphous calcium phosphate), which endow dentin with osteoconductive properties. The hydroxyapatite in dentin is in the form of calcium phosphate with low crystal content, which makes it easily degradable by osteoclast activity. It is composed of 20 % organic content, of which 90 % is a type I collagen network and 10 % non-collagenous proteins (osteocalcin, osteonectin, sialoprotein, and phosphoprotein, which participate in bone calcification) and growth factors (bone morphogenetic proteins: BMPs, and insulin-like growth factor, which give the tooth osteoinductive properties); the remaining 10 % is water (Kabir et al., 2017; Sánchez-Labrador et al., 2020, 2021).

Because of these properties and the inherent similarities between autogenous dentin and autologous bone grafts, various research teams have ventured to apply APD in ARP procedures (Del Canto-Diaz et al., 2019; Joshi et al., 2016; Jung et al., 2018). But as far as the authors are aware, no published systematic review has evaluated the clinical outcomes of ARP with APD.

Therefore, the objectives of this review were to assess the clinical performance of APD in ARP in comparison with other bone substitutes or spontaneous healing (blood clot formation) in terms of volumetric changes, associated complications, and histomorphometric data.

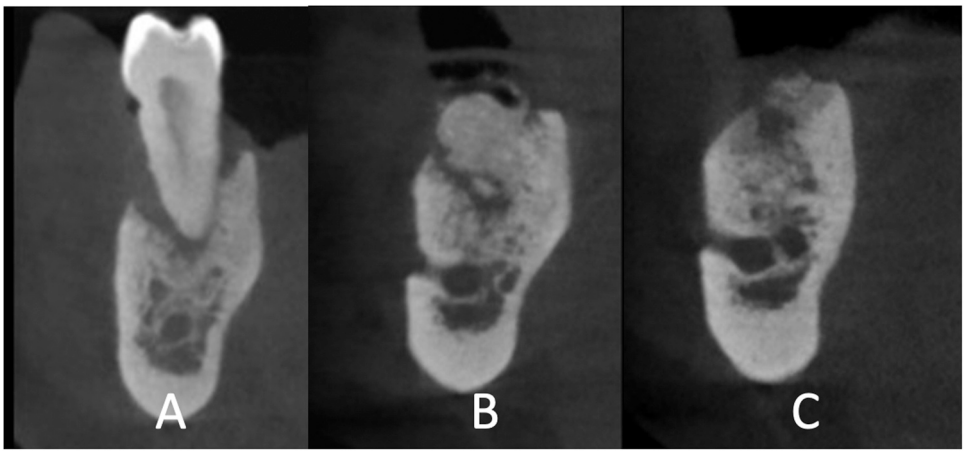

Fig. 2. Alveolar ridge preservation process (cone beam computed tomography): (A) Pre-extraction, (B): Particulated dentin graft placed in fresh post-extraction socket, (C): Bone aspect 4 months after alveolar ridge preservation procedure. Clinical images provided by Dr. Luis Sánchez-Labrador.

2. Material and methods

This systematic review followed guidelines established in the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement and was registered in the International Prospective Register of Systematic Reviews (PROSPERO; Reg. no. CRD42021246353).

It set out to answer the following PICO question (Population, Intervention, Comparison and Outcome): "In patients scheduled for restoration with dental implants after dental extraction(s), is the use of APD appropriate for ARP, in comparison with spontaneous healing or the use of other bone substitutes, in order to maintain bone volume and so avoid structural and compositional changes in the overlying soft tissue?, whereby Population (P) was defined as patients needing dental extraction(s) and subsequent implant placement; Intervention (I) as ARP of the extracted teeth with APD; Comparison (C) as ARP with other bone substitutes or spontaneous healing; and the main primary outcome (O) was volumetric changes.

2.1. Eligibility criteria

2.1.1. Inclusion criteria

- Human clinical studies.
- Randomized controlled clinical trials, cohort studies, case-control studies, cross-sectional studies.
- Case series.
- ARP with APD in comparison with other bone substitutes or blood clot formation (spontaneous healing).
- Dental extraction(s) and alveolar ridge preservation performed in the same session.
- Patient sample (related to the topic) of at least 4 subjects.
- Follow-up continuing until (at least) the time of dental implant placement.
- Articles published up to and including March 10th, 2022.

2.1.2. Exclusion criteria

- Case reports.
- Animal studies.
- In vitro studies.
- Insufficient information about the ARP procedures carried out.

2.2. Type of intervention and comparison

All the articles included enrolled four or more patients undergoing dental extractions and ARP. Due to the scarcity of comparative studies, studies that performed ARP with APD without a comparison group were also included.

2.3. Sources and search strategy

An electronic search was conducted in the online databases PubMed, Web of Science, and Cochrane Library up to and including March 10th, 2022. for articles published in English, German and Spanish, with no limit on publication date. In addition, manual searches were made in relevant oral surgery and implantology journals, in the reference sections of articles identified in the electronic search, as well as a grey literature search via the Open Grey website. The search strategy used for databases PubMed, Web of Science and Cochrane Library consisted of the following Medical Subject Headings (MeSH-Terms) and free terms: (socket preservation OR alveolar preservation OR alveolar ridge preservation OR alveolar reconstruction) AND (dentin OR autologous tooth OR particulated dentin).

2.4. Study selection and screening methods

Two reviewers (L.S.L and S.B.B) screened the titles and abstracts of the articles identified in searches independently. The same reviewers read the full manuscripts of those studies that fulfilled the inclusion criteria, or those with insufficient data in the title and abstract to reach a clear conclusion, before making a final selection. Any disagreement was resolved by discussion with a third reviewer (J.C.B-B). RefWorks Reference Management Software (Ex Libris, Jerusalem, Israel) was used to detect duplicate references in different electronic databases. If more than one study investigated the same patient cohort, the work with the longest follow-up period was selected for inclusion. Inter-reviewer reliability in the selection process and after full-text analysis was calculated to obtain a percentage of agreement and kappa correlation coefficient.

2.5. Data collection and items

The primary outcome was volumetric change (bone volume) between T0 (tooth extraction and ARP) and T1 (subsequent implant placement) Secondary outcomes were histologic/histomorphometric data, and any associated complications.

In addition, various descriptive data were studied, such as the different procedures for dentin preparation, the different devices used, the re-entry time (time between ARP and dental implant placement) and the osseointegration time (time between dental implant placement and second stage surgery).

The same two reviewers performed duplicate data extraction. When data was incomplete or missing from a study, the authors were contacted. If agreement could not be reached, data was excluded until further clarification was available. The data extracted were as follows: authors, year and journal of publication, study design, number of patients, mean age, number and location of alveoli, tooth preparation (Fig. 3, Clinical images provided by Dr. Luis Sánchez-Labrador), and device used, barrier method, post-operative medication, re-entry time, vertical and horizontal socket measurement, osseointegration time, follow-up, implant survival or success rate, complications, histology and/or histomorphometric data.

2.6. Quality assessment in individual studies

Risk of bias assessment of randomized clinical trials was performed using the method detailed in the Cochrane Handbook for Systematic Reviews and Interventions version 5.1.0 that evaluates seven domains: selection bias, allocation bias, blinding of participants and staff, blinding of the outcome assessors, incomplete data, selective notification of results, and other biases. Each was classified as low risk, high risk or uncertain risk (represented by a green (+), red (-) or yellow (?), respectively (Higgins et al., 2011).

Risk of bias assessment of cohort studies was performed using The Newcastle-Ottawa scale (NOS). This scale includes three main categories: selection of study groups, comparability of participants, and outcome. Each individual study received a maximum of 9 points (Wells et al., 2014).

Risk of bias of case series was evaluated by The Joanna Briggs Institute Critical Appraisal tool, evaluating risk through a checklist of 10 questions.

2.7. Statistical analysis

Due to the heterogeneity of the studies reviewed, meta-analysis could not be performed.

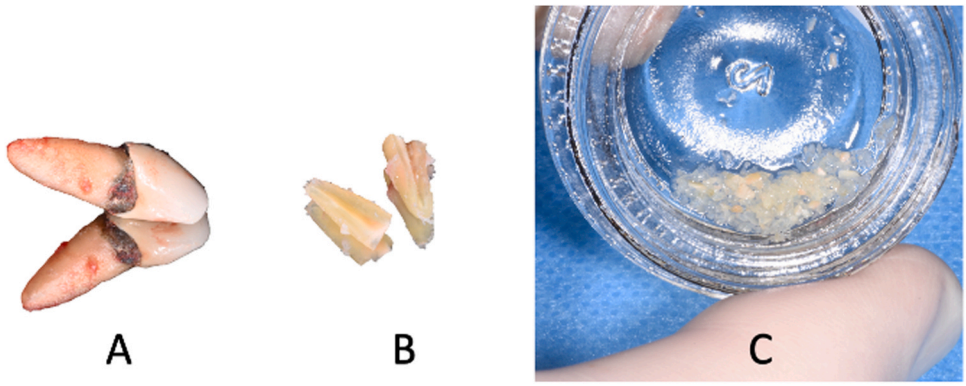

Fig. 3. Autogenous dentin preparation: (A): Extracted tooth, (B) Sectioned root, (C): Particulated dentin graft. Clinical images provided by Dr. Luis Sánchez-Labrador.

3. Results

3.1. Study selection

The initial electronic database search identified 727 articles and the manual search yielded four additional articles (n = 731). Of these studies, 194 were duplicates or triplicates and were removed. After an initial scan to eliminate articles not relevant to the focus question followed by title and abstract screening, a combined total of 27 articles were selected for full text analysis. Sixteen of them were excluded because they did not fulfill the inclusion criteria.

Finally, a total of 11 studies were selected for review and data extraction: six comparative studies and five that exclusively evaluated dentin. Three comparative studies evaluated autogenous dentin versus spontaneous healing (blood clot) and beta-tricalcium phosphate (Joshi et al., 2016), Bio-Oss© (Geistlich Pharma AG, Wolhusen) versus demineralized dentin or demineralized dentin combined with rhBMP-2 (Jung et al., 2018), and autogenous dentin versus spontaneous healing (blood clot) (Del Canto-Diaz et al., 2019). Two studies compared different methods of tooth preparation: Elfana et al. (2021) compared autogenous whole tooth with autogenous demineralized dentin graft, while Minetti et al. (2020) compared autogenous dentin graft from healthy teeth and autogenous dentin graft from endodontically treated teeth. The flow chart of the entire search and article selection process is shown in Fig. 4.

Due to the heterogeneity of the results of the studies, meta-analysis could not be realized.

Inter-investigator agreement.

Cohen's Kappa statistic between the two reviewers (L.S.L and S.B.B) was 0.931 (CI 95 % 1.005–0.857) for title and abstract selection and 0.916 (CI 95 %: 1.315–0.518) for full text assessment. Therefore, the agreement level was considered almost perfect. Third reviewer consensus evaluation was not required.

3.2. Study characteristics

Basic information about the articles such as study design, study objectives, sample size, evaluation methods, follow-up periods, and so on are outlined in Tables 1 and 2. Of the 11 articles analyzed, two were case series, four were randomized clinical trials, and five were cohort studies (four prospective and one retrospective).

All patients attended follow-up periods of at least three months after ARP, the maximum follow-up period being 35 months.

3.3. Synthesis of results

3.3.1. Patient characteristics

Studies were divided into those comparing APD with spontaneous healing or other bone substitutes, and those investigating APD without any comparison.

The six comparative studies included 129 patients, while studies without comparison groups included 86 patients. The total number of patients analyzed totaled 215 patients, with patient ages ranging between 27 and 79 years. Three studies did not mention gender (Mazor et al., 2019; Valdec et al., 2017; Pohl et al., 2020), while the other eight studies recruited 126 women and 72 men.

One study did not report the number of alveoli treated (Valdec et al., 2017). Studies without comparison groups included 199 alveoli, while comparative studies included 138 alveoli, making a total of 337 alveoli.

3.3.2. Volume maintenance

Six studies used pre- and post-surgical CBCT to determine the bone volume maintained (Del Canto-Diaz et al., 2019; Joshi et al., 2016; Jung et al., 2018; Elfana et al., 2021; Pohl et al., 2020; Andrade et al., 2020), while five studies did not evaluate volume maintenance after the ARP procedure (Minetti et al., 2020; Mazor et al., 2019; Valdec et al., 2017; Andrade et al., 2020; Minimizato et al., 2018). As for the two non-comparative studies that compared this outcome, one of them observed that horizontal and vertical dimensions were preserved and even increased (Andrade et al., 2020), while the other study obtained a vertical increase (+0.16 [buccal], +0.4 [lingual]) but a horizontal decrease (−1.39 [1 mm from the highest ridge], −0.82 [3 mm from the highest ridge], −0.44 [5 mm from the highest ridge]) (Pohl et al., 2020).

Regarding comparative studies, these reported that vertical reductions in the grafted area ranged from − 0.28 ± 0.13 to − 0.97 ± 0.39, while horizontal reductions ranged from − 0.15 ± 0.08 to − 1.54 ± 0.74, 4–6 months after the ARP procedure.

In all cases in which APD was used, both vertical and horizontal reduction was less than in the control groups (xenogeneic bone, β-TCP, dentin with rhBMP-2, or blood clot) (Del Canto-Diaz et al., 2019; Joshi et al., 2016; Elfana et al., 2021), with the exception of one study by Jung (Jung et al., 2018) in which the smallest vertical loss was seen with demineralized dentin matrix with rhBMP-2 in comparison with Bio-Oss© (Geistlich Pharma AG, Wolhusen, Switzerland) or demineralized dentin matrix alone (Jung et al., 2018). Table 2 shows all volume maintenance data. (Table 3).

3.3.3. Complications

Eight studies reported no complications (Joshi et al., 2016; Elfana et al., 2021; Minetti et al., 2020; Mazor et al., 2019; Valdec et al.,

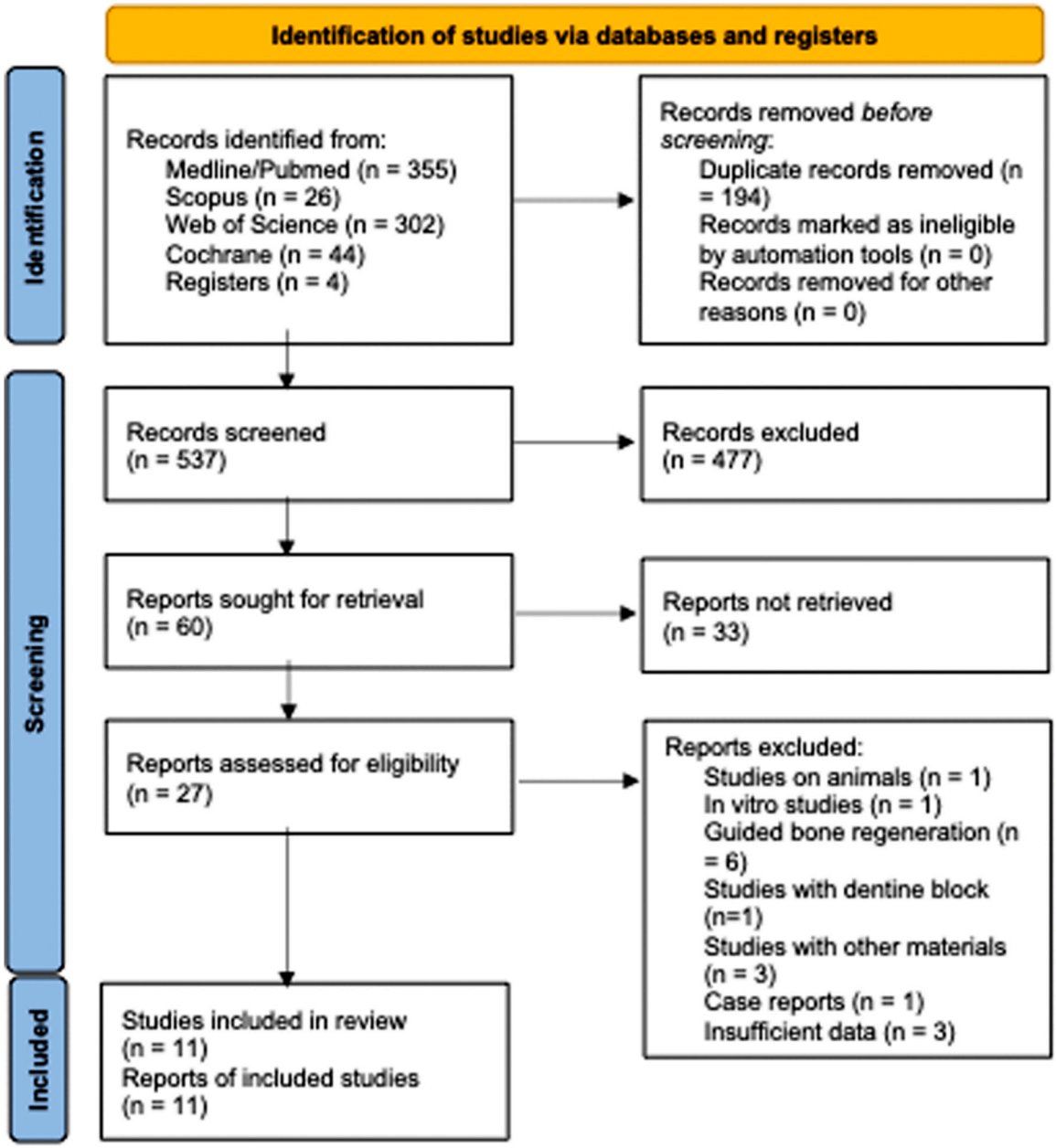

Fig. 4. Flowchart illustrating the selection process.

2017; Andrade et al., 2019; Minimizato et al., 2018; Pohl et al., 2020), one study did not mention complications (Del Canto-Diaz et al., 2019), and just two studies described complications: Minetti et al. (2020) reported one case of infection, while Jung et al. (2018) recorded complications in 4 patients out of a total of 27 (See Tables 1 and 2).

3.3.4. Tooth preparation and device used

Many devices for tooth/dentin preparation have been described in the literature; among the articles reviewed here, the Smart Dentin Grinder® was the most commonly used device (Del Canto-Diaz et al., 2019; Mazor et al., 2019; Pohl et al., 2020; Andrade et al., 2019), followed by the Tooth Transformer® (Minetti et al., 2019, 2020).

3.3.5. Histologic/Histomorphometric data

Only one of the eleven studies provided no information about histology or histomorphometry findings (Del Canto-Diaz et al., 2019). So, histological examinations were carried out in 10 out of the 11 studies (Joshi et al., 2016; Jung et al., 2018; Elfana et al., 2021; Minetti et al., 2020; Mazor et al., 2019; Valdec et al., 2017; Andrade et al., 2019; Minetti et al., 2019; Minimizato et al., 2018; Pohl et al., 2020). Histomorphometric examination was performed in 6 of the 11 studies; a percentage of vital new bone ranging from 20.78 % ± 13.29–66.5 % and a percentage of residual graft ranging from 0.9 % to 19.70 % ± 13.75 % were observed between 4 and 7 months after ARP (Jung et al., 2018; Elfana et al., 2021; Minetti et al., 2020; Mazor et al., 2019; Andrade et al., 2019; Minetti et al., 2019). All histologic and histomorphometric data are shown in Table 4.

3.3.6. Barrier method

Eight of the 11 studies employed resorbable materials (Del Canto-Diaz et al., 2019; Joshi et al., 2016; Jung et al., 2018; Elfana et al., 2021; Minetti et al., 2020; Pohl et al., 2020; Andrade et al., 2020; Minetti et al., 2019); one study performed fundamentally primary

Table 1
Studies evaluating alveolar ridge preservation with autogenous dentin.

Author Journal Year	Study type	Patient (age)	Alveolus (number and location)	Barrier method	Post-operative medication	Re-entry Osseointegration	Follow-up Implant survival/ success	Vertical/Horizontal socket measurement (method)	Complications
Mazor Z et al. Int J Periodontics Restorative Dent 2019	Case series	4 (NM)	4 (non-molars) Non-restorable caries	PTFE membrane (Cytoplast Single Osteogenics) and horizontal mattress sutures Removed 4 weeks after surgery	Amoxicillin 500 mg for 7 days Ibuprofen 400 mg qid or as needed	2–7 (2, 3, 3.5 and 7 months) 3 months	1 year post-loading 100 %	NM	NO
Valdec S et al. Int J Implant Dent 2017	Case series	4 (36–65 years)	NM Trauma (damage to one or two teeth of anterior maxilla each patient)	Autologous soft tissue graft harvested from the palate (punch)	Amoxicillin750 mg 3/day 7 days	3–4 months NM	NM	NM	NO
Andrade C et al. Clin Oral Invest 2020	Pilot study (prospective cohort study)	4 (44–63 years, MA 54 years) All female patients	10 maxillary teeth (4 incisors, 5 canines, 1 premolar)	L-PRF membranes	NM	4–6 months NM	NM NM	4 months after ARP, horizontal and vertical dimensions were preserved and even increased (CBCT)	NO
Minamizato T et al. Int J Oral Maxillofac Surg 2018	Pilot study (prospective single cohort study)	7 (2 male/ 5 female) 54.6 years	8 (3 molars, 3 anterior teeth, 2 premolars, 1 mesiodens)	Primary closure except in two cases was covered with a collagen membrane NM (membrane brand)	NM	4–6 months 3 months	24 months 100 %	NM	NO
Minetti E et al. Appl Sci 2019	Multicenter prospective cohort single arm study	98 (29 male/ 69 female) 53.7 years	119 (60 mandible 59 maxilla) (26 incisors, 8 canines, 36 premolars, 49 molars)	Collagen membrane	Amoxicillin 1 g 2/ day 7–10 days	4 months NM	5–35 months 98,94 %	NM	1 infection
Pohl S et al. Materials 2020	Retrospective cohort single arm study	12 51 ± 14 years NM (gender)	58 (39 maxilla 19 mandible) (22 incisors, 12 canines, 19 premolars, 5 molars)	PRF membranes or collagen sponge. Absorbable monofilament sutures 5.0	NM	4 months NM	NM	4 months: Vertical: + 0.16(buccal) + 0.4 (lingual) Horizontal: -1.39 (1 mm from the highest ridge) -0.82 (3 mm from the highest ridge) -0.44 (5 mm from the highest ridge) (CBCT)	NO

NM: Not Mentioned.

Table 2
Studies evaluating alveolar ridge preservation with autogenous dentin vs other bone substitutes.

Author Journal Year	Study type	Patients (number) Gender/ age (mean)	Alveolus (number and location)	Barrier method	Post-operative medication	Re-entry Osseointegration	Follow-up Implant survival/ success	Vertical/Horizontal socket measurement (method)	Complications
Del Canto-Díaz A et al. Med Oral Patol Oral Cir Bucal 2019	Pilot study (RCT)	6 (3 male/3 female) 47.6 years	12 uni-radicular (6 dentin vs. 6 clot)	15 × 20– mm collagen membrane and the edges sutured using a 5/0 monofilament suture	NM	NM	NM	At 16 weeks: dentin group: -0.42 mm/ - 0.16 mm Clot group: -1.77 mm/− 2.22 mm (CBCT)	NM
Elfana A et al. Clin Oral Implants Res 2021	RCT	10 (3 male/ 7female) 33.5 years	20 non-molar (10 autogenous whole tooth vs. 10 autogenous demineralized dentin graft) 6 maxilla 4 mandible	Collagen membrane (Hypro-Sorb®) and the edges sutured using a 5/0 monofilament suture	Amoxicillin 500 mg 8 h/7 days Ibuprofen 600 mg qid or as needed	6 months NM	NM	At 6 months: Vertical: 0.61 ± 0.20 mm (buccal) 0.66 ± 0.31 mm (lingual) in autogenous whole tooth and 0.72 ± 0.27 mm (buccal) 0.56 ± 0.24 mm (lingual) in autogenous demineralized dentin graft Horizontal: 0.85 ± 0.38 mm in autogenous whole tooth and 1.02 ± 0.45 mm in autogenous demineralized dentin graft (CBCT)	NO
Minetti E et al. Materials 2020	Pilot study (Multicenter double arm cohort prospective)	28 (10 male/ 18 female) 51.79 ± 5.97 years	34 (20 healthy whole teeth vs. 14 teeth with endodontic root canal therapy)	Collagen membrane (Bego oss ®)	2 g of amoxicillin/ clavulanic acid in one solution 2 h before the extractions	4 months NM	NM	NM	NO
Joshi C et al. Indian Soc Periodontol 2016	Pilot Study (RCT)	15 (9 male 6 female) 35.6 ± 5.7 years	45 (15 clot vs. 15 autogenous tooth graft vs. 15 beta-tricalcium phosphate) 26 maxilla 19 mandible	Chorion membrane (Tissue bank, TMH, Mumbai, India)	500 mg of amoxicillin 5 days NM (times per day)	4 months NM	NM	At 4 months: Vertical: - 0.28 ± 0.13 mm (Autogenous tooth graft) - 1.72 ± 0.56 mm (β-TCP) - 2.60 ± 0.88 mm (clot) Horizontal: - 0.15 ± 0.08 mm (Autogenous tooth graft) - 1.45 ± 0.40 mm (β-TCP) - 2.29 ± 0.40 mm (clot) (CBCT)	NO
Jung JU et al. Appl Sci 2018	Prospective randomized controlled trial	27 (16 males, 14 female) 27–79 years	27 (9 Bio-oss collagen, 9 demineralized dentin matrix, 9 demineralized dentin matrix combined with rhBMP-2) Third molars, premolar or molar	An absorbable atelocollagen plug (Rapiplug) and cross-mattress sutures (5–0 non-resorbable nylon)	Analgesics (non-steroidal anti-inflammatory drugs) and antibiotics (amoxicillin plus clavulanic acid or clindamycin for 5–7 days)	4 months NM	NM	At 4 months: Vertical in buccal/lingual: -1.14 ± 0.81/ − 0.65 ± 0.37 mm (bio-oss) -0.97 ± 0.39/ − 0.76 ± 0.29 mm (DDM) -0.82 ± 0.36/− 0.5 ± 0.22 mm (DDM with rhBMP-2) Horizontal 1/3/5 mm: -1.68 ± 1.11/− 1.24 ± 0.65/ − 0.5 ± 0.19 mm (bio-oss) -0.78 ± 0.41/− 0.49 ± 0.47/ − 0.2 ± 0.15 mm (DDM) -1.54 ± 0.74/− 0.79 ± 0.54/ − 0.32 ± 0.21 mm (DDM with	1 patient with swelling and pain (bio-oss), 2 patients with pain (dentin matrix) and 1 patient with bleeding (dentin matrix with rhBMP-2)

(*continued on next page*)

Table 2 (*continued*)

Author Journal Year	Study type	Patients (number) Gender/ age (mean)	Alveolus (number and location)	Barrier method	Post-operative medication	Re-entry Osseointegration	Follow-up Implant survival/ success	Vertical/Horizontal socket measurement (method)	Complications
								rhBMP-2) (CBCT)	

NM: Not Mentioned.

Table 3
Tooth preparation and device employed.

	Enamel	Pulp/CF	Cementum	Calculus	Restorations	PL	ST	Cleaning instrument	Dentin treatment	Device	Particle size
Mazor et al. (2019)	✓			✓	✓	✓		Tungsten carbide bur	Full teeth	SDG	300–1200 µm
Valdec et al. (2017)	✓	✓	✓			✓	✓	Rotating instruments	Cut into pieces	Bone mill	250–2000 µm
Andrade et al. (2019)					✓			Tungsten carbide bur	Mixed with L-PRF	SDG	300–1200 µm
Minimizato et al. (2018)		✓		✓	✓		✓	NM	Teeth crushed Mixed with PRP	Takige	400–800 µm
Minetti et al. (2019)				✓				Piezoelectric/diamond drill	Teeth cut in small pieces	TT	NM
Pohl et al. (2020)	✓	✓		✓	✓	✓		Carbide bur	Full teeth	SDG	300–1200 µm
Del Canto-Díaz et al. (2019)				✓	✓	✓		NM	Full teeth	SDG	300–1200 µm
Elfana et al. (2021)		✓	✓			✓	✓	NM	Full teeth	Gold bone mill	NM
Minetti et al. (2020)					✓			Diamond drill	Teeth cut in pieces	TT	NM
Joshi et al. (2016)			✓					Carbide bur	Full teeth	Conventional grinder	300–500 µm
Jung et al. (2018)		✓			✓	✓		NM	Just roots	Auto BT	NM

PL: Periodontal ligament CF: Canal filling ST: Soft tissues SDG: Smart Dentin Grinder TT: Tooth Transformer ✓Tissues removed.

Table 4
Histology and histomorphometry study.

Author Journal Year	Histology/Histomorphometry
Mazor Z et al. Int J Periodontics Restorative Dent 2019	Histology (3 months post-healing): Grafted area occupied by dentin particles connecting via bridges of woven bone. New bone surrounding the graft particles at all time points. No signs of inflammatory infiltrate. Histomorphometry (7 months post-healing): 63 % new vital bone, with vital osteocytes in the lacunae and signs of remodeling, small fraction of residual particles.
Valdec S et al. Int J Implant Dent 2017	Histology (4 months post-healing) (just in one patient): Evidence of remodeling processes between dentin and bone, without any signs of inflammation. No Histomorphometry
Andrade C et al. Clin Oral Invest 2020	Histology (4–6 months post-healing): The samples in general showed the presence of compact bone tissue with normal osteocytes and with some geometric dentin fragments (5–10 % of total mineralized tissue). The bone tissue showed moderate osteoblastic activity and a medullary space filled with connective tissue showing slight mononuclear infiltrate Histomorphometry (4–6 months post-healing): 56.5 % bone, 3.6 % remaining dentin. In 4/10 alveolus, all dentin disappeared, and in 2/10 was lower than 1 %. At 4 months bone was 26.3 %, 56.5 % at 5 months, 66.5 % at 6 months. Dentin was 10.4 % at 4 months, 4.8 % at 5 months and 0.9 % at 6 months.
Minamizato T et al. Int J Oral Maxillofac Surg 2018	Histology (4–6 months post-healing): New bone formation surrounding autogenous partially demineralized dentin matrix particles was evident, and newly formed bone and autogenous partially demineralized dentin matrix particles were found to be amalgamated. The maturation of new bone with many lacunae containing osteocytes, woven bone formation, and some lining cells on the surface of the newly formed bone. Autogenous partially demineralized dentin matrix particles were surrounded by bone with many collagen fiber-derived lamellar structures, lining of osteoblastic cells on the surface of the bone. Howship's lacunae were identified on the surface of the autogenous partially demineralized dentin matrix particles, but there were very few multinucleated osteoclastic cells. No Histomorphometry
Minetti E et al. Appl. Sci 2019	Histology (4 months post-healing): All dentin granules were almost surrounded by the newly formed bone. No inflammatory or adverse reaction was seen around the particles. Histomorphometry (4 months post-healing): The Bone Volume/Total Volume average (BV %) was 41.47 (S.D. ± 11.51), the Residual Graft/Total Volume average (Graft %) was 16.60 (S.D. ± 7.09), and the Vital Bone/Total Bone average (VB %) was 21.89 (S.D. ± 9.72).
Pohl S et al. Materials 2020	Histology (4 months post-healing): New bone formation in close contact with dentin particles (ankylosis) with no signs of inflammation or fibrous encapsulation of the autologous augmentation material. No Histomorphometry
Del Canto-Díaz A et al. Med Oral Patol Oral Cir Bucal 2019	NM
Elfana A et al. Clin Oral Implants Res 2021	Histology (6 months post-healing): In the autogenous demineralize dentin graft group H&E-stained sections revealed thick mature trabeculae of bone surrounded by fibrovascular stroma. The autogenous whole tooth group showed mature bone formation in fibrovascular stroma without any inflammatory reaction. Histomorphometry (6 months post-healing): The autogenous whole tooth group showed a total bone area of 37.55 ± 8.94 %, a residual graft area of 17.05 ± 5.58 % and a soft tissue area of 45.4 ± 4.06 %, while in the autogenous demineralized dentin graft group the area percentages were 48.4 ± 11.56 %, 11.45 ± 4.13 % and 40.15 ± 7.73 %, respectively.
Minetti E et al. Appl. Materials 2020	Histology (4 months post-healing): Showed that dentin and enamel graft materials, partially resorbed, were surrounded and included in various new bone layers. Histomorphometry (4 months post-healing): Healthy whole teeth biopsies showed a mean of 36.68 % (± 8.90 %) for bone volume, 19.70 % (± 13.75 %) for residual graft, and 20.78 % (± 13.29 %) for vital bone. In the teeth with endodontic root canal therapy group, histomorphometric analysis showed a mean of 39.16 % (± 11.51 %) for bone volume, 17.39 % (± 7.09 %) for residual graft, and 22.89 % (± 9.72 %) for vital bone.
Joshi C et al. Indian Soc Periodontol 2016	Histology (4 months post-healing): Autogenous tooth graft sites showed newly formed bone associated with connective tissue stroma rich in angiogenesis. Autogenous tooth graft particles had started to resorb and were surrounded by osteoid formation indicating new bone formation. Minimum fibrous tissue or no inflammatory cellular infiltration was observed. In comparison, β-TCP-grafted sites showed less osteoid formation. Graft particles were poorly integrated with newly forming bone. The connective tissue stroma surrounding β-TCP graft particles showed minimal evidence of angiogenesis and presence of scattered inflammatory infiltrate at some isolated sites No Histomorphometry
Jung JU et al. Appl Sci 2018	Histology (4 months post-healing): All grafted sites indicated the presence of newly formed bone and remaining parts of tooth. No signs of inflammation. Histomorphometry (4 months post-healing): Bone specimens obtained from 18 patients (6 per group). New bone comprised 22 % in bio-oss group, 33 % in DDM group and 39 % in DDM with BMP-2. There was 65 % of soft tissue in bio-oss group, 56 % in DDM group and 50 % in DDM with BMP-2 group

NM: Not Mentioned.

closure, with the exception of two cases (Minimizato et al., 2018); one study used non-resorbable membranes (Mazor et al., 2019); and the last study used soft tissue grafts punched from the palate (Valdec et al., 2017).

3.3.7. Re-entry and osseointegration time

Re-entry time was described in 10 of the 11 studies and varied between studies from two to seven months (Valdec et al., 2017; Joshi et al., 2016; Jung et al., 2018; Minetti et al., 2020, 2019; Pohl et al., 2020; Andrade et al., 2020; Minimizato et al., 2018; Elfana et al., 2021; Mazor et al., 2019). Only one study did not provide this information (Del Canto-Diaz et al., 2019).

Osseointegration time after implant placement was three months in two of the studies (Mazor et al., 2019; Minimizato et al., 2018), while the rest of the studies did not provide this data.

3.3.8. Quality assessment of individual studies

Quality assessment of the selected case control and cohort studies is summarized in Table 5 (adequate quality of evidence among the studies reviewed), quality of randomized clinical trials in Table 6

Table 5
Quality assessment of included studies using the Newcastle-Ottawa scale.

	Selection				Comparability		Outcome			Number of stars (out of 8)
Study	S1	S2	S3	S4	C1	C2	E1	E2	E3	
Andrade C et al. (2020)	★	★	★	0	★	0	0	★	★	6
Minimizato et al. (2018)	★	0	★	★	★	0	0	0	★	5
Minetti et al. (2019)	★	0	★	★	★	0	0	0	★	5
Pohl et al. (2020)	★	0	★	★	★	0	0	★	★	6
Minetti et al. (2020)	★	0	★	★	★	0	0	0	★	5

Table 6
Quality assessment of included studies using the Cochrane bias assessment tool.

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Del Canto-Diaz A et al. 2019	+	+	?	+	+	?	+
Elfana A et al. 2021	+	+	?	?	?	+	+
Joshi C et al. 2016	+	+	?	+	+	+	?
Jung JU et al. 2018	+	+	?	?	+	+	+

(medium risk of bias), and quality of the case series in Table 7 (medium risk of bias).

4. Discussion

The objectives of the present systematic review were to assess the clinical performance of APD in ARP in comparison with other bone substitutes or spontaneous healing (blood clot formation) in terms of volumetric changes, associated complications, and histomorphometric data. The search for relevant articles identified 11 eligible clinical studies (six comparative studies and five without comparison groups), which applied various devices, forms of preparation, grafting materials, osseointegration times and/or reentry times.

The placement of bone substitutes in the alveolus after dental extraction reduces the collapse of the alveolar bone ridge and facilitates subsequent rehabilitation by means of a dental implant. Although this fact would appear evident and has been described in a recent meta-analysis (Willenbacher et al., 2016), there is greater controversy and diversity of opinion regarding the filling material and/or technique (autografts, allografts, xenografts, alloplasts) that obtain the best outcomes (Willenbacher et al., 2016; Canellas et al., 2019). Autogenous bone is still considered the 'gold standard' for bone regeneration due to its osteogenic, osteoconductive and osteoinductive properties (Velázquez-Iglesias et al., 2022; Bazal-Bonelli et al., 2021) although this material suffers a series of drawbacks: additional surgery to harvest bone from a second site, prolonged surgical time, unpredictable resorption, risk to the donor site, risk of complications, and the limited availability of autologous bone (Heinemann et al., 2015; Stumbras et al., 2019, Shaikh et al., 2022). These disadvantages, as well as the fact that all biomedical specialties are evolving toward minimally invasive therapies, have driven the search for alternative materials for bone regeneration.

The primary objective of our review was to assess the volumetric changes that occur between T0 (tooth extraction and ARP) and T1 (subsequent implant placement). The results of the studies reviewed are encouraging: in all the cases, both vertical and horizontal reduction was less with ADP than in control groups. These results suggest that the technique is ideal for maintaining the existing soft and hard tissue envelope and so facilitates subsequent treatment procedures. Moreover, it should be noted that most of the studies included in this systematic review performed APR in anterior areas – the most critical area – where minimizing the resorptive process is of paramount importance. The results obtained are especially

Table 7
Quality assessment of included studies using the Joanna Briggs Institute Appraisal tool.

Study	Valdec S et al. 2017	Mazor Z et al. 2019
Were there clear criteria for inclusion in the case series?	–	+
Was the condition measured in a standard, reliable way for all participants included in the case series?	+	+
Were valid methods used for identification of the condition for all participants included in the case series?	+	–
Did the case series have consecutive inclusion of participants?	?	?
Did the case series have complete inclusion of the participants?	?	?
Was there clear reporting of the demographics of the participants in the study?	–	–
Was there clear reporting of clinical information of the participants?	+	+
Were the outcomes or follow up results of cases clearly reported?	+	+
Was there clear reporting of the presenting site (s)/clinic (s) demographic information?	–	+
Was statistical analysis appropriate?	–	–
Overall appraisal	Included	Included

+=Yes; -=No; ?=Unclear.

noteworthy considering that volumetric changes were evaluated with CBCT, as this is the most accurate method for evaluating bone changes after ARP procedures (Dominiak et al., 2021; Pickert et al., 2022).

The secondary objectives of the review were to assess histomorphometric data obtained with this new graft material and any possible complications.

Dentin offers both physical and chemical properties suited to stimulating bone tissue formation, so the promising behavior exhibited by APD could be expected. In this context, histomorphometric examinations performed between 4 and 7 months after ARP procedures showed 20.78–66.5 % new bone formation, ranges that were even higher than those obtained using xenogeneic bone grafts (20.6–36.5 %) (Vaia et al., 2021; Santos et al., 2021) or allogeneic grafts (14–42 %) (Iasella et al., 2003). Histomorphometry also observed residual graft percentages of 0.9–19.7 %, these being lower than those obtained with other materials such as xenogeneic (19.0–36.6 %) (Vaia et al., 2021) or allogeneic (19–55 %) bone grafts (Iasella et al., 2003), which may exhibit incomplete resorption in the long term due to their production processes (Minetti et al., 2022). However, it should be noted that the different studies only conducted the histomorphometric assessment once and at different times from each other, except for Andrade et al., who performed histomorphometric studies at three different times (4, 5, and 6 months), observing greater bone formation and less residual dentinal tissue at the longer maturation times. This finding suggests the direction that future research should take to clarify the optimal maturation time of this novel graft material.

Regarding complications, the secondary objective of any surgical procedure is always to prevent adverse events, minimize damage, and improve the overall outcome for the patient (Vivekanantham et al., 2014; Tagar et al., 2019). This is a basic factor that all research must consider, especially when investigating a novel material such as APD. In the present review, APD has been shown to provoke a low rate of complications (2.32 %). These complications are similar to those reported in studies of ARP procedures with other bone substitutes evaluated by other authors (Atieh et al., 2021). Moreover, although autogenous dentin does not present the osteogenic capacity of autogenous bone and the quantity available is also limited, it does exhibit appropriate behavior (as described above), at the same time as eliminating the morbidity and complications associated with autogenous bone harvesting (De Oliveira et al., 2013). In addition, this novel graft material is less costly in comparison with other biomaterials (Dhuvad et al., 2021), is well-accepted by patients, and produces fewer adverse reactions in comparison with some xenografts (Zhang et al., 2021).

The articles analyzed in the present review described a range of devices for preparing autogenous dentin, the most frequently used being the Smart Dentin Grinder® and the Tooth Transformer®. Although both produce similar particle sizes, the Smart Dentin Grinder® takes less time to prepare the dentin. Nevertheless, both devices obtain good results in ARP procedures. In any case, each author/research team prepared the tooth material in a different way, removing some or other dental tissues prior to ARP procedures. It would be interesting to compare different dentin preparation techniques in order to understand whether they produce different histomorphometric outcomes, and to find out whether enamel and/or cementum also play a role in the process of new bone formation.

Lastly, the present systematic review suffered several limitations, namely the small sample sizes in the works reviewed and a generalized failure to assess certain parameters, such as marginal bone loss around dental implants placed in areas regenerated with dentin. Moreover, different devices and tooth preparation methods were used, different grafting materials were compared, and osseointegration time and/or reentry time varied between studies. So, a uniform protocol would obtain more reliable results.

5. Conclusion

Within the limitations of this systematic review, it may be concluded that APD appears a good option as a graft material in ARP procedures due to its osteoconductive and osteoinductive properties. The studies reviewed obtained encouraging results in terms of volume maintenance and histomorphometric data. Furthermore, the dentin graft is less costly in comparison with other bone substitutes and would appear to exhibit a low complication rate. However, these promising results should be treated with caution as the data reported was drawn from studies of the – as yet – early stages of a new clinical development and the studies performed to date are heterogeneous. Further studies – randomized clinical trials, ideally – with adequate protocols, larger sample sizes, longer follow-up periods and comparisons with a wide range of bone substitutes are needed to broaden our understanding of this alternative biomaterial's clinical behavior.

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CRediT authorship contribution statement

Luis Sánchez-Labrador: Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft. **Santiago Bazal-Bonelli:** Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft. **Luis Miguel Sáez-Alcaide:** Methodology, Writing – original draft. **Sáez-Alcaide Luis Miguel:** Methodology, Writing – original draft. **Jorge Cortés-Bretón Brinkmann:** Supervision, Validation, Writing – review & editing, Software. **José María Martínez-González:** Supervision, Validation, Writing – review & editing, Project administration.

Conflict of interest

None of the authors declare conflict of interests.

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