Journal of Dentistry 145 (2024) 104986

Contents lists available at ScienceDirect

Journal of Dentistry

journal homepage: www.elsevier.com/locate/jdent

Review article

Learn, unlearn, and relearn post-extraction alveolar socket healing: Evolving knowledge and practices

Melissa Rachel Fok *, Lijian Jin

Division of Periodontology and Implant Dentistry, Faculty of Dentistry, The University of Hong Kong, Hong Kong SAR, PR China

ARTICLE INFO

Keywords:
Tooth extraction
Tooth socket
Alveolar process
Alveolar bone loss
Socket healing
Extraction healing
Alveolar ridge preservation
Alveolar ridge augmentation
Dimension
Review

ABSTRACT

Objective: This review was to offer a comprehensive analysis of currently available evidence on post-extraction alveolar socket healing, including i) the histological and molecular events during alveolar socket healing, ii) the dimensional ridge alterations after socket healing and controversies relating to sinus pneumatisation, iii) the patient-specific factors, procedural elements, and site-related variables influencing socket healing, iv) techniques and effectiveness of alveolar ridge preservation (ARP) procedure, and v) the philosophies and cost-effectiveness of ARP in clinical practice.

Sources and study selection: To investigate the dimensional profiles of the alveolar ridge following unassisted healing, an overview of systematic reviews was conducted in February 2024 by two independent reviewers. Four electronic databases were searched in Pubmed, Embase, Web of science and Cochrane Library between 2004 and 2024 to identify all relevant systematic reviews on post-extraction healing. A further manual search of reviews was also conducted. The articles were further reviewed in full text for relevance. The AMSTAR-2 appraisal tool was adopted to assess methodological quality. Current research pertaining to other listed objectives was objectively analysed in narration.

Data: 11 out of 459 retrieved studies were selected and ultimately covered in this review on the dimensional changes of alveolar ridge following natural healing: Seven systematic reviews and four systematic reviews with meta-analyses. The methodological quality of all included reviews was critically low.

Conclusion: This review thoroughly examines the healing profiles of post-extraction alveolar sockets and highlights the dynamic process with overlapping phases and the inter-individual variability in outcomes. ARP procedure is a potential strategy for facilitating prosthetic site development, while the current evidence is limited. Herein, an individualised and prosthetically driven approach is crucial. Further well sized and designed trials with novel biomaterials need to be undertaken, and the role of artificial intelligence in predicting healing and assisting clinical decision-making could be explored.

Clinical significance: By advancing our understanding of alveolar socket healing and its management strategies, clinicians can make more informed decisions regarding patient and site level assessment and selection, surgical techniques, and biomaterial choices, ultimately contributing to the enhanced healing process with reduced complications and improved quality of life for patients undergoing tooth extraction and dental implant treatments.

1. Introduction

The earliest evidence of dental extractions, or tooth removal, dates back to the ancient civilisations of China and Egypt around 3000–6000 BC [1,2]. In these early societies, rudimentary tools and instruments like forceps, chisels, mallets, or even fingers were used for tooth removal, typically without anaesthesia. Tooth forceps were the last resort to treat toothache in the ancient world, and it is a ubiquitous dental procedure. Intriguingly, the tools and procedures to extract hopeless teeth in modern dentistry have remained mostly unaltered from the past. Fortunately, our comprehension of alveolar healing and sinus pneumatisation following tooth extraction has advanced with time. This hastened understanding is fueled by the advent of dental implants and the clinicians' desire to understand the post-extraction healing patterns of

* Corresponding author at: Clinical Assistant Professor, Division of Periodontology and Implant Dentistry, Faculty of Dentistry, The University of Hong Kong, Address: Room 3B51B, 34 Hospital Road, Sai Yin Pun, Hong Kong SAR, PR China.
E-mail address: melfok@hku.hk (M.R. Fok).

https://doi.org/10.1016/j.jdent.2024.104986
Received 11 January 2024; Received in revised form 31 March 2024; Accepted 2 April 2024
Available online 3 April 2024

the alveolar process – the basis for implant osseointegration, which is crucial for prosthetically driven implant planning [3,4] and optimising esthetic outcome [5], function and post-treatment tissue stability. This review aims to emphasise the current knowledge on post-extraction healing, sinus changes, and their relationship with contemporary concepts of implant site development and implant rehabilitation of the partially edentulous ridge.

2. The alveolar process

The alveolar process as a tooth-dependent structure develops in parallel with tooth eruption and yet supports the tooth [6,7]. It is bounded coronally by the bone crest and apically by an imaginary horizontal line perpendicular to the axis of tooth at the apex. Hence, its morphologic characteristics are dependent on the root form and length, size and orientation of the developing tooth [8]. The bone below the apical limit of the tooth apex is identified as the basal bone of the maxilla and mandible [6]. The height and thickness of the alveolus are of moderate to high heritability, with heritability values ranging from 0.52 to 0.55 [9,10]. The majority of the facial alveolar bone at the anterior maxilla and mandible across populations have been consistently found to be $\leq$1 mm thin [11–14]. Heimes et al., in their meta-analysis that included 45 studies, showed a buccal plate thickness of 0.76 $\pm$ 0.49 mm in the maxillary frontal, 1.40 $\pm$ 0.75 mm in the maxillary premolar, 1.42 $\pm$ 0.74 mm in the maxillary molar, 0.95 $\pm$ 0.58 mm in the mandibular frontal, 0.86 $\pm$ 0.51 mm in the mandibular premolar, and 1.20 $\pm$ 0.96 mm in the mandibular molar region respectively. These results suggest that the maxillary premolar and molar buccal plates are morphologically more similar, the same with the lower anterior and premolar regions. A recent systematic review has accounted for 87 % of facial alveolar bone thickness heterogeneity in geographical settings, with Asian populations showing the lowest thickness values [15]. It has important implications as the thickness of the alveolar plate has been shown to critically influence the amount of post-extraction ridge resorption [11,16].

3. Histological and molecular changes in alveolar socket healing

Following tooth extraction, a series of orchestrated tissue changes occur, typically resulting in morphological alterations, ridge height, width, and volume loss. These changes display high inter-individual variation [17–19] and depend on various intrinsic and extrinsic modifying factors, including individual healing capacity, systemic status, pre-existing destruction of tooth-supporting tissues (e.g., reasons for extraction), tissue trauma imposed during extraction, denture wear [20], age, pressure exerted on wound during healing, size of the extraction defect and other environmental factors [17]. The first documented evaluation of this healing process was performed in a healthy canine with intact periodontium [21]. Since then, the post-extraction histological events and tissue changes have been extensively studied in animals (rats, dogs, sheep, and monkeys) and humans (autopsy and biopsy material) with heterogeneous methodologies [17,22–37]. In animal studies, the whole alveolar healing socket was often subjected to histological analysis, while in humans, biopsies of marginal tissue or central socket were obtained for analysis. The extraction wound healing process is a dynamic sequence consisting of four overlapping and precisely orchestrated phases, each with distinct physiological roles [38]. The general histogenesis of repair following extraction is conserved among mammals and resembles intramembranous ossification with direct bone formation and no intermediate cartilage formation [39]. However, the timing of tissue replacement varies as the experimental animals used were not consistent in terms of confounding factors such as age, sex, species and diet. Healing in rats is rapid, with observed complete cortication between buccal and lingual crests on the twenty-fifth day [27]. Meanwhile, healing in the canine model is 3–5 times faster than in humans [8]. The distinguished patterns of tissue transition observed in the canine and rat extraction healing models could not be observed in humans [17].

3.1. Haemostasis and coagulation phase

Immediately after extraction, the periodontal ligaments joining the alveolus and root cementum are severed, vascular injury exists, and the socket occurs with the formation of blood clots. The process of haemostasis sets in to control bleeding [40]. Haemostasis involves the intricate and coordinated interplay of platelets, plasma and fibrinolytic proteins, blood vasculatures and cytokine mediators to seal off impaired vessels from surrounding tissue. In primary hemostasis, vascular spasm and vasoconstriction occur; platelets in the blood are exposed to the extracellular matrix, roll and adhere to exposed subendothelial extracellular matrix at sites of vascular injury mediated by von Willebrand Factor, undergo platelet activation, degranulation, aggregation and platelet plug formation. Secondary haemostasis is marked by the activation of a coagulation cascade consisting of both intrinsic and extrinsic pathways. This process leads to the conversion of soluble fibrinogen to insoluble fibrin for forming a crosslinked fibrin meshwork, thereby further stabilising and consolidating the platelet plug and blood clot. The resultant thrombus functions as a provisional matrix to support the migration of inflammatory cells. Enmeshed platelets release a range of cytokines and growth factors such as interleukin-1ß (IL-1β), platelet-derived growth factor (PDGF-AA,-AB), transforming growth factor 1β (TGF- 1β), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF) and insulin-like growth factor (IGF), essentially signaling the subsequent inflammatory and proliferative phases of wound healing [41,42]. The final stage of tertiary hemostasis involves the plasmin-mediated dissolution of fibrin clots to restore normal blood flow [40].

3.2. Inflammatory phase

The inflammatory phase sets in within 24 to 72 h shortly after the commencement of primary haemostasis and activates the innate immune system. Unlike skeletal healing, the healing of an extraction site in the oral cavity presents a distinct micro-environment subjected to the constant bathing of saliva and microbial contamination. The microbial challenge stems from distinct sites in the oral environment, as well as locally, from the pathogenic microorganisms that cause tooth decay, periodontal destruction, and non-resolving infections and necessitate the eventual need for tooth extraction. The continued presence of pathogenic biofilm and high bacterial load at the wound site are known to sustain a pro-inflammatory state, leading to delayed healing [43]. Locally injured cells release calcium waves, reactive oxygen species (ROS), lipid mediators and chemokines within a few minutes of the insult. Polymorphonuclear neutrophils (PMN), as the first responders at wound site defence, can sense the ‘calcium alarm’ and switch from exploratory patrolling to coordinated swarming migration mode via connexin-43 (Cx43) hemichannels [44]. They also respond via pattern-recognition receptors (PRR) to damaged-associated molecular patterns (DAMPs) released from damaged tissue through inflammasome activation and cell death [45], pathogen-associated molecular patterns from pathogens (i.e. lipopolysaccharide, lipoteichoic acid, flagellin) [46], complement proteins and chemokines. PMN performs phagocytosis, utilises oxidant- or protease-dependent mechanisms, secretes anti-microbial peptides, and releases aurophilic granules and neutrophil extracellular traps (NETs) to aid pathogen clearance [47]. PMNs will also coordinate downstream inflammatory cell recruitment, migration, differentiation and proliferation. As platelet degranulation takes place, the release of growth factors, inflammatory cytokines (IL-1β, TNF-α), and chemokines (PDGF, PF4, TGF-β, HIF, SDF1/CXCL12) will signal inflammatory cells to the wound site to fight bacterial ingress and to clear up dead cells and bacteria for new tissue to form [41]. Monocytes translocate to the wound site and transdifferentiate to macrophage in response to TGF-β a few days after injury [48]. Early macrophages are in an M1 proinflammatory state that synthesises matrix metalloproteinases

(MMPs) to digest ECM and thrombus, and they are responsible for killing and engulfing pathogens. Macrophages also participate in the critical clearance of neutrophils through neutrophil efferocytosis. Failure of neutrophil clearance will lead to a persistent inflammatory state and failure of the wound to progress to the proliferative phase [49]. The resolution of inflammation is characterised by macrophage transition to reparative M2 phenotype. M2 macrophage has spatial and phenotypic similarities to endothelial cells. They mediate angiogenesis and vessel anastomosis via 'vascular mimicry' [50]. Anti-inflammatory macrophages also release anti-inflammatory mediators (e.g., IL-1R antagonist and IL-10) and growth factors like VEGF, FGF, TGF-β, and IGF1, in turn promoting fibroblast proliferation, ECM synthesis, angiogenesis and activating osteoblast [49,51]. Macrophages can also acquire profibrotic (M2a) or fibrinolytic (M2c) phenotypes depending on the stage of wound healing and the biological cues. Adaptive immunity will also be called into play to mount more delayed but specific immune responses mediated by B and T cells [49]. During the inflammatory phase, the composite of inflammatory cells like macrophages, immature fibroblasts and vascular sprouts in the socket collectively form the granulation tissue [8]. Amler [22] and Trombelli et al. [17] were consistent in their findings that by one week and 2–4 weeks, the initial blood clot and fibrin meshwork embedding platelet, erythrocytes and leukocytes were completely remodelled into granulation connective tissue with erythrocytes scattered between mesenchymal cells. This process is centrifugal and starts from the outer border and gradually spreads to the centre of the socket [52]. The proliferative phase is instituted as the inflammatory cells phagocytose debris and 'sterilise' the site.

3.3. Proliferative phase

The proliferative phase in extraction healing can consist of fibroplasia and formation of woven bone, which progressively replace the granulation tissue into the provisional matrix and woven bone by 6–8 weeks in human extraction sockets [17]. Fibroplasia is characterised by the rapid fibroblast migration and proliferation, collagen synthesis and deposition of extracellular matrix proteins, constituting the provisional matrix. Fibroblasts are activated and attracted to the wounds via various growth factors (e.g., TGF-β, FGF-2 and PDGF) [53]. Then, ECM components are synthesised and deposited, such as collagen, elastin and proteoglycans, creating a provisional matrix for supporting cell migration and new tissue formation. The tissue is enriched with mesenchymal cells, vascular structures and collagen fibres, with a provisional matrix occupying a mean of approximately 60 % of the area [17]. The mature ECM supports cell migration and enhances cell adhesion mediated by the interaction between filopodia and pseudopodia extension with fibronectin and collagen proteins in the matrix [52]. High expression of collagen type I and MMPs (i.e. MMP-2, MMP-9) has been reported in this phase, where collagen I serve as an early bone formation marker and MMPs are responsible for ECM remodelling and angiogenesis [28]. More than half of the cells in this provisional matrix had been found to possess osteogenic potential by studying Cbfa1/Runx2 and osteocalcin cell marker expression profiles [54,55]. The process of angiogenesis co-occurs and is essential for delivering oxygen, nutrients, and growth factors to the wound site. Endothelial cells, which line the interior surface of blood vessels, proliferate and migrate to form new capillaries. Oxygen-deprived circumstances can support endothelial cell growth and specialisation, contributing to the orderly sequence of angiogenesis. This process is marked by enzyme-driven basal lamina breakdown, enabling vessel crawling, cell expansion, differentiation, and ultimately, maturation and remodelling [56]. VEGF and FGF are among the key molecules that stimulate angiogenesis [57]. VEGF increases endothelial cell differentiation and proliferation, and it also increasingly recruits endothelial progenitor cells [56]. Scala et al. studied experimental extraction healing in monkeys, they observed the occupation of alveolus by provisional matrix and newly formed bone lining the socket bony walls at ten days. Nahles et al. also demonstrated that the highest osteoblastic activity occurs within the first four weeks of healing, simultaneous with CD31 endothelial cell expression patterns that initiate from the apical portion and propagate to the coronal portion of the socket at 12 weeks [54]. Residual periodontal ligament (PDL) fibres have been reported to disappear after two weeks in dogs [25], while small amounts can remain for up to 30 days of healing in monkeys [34], and epithelia remain of Malasseza and cementicles in the extraction sockets of humans [58] which progressively gets replaced by the matrix. The woven bone formation could be observed as early as 2–4 weeks of healing in humans, presenting as finger-like projections of new bone, occupying a mean of 6 % of tissue area; the proportion increases to a mean of 32–34 % tissue area at 6–8 weeks and 12–24 weeks of healing [17]. The deposition of woven bone from the provisional matrix is characterised by the differentiation of mesenchymal cells to osteogenic lineage and the high expression of BMP-7 from 2 to 4-weeks to 6–8 weeks of healing, and this process of bone morphogenesis and osteoblast differentiation has been shown to be mediated by TGF-β and BMPs [59]. BMPs have also been demonstrated to stimulate the synthesis and secretion of growth factors like VEGF, FGF, PDGF and IGF that synergistically regulate angiogenesis [60]. The source of osteogenic lineage cells has been shown to originate from the hematopoietic organs such as the bone marrow [61], periosteum, periodontal ligament, adipocytes and pericytes [62–65]. Few osteoclasts were identified in the marrow spaces of the bundle bone that lines the socket walls, contributing to the remodelling of the socket. In parallel with the loss of PDL fibre and modelling of outer bundle bone, the osteoid matrix is being laid down within the socket [57]. The provisional matrix is progressively penetrated by bone-forming cells and newly formed blood vessels, where woven bone gradually lies around vascular structures to form primary osteon or the Harversian system [17,34]. The primary osteon may occasionally be reinforced by paralleled-fibered bone [8]. This poor load-bearing woven bone will subsequently undergo replacement and remodelling to mature lamellar bone and bone marrow. The socket peripheral epithelium proliferates towards the socket centre over the provisional matrix to gradually close the wound [52].

3.4. Bone modelling and remodelling phase

Both bone modelling and remodelling mark the last phase of the socket healing, subsequently bringing about qualitative and quantitative changes in the alveolar ridge. Bone modelling refers to a change in the topography and structural architecture, translating to the resorption of the socket wall, bundle bone and the resultant dimensional changes of the alveolar ridge following extraction healing. Whilst bone remodelling reflects the alteration without concomitant change in the topography and architecture of the bone, translating to replacing the immature woven bone with lamellar bone and bone marrow in the healing process [8]. The modelling/remodelling process is tightly regulated by complex signaling cascades and pathways, such as receptor activator of nuclear factor kappa B (RANK), RANK ligand (RANKL), osteoprotegerin (OPG), osteocalcin (OC), osteopontin (OPN), osterix (OST), macrophage colony-stimulating factor (M-CSF) and runt-related transcription factor 2 (RUNX2), which is coordinated by the activities of osteoblasts and osteoclasts [59,66].

The remodelling process starts apically (at four weeks) as it propagates to the coronal portion at about 12 weeks [54] and ends with the bridging of the cortical plates at the crestal level with the cortical bone. Bone remodelling can take months and years, and the process shows high variability among individuals [8,17]. To illustrate the range of variability, study results across research groups will be briefly described. Evian et al. identified the period between 8 and 12 weeks when osteogenesis slows down and a substantial amount of mature trabecular bone containing osteoblasts and an osteoid seam is formed [67]. Ahn et al. reported socket 'cortication' as early as ten weeks post-extraction [68]. Lindhe et al. reported 60–65 % of tissue volume consisting of lamellar bone (including parallel-fibred, concentric and interstitial lamella) and

bone marrow in the posterior maxilla following over 16-week healing response. At the same time, only a few samples presented a ridge of dense cortical bone at the coronal portion, termed the 'corticalization' of the ridge [69]. Nahles et al. reported complete site ossification at 12 weeks following extraction in one-fourth of the sites, while one-fourth of sites showed apical ossification with the coronal region of the specimen still occupied by the provisional matrix [54]. Carlsson et al. noted that significant variations occurred in the amount of newly formed bone in 30 subjects [70]. Trombelli et al. also corroborated 'the great variation between samples with respect to tissue formation and maturation' [17]. Their study results displayed substantially slower patterns of lamellar bone/bone marrow deposition, with only 1 out of 11 biopsies demonstrating lamellar bone/bone marrow formation at 12 to 24 weeks of healing. Bertl et al., in a retrospective radiographic study, also reported similar findings that three-quarters of sockets were not completely corticated at 3 to 6 months, and complete cortication was observed in around 80 % of sockets following 9–12 months of healing [71]. It can be concluded that complete bone healing and remodelling may sometimes take longer than 24 weeks.

The process of bone modelling was shown to proceed with remodelling, as it is evident that two-thirds of the ridge dimensional alteration occurred within the first three months [19]. After extraction, osteoclasts are identified around the buccal and lingual bone crest walls and the outer and inner (bundle bone) socket bone walls [8,23,72–74]. Here, bone resorption was more dependent on postmitotic osteoclast precursor cells derived from hematopoietic organs rather than from the socket during the initial period of wound healing [72]. The canon that bone modelling occurs primarily at the buccal surfaces following extraction is derived from evidence from an experimental canine extraction study demonstrating the apical positioning of the buccal about the lingual wall by 2 mm after eight weeks of healing at the premolar region [75]. However, the lingual walls are also equally susceptible to modelling, with the extent of resorption dictated more by the initial thickness of the socket wall, as observed from other human studies [76,77] and also consistent with our unpublished human data at the molar sites. The thickness of the lingual wall in animal studies was usually wider than the buccal walls, thus explaining the greater vertical and horizontal modelling at the side of the thin buccal plate. Major morphological and dimensional changes following extraction are known to occur during the first year following tooth extraction, with the most significant change occurring during the first eight weeks due to the initial elevated osteoclastic activity [19,77]. The histological tissue constitution and topographical and dimensional alterations appear to be influenced by a range of patient-related, procedural-related and site-related modifying factors that will be described later.

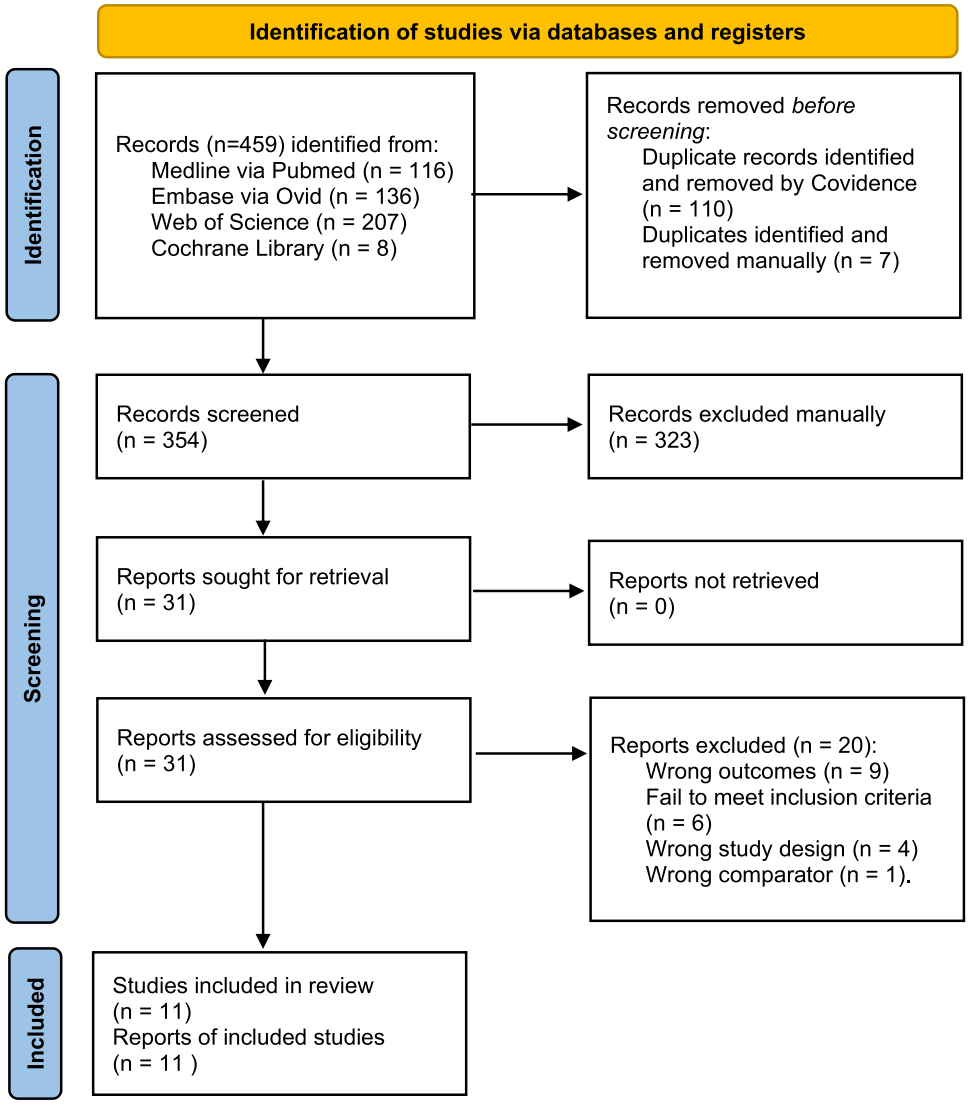

Fig. 1. PRISMA flowchart of search strategy and selection process (PRISMA 2020) [90].

Table 1
Descriptive summary of included systematic reviews.

Publication Author (Year)	Journal	Country	Study type	Study focus question	Total number of included studies	Number of included studies in meta-analysis
Barootchi et al. (2023) [89]	Periodontology 2000	USA	Systematic review	To provide a complete evidence-based assessment of the complications and cost-effectiveness of different modalities of ARP.	36. All included studies are RCCTs.	NA
Chatzopoulos et al. (2024) [86]	The Journal of Prosthetic Dentistry	USA	Systematic review and meta-analysis	To assess the efficacy of ARP with dPTFE membranes with or without grafting materials in post extraction sites.	23. 14 RCCTs, 4 retrospective cohort studies, 3 case series, 2 prospective CCTs.	5
Couso-Queiruga et al. (2021) [78]	Journal of Clinical Periodontology	USA	Systematic review and meta-analysis	To analyse the evidence on post-extraction dimensional changes in the alveolar ridge after unassisted socket healing	28. 25 RCCTs, 3 non-RCTs	20
Fischer et al. (2022) [81]	International Journal of Implant Dentistry	Switzerland	Systematic review and meta-analysis	To assess the dimensional establishment of bony envelop after ARP with DBBM to estimate the surgical feasibility for standard diameter implants without additional augmentation	9. All included studies are RCCTs.	9
Horvath et al. (2013) [82]	Clinical Oral Investigation	UK	Systematic review	To examine the effect of ARP compared to unassisted socket healing	14. 8 RCCTs, 6 CCTs	NA
Jambhekar et al. (2015) [83]	The Journal of Prosthetic Dentistry	USA	Systematic review	To analyse the clinical outcomes of ARP following flapless tooth extraction and identify the graft material that results in the least loss of ridge dimensions, maximum amount of vital bone, the least remnant graft material, and the least connective tissue	32. All included studies are RCCTs.	NA
Morjaria et al. (2014) [79]	Clinical Implant Dentistry and Related Research	UK	Systematic review	To assess if there is any benefit in grafting and/or GBR in the management of extraction socket.	9. All included studies are RCCTs.	NA
Natto et al. (2017) [85]	International Journal of Periodontics an Restorative Dentistry	Saudi Arabia	Systematic review and network meta-analysis	To identify and rank the performance of different ARP modalities by dimensional changes in ridge after tooth extractions.	8. All included studies are RCCTs	8
Tan et al. (2012) [77]	Clinical Oral Implants Research	Hong Kong, China	Systematic review	To assess the magnitude of dimensional changes of the alveolar ridge up to 12 months following tooth extraction in humans.	20. 11 RCCTs, 5 CCTs, 4 cohort studies.	NA
Ten Heggeler et al. (2010) [84]	Clinical Oral Implants Research	The Netherlands	Systematic review	To assess the effect of socket preservation therapies in non-molar regions versus spontaneous healing with respect to ridge dimensions	9. 6 RCCTs, 3 CCTs	NA
Van der Weijden et al. (2009) [76]	Journal of Clinical Periodontology	The Netherlands	Systematic review	To assess the dimensional changes of the alveolar ridge after tooth extraction	12. 6 RCCTs, 4 CCTs, 1 case-series, 1 prospective clinical trial	NA

ARP, alveolar ridge preservation; dPTFE, high-density polytetrafluoroethylene; RCCTs: randomised controlled clinical trials; CCTs: controlled clinical trials; NA, not applicable; DBBM, deproteinised bovine bone mineral; GBR, guided bone regeneration.

4. Dimensional changes in unassisted alveolar socket healing

Post-extraction alterations in both hard and soft tissues have been investigated with various clinical and radiographic methodologies. Methods in hard tissue assessment included lateral cephalometric radiographs, peri-apical radiographs, computed tomography, cone-beam computed tomography, and re-entry using the reference tools like stents or pins. Soft tissue assessments were often made on physical study casts, digitised casts, or digital intra-oral scans. A series of systematic reviews on the topic of socket healing had been conducted by the scientific community to address knowledge gaps pertaining to treatment planning for an aesthetic, functional and maintenance friendly prosthetic rehabilitation following tooth loss. However, the majority of reviews focus on the efficacy of various alveolar ridge preservation modalities and not spontaneous healing per se. The most recent quality assessment review on systematic review on alveolar ridge preservation was published in 2022 [78], while no such quality assessment of reviews was conducted in relation to our chosen topic. Given the increased number of studies on alveolar ridge preservation and the increased observations on the comparative arm of a portion of these studies for spontaneous healing after extraction. This overview of systematic reviews aims to summarise the data pertaining to the hard tissue dimensional changes of the alveolar ridge following post-extraction spontaneous healing.

4.1. Materials and methods

This review adheres to the PRIOR guidelines [79]. The protocol has been registered in Open Science Framework (OSF) database hosted by the Center for Open Science and can be publicly accessed at https://doi.org/10.17605/OSF.IO/5BAFG. Ethical approval was not needed for this overview.

4.1.1. Eligibility criteria

Systematic reviews published in indexed peer-reviewed journals with or without meta-analysis of controlled or non-controlled clinical trials or case series on adult humans ≥18 years, with reported pooled estimate from ≥2 studies on non-third molar post-extraction hard tissue dimensional changes following spontaneous/natural extraction healing. The definition of systematic review in this overview encompasses the systematic search of ≥2 databases following a pre-defined search strategy for identification of studies, and a systematic multi-stage process of screening, full texts review and selection of studies following a predefined set of inclusion/exclusion criteria. The search was limited to

Table 2
Summary of AMSTAR-2 assessments of included reviews.

	Barootchi et al. (2023) [89]	Chatzopoulos et al. (2024) [86]	Couso-Queiruga et al. (2021) [78]	Fischer et al. (2022) [81]	Horvath et al. (2013) [82]	Jambhekar et al. (2015) [83]	Morjaria et al. (2014) [79]	Natto et al. (2017) [85]	Tan et al. (2012) [77]	Ten Heggeler et al. (2010) [84]	Van der Weijden et al. (2009) [76]
1. Complete research PICO question and inclusion criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Registered protocol	No	Yes	Yes	No	No	No	No	No	No	No	No
3. Study selection explanation	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
4. Comprehensive search strategy	Partial Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes
5. Duplicate study selection	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Duplicate data extraction	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
7. List and explanation of excluded studies	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	No
8. Description of included studies	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	Partial yes	Yes	Yes	Yes
9. Satisfactory RoB assessment	No	Yes	Yes	Yes	Yes	No	Yes	Partial yes	Yes	Yes	Yes
10. Report the source of funding of included studies	No	No	No	No	Yes	No	No	No	No	No	No
11. Appropriate meta-analytical methods	No meta-analysis	Yes	Yes	Yes	No meta-analysis	No meta-analysis	No meta-analysis	No	No meta-analysis	No meta-analysis	No meta-analysis
12. Meta-analytical assessment of impact of RoB on the results	No meta-analysis	No	Yes	Yes	No meta-analysis	No meta-analysis	No meta-analysis	No	No meta-analysis	No meta-analysis	No meta-analysis
13. Consideration of RoB when interpreting results	No	No	No	Yes	Yes	No	Yes	Yes	No	Yes	No
14. Discussion of any heterogeneity	No	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes
15. Assessment of the impact of publication bias	No meta-analysis	No	No	Yes	No meta-analysis	No meta-analysis	No meta-analysis	No	No meta-analysis	No meta-analysis	No meta-analysis
16. Report conflicts of interest for conducing the review	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes
Overall quality	**Critically low**	**Critically low**	**Critically low**	**Critically low**	**Critically low**	**Critically low**	**Critically low**	**Critically low**	**Critically low**	**Critically low**	**Critically low**

AMSTAR, A Measurement Tool to Assess Systematic Reviews; RoB, risk of bias; PICO, Population, Intervention, Comparison, and Outcome.

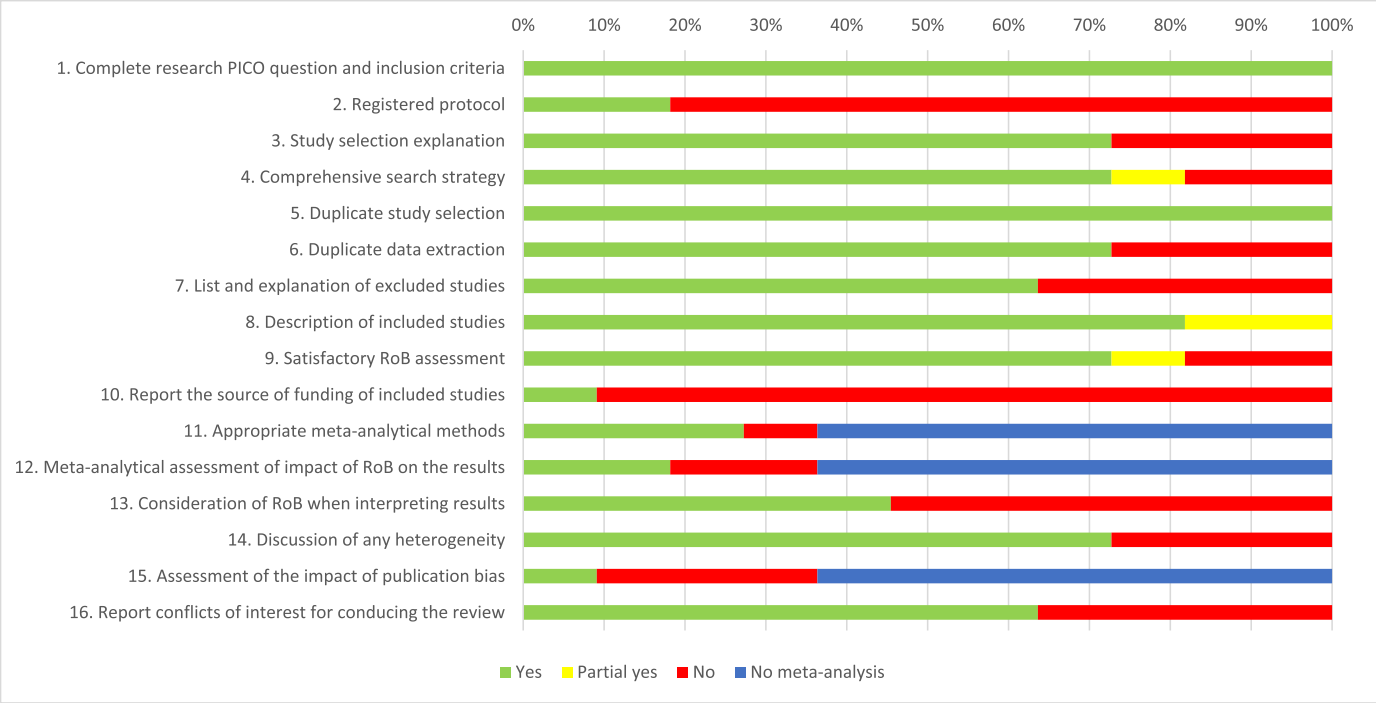

Fig. 2. Visual representation of findings from AMSTAR-2 domains (RoB, risk of bias).

the period between 2004 and 2024 and publication language in English. Such restrictions balances pragmatic consideration in resources and inclusion of reviews of reasonable scientific rigor. Primary studies, literature reviews and critical reviews were excluded.

4.1.2. Information sources and search strategy

Four databases were systematically searched on 29 Feb 2024: Medline via Pubmed, Embase via Ovid, Web of Science and Cochrane Library. The literature search was performed using a combination of MeSH term and free keyword listed in Supplementary Table 1. The search was limited to systematic reviews published in the last 20 years (2004–2024/2). To identify additional reviews, a thorough examination of the bibliographies of all included studies was performed manually. Detailed search strategies for each database can be found in Supplementary Table 1.

4.1.3. Study selection

The Covidence platform (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia, accessible at www.covidence.org) was utilised for the screening process. Two reviewers (M.F. & T.F.) independently and in duplicate screened the titles, abstracts, and keywords derived from the search results. Manual and automated detection methods, provided by the Covidence platform, were employed to eliminate duplicate records. Subsequently, the full texts of the remaining articles were retrieved. Two reviewers (M.F. & T.F.) independently evaluated these articles in full text for eligibility according to the criteria outlined in Section 4.1.1. Throughout the selection process, any discrepancies regarding the eligibility of articles were resolved through discussions among the reviewers and a third reviewer was available but not required to resolve conflict in this review. Articles that did not meet the eligibility criteria were excluded and the reasons for their exclusion were documented in Supplementary Table 2. Inter-examiner agreement was assessed and reported using Cohen's Kappa statistics.

4.1.4. Data extraction

An electronic data extraction spreadsheet in excel was developed to facilitate the systematic collection of data from the included studies. The initial data extraction was performed by a single reviewer (M.F.), while a second reviewer (T.F.) verified and examined the entire process. Any discrepancies in the extracted data were resolved through discussions until a consensus was reached. For each study, the recorded data included the following aspects: author, publication year, journal, country, study type, study focus question/objective, total number of included studies, number of included studies in meta-analysis, tooth location, duration of healing, method of assessment, pooled estimate of post-extraction dimensional change, number of included studies for pooled estimate calculation.

4.1.5. Quality assessment

The methodological quality of the included systematic reviews was evaluated using the AMSTAR-2 tool [80]. This recently developed instrument comprises 16 items and focuses on categorising the overall confidence of each systematic review into four groups (high, moderate, low, and critically low quality) based on the adherence to certain critical domains that may impact the validity of a review and its conclusions. Thus, when one or more critical weaknesses are present, an SR should be regarded as having low or critically low quality. Two independent reviewers (M.F. & T.F.) conducted the quality assessment, and any disagreements were resolved by open discussion. The outcomes of the quality assessment were summarised in a table, and a visual chart illustrating the quality of each domain was constructed with excel.

4.2. Results

4.2.1. Included studies

459 articles were identified through the electronic search, from which 31 were retained after screening titles and abstracts for full-text analysis. Subsequently, 20 articles were excluded for reasons detailed in Fig. 1 and Supplementary Table 2. The manual search did not yield any additional publications. Ultimately, 11 pertinent systematic reviews were incorporated into this overview [76,77,81–89]. A flowchart illustrating the progression of study selection during the systematic review process can be found in Fig. 1. The inter-examiner agreement, as

Table 3
Summary table for post-extraction dimensional changes across systematic reviews.

Study (Year)	Tooth location	Duration of healing (months)	Method of assessment	Number of included studies for quantitative analyses	Pooled estimate
Barootchi et al. (2023) [93]	Non-molars	4 months	Clinical and radiographic observations	Unclear, ≦17	Width reduction: Crest (up to 1 mm below) 3.38 mm (95 % CI: 3.25, 3.52); 3 mm below crest: 1.88 mm (95 % CI: 1.50, 2.25); 5 mm below crest (95 % CI: 0.80, 1.24); percentage width reduction at crest: 40 % Mid-facial height reduction: 1.94 mm (95 % CI: 1.70, 2.18) Mid-lingual height reduction: 1.33 mm (95 % CI: 1.17, 1.49) Mesial height reduction: 0.53 mm (95 % CI: 0.43, 0.63) Distal height reduction: 0.53 mm (95 % CI: 0.43, 0.63)
Chatzopoulos et al. (2024) [89]	All pooled	3–4 months	Clinical and radiographic observations	3	Width: −3.23 mm, 95 % CI: −5.37, 1.10
					Height: −2.17, 95 % CI: −2.84, 1.51
Couso-Queiruga et al. (2021) [81]	Non-molars	2–9 months	Clinical re-entry observation	8	Width reduction: MD: 2.73 mm, 95 % CI: 2.36, 3.11
				8	Mid-facial height reduction: MD: 1.71 mm, 95 % CI: 1.30, 2.12
				6	Mid-lingual height reduction: MD: 1.44 mm, 95 % CI: 0.78, 2.10
	Non-molars		Radiographic observations	7	Width reduction: MD: 2.54 mm, 95 % CI: 1.97, 3.11
				6	Mid-facial height reduction: MD: 1.65 mm, 95 % CI: 0.42, 2.88
				6	Mid-lingual height reduction: MD: 0.87 mm, 95 % CI: 0.36, 1.38
	Molars		Radiographic observations	4	Width reduction: MD: 3.61 mm, 95 % CI: 3.24, 3.98
				3	Mid-facial height reduction: MD: 1.46 mm, 95 % CI: 0.73, 2.20
				3	Mid-lingual height reduction: MD: 1.20 mm, 95 % CI: 0.56, 1.83
Fischer et al. (2022) [84]	Anterior	2–12 months	Clinical and radiographic observations	5	Crest width: 3.99 mm (SD 1.30) - 5.77 mm (SD 1.24)
	All pooled			4	Crest width: 4.04 mm (SD 3.83) - 9.80 mm (SD 1.50)
Horvath et al. (2013) [85]	All pooled	1–9 months	Clinical re-entry observation	3	Width reduction: 2.5 mm to 4.6 ± 0.3mm
				4	Height reduction: 0.8 ± 1.6 to 3.6 ± 1.5mm
Jambhekar et al. (2015) [86]	All pooled	mean: 17.2 weeks	Clinical re-entry observation	9	Width reduction at ridge crest: 2.79mm
				10	Height reduction from ridge crest: 1.74mm
Morjaria et al. (2014) [82]	All pooled	3 - 12 months	Clinical re-entry observation	5	Width reduction: 2.47 mm (SD 0.4 mm) to 4.56 mm (SD 0.33 mm)
				5	Height reduction: 0.9 mm (SD 1.6 mm) to 3.6 mm (SD 1.5 mm)
			Radiographic observations	3	Height reduction: 0.51 mm (no SD) to 1.17 mm (SD 1.23 mm)
Natto et al. (2017) [88]	All pooled	4–9 months	Clinical and radiographic observations	6 (height), 8 (width)	Width: −2.01 mm (credible interval −2.92 to −1.04) Height: −1.11 mm (credible interval −6.21 to 3.88
Tan et al. (2012) [77]	All pooled	6 months	Clinical re-entry observation	6	Width reduction: 3.79 ± 0.23 mm; percentage width reduction: 32 % (3 months), 29–63 % (6–7 months)
				6	Height reduction: 1.24 ± 0.11 mm on buccal; percentage height reduction: 11–22 % (6 months)
				2	Height reduction: 0.84±0.62 mm on mesial
				2	Height reduction: 0.80±0.71 mm on distal
Ten Heggeler et al. (2011) [87]	Non-molars	3–7 months	Clinical and radiographic observations	9	Width reduction: 2.6 to 4.6mm
				9	Height reduction 0.4 to 3.9mm
Van der Weijden et al. (2009) [76]	Non-molars	3–6 months	Clinical and radiographic observations	9	Width reduction: 2.6 to 4.6mm
				9	Height reduction: 0.4 to 3.9mm

CI: confidence interval, MD: mean difference, SD: standard deviation.

measured by Cohen's kappa coefficient, was 0.93.

The characteristics of included systematic reviews are summarised in Table 1. All of the reviews were published between 2009 and 2024. Of the 11 systematic reviews, 3 included meta-analysis and 1 conducted a network meta-analysis. Only three systematic reviews were focused on assessing the dimensional changes of alveolar ridge after unassisted tooth extraction. The remaining systematic reviews were focused on assessing the effect of ARP.

4.2.2. Quality assessment of included studies

The methodological quality of included systematic review was assessed using the AMSTAR-2 tool, with findings summarised in Table 2. All systematic reviews possess more than 1 critical weakness in the 16 AMSTAR-2 domains. Hence all studies are ranked critically low in methodological quality. A visual representation of the findings for each domain can be found in Fig. 2. Majority of reviews failed to register protocol, report source of funding of the included studies and consider risk of bias in interpretation of results. Considering the outcome of interest of this review is the ridge dimensional change of unassisted socket healing, the impact of funding information on reporting bias of this outcome may be minimal.

4.3. Data synthesis and commentary

Eleven relevant systematic review with meta-analysis were identified reporting hard tissue dimensional changes in alveolar socket healing [76,77,81–89] and findings are summarised in Table 3. There is a general pattern of greater buccal and lingual height reduction as compared to mesial and distal one, while the width reduction reduces with increasing distance from the alveolar crest [77]. The proximal bone is maintained by periodontal ligaments of the adjacent teeth if present [5]. The amount of ridge horizontal reduction (29–63 %) is more significant than the vertical reduction (11–22 %) during a period of 3 to 7 months, with major modelling occurring in the first three months [77]. A review by Tan et al. concluded from 6 re-entry studies a vertical reduction of 1.24 ± 0.11 mm (buccal), 0.84 ± 0.62 mm (mesial) and 0.80 ± 0.71 mm (distal) at 6-month healing, and from 5 studies a horizontal dimensional reduction of 3.79 ± 0.23 mm at six months of healing with considerable heterogeneity. However, the review could not analyse different assessment methods, tooth location, type, reasons for extraction and socket integrity due to insufficient studies with similar methodology reporting outcomes and a lack of reporting from the primary studies.

A more recent report by Couso-Queiruga and co-workers included 28 articles for quantitative analysis. They gave additional insights into the anatomical difference between molar and non-molar sites in terms of post-extraction dimensional changes (Fig. 3). Pooled estimates were comparable in non-molar sites regardless of assessment methods. Mean vertical mid-facial, mid-lingual and horizontal reduction examined radiographically was 1.65 mm (95 % CI: 0.42–2.88), 0.87 mm (95 % CI: 0.36–1.38) and 2.54 mm (95 % CI: 1.97–3.11) respectively in non-molar sites. Mean vertical mid-facial, mid-lingual and horizontal ridge reduction assessed radiographically was 1.46 mm (95 % CI: 0.73–2.20), 1.20 mm (95 % CI: 0.56–1.83) and 3.61 mm (95 % CI: 3.24–3.98) respectively in molar sites. The magnitude of post-extraction ridge width reduction was found to be greater in molar than non-molar sites (3.61 vs 2.54 mm); mid-facial ridge height reduction was slightly higher in non-molar sites compared to molar sites (1.65 vs 1.46 mm), mid-lingual ridge height reduction was higher in molar sites with reference to non-molar sites (1.2 vs 0.79 mm). Maxillary non-molar sites with facial bone plate >1 mm were found to have significantly less ridge width reduction and mid-facial ridge height reduction (1.17 mm, 95 % CI: 0.84–1.50; 1.17 mm, 95 % CI: 0.86–1.48) [81]. Similar to the limitations in other reviews, the effect of local (i.e. socket integrity, reasons for extraction), systemic (i.e. smoking, diabetes) and surgical factors (i.e. primary/secondary intention healing, atraumatic extraction) could not be assessed due to heterogeneous methodologies and a lack of reporting in the included studies. Future studies with improved reporting on local, systemic, and surgical variables are recommended.

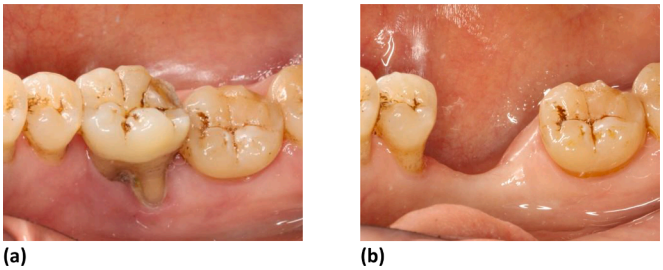

Fig. 3. An example of alterations in the ridge dimensions during the natural healing process of a tooth extraction socket over six months (a) Baseline (b) 6 months.

The predictive value of facial bone thickness and supra-crestal soft tissue height, collectively termed as the periodontal phenotype, in post-extraction ridge width and height reduction only pertained to non-molar sites [11,91,92] due to the lack of studies that investigated their predictive value in molar sites alveolar ridge resorption [81]. Araujo et al. proposed that the bundle bone is a tooth-dependent structure, and a larger proportion of the buccal plate comprises bundle bone as compared to the lingual plate. Hence, once the tooth is lost, the buccal plate will be lost significantly through bone modelling [23]. However, the buccal and lingual relative height difference was found to be less pronounced than what was reported in a canine lower premolar extraction model by Araujo et al.. Tan et al. calculated a relative difference of 0.3–0.6 mm over 3 and 7 months, while Couso-Queiruga et al. calculated a relative difference of around 0.27 mm at non-molar sites and 0.26 mm at molar sites. The classical human study by Schropp et al. also concluded an increased reduction of ridge width in the molar region versus the premolar area, and similarly in the mandible versus the maxilla [19]. The discrepancy between animal and human studies and the post-extraction dimensional changes presented in the literature can be better appreciated by putting into perspective the previously described buccal bone thickness data from Heimes et al. [14]. The mean thickness of buccal bone for the upper posterior teeth is >1 mm, and the mean buccal bone thickness of the lower anterior and premolar teeth is <1 mm, thus explaining the reported patterns of vertical dimensional changes in other studies. This notion was also in alignment with new evidence in the literature. Barootchi et al. demonstrated, in spontaneously healed non-molar sites, the significant association of an increase in facial bone thickness with the attenuation of mid-crestal resorption of horizontal and vertical ridge within the most coronal 2 mm [93].

5. Sinus pneumatisation

The maxillary sinus is the largest among all sinus spaces and most relevant to dentistry, as it borders the maxillary alveolus and lies in close proximity to the maxillary teeth. The phenomenon of sinus pneumatisation has been frequently attributed as the main reason for inadequate bone height at the maxillary region for implant placement, necessitating the need for sinus floor elevation procedures to gain bone height. Pneumatisation of all paranasal sinuses is a normal physiologic process that occurs during growth. The pneumatisation process is initiated by osteoclastic resorption of cortical walls in the sinus and the deposition of osteoid inferiorly [94]. In a Japanese study analysing 115 CT scans, the maxillary sinus volume increased up to 20 years of age but decreased afterwards with a correlation coefficient of −0.43 [95,96]. Most of the studies on sinus pneumatisation are cross-sectional and retrospective, comparing contralateral dentate and edentulous sites of the same subject, limiting the validity of the findings and only giving a general impression of the topic. Some authors suggest the occurrence of

post-extraction sinus pneumatisation through the floor remodelling in the sinus could result in 'paper-thin' cortical basal and lateral bone [97,98]. Sharon et al. studied 152 panoramic radiographs with contralateral comparisons of dentate and edentulous sites and concluded that posterior maxillary tooth extraction caused inferior sinus expansion. More expansion (up to 5.27 ± 1.59 mm) was observed after tooth extraction surrounded by a superiorly curving sinus floor, extraction of multiple adjacent posterior teeth and maxillary second molars [99]. Farina et al., in a retrospective analysis of 32 CT scans comparing dentate and edentulous sextants, reported sinus pneumatisation accounting for up to 46 % of the variation in bone height [100]. However, multiple studies challenged the notion of extensive post-extraction sinus pneumatisation, as no significant difference in sinus volume and sinus dimensions between the dentate and edentulous group in older adults was found [95,101–103], pointing to the fact limited pneumatisation occurs in sinus after tooth loss. Cavalcanti et al. recently conducted a cross-sectional analysis of 183 CBCTs and compared a single edentulous space with its contralateral tooth. The mean amount of sinus pneumatisation was reported to be 0.9 ± 2.93 mm, a value much less than what was reported by Sharan et al. [104]. They also observed that when a sinus recess/pneumatisation was present before extraction, virtually no pneumatisation at that site would occur. Instead, pneumatisation happened in regions without previous pneumatisation. In addition, the presence of localised sinus pneumatisation/sinus recess was associated with reduced healed ridge height (4.28 ± 2.45 mm). The reduced healed ridge height may be a misnomer as the baseline ridge height may already be reduced for sites presented with localised sinus pneumatisation/ interradicular sinus recess. Similarly, in another retrospective CBCT study by Hameed et al., minimal sinus floor alteration was found following extraction (0.47 ± 0.32 mm), and alveolar crest height alterations account for 88 % of post-extraction dimensional change [103]. Considering the average error of 0.98 % for CBCT imaging, the small amount of sinus floor change may be due to imaging error instead of actual changes [105]. In a recent alveolar ridge preservation RCT by Cha et al. focusing on upper molars, the extent of sinus floor level change in sites allowed for spontaneous healing was reported to be −1.16 mm (−1.73, −0.61), which was also in alignment with values from previous CBCT studies.

An attempt to classify the association of the sinus with the roots of the upper teeth was first proposed by Friedfeld et al. [106] and was subsequently modified by various authors [107,108]. The latter two classifications were similar regarding the vertical relationship assessment, with the classification proposed by Kwak et al. more comprehensive regarding 3-dimensional assessment in computer tomography. These classification systems aim to help clinicians assess the amount of protrusion of roots into the sinus and estimate the risk of pneumatisation, which are crucial for pre-prosthetic treatment consideration and surgical implant planning. Sharan et al. demonstrated an overestimation of root protrusion into the sinus by panoramic radiograph compared to CT, and only 39 % of teeth with roots appearing to project on the sinus cavity in panoramic radiograph agree with paired CT findings [108]. This highlights the limited diagnostic capability of panoramic radiographs, the difficulty of using plain radiographs to assess the true relationship of the sinus recesses about the maxillary tooth roots, the location and inferior extent of the sinus recess, and hence justifies the need for additional pre-operative 3D diagnostic imaging in line with recent guidelines [109]. Therefore, the earlier studies that reported progressive pneumatisation following extraction based on panoramic radiograph assessments must be interpreted cautiously.

6. Clinical factors affecting alveolar socket healing

A pleiomorph of patient-related, procedural-related and site-related modifying factors appear to interact and influence the temporal histogenesis of repair, topographical and dimensional alterations following extraction.

6.1. Patient-related factors

Significant inter-individual variation in tissue formation and maturation has been observed in the literature. Yet the specific individual factors that affect bone physiology are not yet fully understood and are scarcely reported in the literature. Regardless, animal studies have demonstrated that angiogenesis and osteogenesis decrease in older organisms [54,110,111]. As age increases, a decline in endothelial potential has been observed, driven by ageing-related changes in ECM and cellular senescence [112,113]. Sex and race also profoundly affect human skull anatomy and dental morphometry, partially contributing to anatomical variations that affect the healing pattern [114,115].

Smoking is known to post deleterious effects on multiple systems and organs, including the oral cavity. An examination of biopsy specimens taken from extraction sites in both non-smokers and smokers showed that smokers exhibited higher amounts of osteoid and fibrous tissue. In contrast, non-smokers showed more bone marrow and lamellar bone, suggesting that non-smokers can experience more advanced remodelling compared to smokers [69]. Findings from Lindhe et al. aligned with previous research, which shows that smoking affects inflammation processes (involving neutrophils and macrophages), wound recovery (including fibroblast function and collagen creation), and bone modelling and remodelling processes [69,116,117]. A more extensive alveolar ridge dimensional reduction (0.5 mm increased height reduction) in the maxillary non-molar region, as well as delayed post-extraction socket healing in smokers, were reported from a prospective study after six months of healing [118]. Urban et al. also reported a higher early failure rate for immediate implant placement in molar regions among smokers [119]. Poorly controlled or untreated diabetes mellitus is also known to impact healing outcomes negatively [120]. Tooth extraction healing was found to be slower in diabetic compared to a healthy patient at seven days postoperatively, with greater socket dimensions and more complications like swelling and infection reported among the diabetic group [121]. Hypertension and age were associated with increased odds for erratic socket healing with fibrous scare following ≥12 weeks of healing [122]. The majority of pre-clinical studies presented negative impacts of osteoporosis on extraction healing. However, most studies are rated with unclear bias, making it difficult to draw broader conclusions [123]. There are contradictory results in the existing literature, and the influence of osteoporosis on oral bone loss is yet to be determined, awaiting further clarification [124,125].

6.2. Procedural-related factors

The elevation of a coronal mucoperiosteal flap has been shown in both animal and human studies to induce osteoclastic activities and vertical bone resorption [126–128]. The elevation of a mucoperiosteal flap was demonstrated to account for loss of attachment and bone resorption (0.6 mm) from classical periodontal literature v. Keeping the periosteum intact during extraction was shown to reduce the resorption rate of the socket. At the same time, the detected difference was diminished with time [129], in alignment with later findings from Araujo & Lindhe [130].

Atraumatic extraction techniques play a critical role in preventing alveolar bone loss regardless of how the socket is treated after extraction, as evident from the minimal and non-significant bone resorption values among all three atraumatic extraction treatment arms in a total of 125 patients [131].

Multiple adjacent extractions have been associated with a greater extent of crestal resorption. This notion is mainly based on two pieces of evidence. The first originates from Pietrokovski and colleagues. By examining 120 dried skulls, they observed that having multiple neighbouring toothless areas results in a more pronounced concavity [132]. In another retrospective study, Pramstraller studied 127 CT scans and noted that the absence of teeth adjacent to the edentulous site could affect the relative vertical ridge position (cementoenamel junction of

canine as reference) but not the bone height or width [133]. Al-Askar et al. demonstrated that contiguous teeth extraction in dogs leads to more ridge width loss, especially in the lower posterior region when three teeth are extracted. However, no ridge height data was reported [134]. To summarise, the relevant studies are either performed on the canine model or are retrospective. The touted findings from human studies may be more related to periodontal destructions before extraction or the time-dependent disuse atrophy rather than the actual effect of multiple extractions. Further time-controlled prospective clinical studies are required to clarify the exact relationship.

The use of chlorhexidine digluconate mouthrinse for 30 days after extraction was shown to reduce approximal bone height reduction by 0.94 mm [135,136]. However, the practicality and cost-effectiveness of instructing patients to rinse with 0.12 % chlorhexidine for 30 days after extraction is debatable.

The use of hyaluronic acid for wound healing enhancement has recently received considerable attention given its antibacterial, anti-inflammatory properties and versatility in application [137–140]. A recent systematic review and meta-analysis including five preclinical and 22 clinical studies concluded that the positive effects of hyaluronic acid as an adjunct to tooth extraction demonstrated in pre-clinical studies failed to be translated in clinical studies in terms of reducing alveolar ridge modelling and enhancing bone formation [141]. On the other hand, their meta-analysis demonstrated a significant reduction in pain perception after lower third molar extraction and enhanced soft tissue healing with its adjunct use [141].

6.3. Site-related factors

Local factors that may affect socket healing outcomes encompass the periodontal phenotype (bone morphotype and gingival phenotype, anatomical location, tooth angulation, the integrity of the extraction sockets, which may also be linked to the reasons for extraction, the use of prosthesis and other differences in anatomy at the various tooth sites [142]. These factors may interact and show multicollinearity.

Thin buccal bone was associated with more extensive bone resorption [92], while the effect of ARP could be negligible in thick bones [16]. The molar sites were also demonstrated to harbour slightly less lamellar bone and more bone marrow than tissue sampled from premolar locations [69], suggesting potential histological variations dependent on anatomical site. In a retrospective analysis of 1226 records, Kim and colleagues found that the highest incidence of erratic socket healing was observed in mandibular molar locations [122]. It was hypothesised that extracting posterior teeth is more challenging, and their socket dimensions are naturally bigger, resulting in greater dimensional changes compared to premolar locations [133]. As previously described in Sections 4 and 5 on the topics of dimensional ridge alterations and sinus pneumatisation, depending on the intrinsic anatomical differences (pre-extraction ridge width, bone plate thickness, sinus recess, etc.) allied with the location of extraction (incisors, premolars, molars), the patterns of alveolar healing will vary.

The socket integrity at the time of extraction and the extent of bone destruction from periodontal disease were found to affect the extent of socket remodelling. In a prospective study involving 17 extracted molars due to advanced periodontal disease, Zhao et al. demonstrated that the impact of extraction may be overshadowed by bone destruction from periodontal disease, as the ridge height and width changes reported in their study were less pronounced than those reported in other extraction studies with intact sockets [143,144]. Cha et al. reported more pronounced palatal bone resorption attributing to the more severely damaged palatal wall at baseline of the ARP test group sites compared to the spontaneous healing group, indicating that the baseline socket configuration can affect the efficacy of ARP and bone modelling patterns [145]. Sabri et al. summarised up to 13 classification systems for single-rooted extraction sockets in a recent systematic review. Based on combining all important parameters from the systematic synthesis of evidence, they proposed a new classification system that also integrated patient and extraction-related factors as class modifiers, aiming to inform prognosis and treatment planning before extractions [146]. These classification models remain to be validated for their conceptual soundness and fit for clinical decision-making purposes in clinical studies.

Long-term denture wearing contributes to notably increased resorption of residual alveolar ridges than non-denture wearers. It is partially attributed to the pressure from the prostheses [147–150]. The loss of alveolar height under complete denture wear was found to be more severe in the mandible than in the maxilla [148,151].

7. Alveolar ridge preservation (ARP) procedure

ARP, as the name implies, is a procedure intended to preserve the alveolar ridge and limit bone resorption following tooth extraction, either for implant site development to reduce the need for auxiliary grafting or to facilitate other prosthetic rehabilitation. Various grafting materials derived from human, animal, or synthetic sources, in combination with or without different socket sealing techniques, have been reported aiming to mitigate post-extraction dimensional changes, maximising the quality and quantity of bone, and improve patient outcomes [85,152–156]. The list of grafting materials utilised in this process consists of particulate autogenous bone chips and dentine chips [157,158], allografts, xenografts, and alloplasts; biologics include growth factors like enamel matrix derivative (EMD), rhBMP-2, platelet-rich fibrin/autologous blood-derived products (ABPs) and hyaluronic acid [154,156]. Sockets sealing materials include resorbable bovine and porcine collagen matrices, collagen plugs, non-resorbable expanded polytetrafluoroethylene (ePTFE) and dense polytetrafluoroethylene membrane (dPTFE) membranes [152,154,155,159]. Advocates of ARP postulated that based on principles of guided bone regeneration, the added graft materials will act as space maintainers and scaffold to stabilise blood clots and protect the site from external destabilising factors, thus allowing osteo-conduction, progressive mineralisation of tissue, and eventually replacement of graft with host tissue [57,59]. Araujo et al., in a series of beagle dog studies, demonstrated histologically that minimal woven bone trabeculae were detected around the lateral socket walls and apical of the graft materials in the grafted sites after two weeks of healing, while the inserted bovine xenograft particles in the socket central and marginal portion were encapsulated by non-mineralised connective tissue lined by multinucleated cells [160,161].

7.1. Efficacy of ARP

To date, the existing collection of systematic reviews assessing the efficacy of ARP is consistent in their findings, confirming that ARP techniques can attenuate but not eliminate dimensional changes following extraction [152,154]. Evidence suggests that the use of bone graft substitutes in slower resorbing modes, such as xenografts, allografts, and autogenous partially demineralised dentin matrix (APDDM), seems to yield improved outcomes [154,157,158]. The most recent Cochrane systematic review shows that the reported reduction in loss of width and height of alveolar ridge comparing xenografts with extraction were (MD −1.18 mm, 95 % CI −1.82) and (MD −1.35 mm, 95 % CI −2.00 to −0.70, 6 studies, 184 participants, 201 extraction sites) respectively; reduction in loss of alveolar height comparing allograft with extraction was (MD −3.73 mm; 95 % CI −4.05 to −3.41; 1 study, 15 participants, 60 extraction sites) [152]. Here, there was no significant difference in the need for additional augmentation or implant failure among groups. However, the overall certainty evidence was graded low to very low, and the majority of the studies included were restricted to the assessment of relatively intact extraction sites and did not inform the behaviour of molar sites. A subsequent review investigated the effectiveness of ARP in damaged extraction sockets [162] and reached a similar conclusion. In contrast, there was a significantly less need of

further bone grafting for placing implants. Only one molar study was included in their review, and the magnitude of the positive effect from ARP was discounted at the palatal side by the severe pre-extraction periodontal destruction [145,162]. It is unclear if such an effect is attributed to morphological features, the site-specific inflammatory burden, or host-related factors. Cha et al. also reported a difference of around 1 mm between the ARP and control group in terms of preventing sinus pneumatisation and the reduced proportion of subjects needing lateral window sinus grafts. However, they did not inform the need for additional lateral augmentation. A previous report by Levi et al. [163] showed a less intense pneumatisation in the subjects treated with socket preservation procedure (0.30 ± 0.10 mm) in line with the observations of Rasperini et al. [164]. Another review by Fischer and co-workers also demonstrated MD of 1.13 mm in the width of alveolar ridge in favour of ARP with xenograft and, importantly, no ARP or additional grafting procedures were needed in 4 out of 5 cases [84]. An undesirable situation arises when a patient, following an ARP procedure, still requires a lateral window sinus graft or major staged augmentation, rendering the cost of ARP unjustifiable. Consequently, it is essential to identify such patients that are unlikely to benefit from ARP before the extraction process. When evaluating a potential extraction site for ARP, it is crucial to conduct a comprehensive assessment of the final implant positioning from a prosthetically driven perspective. This assessment should also consider the future implant's apical coronal position and ensure adequate space for developing the emergence profile rather than merely performing ARP to preserve crestal bone that may later need removal. Additionally, the preservation site should be strategically located in an area critical for implant placement. In cases involving upper molars with significant root divergence and inter-radicular sinus recesses, ridge preservation in root-occupied areas may complicate sinus morphology for subsequent needed sinus lift procedures. Ridge width reduction has been reported to be greater for molar sites, yet given the posterior anatomical characteristics, they possess a greater baseline ridge width. Hence, posterior teeth with a reasonably intact socket at the time of extraction and good basal bone height apical to root apex may not require ARP.

The Cochrane systematic review by Atieh and co-workers could not detect a difference in the performance of different grafting materials in ARP. In another network meta-analysis by Canullo et al., they reported that ARP techniques with xenograft and allograft in sole or in combination with bioactive agents performed better in reducing post-extraction dimensional changes with reference to other grafting materials or spontaneous healing, despite presenting the worst histological outcomes. Platelet concentrate yields the best outcome of new bone formation, which is in alignment with earlier findings in pre-clinical studies [154,160]. It is interesting to note that the soft tissue volume contours did not differ significantly between the ARP and natural healing group, suggesting the replacement of the hard tissue space with soft tissue at the anterior sites [92], in alignment with the findings from the previous studies [5,11].

The dimensional changes of the ridge following ARP, despite being the most common primary outcome measure in assessing the efficacy of ARP [165], serve as a surrogate outcome at best. From the clinicians' and patients' point of view, other outcomes, such as the need of additional augmentation simultaneously or before implant placement, complication rate, cost-effectiveness, time of procedure, implant success rate, patient-related outcome measures, may be more relevant. The establishment and standardised reporting of a core outcome set and measurements will enable more meaningful comparison and synthesis of evidence-based clinical recommendations [166].

7.2. Technical variables

Various surgical techniques, bone replacement grafts, socket sealing material, biologics and their combinations have been utilised for ARP. The currently available evidence is unclear whether a particular biomaterial or their combination will be superior to one another [152]. In a different vein, the effect of a flapped or flapless technique on ARP has been a subject matter for debate. The study of Atieh and co-workers on 149 extraction sockets from 5 randomised controlled trials [167] showed no significant difference in the changes of ridge width and height between the two techniques. However, the flapless approach was associated with more favourable patient-reported outcomes, facial keratinised tissue width and thickness. In contrast, a recent review conducted by Barootchi et al. restricted analysis to non-molar sites and reported a significant association of flap elevation and primary wound closure with increased midbuccal vertical and horizontal bone loss [93]. Although guided bone regeneration and ARP share similarities regarding the need for biomaterials application and the goal to achieve favourable ridge morphology and dimension, the current evidence suggests that flap advancement and primary closure are not mandatory for ARP to achieve positive outcomes [168], provided that a socket seal procedure is carried out (collagen barrier membrane/ collagen plug/ free gingival graft/ dPTFE), and the bone replacement graft is well protected [155,159].

7.3. Cost-effectiveness of ARP

An elegant cost-effectiveness analysis has been recently conducted by Barootchi et al. [93]. They have limited analysis only of non-molar sites owing to potential multicollinearity in relation to anatomical differences and cost implications. In addition, only a few clinical studies focused on dealing with the extraction sockets of molars at that juncture. By US market price, xenogenic bone was associated with the highest cost, followed by allograft and alloplast. They have also identified xenograft and allograft-based approaches to be associated with superior performance, in agreement with the conclusion drawn by Canullo et al. [93,154]. In contrast to the findings of Del Fabbro et al. that there was no definitive evidence to suggest that a particular sealing technique or biomaterial offers superior outcomes as compared to other available options [155], Canullo et al. correlated the utilisation of membranes with improved anticipated return on investment (ridge width and mid buccal height reduction). Nevertheless, the cost-effectiveness analysis failed to consider the likelihood of a site requiring re-grafting before or concurrent with the implant placement. Additionally, it did not account for the total volume of biomaterial utilised or the overall time investment for both the ARP and implant procedures under the best or worst-case scenarios. This limited analysis restricts the ability to make comprehensive comparisons with alternative protocols for immediate, early or delayed implant placement.

8. Conclusions and future perspectives

In summary, this literature review has extensively assessed the existing evidence pertaining to the post- extraction socket healing. The wound healing process of extraction sockets is a dynamic sequence consisting of four overlapping phases with distinct physiological roles, including hemostasis and coagulation, inflammation, proliferation and bone modelling & remodelling. Following tooth extraction, a series of tissue changes occur, resulting in morphological alterations, decrease of ridge height and width as well as loss of bone volume. These changes display high inter-individual variability variation, and it depends on various factors (e.g., individual healing capacity, systemic conditions, pre-existing destruction of tooth-supporting tissues, trauma inflicted during extraction, denture wear, age, size of the extraction defect, consecutive extractions and other environmental factors). Whereas, many of these factors remained to be further investigated systematically via both pre-clinical and clinical studies.

In the context of alveolar socket healing, the role of ARP has been critically examined as a potential strategy for facilitating future prosthetic site development. The current evidence suggests that ARP could be a useful technique to limit dimensional change and, in part, reduce

the need for additional bone augmentation procedures in selective cases. Whereas, it is crucial to acknowledge the limitations of the current evidence related to the efficacy of ARP. The heterogeneity of study designs, methodologies and outcome measures makes it challenging to draw definitive conclusions. Future research work should focus on well-designed, randomised controlled trials with large sample sizes and standardised outcome measures including cost-effectiveness and PROMs, to generate more reliable evidence on the efficacy of ARP procedures for enhancing alveolar socket healing.

The significance of employing a prosthetically driven approach when evaluating extraction sites for potential implant placement has been addressed in the consideration of ARP procedures. Furthermore, the review has highlighted the importance of identifying the individuals who may benefit the most from specific socket healing strategies and vice versa. By doing so, clinicians can optimise the cost-effectiveness of the treatment and ensure that patients receive the most appropriate care for their specific needs. Looking into the future, narrow artificial intelligence technologies may be developed and employed to predict post-extraction ridge topography on diagnostic imagery with large training and validation datasets, thereby facilitating appropriate decision-making prior to dental extractions. This approach demonstrates the potential of AI to facilitate decision-making processes in the field of dentistry.

The choice of biomaterials used during the socket healing process has also emerged as an important factor in determining the success of the treatment. However, further studies are essential to identify the most effective biomaterials and combined usage in different clinical situations for improving clinical and histological outcomes.

By advancing our understanding of alveolar socket healing and its management strategies, clinicians can make more informed decisions regarding patient selection, surgical techniques and biomaterial choices, ultimately contributing to better patient management and the long-term success of dental implants.

CRediT authorship contribution statement

Melissa Rachel Fok: Conceptualization, Writing – original draft. **Lijian Jin:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jdent.2024.104986.

References

[1] D.C. Koutroumpas, E. Lioumi, G. Vougiouklakis, Tooth Extraction in Antiquity, J. Hist. Dent. 68 (3) (2020) 127–144.
[2] Y. Xu, M.I. MacEntee, The roots of dentistry in ancient China, J. Can. Dent. Assoc. 60 (7) (1994) 613–616.
[3] D.A. Garber, U.C. Belser, Restoration-driven implant placement with restoration-generated site development, Compend. Contin. Educ. Dent. 16 (8) (1995) 798–802, 796804.
[4] U. Grunder, S. Gracis, M. Capelli, Influence of the 3-D bone-to-implant relationship on esthetics, Int. J. Periodont. Restorat. Dent. 25 (2) (2005) 113–119.
[5] V. Chappuis, M.G. Araújo, D. Buser, Clinical relevance of dimensional bone and soft tissue alterations post-extraction in esthetic sites, Periodontol 73 (1) (2017) 73–83, 2000.
[6] H.E. Schroeder, The Periodontium, 12, Springer-Verlag, Berlin/Heidelberg/New York/Tokyo, 1986.
[7] T. Berglundh, W.V. Giannobile, P. Niklaus, N.P. Lang, M. Sanz, Clinical Periodontology and Implant Dentistry, Wiley-Blackwell, 2021.
[8] M.G. Araújo, C.O. Silva, M. Misawa, F. Sukekava, Alveolar socket healing: what can we learn? Periodontol 68 (1) (2015) 122–134, 2000.
[9] B.S. Michalowicz, D.P. Aeppli, R.K. Kuba, J.E. Bereuter, J.P. Conry, N.L. Segal, T. J. Bouchard Jr., B.L. Pihlstrom, A twin study of genetic variation in proportional radiographic alveolar bone height, J. Dent. Res. 70 (11) (1991) 1431–1435.
[10] N. Goshtasbi, J. Hazzard, N. Mehrkhodavandi, R. Al-Qawasmi, The heritability of alveolar bone thickness in siblings seeking orthodontic treatment, Am. J. Orthod. Dentofacial Orthop. 157 (6) (2020) 803–808.
[11] V. Chappuis, O. Engel, M. Reyes, K. Shahim, L.P. Nolte, D. Buser, Ridge alterations post-extraction in the esthetic zone: a 3D analysis with CBCT, J. Dent. Res. 92 (12 Suppl) (2013) 195s–201s.
[12] A.L. Januário, W.R. Duarte, M. Barriviera, J.C. Mesti, M.G. Araújo, J. Lindhe, Dimension of the facial bone wall in the anterior maxilla: a cone-beam computed tomography study, Clin. Oral Implant. Res. 22 (10) (2011) 1168–1171.
[13] V.S. Todorovic, T.C. Postma, J. Hoffman, A.W. van Zyl, Buccal and palatal alveolar bone dimensions in the anterior maxilla: a micro-CT study, Clin. ImPlant Dent. Relat. Res. 25 (2) (2023) 261–270.
[14] D. Heimes, E. Schiegnitz, R. Kuchen, P.W. Kämmerer, B. Al-Nawas, Buccal bone thickness in anterior and posterior teeth-a systematic review, Healthc. (Basel) 9 (12) (2021).
[15] J. Rojo-Sanchis, D. Soto-Peñaloza, D. Peñarrocha-Oltra, M. Peñarrocha-Diago, J. Viña-Almunia, Facial alveolar bone thickness and modifying factors of anterior maxillary teeth: a systematic review and meta-analysis of cone-beam computed tomography studies, BMC. Oral Health 21 (1) (2021) 143.
[16] C. Tomasi, M. Donati, D. Cecchinato, I. Szathvary, E. Corrà, J. Lindhe, Effect of socket grafting with deproteinized bone mineral: an RCT on dimensional alterations after 6 months, Clin. Oral Implants Res. 29 (5) (2018) 435–442.
[17] L. Trombelli, R. Farina, A. Marzola, L. Bozzi, B. Liljenberg, J. Lindhe, Modeling and remodeling of human extraction sockets, J. Clin. Periodontol. 35 (7) (2008) 630–639.
[18] K. Johnson, A study of the dimensional changes occurring in the maxilla following tooth extraction, Aust. Dent. J. 14 (4) (1969) 241–244.
[19] L. Schropp, A. Wenzel, L. Kostopoulos, T. Karring, Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study, Int. J. Periodont. Restorat. Dent. 23 (4) (2003) 313–323.
[20] J. Pietrokovski, J. Harfin, F. Levy, The influence of age and denture wear on the size of edentulous structures, Gerodontology 20 (2) (2003) 100–105.
[21] H. Euler, Die Heilung von Extraktionswunden, Dtsch Monatsschr Zahnheilkd 41 (1923) 685.
[22] M.H. Amler, The time sequence of tissue regeneration in human extraction wounds, Oral Surg. Oral Med. Oral Pathol. 27 (3) (1969) 309–318.
[23] M.G. Araújo, J. Lindhe, Dimensional ridge alterations following tooth extraction. An experimental study in the dog, J. Clin. Periodontol. 32 (2) (2005) 212–218.
[24] G. Cardaropoli, M. Araújo, R. Hayacibara, F. Sukekava, J. Lindhe, Healing of extraction sockets and surgically produced - augmented and non-augmented - defects in the alveolar ridge. An experimental study in the dog, J. Clin. Periodontol. 32 (5) (2005) 435–440.
[25] G. Cardaropoli, M. Araújo, J. Lindhe, Dynamics of bone tissue formation in tooth extraction sites. An experimental study in dogs, J. Clin. Periodontol. 30 (9) (2003) 809–818.
[26] M.B. Guglielmotti, R.L. Cabrini, Alveolar wound healing and ridge remodeling after tooth extraction in the rat: a histologic, radiographic, and histometric study, J. Oral Maxillofac. Surg. 43 (5) (1985) 359–364.
[27] R.F. Huebsch, R.D. Coleman, A.M. Frandsen, H. Becks, The healing process following molar extraction. I. Normal male rats (long-evans strain), Oral Surg. Oral Med. Oral Pathol. 5 (8) (1952) 864–876.
[28] M. Kanyama, T. Kuboki, K. Akiyama, K. Nawachi, F.M. Miyauchi, H. Yatani, S. Kubota, T. Nakanishi, M. Takigawa, Connective tissue growth factor expressed in rat alveolar bone regeneration sites after tooth extraction, Arch. Oral Biol. 48 (10) (2003) 723–730.
[29] Y. Kuboki, F. Hashimoto, K. Ishibashi, Time-dependent changes of collagen crosslinks in the socket after tooth extraction in rabbits, J. Dent. Res. 67 (6) (1988) 944–948.
[30] W.L. Lin, C.A. McCulloch, M.I. Cho, Differentiation of periodontal ligament fibroblasts into osteoblasts during socket healing after tooth extraction in the rat, Anat. Rec. 240 (4) (1994) 492–506.
[31] S. Marconcini, M. Denaro, S. Cosola, M. Gabriele, P. Toti, E. Mijiritsky, A. Proietti, F. Basolo, E. Giammarinaro, U. Covani, Myofibroblast gene expression profile after tooth extraction in the rabbit, Mater. (Basel) 12 (22) (2019).
[32] J. Pietrokovski, M. Massler, Residual ridge remodeling after tooth extraction in monkeys, J. Prosthet. Dent. 26 (2) (1971) 119–129.
[33] H. Sato, Y. Takeda, Proliferative activity, apoptosis, and histogenesis in the early stages of rat tooth extraction wound healing, Cell. Tissue. Organ. 186 (2) (2007) 104–111.
[34] A. Scala, N.P. Lang, M.T. Schweikert, J.A. de Oliveira, I. Rangel-Garcia Jr., D. Botticelli, Sequential healing of open extraction sockets. An experimental study in monkeys, Clin. Oral Implant. Res. 25 (3) (2014) 288–295.

[35] R.L. Smith, The role of epithelium in the healing of experimental extraction wounds, J. Dent. Res. 37 (2) (1958) 187–194.
[36] J. Liu, P.R. Schmidlin, A. Philipp, N. Hild, A. Tawse-Smith, W. Duncan, Novel bone substitute material in alveolar bone healing following tooth extraction: an experimental study in sheep, Clin. Oral Implant. Res. 27 (7) (2016) 762–770.
[37] A. Ram, W.J. Duncan, D.E. Coates, S. Nobakht, T. Tkatchenko, T.J. Milne, Bone remodelling marker expression in grafted and ungrafted sheep tooth extraction sockets: a comparative randomised study, Arch. Oral Biol. 153 (2023) 105738.
[38] S. Guo, L.A. Dipietro, Factors affecting wound healing, J. Dent. Res. 89 (3) (2010) 219–229.
[39] G. Breeland, M.A. Sinkler, R.G. Menezes, Embryology. Bone Ossification, StatPearls, StatPearls Publishing Copyright © 2023, StatPearls Publishing LLC., Treasure Island (FL), 2023.
[40] M.H. Periayah, A.S. Halim, A.Z. Mat Saad, Mechanism action of platelets and crucial blood coagulation pathways in hemostasis, Int. J. Hematol. Oncol. Stem Cell Res. 11 (4) (2017) 319–327.
[41] M. Rodrigues, N. Kosaric, C.A. Bonham, G.C. Gurtner, Wound healing: a cellular perspective, Physiol. Rev. 99 (1) (2019) 665–706.
[42] X. Wang, M.R. Fok, G. Pelekos, L. Jin, M.S. Tonetti, In vitro and ex vivo kinetic release profile of growth factors and cytokines from leucocyte- and platelet-rich fibrin (L-PRF) preparations, Cells 11 (13) (2022).
[43] S.L. Percival, J.G. Thomas, D.W. Williams, Biofilms and bacterial imbalances in chronic wounds: anti-Koch, Int. Wound J. 7 (3) (2010) 169–175.
[44] H. Poplimont, A. Georgantzoglou, M. Boulch, H.A. Walker, C. Coombs, F. Papaleonidopoulou, M. Sarris, Neutrophil swarming in damaged tissue is orchestrated by connexins and cooperative calcium alarm signals, Curr. Biol. 30 (14) (2020) 2761–2776, e7.
[45] A. Murao, M. Aziz, H. Wang, M. Brenner, P. Wang, Release mechanisms of major DAMPs, Apoptosis. 26 (3–4) (2021) 152–162.
[46] H. Kumar, T. Kawai, S. Akira, Pathogen recognition by the innate immune system, Int. Rev. Immunol. 30 (1) (2011) 16–34.
[47] T.N. Mayadas, X. Cullere, C.A. Lowell, The multifaceted functions of neutrophils, Annu Rev. Pathol. 9 (2014) 181–218.
[48] M. Hunter, Y. Wang, T. Eubank, C. Baran, P. Nana-Sinkam, C. Marsh, Survival of monocytes and macrophages and their role in health and disease, Front. Biosci. (Landmark. Ed) 14 (11) (2009) 4079–4102.
[49] N.X. Landén, D. Li, M. Ståhle, Transition from inflammation to proliferation: a critical step during wound healing, Cell Mol. Life Sci. 73 (20) (2016) 3861–3885.
[50] A. Fantin, J.M. Vieira, G. Gestri, L. Denti, Q. Schwarz, S. Prykhozhij, F. Peri, S. W. Wilson, C. Ruhrberg, Tissue macrophages act as cellular chaperones for vascular anastomosis downstream of VEGF-mediated endothelial tip cell induction, Blood 116 (5) (2010) 829–840.
[51] T.J. Koh, L.A. DiPietro, Inflammation and wound healing: the role of the macrophage, Expert. Rev. Mol. Med. 13 (2011) e23.
[52] G. Pagni, G. Pellegrini, W.V. Giannobile, G. Rasperini, Postextraction alveolar ridge preservation: biological basis and treatments, Int. J. Dent. 2012 (2012) 151030.
[53] J.R. Lieberman, A. Daluiski, T.A. Einhorn, The role of growth factors in the repair of bone. Biology and clinical applications, J. Bone Joint Surg. Am. 84 (6) (2002) 1032–1044.
[54] S. Nahles, C. Nack, K. Gratecap, H. Lage, J.J. Nelson, K. Nelson, Bone physiology in human grafted and non-grafted extraction sockets–an immunohistochemical study, Clin. Oral Implant. Res. 24 (7) (2013) 812–819.
[55] S. Heberer, A. Wustlich, H. Lage, J.J. Nelson, K. Nelson, Osteogenic potential of mesenchymal cells embedded in the provisional matrix after a 6-week healing period in augmented and non-augmented extraction sockets: an immunohistochemical prospective pilot study in humans, Clin. Oral Implant. Res. 23 (1) (2012) 19–27.
[56] K.D. Hankenson, M. Dishowitz, C. Gray, M. Schenker, Angiogenesis in bone regeneration, Injury 42 (6) (2011) 556–561.
[57] R. Farina, L. Trombelli, Wound healing of extraction sockets, Endod. Topics. 25 (1) (2011) 16–43.
[58] H. Devlin, P. Sloan, Early bone healing events in the human extraction socket, Int. J. Oral Maxillofac. Surg. 31 (6) (2002) 641–645.
[59] P. de Sousa Gomes, P. Daugela, L. Poskevicius, L. Mariano, M.H. Fernandes, Molecular and cellular aspects of socket healing in the absence and presence of graft materials and autologous platelet concentrates: a focused review, J. Oral Maxillofac. Res. 10 (3) (2019) e2.
[60] R. Dimitriou, E. Tsiridis, P.V. Giannoudis, Current concepts of molecular aspects of bone healing, Injury 36 (12) (2005) 1392–1404.
[61] Y. Hosokawa, Y. Sakakura, K. Irie, K. Kudo, I. Kashiwakura, Effects of local and whole body irradiation on the appearance of osteoblasts during wound healing in tooth extraction sockets in rats, J. Radiat. Res. 51 (2) (2010) 181–186.
[62] S. Supakul, K. Yao, H. Ochi, T. Shimada, K. Hashimoto, S. Sunamura, Y. Mabuchi, M. Tanaka, C. Akazawa, T. Nakamura, A. Okawa, S. Takeda, S. Sato, Pericytes as a source of osteogenic cells in bone fracture healing, Int. J. Mol. Sci. 20 (5) (2019).
[63] J. Liu, Z. Zhao, J. Ruan, M.D. Weir, T. Ma, K. Ren, A. Schneider, T.W. Oates, A. Li, L. Zhao, H.H.K. Xu, Stem cells in the periodontal ligament differentiated into osteogenic, fibrogenic and cementogenic lineages for the regeneration of the periodontal complex, J. Dent. 92 (2020) 103259.
[64] G. Ceccarelli, A. Graziano, L. Benedetti, M. Imbriani, F. Romano, F. Ferrarotti, M. Aimetti, G.M. Cusella de Angelis, Osteogenic potential of human oral-periosteal cells (PCs) isolated from different oral origin: an in vitro study, J. Cell Physiol. 231 (3) (2016) 607–612.
[65] B.E. Grottkau, Y. Lin, Osteogenesis of adipose-derived stem cells, Bone Res. 1 (2) (2013) 133–145.
[66] J.S. Hassumi, G. Mulinari-Santos, A. Fabris, R.G.M. Jacob, A. Gonçalves, A. C. Rossi, A.R. Freire, L.P. Faverani, R. Okamoto, Alveolar bone healing in rats: micro-CT, immunohistochemical and molecular analysis, J. Appl. Oral Sci. 26 (2018) e20170326.
[67] C.I. Evian, E.S. Rosenberg, J.G. Coslet, H. Corn, The osteogenic activity of bone removed from healing extraction sockets in humans, J. Periodontol. 53 (2) (1982) 81–85.
[68] J.J. Ahn, H.I. Shin, Bone tissue formation in extraction sockets from sites with advanced periodontal disease: a histomorphometric study in humans, Int. J. Oral Maxillofac. Implant. 23 (6) (2008) 1133–1138.
[69] J. Lindhe, D. Cecchinato, E.A. Bressan, M. Toia, M.G. Araújo, B. Liljenberg, The alveolar process of the edentulous maxilla in periodontitis and non-periodontitis subjects, Clin. Oral Implant. Res. 23 (1) (2012) 5–11.
[70] G.E. Carlsson, G. Persson, Morphologic changes of the mandible after extraction and wearing of dentures. A longitudinal, clinical, and x-ray cephalometric study covering 5 years, Odontol. Revy. 18 (1) (1967) 27–54.
[71] K. Bertl, E.B. Kukla, R. Albugami, F. Beck, A. Gahleitner, A. Stavropoulos, Timeframe of socket cortication after tooth extraction: a retrospective radiographic study, Clin. Oral Implant. Res. 29 (1) (2018) 130–138.
[72] Y. Hosokawa, Y. Sakakura, L. Tanaka, K. Okumura, T. Yajima, M. Kaneko, Effects of local and whole body irradiation on appearance of osteoclasts during wound healing of tooth extraction sockets in rats, J. Radiat. Res. 48 (4) (2007) 273–280.
[73] M.G. Araújo, F. Sukekava, J.L. Wennström, J. Lindhe, Tissue modeling following implant placement in fresh extraction sockets, Clin. Oral Implant. Res. 17 (6) (2006) 615–624.
[74] M.G. Araújo, J.L. Wennström, J. Lindhe, Modeling of the buccal and lingual bone walls of fresh extraction sites following implant installation, Clin. Oral Implant. Res. 17 (6) (2006) 606–614.
[75] M.G. Araújo, F. Sukekava, J.L. Wennström, J. Lindhe, Ridge alterations following implant placement in fresh extraction sockets: an experimental study in the dog, J. Clin. Periodontol. 32 (6) (2005) 645–652.
[76] F. Van der Weijden, F. Dell'Acqua, D.E. Slot, Alveolar bone dimensional changes of post-extraction sockets in humans: a systematic review, J. Clin. Periodontol. 36 (12) (2009) 1048–1058.
[77] W.L. Tan, T.L. Wong, M.C. Wong, N.P. Lang, A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans, Clin. Oral Implant. Res. 23 (Suppl 5) (2012) 1–21.
[78] C. Aribau-Gumà, A. Jorba-García, A. Sánchez-Torres, M. Sànchez-Garcés, Alveolar ridge preservation: an overview of systematic reviews, Int. J. Oral Maxillofac. Surg. 51 (2) (2022) 234–242.
[79] M.A. Atieh, N.H.M. Alsabeeha, A.G.T. Payne, S. Ali, C.M. Faggion Jr., M. Esposito, Interventions for replacing missing teeth: alveolar ridge preservation techniques for dental implant site development, Cochrane Datab. System. Rev. (4) (2021).
[80] B.J. Shea, B.C. Reeves, G. Wells, M. Thuku, C. Hamel, J. Moran, D. Moher, P. Tugwell, V. Welch, E. Kristjansson, D.A. Henry, AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both, BMJ 358 (2017) j4008.
[81] E. Couso-Queiruga, S. Stuhr, M. Tattan, L. Chambrone, G. Avila-Ortiz, Post-extraction dimensional changes: a systematic review and meta-analysis, J. Clin. Periodontol. 48 (1) (2021) 126–144.
[82] K.R. Morjaria, R. Wilson, R.M. Palmer, Bone healing after tooth extraction with or without an intervention: a systematic review of randomized controlled trials, Clin. ImPlant Dent. Relat. Res. 16 (1) (2014) 1–20.
[83] S. Barootchi, H.L. Wang, A. Ravida, F. Ben Amor, F. Riccitiello, C. Rengo, A. Paz, L. Laino, G. Marenzi, R. Gasparro, G. Sammartino, Ridge preservation techniques to avoid invasive bone reconstruction: a systematic review and meta-analysis: naples Consensus Report Working Group C, Int. J. Oral Implantol. (Berl) 12 (4) (2019) 399–416.
[84] K.R. Fischer, A. Solderer, K. Arlt, C. Heumann, C.C. Liu, P.R. Schmidlin, Bone envelope for implant placement after alveolar ridge preservation: a systematic review and meta-analysis, Int. J. ImPlant Dent. 8 (1) (2022) 56.
[85] A. Horváth, N. Mardas, L.A. Mezzomo, I.G. Needleman, N. Donos, Alveolar ridge preservation. A systematic review, Clin. Oral Investig. 17 (2) (2013) 341–363.
[86] S. Jambhekar, F. Kernen, A.S. Bidra, Clinical and histologic outcomes of socket grafting after flapless tooth extraction: a systematic review of randomized controlled clinical trials, J. Prosthet. Dent. 113 (5) (2015) 371–382.
[87] J.M. Ten Heggeler, D.E. Slot, G.A. Van der Weijden, Effect of socket preservation therapies following tooth extraction in non-molar regions in humans: a systematic review, Clin. Oral Implant. Res. 22 (8) (2011) 779–788.
[88] Z.S. Natto, A. Parashis, B. Steffensen, R. Ganguly, M.D. Finkelman, Y.N. Jeong, Efficacy of collagen matrix seal and collagen sponge on ridge preservation in combination with bone allograft: a randomized controlled clinical trial, J. Clin. Periodontol. 44 (6) (2017) 649–659.
[89] G.S. Chatzopoulos, V.P. Koidou, M. Sonnenberger, D. Johnson, H. Chu, L.F. Wolff, Postextraction ridge preservation by using dense PTFE membranes: a systematic review and meta-analysis, J. Prosthet. Dent. 131 (3) (2024) 410–419.
[90] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, L. Shamseer, J.M. Tetzlaff, E.A. Akl, S.E. Brennan, R. Chou, J. Glanville, J. M. Grimshaw, A. Hróbjartsson, M.M. Lalu, T. Li, E.W. Loder, E. Mayo-Wilson, S. McDonald, L.A. McGuinness, L.A. Stewart, J. Thomas, A.C. Tricco, V.A. Welch, P. Whiting, D. Moher, The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, BMJ 372 (2021) n71.
[91] E. Couso-Queiruga, Z.A. Graham, T. Peter, O. Gonzalez-Martin, P. Galindo-Moreno, G. Avila-Ortiz, Effect of periodontal phenotype characteristics on post-extraction dimensional changes of the alveolar ridge: a prospective case series, J. Clin. Periodontol. 50 (5) (2023) 694–706.

[92] G. Avila-Ortiz, M. Gubler, M. Romero-Bustillos, C.L. Nicholas, M.B. Zimmerman, C.A. Barwacz, Efficacy of alveolar ridge preservation: a randomized controlled trial, J. Dent. Res. 99 (4) (2020) 402–409.
[93] S. Barootchi, L. Tavelli, J. Majzoub, M. Stefanini, H.L. Wang, G. Avila-Ortiz, Alveolar ridge preservation: complications and cost-effectiveness, Periodontol 92 (1) (2023) 235–262, 2000.
[94] H. Wehrbein, P. Diedrich, The initial morphological state in the basally pneumatized maxillary sinus–a radiological-histological study in man, Fortschr. Kieferorthop. 53 (5) (1992) 254–262.
[95] Y. Ariji, T. Kuroki, S. Moriguchi, E. Ariji, S. Kanda, Age changes in the volume of the human maxillary sinus: a study using computed tomography, Dentomaxillofac. Radiol. 23 (3) (1994) 163–168.
[96] D. Lorkiewicz-Muszyńska, W. Kociemba, A. Rewekant, A. Sroka, K. Jończyk-Potoczna, M. Patelska-Banaszewska, A. Przystańska, Development of the maxillary sinus from birth to age 18. Postnatal growth pattern, Int. J. Pediatr. Otorhinolaryngol. 79 (9) (2015) 1393–1400.
[97] S.V. Raja, Management of the posterior maxilla with sinus lift: review of techniques, J. Oral Maxillofac. Surg. 67 (8) (2009) 1730–1734.
[98] S. Alqahtani, A. Alsheraimi, A. Alshareef, R. Alsaban, A. Alqahtani, M. Almgran, M. Eldesouky, A. Al-Omar, Maxillary sinus pneumatization following extractions in Riyadh, Saudi Arabia: a cross-sectional study, Cureus 12 (1) (2020) e6611.
[99] A. Sharan, D. Madjar, Maxillary sinus pneumatization following extractions: a radiographic study, Int. J. Oral Maxillofac. Implant. 23 (1) (2008) 48–56.
[100] R. Farina, M. Pramstraller, G. Franceschetti, C. Pramstraller, L. Trombelli, Alveolar ridge dimensions in maxillary posterior sextants: a retrospective comparative study of dentate and edentulous sites using computerized tomography data, Clin. Oral Implant. Res. 22 (10) (2011) 1138–1144.
[101] M. Schriber, M.M. Bornstein, V.G.A. Suter, Is the pneumatisation of the maxillary sinus following tooth loss a reality? A retrospective analysis using cone beam computed tomography and a customised software program, Clin. Oral Investig. 23 (3) (2019) 1349–1358.
[102] Y. Uchida, M. Goto, T. Katsuki, T. Akiyoshi, A cadaveric study of maxillary sinus size as an aid in bone grafting of the maxillary sinus floor, J. Oral Maxillofac. Surg. 56 (10) (1998) 1158–1163.
[103] S. Hameed, N. Bakhshalian, E. Alwazan, S.S. Wallace, H.H. Zadeh, Maxillary sinus floor and alveolar crest alterations following extraction of single maxillary molars: a retrospective CBCT analysis, Int. J. Periodontics Restorative Dent. 39 (4) (2019) 545–551.
[104] M.C. Cavalcanti, T.E. Guirado, V.M. Sapata, C. Costa, C.M. Pannuti, R.E. Jung, J. B. César Neto, Maxillary sinus floor pneumatization and alveolar ridge resorption after tooth loss: a cross-sectional study, Braz. Oral Res. 32 (2018) e64.
[105] R.A. Mischkowski, R. Pulsfort, L. Ritter, J. Neugebauer, H.G. Brochhagen, E. Keeve, J.E. Zöller, Geometric accuracy of a newly developed cone-beam device for maxillofacial imaging, Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 104 (4) (2007) 551–559.
[106] M. Freisfeld, D. Drescher, B. Schellmann, H. Schüller, The maxillary sixth-year molar and its relation to the maxillary sinus. A comparative study between the panoramic tomogram and the computed tomogram, Fortschr. Kieferorthop. 54 (5) (1993) 179–186.
[107] H.H. Kwak, H.D. Park, H.R. Yoon, M.K. Kang, K.S. Koh, H.J. Kim, Topographic anatomy of the inferior wall of the maxillary sinus in Koreans, Int. J. Oral Maxillofac. Surg. 33 (4) (2004) 382–388.
[108] A. Sharan, D. Madjar, Correlation between maxillary sinus floor topography and related root position of posterior teeth using panoramic and cross-sectional computed tomography imaging, Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 102 (3) (2006) 375–381.
[109] M.M. Bornstein, K. Horner, R. Jacobs, Use of cone beam computed tomography in implant dentistry: current concepts, indications and limitations for clinical practice and research, Periodontol 73 (1) (2017) 51–72, 2000.
[110] J. Aronson, Modulation of distraction osteogenesis in the aged rat by fibroblast growth factor, Clin. Orthop. Relat. Res. (425) (2004) 264–283.
[111] A.P. Kusumbe, S.K. Ramasamy, R.H. Adams, Coupling of angiogenesis and osteogenesis by a specific vessel subtype in bone, Nature 507 (7492) (2014) 323–328.
[112] M.J. Reed, J.M. Edelberg, Impaired angiogenesis in the aged, Sci. Aging Knowledge Environ. (7) (2004) pe7, 2004.
[113] J. Lähteenvuo, A. Rosenzweig, Effects of aging on angiogenesis, Circ. Res. 110 (9) (2012) 1252–1264.
[114] C. Leao de Queiroz, A.S. Terada, T.U. Dezem, L. Gomes de Araújo, R. Galo, C. Oliveira-Santos, R.H. Alves da Silva, Sex Determination of Adult Human Maxillary Sinuses on Panoramic Radiographs, Acta Stomatol. Croat. 50 (3) (2016) 215–221.
[115] T. Mello-Gentil, V. Souza-Mello, Contributions of anatomy to forensic sex estimation: focus on head and neck bones, Forensic Sci. Res. 7 (1) (2022) 11–23.
[116] R.A. Patel, R.F. Wilson, P.A. Patel, R.M. Palmer, The effect of smoking on bone healing: a systematic review, Bone Joint. Res. 2 (6) (2013) 102–111.
[117] A. Ozkan, G.R. Bayar, H.A. Altug, M. Sencimen, N. Dogan, Y. Gunaydin, E. Ergodan, The effect of cigarette smoking on the healing of extraction sockets: an immunohistochemical study, J. Craniofac. Surg. 25 (4) (2014) e397–e402.
[118] J.B. Saldanha, M.Z. Casati, F.H. Neto, E.A. Sallum, F.H. Nociti Jr., Smoking may affect the alveolar process dimensions and radiographic bone density in maxillary extraction sites: a prospective study in humans, J. Oral Maxillofac. Surg. 64 (9) (2006) 1359–1365.
[119] T. Urban, L. Kostopoulos, A. Wenzel, Immediate implant placement in molar regions: risk factors for early failure, Clin. Oral Implant. Res. 23 (2) (2012) 220–227.
[120] X. Shen, X. Shen, B. Li, W. Zhu, Y. Fu, R. Xu, Y. Du, J. Cheng, H. Jiang, Abnormal macrophage polarization impedes the healing of diabetes-associated tooth sockets, Bone 143 (2021) 115618.
[121] S. Gadicherla, K. Smriti, S. Roy, K.C. Pentapati, J. Rajan, A. Walia, Comparison of extraction socket healing in non-diabetic, prediabetic, and type 2 diabetic patients, Clin. Cosmet. Investig. Dent. 12 (2020) 291–296.
[122] J.H. Kim, C. Susin, J.H. Min, H.Y. Suh, E.J. Sang, Y. Ku, U.M. Wikesjö, K.T. Koo, Extraction sockets: erratic healing impeding factors, J. Clin. Periodontol. 41 (1) (2014) 80–85.
[123] B.B. Só, F.M. Silveira, G.S. Llantada, L.C. Jardim, T. Calcagnotto, M.A.T. Martins, M.D. Martins, Effects of osteoporosis on alveolar bone repair after tooth extraction: a systematic review of preclinical studies, Arch. Oral Biol. 125 (2021) 105054.
[124] J.S. Mattson, D.R. Cerutis, L.C. Parrish, Osteoporosis: a review and its dental implications, Compend. Contin. Educ. Dent. 23 (11) (2002), 1001-4, 1006, 1008 passim; quiz 1014.
[125] J. Wactawski-Wende, S.G. Grossi, M. Trevisan, R.J. Genco, M. Tezal, R. G. Dunford, A.W. Ho, E. Hausmann, M.M. Hreshchyshyn, The role of osteopenia in oral bone loss and periodontal disease, J. Periodontol. 67 (10 Suppl) (1996) 1076–1084.
[126] I. Binderman, M. Adut, R. Zohar, H. Bahar, D. Faibish, A. Yaffe, Alveolar bone resorption following coronal versus apical approach in a mucoperiosteal flap surgery procedure in the rat mandible, J. Periodontol. 72 (10) (2001) 1348–1353.
[127] S. Fickl, M. Kebschull, P. Schupbach, O. Zuhr, U. Schlagenhauf, M.B. Hürzeler, Bone loss after full-thickness and partial-thickness flap elevation, J. Clin. Periodontol. 38 (2) (2011) 157–162.
[128] M.H.A. Saleh, E. Couso-Queiruga, A. Ravidà, H. Dukka, N. Paiva De Andrade, A. Ou, H.L. Wang, Impact of the periodontal phenotype in premolar and molar sites on bone loss following full-thickness mucoperiosteal flap: a 1-year prospective clinical trial, J. Periodontol. 93 (7) (2022) 966–976.
[129] S. Fickl, O. Zuhr, H. Wachtel, W. Bolz, M. Huerzeler, Tissue alterations after tooth extraction with and without surgical trauma: a volumetric study in the beagle dog, J. Clin. Periodontol. 35 (4) (2008) 356–363.
[130] M.G. Araújo, J. Lindhe, Ridge alterations following tooth extraction with and without flap elevation: an experimental study in the dog, Clin. Oral Implant. Res. 20 (6) (2009) 545–549.
[131] A.A. Oghli, H. Steveling, Ridge preservation following tooth extraction: a comparison between atraumatic extraction and socket seal surgery, Quintessence Int. 41 (7) (2010) 605–609.
[132] J. Pietrokovski, The bony residual ridge in man, J. Prosthet. Dent. 34 (4) (1975) 456–462.
[133] M. Pramstraller, R. Farina, G. Franceschetti, C. Pramstraller, L. Trombelli, Ridge dimensions of the edentulous posterior maxilla: a retrospective analysis of a cohort of 127 patients using computerized tomography data, Clin. Oral Implant. Res. 22 (1) (2011) 54–61.
[134] M. Al-Askar, R. O'Neill, P.C. Stark, T. Griffin, F. Javed, K. Al-Hezaimi, Effect of single and contiguous teeth extractions on alveolar bone remodeling: a study in dogs, Clin. ImPlant Dent. Relat. Res. 15 (4) (2013) 569–575.
[135] U. Brägger, U. Schild, N.P. Lang, Effect of chlorhexidine (0.12 %) rinses on periodontal tissue healing after tooth extraction. (II). Radiographic parameters, J. Clin. Periodontol. 21 (6) (1994) 422–430.
[136] N.P. Lang, U. Schild, U. Brägger, Effect of chlorhexidine (0.12 %) rinses on periodontal tissue healing after tooth extraction. (I). Clinical parameters, J. Clin. Periodontol. 21 (6) (1994) 415–421.
[137] C.L. Romanò, E. De Vecchi, M. Bortolin, I. Morelli, L. Drago, Hyaluronic acid and its composites as a local antimicrobial/antiadhesive barrier, J. Bone Jt. Infect. 2 (1) (2017) 63–72.
[138] J. Andrade Del Olmo, L. Pérez-Álvarez, V. Sáez Martínez, S. Benito Cid, R. Pérez González, J.L. Vilas-Vilela, J.M. Alonso, Drug delivery from hyaluronic acid-BDDE injectable hydrogels for antibacterial and anti-inflammatory applications, Gels 8 (4) (2022).
[139] W. Han, Y. Lv, Y. Sun, Y. Wang, Z. Zhao, C. Shi, X. Chen, L. Wang, M. Zhang, B. Wei, X. Zhao, X. Wang, The anti-inflammatory activity of specific-sized hyaluronic acid oligosaccharides, Carbohydr. Polym. 276 (2022) 118699.
[140] R. Al-Khateeb, I. Olszewska-Czyz, Biological molecules in dental applications: hyaluronic acid as a companion biomaterial for diverse dental applications, Heliyon. 6 (4) (2020) e03722.
[141] D. Domic, K. Bertl, T. Lang, N. Pandis, C. Ulm, A. Stavropoulos, Hyaluronic acid in tooth extraction: a systematic review and meta-analysis of preclinical and clinical trials, Clin. Oral Investig. 27 (12) (2023) 7209–7229.
[142] M. Misawa, J. Lindhe, M.G. Araújo, The alveolar process following single-tooth extraction: a study of maxillary incisor and premolar sites in man, Clin. Oral Implant. Res. 27 (7) (2016) 884–889.
[143] L. Zhao, Y. Wei, T. Xu, B. Zhang, W. Hu, K.H. Chung, Changes in alveolar process dimensions following extraction of molars with advanced periodontal disease: a clinical pilot study, Clin. Oral Implant. Res. 30 (4) (2019) 324–335.
[144] C.J. Walker, T.J. Prihoda, B.L. Mealey, D.J. Lasho, M. Noujeim, G. Huynh-Ba, Evaluation of healing at molar extraction sites with and without ridge preservation: a randomized controlled clinical trial, J. Periodontol. 88 (3) (2017) 241–249.
[145] J.K. Cha, Y.W. Song, S.H. Park, R.E. Jung, U.W. Jung, D.S. Thoma, Alveolar ridge preservation in the posterior maxilla reduces vertical dimensional change: a randomized controlled clinical trial, Clin. Oral Implant. Res. 30 (6) (2019) 515–523.
[146] H. Sabri, S. Barootchi, T. Heck, H.L. Wang, Single-rooted extraction socket classification: a systematic review and proposal of a new classification system

based on morphologic and patient-related factors, J. Esthet. Restor. Dent. 35 (1) (2023) 168–182.
[147] A. Alsaggaf, M.R. Fenlon, A case control study to investigate the effects of denture wear on residual alveolar ridge resorption in edentulous patients, J. Dent. 98 (2020) 103373.
[148] A. Tallgren, The continuing reduction of the residual alveolar ridges in complete denture wearers: a mixed-longitudinal study covering 25 years, J. Prosthet. Dent. 27 (2) (1972) 120–132.
[149] C.C. Wyatt, The effect of prosthodontic treatment on alveolar bone loss: a review of the literature, J. Prosthet. Dent. 80 (3) (1998) 362–366.
[150] J. Pietrokovski, The residual edentulous arches–foundation for implants and for removable dentures; some clinical considerations. A review of the literature 1954-2012, Refuat. Hapeh. Vehashinayim 30 (1) (1993) 68 (2013) 14-24.
[151] L.R. Bairam, W.A. Miller, Mandible bone resorption as determined from panoramic radiographs in edentulous male individuals ages 25-80 years, Gerodontology 11 (2) (1994) 80–85.
[152] M.A. Atieh, N.H. Alsabeeha, A.G. Payne, S. Ali, C.M.J. Faggion, M. Esposito, Interventions for replacing missing teeth: alveolar ridge preservation techniques for dental implant site development, Cochr. Datab. Syst. Rev. 4 (4) (2021) Cd010176.
[153] G. Avila-Ortiz, L. Chambrone, F. Vignoletti, Effect of alveolar ridge preservation interventions following tooth extraction: a systematic review and meta-analysis, J. Clin. Periodontol. 46 (Suppl 21) (2019) 195–223.
[154] L. Canullo, M. Del Fabbro, S. Khijmatgar, S. Panda, A. Ravidà, G. Tommasato, A. Sculean, P. Pesce, Dimensional and histomorphometric evaluation of biomaterials used for alveolar ridge preservation: a systematic review and network meta-analysis, Clin. Oral Investig. 26 (1) (2022) 141–158.
[155] M. Del Fabbro, G. Tommasato, P. Pesce, A. Ravidà, S. Khijmatgar, A. Sculean, M. Galli, D. Antonacci, L. Canullo, Sealing materials for post-extraction site: a systematic review and network meta-analysis, Clin. Oral Investig. 26 (2) (2022) 1137–1154.
[156] F. Suárez-López Del Amo, A. Monje, Efficacy of biologics for alveolar ridge preservation/reconstruction and implant site development: an American Academy of Periodontology best evidence systematic review, J. Periodontol. 93 (12) (2022) 1827–1847.
[157] L. Sánchez-Labrador, S. Bazal-Bonelli, F. Pérez-González, L.M. Sáez-Alcaide, J. Cortés-Bretón Brinkmann, J.M. Martínez-González, Autogenous particulated dentin for alveolar ridge preservation. A systematic review, Ann. Anat. 246 (2023) 152024.
[158] Y. Feng, R. Zhao, J. Li, Z. Yuan, X. Xu, J. Gong, Efficacy of autogenous particulated dentin graft for alveolar ridge preservation: a systematic review and meta-analysis of randomized controlled trials, Med. (Baltimore) 102 (48) (2023) e36391.
[159] J.R. Martins, T.P. Wagner, A.C. Vallim, W. Konflanz, F. Schwendicke, R. K. Celeste, A.N. Haas, Comparison of the efficacy of different techniques to seal the alveolus during alveolar ridge preservation: meta-regression and network meta-analysis, J. Clin. Periodontol. 49 (7) (2022) 694–705.
[160] M. Araújo, E. Linder, J. Lindhe, Effect of a xenograft on early bone formation in extraction sockets: an experimental study in dog, Clin. Oral Implants Res. 20 (1) (2009) 1–6.
[161] M. Araújo, E. Linder, J. Wennström, J. Lindhe, The influence of Bio-Oss Collagen on healing of an extraction socket: an experimental study in the dog, Int. J. Periodont. Restorat. Dent. 28 (2) (2008) 123–135.
[162] M.A. Atieh, M. Alnaqbi, F. Abdunabi, L. Lin, N.H.M. Alsabeeha, Alveolar ridge preservation in extraction sockets of periodontally compromised teeth: a systematic review and meta-analysis, Clin. Oral Implant. Res. 33 (9) (2022) 869–885.
[163] I. Levi, M. Halperin-Sternfeld, J. Horwitz, H. Zigdon-Giladi, E.E. Machtei, Dimensional changes of the maxillary sinus following tooth extraction in the posterior maxilla with and without socket preservation, Clin. ImPlant Dent. Relat. Res. 19 (5) (2017) 952–958.
[164] G. Rasperini, L. Canullo, C. Dellavia, G. Pellegrini, M. Simion, Socket grafting in the posterior maxilla reduces the need for sinus augmentation, Int. J. Periodont. Restorat. Dent. 30 (3) (2010) 265–273.
[165] J.Y. Shi, E. Montero, X.Y. Wu, D. Palombo, S.M. Wei, I. Sanz-Sánchez, Bone preservation or augmentation simultaneous with or prior to dental implant placement: a systematic review of outcomes and outcome measures used in clinical trials in the last 10 years, J. Clin. Periodontol. 50 Suppl 25 (2023) 67–82.
[166] M.S. Tonetti, M. Sanz, G. Avila-Ortiz, T. Berglundh, F. Cairo, J. Derks, E. Figuero, F. Graziani, F. Guerra, L. Heitz-Mayfield, R.E. Jung, H. Lai, I. Needleman, P. N. Papapanou, I. Sailer, I. Sanz-Sanchez, F. Schwarz, J. Shi, D. Thoma, Relevant domains, core outcome sets and measurements for implant dentistry clinical trials: the Implant Dentistry Core Outcome Set and Measurement (ID-COSM) international consensus report, J. Clin. Periodontol. 50 (Suppl 25) (2023) 5–21.
[167] M.A. Atieh, L. Alfardan, N.H.M. Alsabeeha, Flapped versus flapless alveolar ridge preservation: a systematic review and meta-analysis, Int. J. Oral Maxillofac. Surg. 51 (1) (2022) 133–142.
[168] J. Lee, J.B. Lee, K.T. Koo, Y.J. Seol, Y.M. Lee, Flap management in alveolar ridge preservation: a systematic review and meta-analysis, Int. J. Oral Maxillofac. Implants 33 (3) (2018) 613–621.