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Review article

Genetic bases in the reabsorption of the mandibular residual crest

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ABSTRACT

The increase in life span of the human being leads to the appearance of new challenges for the health sciences. As a result of getting old, chronic and degenerative diseases started to occupy a predominant role in clinical research in the last decades. It is the case of degenerative processes that occur in the oral cavity after teeth loss.Mandibular residual ridge resorption is a widely studied process from the middle of last century and muchresearch relate this process with multiple factors. Recently, the understanding of the biological processes that occur after tooth extraction has been amplified.In this work, genetic factors involved in mandibular residual ridge resorption are discussed and the relationship between single nucleotide polymorphisms of some genes and mandibular residual ridge resorptionare stablished.

Keywords: Mandibular residual ridge resorption, Associated genetic factors, Single nucleotide polymorphism

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INTRODUCTION

With the increase in life expectancy of the elderly population, rehabilitation treatment for total tooth loss is common in old age and maintaining the residual ridge after tooth extraction is essential for successful treatment [1]. There are individual differences in the residual resorption process of the alveolar crest, which is chronic, progressive, irreversible and cumulative, and characterized by sequential stages that first affect the buccal and lingual surfaces and, eventually, the alveolar bone crest [2].

In prosthetic rehabilitation, bone is the base providing support for prostheses, being an area where biting and chewing forces are transmitted [3]. In oral rehabilitation, when the insertion of end osseous implants is planned, one of the most frequent problems is the reduced amount of available support bone. Therefore, it is important to know the quantity and quality of the mandibular bone, as it has an impact on long-term survival of total oral rehabilitation [4].

This diagnosis should be made with the highest accuracy with analytic software. Magnetic Resonance Imaging has as principal advantages no radiation is used to obtain the images, and no biological damage has been reported thus far [5].

After tooth loss, the jaw can lose up to 50% of its volume. Atwood was the first to classify the various stages of alveolar crest resorption by means of morphological criteria [6]. Based on these studies, later, Cawood and Howell established the classification of edentulous mandibles that still is the most used nowadays [7].

Bone is a highly dynamic organized tissue, consisting of a protein matrix, comprising mainly type 1 collagen, minerals and cells from multiple lineages. In 1760, John Hunter proposed that the integrity of the vertebrate skeleton be maintained through the remodelling process, a precise space-time sequence in which the old bone packages are removed and replaced by new ones [8]. Deregulated bone remodelling would cause a series of skeletal disorders. Research of this scientist led to an increased understanding of the genetic and epigenetic bases of bone remodelling and the provision of new molecular targets potentially amenable to treatment [9].

Residual crest resorption (RCR) is a multifactorial condition, involving bone resorption of the residual mandibular crest. After tooth extraction, wound healing involves bone formation in the tooth socket and bone resorption on the external surface of the alveolar bone, forming a residual crest with the shape of a saddle [10]. There is resorption of the residual crest in most patients and the extent of crest loss (volume and height) differs significantly between patients. In most patients, even after healing, active bone resorption persists, and part of the jaw structure is removed due to excessive atrophy of the jaw bone. RCR is thought to have a multifactorial etiology, with influence of the immune response at the bone site [10].

Several factors have been implicated in the pathophysiology of RCR, including osteoclast activation factor, dental plaque endotoxins, prostaglandins, stimulating factor of human

gingival bone resorption, physical activity, heredity, factors that influence age-related bone loss, such as diet, race, decreased Strogen secretion and those affecting gene expression of specific proteins [11]. The observed differences in occurrence, severity, and complications resulting from RCR must have a genetic basis [10].

Genetic variability underlies differences in disease susceptibility, severity and body response [12]. In an attempt to unravel the role of genetic factors in the development of RCR, some studies have explored single nucleotide polymorphisms (SNPs) in genes encoding cytokines and growth factors, matrix metalloproteinases (MMPs), receptor 1 fibroblast growth factor (FGFR1) and hypoxia inducing factor 1α (HIF-1α). These works highlighted significant associations between some polymorphisms and the development of RCR [13-18].

MATERIALS AND METHODS

For this research, the following databases were used: PubMed Central (PMC), Online Knowledge Library (B-ON), Cochrane Library and Scientific Electronic Library Online (SciELO). Google Scholar was also used. The keywords used in the search, in English and Portuguese, were, respectively: mandibular residual ridge resorption; associated genetic factors; single nucleotide polymorphisms.

Priority was given to publications from 2009 till nowadays, but also those published prior to this period if considered relevant to the work.

Mandibular residual crest

Mandibular residual crest is the portion of the residual bone and its soft covering tissue that remains after removal of the teeth. It consists of mucosa bearing of the denture, submucosa, periosteum and underlying residual alveolar bone. Residual ridges are formed after extraction of teeth by cortical and trabecular bone, connective tissue and cover epithelium. The edentulous arch is a vital structure present throughout the patient's entire life, regardless of the presence or function of the tooth. The continuous bone resorption during life often results in inadequate conditions for prosthetic rehabilitation [11].

Reabsorption of the Mandibular Residual Crest

RCR resorption is a pathological, progressive, irreversible and cumulative phenomenon characterized by sequential stages that primarily affect the buccal and lingual surfaces and, eventually, the alveolar bone crest [2]. According to Atwood, the degree of mandibular loss of its alveolar portion is 3-4 times greater than alveolar resorption in the maxilla, due to a smaller support area for dental prostheses in the mandible and, therefore, a greater load per cm^2 [19]. Alveolar loss in the maxilla runs from the cheek to the palate in the horizontal plane. In the mandible, the alveolar crest becomes atrophic on its sides in the glosso-buccal direction, while in the anterior part it occurs in the oral vestibule [3]. Twelve months after extraction, it was estimated a 50% reduction in the bucco-lingual width of the bone with a decrease in its height too. Two-thirds of that reduction occurs in three months. Tan et al. reported an average alveolar bone resorption of 3.8 mm in width and 1.24 mm in height in the first six months [20]. The buccal region of the bone undergoes a faster rate of resorption, resulting in a lingual change in the bone crest with more pronounced resorption in the mandible [7],[21-22]. When after dental extraction, the buccal bone wall is 1 mm or narrower, an average vertical bone loss of 7.5 mm in that buccal wall can be expected eight weeks after the extraction. On the other hand, if after tooth extraction the thickness of the buccal bone is greater than 1 mm, there is only a vertical loss of 1.1 mm of the buccal wall. It has been suggested that crest resorption occurs due to disuse atrophy, lack of blood supply and inflammation [23].

Classification system of the *American College of Prosthodontists* for complete edentulism

The American College of Prosthodontists (ACP) has developed a classification system for complete edentulism based on diagnostic data that is the most implemented worldwide by specialists in the field of oral rehabilitation [24]. The diagnostic criteria used are bone height (mandible), morphology of the residual ridge (maxilla), muscular ligaments (mandible), and maxillomandibular relationship. These criteria are decisive in the classification, but other variables can contribute to increased difficulty of treatment. In class I all four diagnostic criteria are favourable and characterizes the stage of edentulism most apt to be successfully treated with full removable (conventional) prostheses. Class II can be distinguished by the continuous physical degradation of the supporting anatomy of the prosthesis, and, in addition, is characterized by the early onset of systemic disease interactions, patient management and/or lifestyle considerations. Class III is characterized by the need for surgical revision of the support structures to allow adequate prosthodontic function. Class IV describes the most debilitating edentulous condition. Surgical reconstruction is almost always indicated, but it cannot always be performed due to the patient's health, preferences, dental history and financial considerations.

Pathophysiology of Mandibular Residual Crest Reabsorption

The height of the residual crest is maintained when the alveolar bone is in balance with the surrounding tissues, including the teeth, periodontal ligament, oral mucosa and connective tissue. The volume and shape of the alveolar crest, which is a tooth-dependent tissue that develops together with tooth eruption, undergo atrophy after tooth removal [15]. The bone that anchors the tooth in the jaw loses its function and disappears [25][26]. After extraction of the tooth, a cascade of inflammatory reactions is immediately activated, and the extraction socket is temporarily closed by the blood clot. Epithelial tissue begins to proliferate and migrate within the first week and the

integrity of the ruptured tissue is restored by newly formed bone in about 6 months [27]. The rate of changes in the contour of the alveolar crest reaches its peak of activity within 3-4 weeks after tooth extractions, after which it is less pronounced, although it continues to occur until the fourth and fifth months. The size of the residual crest is reduced more rapidly in the first 6 months, but bone resorption activity continues throughout life at a slower rate, resulting in the removal of a large amount of structure from the jaw [28-29].

This phenomenon has been described as reabsorption of the residual mandibular crest (RCR). The RCR rate is different between people and, even in the same person, at different locations. Annual increases in bone loss have a cumulative effect [30]. Anatomical changes will invariably occur within the edentulous alveolar crest after tooth extractions. The loss of teeth and loss or alteration of function within and around the socket result in a series of adaptive changes in the edentulous jaw [31]. Systemic and anatomical factors are likely to influence the amount of resorption. These factors include immunosuppression, impaired healing, genetics, smoking, periapical infection, chronic periodontitis, trauma, alveolar walls integrity, number of adjacent extracted teeth and prosthetic adaptation [32].

Genes involved in the healing process and bone remodelling

Table 1: Studies on genes involved in the healing process and bone remodelling and its relationship with RCR.

Study	Genes	Sample	RCR	Results
[14]	GFGFR1OP 2/wit3.0	20 Long term toothless (66.469,4 years old)	ACP	rs840869 or rs859024 were associated to RCR.
[15]	GFGFR1OP2	134 partial or complete toothless (70.4669,02 years old)	ACP	Minor allele of ss518063493 may be associated to RCR. SPNrs840869 is not associated to RCR in the Korean population.
[18]	FGFR1OP 2/ wit3.0	192 Saudis (RCR = 96; controls = 96) (50.00 years old)	ACP	The SNP rs2279351 was significantly associated to RCR and the mutant C allele is highly predisposing.
[1]	HIF-1 α.	202 Koreans (70,80 ± 9,40 years old) partial or complete toothless	ACP	The rs11549467 allele was associated to RCR.
[16]	VEGF	120 (70,93 ± 9,28 years old) toothless	ACP	Remarkable association with the rs1570360 in the dominant group and the ACC haplotype showed statistically significant association to RCR.

Several studies have been developed with the aim of relating the processes of healing and bone remodelling with the development of RCR (Table1).

FGFR1OP2/wit3.0 gene

The *FGFR1OP2* gene encodes a factor involved in the process of rapid wound healing that occurs in the oral cavity. SNPs in this gene have been shown to be associated with excessive toothless jaw atrophy. It is possible that the *FGFR1OP2* gene also influences bone formation in the oral cavity and changes in its activity level have effects on wound healing and bone resorption [33]. By overexpression of this gene, these authors concluded that it may be involved in the regulation of cell motility necessary to stimulate wound closure. It has also been shown that this cytoskeletal protein induces contraction of the oral mucosa after extraction and accelerates wound healing. Contraction of connective tissue after tooth loss can create tension that disturbs the balance in bone remodelling and, consequently, leads to residual resorption of the crest. Excessive atrophy of the mandible after tooth extraction may be associated with abnormal contraction of the oral mucosa induced by the *FGFR1OP2/wit 3.0* gene [15].

SNPs rs840869 and rs859024

Suwanwela et al. examined the possible association between *FGFR1OP2/wit 3.0* gene SNPs and RCR [14]. The expression of this gene was determined in the gingival tissues of 8 individuals before and after tooth extraction. In the postoperative period, all individuals had increased expression of this gene in the oral mucosa. However, significantly high levels of this expression were only observed in 3 of the 8 individuals [14].

In a sample of 20 long-toothed individuals, the ones having the rs840869 or rs859024 alleles were inserted in the highly atrophied group by using the ACP classification. Linear regression analysis indicated a suggestive association between SNP rs859024 and decreased bone height. The study demonstrated that the genotype of the *FGFR1OP2/wit3.0* alleles can predict the severity of mandibles atrophy after tooth extraction. In particular, the SNPs rs840869 and rs859024 showed a possible association with severely reabsorbed edentulous jaws. Toothless individuals with rs840869 and/or rs859024 SNPs belonged to the ACP type III/IV group, being associated with excessive toothless jaw atrophy. None of the individuals with this genetic profile belonged to other ACP groups. This study demonstrated the first evidence of a genetic basis for atrophic resorption of the jaw [14].

ss518063493 allele

Kim et al. examined the genetic association between polymorphisms in the *FGFR1OP2* gene and residual resorption of the mandible in a Korean population composed of 134 individuals with partially or completely edentulous mandible. Seven variants of this gene were identified, four of which were new [15]. The SNP rs859024 was not identified in the Korean population. Moreover, SNP rs840869 was not associated with residual crest resorption. This study did not demonstrate SNPs associated with RCR in the Korean population with statistical relevance. However, one individual with the ss518063493 allele falls within the ACP type IV group. Although

this is not statistically significant, it can be assumed that individuals with this allele have a potential risk of developing RCR [15].

SNP rs2279351

Alzain et al. investigated the role of SNPs of the *FGFR1OP2* gene in the development of RCR in Saudi individuals (sample of 192 individuals (RCR = 96; controls = 96)). SNPs rs2279351, rs78054962 and rs2306852, present in the *FGFR1OP2* gene promoter region, were identified [18]. SNP rs2279351 showed a significant association with RCR. This allele is highly predisposing to RCR having a dominant influence. Furthermore, the other two SNPs studied, did not show a significant influence on the development of RCR. Thus, the *FGFR1OP2* gene, which plays a role in the process of rapid wound healing in the oral cavity, may be involved in the development of RCR, influencing the rate of resorption of the jaw [18].

***HIF-1α*gene**

After tooth extraction, the bone tissues in the residual crest become hypoxic due to the reduction of the mechanical load. The bone tissues in the residual crest face a new situation that requires glycolytic production of ATP due to hypoxia, which, from an energy point of view, is very unprofitable. Therefore, the formation of new blood vessels to increase the supply of oxygen to bone tissue, is inevitable.

Disuse atrophy is observed when the normally developed bone decreases in size as a result of reduced mechanical load. This load is drastically reduced after tooth extraction, and the continuous pattern of bone resorption is probably related to this change. The hypoxia-inducing factor (HIF-1), a plexus transcriptional component, plays an important role in systemic oxygen homeostasis in mammalian cells. HIF-1 effectors are involved in angiogenesis, vascular tone, epithelial homeostasis and extracellular matrix metabolism, which is very critical for the healing process after tooth extraction. A recent study suggests that a significant difference in the expression of the *HIF-1α* gene may be responsible for a different rate of healing of the skin and wounds on the oral mucosa. An injury to the skin induces significantly higher expression of the *HIF-1α* gene and its signalling pathway than an injury to the tongue, which may partially explain a more robust angiogenesis observed in the skin versus the oral mucosa [34].

SNP rs11549467

Paek et al. examined the possible genetic association between a SNP of the *HIF-1α* gene, known to have high genetic diversity, and RCR [1]. This study used a sample of 202 Korean individuals with partially or completely edentulous jaws. By sequencing the *HIF-1α* gene, four new variants were identified, and the SNP rs11549467 was associated with RCR. This SNP increases the activity of the *HIF-1α* gene, improving angiogenesis and increasing the formation of new blood vessels. Thus, this SNP may play an important role in restoring disturbed bone remodelling balance, leading to RCR [1].

***VEGF* gene**

During the process of homeostasis, the osteocyte functions as a biological signal that regulates several other mediators. Among these mediators, HIF-1 is the main regulator of oxygen-dependent genes. Of the more than 60 genes whose expression is regulated by HIF-1, VEGF (vascular endothelial growth factor) is involved in angiogenesis and is one of the target genes for bone remodelling [35]. The *VEGF* gene is important for osteoclastic bone resorption and acts as a vital factor for normal bone remodelling. Low oxygen pressure is the most prominent event that develops after the decrease of the mechanical load resulting from tooth extraction. The relationship between VEGF, regulated by HIF-1, with angiogenesis and bone reduction is known [36].

SNP rs1570360

Song and Lee studied the association between SNPs of the *VEGF* gene and RCR. This study investigated three SNPs (rs1570360, rs25648 and rs3025039) of this gene and established an association between rs1570360 and RCR [16].

Genes involved in the immune response and antibacterial action

Table 2 presents the main studies that aimed to relate the immune response and antibacterial action to the development of RCR.

Table 2: Studies on genes involved in the immune response and antibacterial action and their relationship with the mandibular residual crest.

Study	Genes	Sample	RCR	Results
[10]	TNF- α, IL10, IL1RN TNFRSF11B and A NOD2, MMP1	192 Saudi (RCR = 96; controls = 96) (50.00 years old)	ACP	*IL-10* gene (rs1800896e) *NOD2* gene (rs5743289) Showed significant association to RCR.
[17]	MMP1	33 toothless		Patients with RCR exhibited more frequently the 2G allele, while only 21,2% of them presented the 1G allele.

***IL-10*gene (SNP rs1800896) andNOD2gene (SNPrs5743289)**

Al Sheikh et al. conducted a study in Saudi Arabia that included 192 Saudi individuals with full and partial edentulous mandibula. The SNPs analyzed were: *TNF-α* (rs1800629), *IL-10* (rs1800872 and rs1800896), *IL1RN* (rs419598), *TNFRSF11B* (rs11573847), *TNFRSF11A* (rs4485469), *NOD2* (rs5743289) and *MMP1* (rs1799750, rs554499 e rs5854). The distribution frequency of the SNPs rs1800629, rs1800872, rs419598, rs11573847, rs4485469, rs1799750, rs554499 and rs5854 did not show a statistically significant difference between patients with RCR and healthy controls [10].

Two SNPs of the *IL-10* gene, which encode a highly pleiotropic anti-inflammatory cytokine produced by various types of cells, were investigated. This cytokine is also implicated in the

inflammatory response, autoimmune diseases and cancer [37]. Some studies have reported the association of these two SNPs with various pathologies. The results of Mannino et al. showed that the SNP rs1800896 (-1082T> C) in the promoter region of the *IL-10* gene and a mutation by transversion are significantly associated with RCR [37]. The wild-type T allele has been shown to lead to four times greater predisposition to RCR than the mutant C allele [38][39].

The SNP rs5743289 in the *NOD2* gene showed a significant association with RCR. It is possible that the SNP rs5743289 T allele interrupts this response and influences innate immunity, which in turn is not able to detect intracellular bacterial growth and leads to the activation of mechanisms that influence bone resorption [10].

The mechanisms by which bacterial infections influence RCR need further elucidation and clarification. For the SNP rs5743289, the frequency of the GG genotype of patients with RCR was associated with a 13.8 times greater risk when compared to that of the TC genotype. The relationship between genotype and clinical characteristics of patients with RCR was assessed, but it was not possible to determine an association. The study reports polymorphism in genes involved in the immune response and antibacterial action and its association with RCR in the Saudi population. Of the ten polymorphic sites investigated in seven genes, two SNPs were significantly associated with RCR: the SNP rs1800896 in the *IL-10* gene and the SNP rs5743289 in the *NOD2* gene. This confirms that genetics plays a role in the etiology of RCR [10].

***MMP-1* gene**

In cases of individuals with teeth, most pathogenic bacteria reside in the periodontal pockets, and do not invade the periodontal tissue. The immune system is never able to efficiently eliminate microorganisms. This leads to chronic inflammation and continuous host response, resulting in tissue destruction [40-41]. MMPs are secreted by inflammatory cells in response to stimuli such as lipopolysaccharides and cytokines [42]. Sundar et al. designed a study to find out whether the polymorphism of the *MMP-1* gene can be related to residual crest reabsorption in a completely edentulous population [17]. This study showed that 78% of analysed individuals had the 2G polymorphism and 22% had 1G polymorphism, which may be associated with disease susceptibility. Furthermore, this study showed that patients with alveolar bone resorption exhibited more frequently the 2G allele, while 21.2% of them had 1G allele, associated with excessive toothless jaw atrophy [17].

RESULTS AND DISCUSSION

The resorption of the residual mandible crest in its most severe phases deserves treatments that aim to restore conditions required for prosthetic rehabilitation, as proposed in the ACP classification [24]. There is no single protocol for the treatment of the most severe forms of RCR. Currently, the quickest treatment is called "preservation of the alveolar crest", which aims to reduce unwanted bone resorption after tooth extraction. To do this, a bone graft is made inside the alveolus, being covered by a membrane that prevents soft tissue invasion during the bone healing process [32][43]. Other treatments had relative success in stages of RCR already established. Osteogenic distraction is a widely used technique that uses basic knowledge of bone biology to grow new bones. In this technique, a bone segment is fractured in the area where the increase in bone mass is desired and during the healing process of the referred fragment, it is stretched in a controlled and constant manner, which stimulates the formation of new bone in the desired direction [44]. Guided bone regeneration, block grafts, growth factors and other techniques have already been successfully used [32]. All these techniques require surgical acts, and long post-operative periods before patient rehabilitation with a permanent prosthesis and all involve a significant increase in treatment costs [32][43][45].

Currently, it is not possible to fully predict the behaviour of RCR, and therefore, available treatments may fail, be deficient or overtreatment may occur.

Differences in the occurrence, severity and complications resulting from RCR are thought to have a genetic basis. Thus, polygenic disorders, with small contributions from many genes and other genome *loci*, suggest genetic susceptibility. These genetic contributions together with environmental factors, may be the reason for the variability observed in the extent and severity of RCR [18].

So far, work on the relationship of genes to the severity of RCR is still scarce. This research found investigations where the relationship between RCR and genes involved in the bone healing and remodelling process was studied, and other studies focused on the relationship with genes involved in the immune response and antibacterial action. In most studies, the relationship of certain SNPs with the severity of RCR was determined [14][16][18][20]. Although the methods used in these studies were very similar, they have limitations due to the sample size and because they focused on specific populations, being probably inconclusive for other populations.

Regarding the genes involved in the bone healing and remodelling process, the *FGFR1OP2/wit3.0* gene is, so far, the most studied, with three RCR-related SPNs identified [14][15][18]. The *HIF-1* and the *VEGF* genes, involved in bone remodelling and osteoclastic bone resorption, were also studied, and SPNs were found in patients with class IV bone resorption [1][16].

The study of Al Sheikh et al. tried to relate genes involved in the immune response and antibacterial action with RCR. Seven genes were analysed (*TNF-α*, *IL-10*, *IL1RN*, *TNFRSF11B*, *TNFRSF11A*, *NOD2* and *MMP1*), and only two showed a relationship

with RCR [10]. Greenlee et al. tried to find out whether the polymorphism of the *MMP-1* gene can be related to RCR in a completely edentulous population. The 2G allele was more frequent in patients with alveolar bone resorption, whereas only 21.2% of these individuals had the 1G allele, associated with excessive toothless jaw atrophy [42].

CONCLUSION

Functional and aesthetic rehabilitation of the oral cavity involves prosthetic rehabilitation of dental structures and consequent restoration and maintenance of functions such as chewing of food, among others. The variability of the resorption processes of the residual mandible crest represents a challenge for the dentist and, in the most severe cases, it may involve performing invasive surgical procedures to restore function and adequately adapt a prosthesis. The placement of dental implants and bone grafts may be necessary and the possibility of complications such as neurological injury or pathological fracture of the jaw increases.

The molecular study of the genes involved in the pathophysiology of RCR, helps to expand the knowledge of this pathology and raises new possibilities of its clinical application in diagnosis, prognosis and treatment. Studies in immuno-genetics or genetic engineering may provide answers and change the way these patients are treated, just like in other medical science areas.

REFERENCES

1. Paek J, Oh Y, Kim J, et al, 2015. Single nucleotide polymorphisms in HIF-1α gene and Residual Ridge Resorption (RRR) of mandible in korean population. Gene Expr. 16(3), Pages-137-144. Doi: 10.3727/105221615 X1418144006549 0.

2. Springe B, Slaidina A, Soboleva U, et al, 2014. Bone mineral density and mandibular residual ridge resorption. International Journal of Prosthodontics. 27(3), Pages-270-276.

3. Zmysłowska E, Ledzion S, Jedrzejewski K, 2007. Factors affecting mandibular residual ridge resorption in edentulous patients: A preliminary report. Folia Morphologica. 66(4), Pages-346-352.

4. Blahout R, Hienz S, Solar P, et al, 2007. Quantification of bone resorption in the interforaminal region of the atrophic mandible. International Journal of Oral and Maxillofacial Implants. 22, Pages-609-615.

5. Parkarwar P, Dental PDU, 2019. Magnetic Resonance Imaging. Journal of Medical Pharmaceutical and Allied Sciences. 8(3), Pages-2192-2203.

6. Atwood DA, 1963. Postextraction changes in the adult mandible as illustrated by microradiographs of midsagittal sections and serial cephalometric roentgenograms. Journal of Prosthetic Dentistry. 13(5), Pages-810-824. Doi: 10.101 6/0022-3913(63)90 225-7.

7. Cawood JI, Howell RA, 1988. A classification of the edentulous jaws. Interntional Journal of Oral and Maxillofacial Surgery. 17(4), Pages-232-236. Doi: 10.1016/ S0901-5027(88)80047-X.

8. Evans CH, 2007. John Hunter and the origins of modern orthopaedic research. Journal of Orthopaedic Research. 25(4), Pages-556-560. Doi: 10.1002/jor.20386.

9. Zaidi M, Yuen T, Sun L, et al, 2018. Regulation of skeletal homeostasis. Endocrine Review. 39(5), Pages-701-718. Doi:10. 1210/er.2018-00050.

10. Al Sheikh H, AlZain S, Shaik JP, et al, 2020. Two novel SNPs in genes involved in immune response and their association with mandibular residual ridge resorption. Saudi Journal of Biolgical Sciences. 27(3), Pages – 846 - 852. Doi: 10.1016/j. sjbs.2020.01.016.

11. Singh OP, Kaur R, Nanda SM, et al, 2016. Residual ridge resorption: A major oral disease entity in relation to bone density. Indian Journal of Oral Sciences. 7(1), Pages-3-6.

12. Shaw G, 2013. Polymorphism and single nucleotide polymorphisms (SNPs). BJU International. 112(5),Pages- 664-665. Doi:10.1111/bju.12298.

13. Jahangiri L, Devlin H, Ting K, 1995. Current perspectives in residual ridge remodeling and its clinical implications : A review. Journal of Prosthetic Dentistry. 80(2),Pages-224-237. Doi: 10.1016/S0022-3913(98)70116-7.

14. Suwanwela J, Lee J, Lin A, et al, 2011. A genetic association study of single nucleotide polymorphisms in FGFR1OP2/wit3.0 and long-term atrophy of edentulous mandible. PLOS ONE. 6(1), Pages-e16204. Doi: 10.1371/ journal.pone.0016204.

15. Kim JH, Oh MY, Paek J, et al, 2012. Association between FGFR1OP2/wit3.0 polymorphisms and residual ridge resorption of mandible in Korean population. PLOS ONE. 7(8),Pages-1-7. Doi: 10.1371/journal.pone.0042734.

16. Song J-H, Lee J-H, 2014. Single nucleotide polymorphisms and haplotypes in vascular endothelial growth factor gene and residual ridge resorption of mandible in Korean population. Journal of Biomaterial Nanobiotechnol. 05(01), Pages-39-43. Doi: 10.4236/jbnb.2 014.51006.

17. Sundar SS, Jayesh SR, Hussain S, 2015. Association of matrix metalloproteinase 1 gene promoter mutation and residual ridge resorption in edentulous patients of South Indian origin. Journal of Pharmaceutical Biological allied Science7(Suppl 2), Pages-S652-S655. Doi: 10.4103/0975-7 406.163591.

18. Alzain S, Al Sheikh H, Al Thomali A, et al, 2020. Significant association of a single nucleotide polymorphism in the upstream region of FGFR1OP2/wit3.0 gene with residual ridge resorption of mandible in Saudis. Biocell. 44(1), Pages-55-62. Doi: 10.32604/biocell.2020.07974.

19. Atwood DA, 1979. Bone loss of edentulous alveolar ridges. Journal of Periodontology. 50(4s), Pages-11-21. Doi: 10.19 02/jop.1979.50.4s.11.

20. Tan WL, Wong TLT, Wong MCM, et al, 2012. A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. Clinical Oral Implants Research. 23(Suppl 5), Pages-1-21. Doi: 10. 1111/j.1600-0501.2011.02375.x.

21. Atwood DA, 1971. Reduction of residual ridges: A major oral disease entity. Journal of Prosthetic Dentistry. 26(3), Pages-266-

279. Doi: 10.1016/0022-3913(71)90069-2.

22. Pietrokovski J, 1975. The bony residual ridge in man. Journal of Prosthetic Dentistry. 34(4), Pages-456-462. Doi: 10.1016/0022-3913(75)90166-3.

23. Chappuis V, Engel O, Reyes M, et al, 2013. Ridge alterations post-extraction in the esthetic zone: A 3D analysis with CBCT. Journal of Dental Research. 92(12), Pages-195S. Doi: 10.1177/0022034513506713.

24. McGarry TJ, Nimmo A, Skiba JF, et al, 1999. Classification system for complete edentulism. Journal of Prosthodontics. 8(1), Pages-27-39. Doi: 10.1111/j.1532-84 9X.1999.tb00005.x.

25. Botticelli D, Berglundh T, Lindhe J, 2004. Hard-tissue alterations following immediate implant placement in extraction sites. Journal of Clinical Periodontology. 31(10), Pages-820-828. Doi: 10.1111/j.1600-051X.2004.00565.x.

26. Araújo M, Linder E, Wennström JLJ, 2008. The influence of bio-oss collagen on healing of an extraction socket: an experimental study in the dog. Intrnatonal Journal of Periodontics and Restoractive Dentistry. 28(2), Pages-123-135.

27. Darby I, Chen STBD, 2009. Ridge preservation techniques for implant therapy. International Journal of Oral Maxillofacial Implants. 24, Pages-260-271.

28. Hämmerle CHF, Araújo MG, Simion M, 2012. Evidence-based knowledge on the biology and treatment of extraction sockets. Clinical Oral Implants Research. 23(Suppl 5), Pages-80-82. Doi: 10.1111/j.1600-0501.2011.02370.x.

29. Jung RE, Philipp A, Annen BM, et al, 2013. Radiographic evaluation of different techniques for ridge preservation after tooth extraction: A randomized controlled clinical trial. Journal of Clinical Periodontology. 40(1), Pages-90-98. Doi: 10.1111/ jcpe.12027.

30. Horváth A, Mardas N, Mezzomo LA, et al, 2013. Alveolar ridge preservation. A systematic review. Clinical Oral Investigation. 17(2), Pages-341-363. Doi: 10.1007/s00784-0 12-0758-5.

31. Morjaria KR, Wilson R, Palmer RM, 2014. Bone healing after tooth extraction with or without an intervention: A systematic review of randomized controlled trials. Clinical Implant Dental Related Research. 16(1), Pages-1-20. Doi: 10.1111/j.1708-8208. 2012.00450.x.

32. Kalsi AS, Kalsi JS, Bassi S, 2019. Alveolar ridge preservation: why, when and how. British Dental Journal. 227(4), Pages-264-274. Doi: 10.1038/s41415-019-0647-2

33. Lin A, Hokugo A, Choi J, et al, 2010. Small cytoskeleton-associated molecule, fibroblast growth factor receptor 1 oncogene partner 2/wound inducible transcript-3.0 (FGFR1OP2/wit3.0), facilitates fibroblast-driven wound closure. American Journal of Pathology. 176(1), Pages-108-121. Doi: 10.2353/ajpath.2010.090256.

34. Chen L, Gajendrareddy PK, Dipietro LA, 2012. Differential expression of HIF-1α in skin and mucosal wounds. Journal of Dental Research. 91(9), Pages-871-876. Doi: 10.1177/00220345

35. Lee JW, Bae S-H, Jeong J-W, et al, 2004. Hypoxia-inducible factor (HIF-1) α: Its protein stability and biological functions. Experimental and Molecular Medicine. 36(1), Pages-1-12. Doi: 10.1038/emm.2004.

36. Ferrara N, Gerber HP, LeCouter J, 2003. The biology of VEGF and its receptors. Nature Medicine. 9(6), Pages-669-676. Doi: 10.1038/nm0603-669.

37. Mannino MH, Zhu Z, Xiao H, et al, 2015. The paradoxical role of IL-10 in immunity and cancer. Cancer Letters. 367(2), Pages-103-107. Doi: 10.1016/j.canlet.2015.07.009.

38. Sun JM, Li Q, Gu H-Y, et al, 2013. Interleukin 10 rs1800872 T>G polymorphism was associated with an increased risk of esophageal cancer in a chinese population. Asian Pacific Journal of Cancer Prevention. 14(6), Pages-3443-3447.

39. Zhang Y, Cui X, Nin L, et al, 2017. The effects of tumor necrosis factor-α (TNF-α) rs1800629 and rs361525 polymorphisms on sepsis risk. Oncotarget. 8(67), Pages-111456-111469. Doi: 10.18632/oncotarget.22824.

40. De Souza AP, Trevilatto PC, Scarel-Caminaga RM, et al, 2003. MMP-1 promoter polymorphism: association with chronic periodontitis severity in a Brazilian population. Journal of Clinical Periodontology. 30(2), Pages-154-158. Doi: 10.1034/j.1600-051X.2003.300202.x.

41. Izakovicova Holla L, Jurajda M, Fassmann A, et al, 2004. Genetic variations in the matrix metalloproteinase-1 promoter and risk of susceptibility and/or severity of chronic periodontitis in the Czech population. Journal of Clinical Periodontology. 31(8), Pages-685-690. Doi: 10.1111/j.1600-051X.2004.00547.x.

42. Greenlee KJ, Werb Z, Kheradmand F, 2007. Matrix metalloproteinases in lung: Multiple, multifarious, and multifaceted. Physiological Review. 87(1), Pages-69-98. Doi: 10.1152/physrev.00022.2006.

43. Avila-Ortiz G, Gubler M, Romero-Bustillos M, et al, 2020. Efficacy of alveolar ridge preservation: A randomized controlled trial. Journal of Dental Research. 99(4), Pages-402-409. Doi: 10.1177/0022034520905660.

44. Guerrero CA, Contasti-Bocco GI, Rodriguez AM, 2016. Mandibular Intraoral Distraction Osteogenesis. Orthognathic Surgery. 2016, Pages-701-712. Doi: 10.1002/9781119004370.ch 45.

45. Rachmiel A, Shilo D, Aizenbud D, et al, 2017. Vertical alveolar distraction osteogenesis of the atrophic posterior mandible before dental implant insertion. Journal of Oral Maxillofacial Surgery.75 (6), Pages – 1164 -1175. Doi: 10.1016/j. joms.2017.01.01. 013.

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