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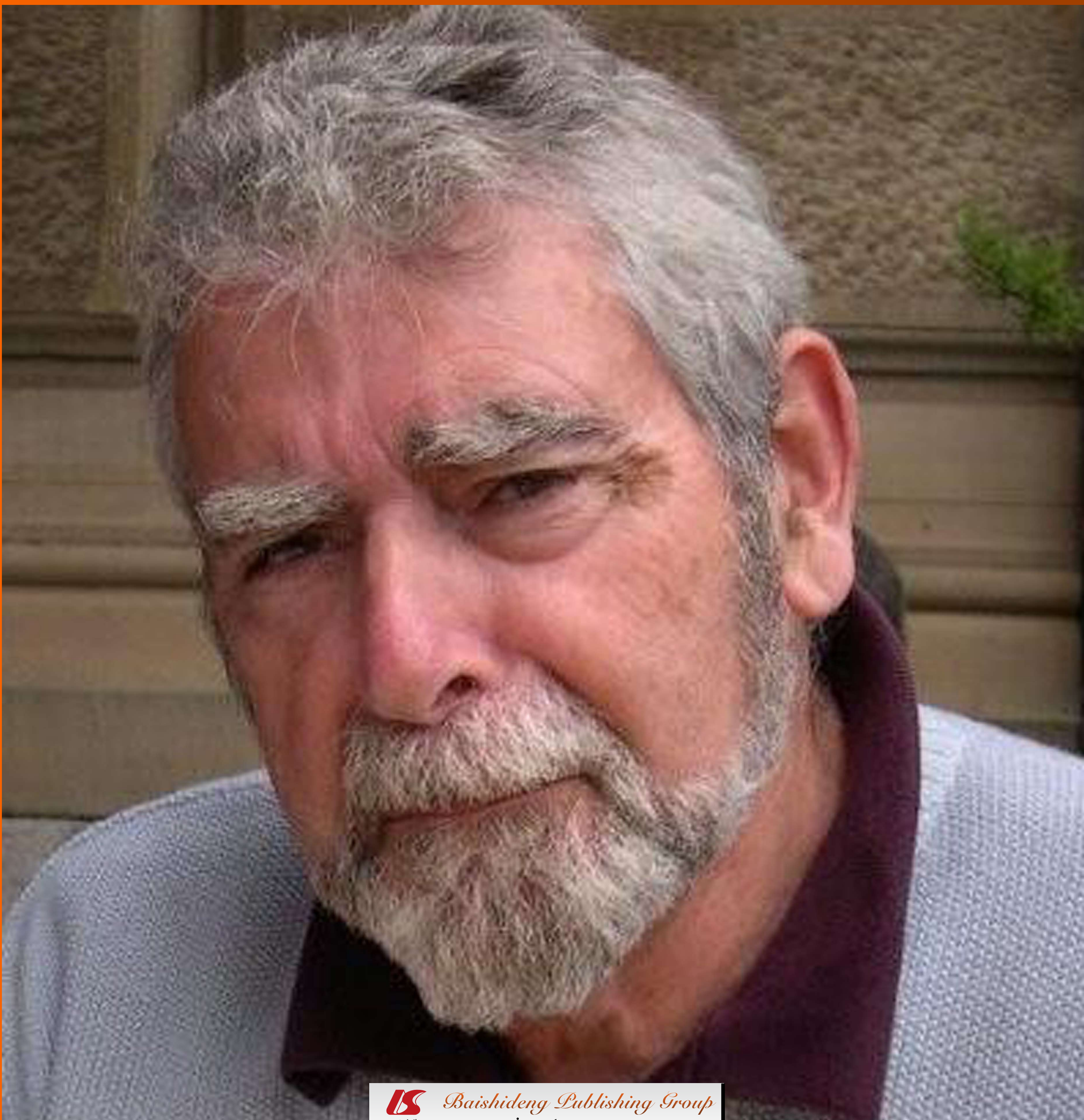

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Contents

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Contents

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WJS covers topics concerning oral and craniofacial sciences, oral and craniofacial development/growth, dental tissue regeneration, craniofacial bone and cartilage research, oral and maxillofacial genetic diseases, developmental abnormalities and soft tissue defects, pulpal and periapical diseases, periodontal diseases and oral mucosal diseases, salivary gland diseases, oral and maxillofacial vascular/nervous diseases, jaw bone diseases, taste abnormalities, oral and maxillofacial pain, occlusion and temporomandibular diseases, repair and treatment of tooth defects, loss and dento-maxillofacial deformities, oral and maxillofacial biomechanics and biomaterials, new techniques for diagnosis/treatment of oral and maxillofacial diseases; and stomatology-related evidence-based medicine, epidemiology and nursing. Priority publication will be given to articles concerning diagnosis and treatment of stomatologic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

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MINIREVIEWS

Dental stem cells: Progress and perspectives

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Abstract

Dental pulp stem cells (DPSCs) are thought to contribute to reparative dentin formation, and that they may correspond to heterogenous populations of precursor cells or represent distinct differentiation stages along the odontoblastic lineage. DPSCs share many similarities with mesenchymal stem cells of the bone marrow (BMSCs). It appears that the distribution of tissue stem cells is not random and, within the dental pulp, there are potentially several distinct niches of stem/progenitor cells. In addition to DPSCs, other dental stem cell populations have been isolated. As for DPSCs, further studies are still needed to evaluate their potential of differentiation and their regenerative activity. Up today, (1) the formal demonstration that pulpal resident stem cells are actually the reparative dentin-forming cells recruited in response to injury is still lacking; and (2) the origin, localization and precise identity of odontogenic stem cells remain largely unknown. Dental clonal cell lines may represent valuable tool to answer some fontamental questions concerning the dental stem cell biology. Altogether, the presence of dental cell populations displaying stem cell properties has opened new paths for considering regenerative therapies. This might be a prerequisite to design alternative strategies for capping and endodontic treatment, using stem cells.

Key words: Dental pulp; Stem cells; Dentin repair; Niche

Core tip: The presence of cell populations displaying stem cell properties within the pulp has opened new paths for considering more conservative therapies. Still, dental stem cells research is still confronted with the lack of precise knowledge related to the location and identity of the cells participating to reparative dentin formation. Clonal cell lines derived from the dental sphere may represent valuable tool to answer some questions that are of fundamental importance to stem cell biology and clinical applications. This review discusses some fundamental concepts of dental stem cell biology within the context of regenerative dentistry.

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INTRODUCTION

Tooth development requires a series of sequential and reciprocal interactions between the ectodermally derived oral epithelium at the origin of ameloblasts and neural crest-derived ectomesenchyme at the origin of odontoblasts. Tooth patterning proceeds through sequential morphogenetic events (bud, cap, bell) leading to crown and subsequently to root formation. During embryogenesis, morphogenesis is coupled to differentiation of commited cells that progressively elaborate enamel and dentin and in turn reach the terminal stages of amelogenic and odontogenic lignages. This cascade of events relies on epithelial-mesenchymal interactions that progressely lead to transformation of the tooth germ into complex mineralized structures[1].

Ameloblasts are lost following enamel maturation and tooth eruption, and hence enamel cannot be regenerated. Dental papilla ectomesenchymal cells give rise to the embryonic pulp and odontoblasts. Dental pulp cells maintain tooth homeostasis and odontoblasts synthesize dentin extracellular matrix. Dentin and pulp are related embryologically, histologically, and are functionally associated although the term of dentin-pulp complex is a notion underlying an oversimplification.

Odontoblasts are polarized postmitotic cells. These terminally differentiated cells cannot undergo further cell division and proliferate to replace irreversibly injured odontoblasts. Only the postmitotic cells forming the sub-odontoblastic Hoehl's cell layer, have the capacity to acquire a polarized phenotype and become functionnal odontoblasts. Odontoblasts are responsible for the secretion of primary and secondary dentin. They have a natural regenerative potential leading to the formation of reactionary dentin[2]. Odontoblasts can be up-regulated to secrete a reactionary dentin matrix when a mild injury occurs, such as attrition or early caries. However, injury of greater intensity, such as deep caries or restorative procedures, may lead to the death of the pre-existing odontoblasts and Hoehl's cells[3]. In such cases, recruitment of stem/precursor cells within the pulp will give rise to a new generation of odontoblast-like cells capable to elaborate reparative dentin.

The process of dental tissue repair may share many similarities with the embryological mechanisms of tooth development. It is assumed that many genes and signaling pathways involved in odontogenesis are also implicated in the tooth repair. Still, the mechanisms underlying reparative dentin formation are "open research areas" and offer exciting opportunities for possible tooth regeneration and dental tissue engineering.

DENTAL PULP STEM CELLS

The post-natal dental pulp contains heterogeneous cell populations responsible for its maintenance, defence and capacity of repair: stromal fibroblasts, odonto-osteoprogenitors, neuronal and vascular cells as well as inflammatory and immune system cells such as dentritic cells, neutrophils, macrophages, lymphocytes[4]. The ability of the pulp to respond to a variety of pathological conditions and injuries by deposition of a reparative dentin by pulp "progenitors" is well recognized[5] but the origin, localization and precise identity of odontogenic stem cells remain largely unknown. Identifying cells mobilized in response to pulp injury is a prerequisite to design alternative strategies for capping and endodontic treatment, using stem cells.

A decade ago, a population of odontogenic progenitors, inferred as dental pulp stem cells (DPSCs), was isolated from the pulp of human permanent third molars[6]. Upon subcutaneous transplantation into immunocompromised mice, *in vitro* expanded DPSCs mixed with hydroxyapatite formed dentin/pulp like complexes at an ectopic site. Populations of DPSCs possesses (1) generic mesenchymal stem cells-like properties (MSCs); (2) colony forming ability; and (3) were shown to express *in vitro* osteoblastic, adipogenic, chondrogenic or even neuronal markers[7-9]. DPSCs share many similarities with mesenchymal stem cells of the bone marrow (BMSCs) which are the most studied stromal stem cell populations. More than 4000 human genes are expressed either by BMSCs or DPSCs[10]. Dental stem cell populations also express different panels of stem cell surface markers such as 3G5, STRO-1, CD44, CD106, CD146, CD90 and Sca-1 used to characterize hematopoetic stem cells. However, it is important to note that DPSCs and BMPCs have not the same embryonic origin and that cells derived from the human or animal dental pulps have not been able to support hematopoiesis in transplantation assays[11]. DPSCs are thought to contribute to reparative dentin formation, and it appears that they may correspond to heterogenous populations of precursor cells or represent distinct differentiation stages along the odontoblastic lineage.

The presence of cell populations displaying stem cell properties within the pulp has opened new paths for considering more conservative therapies[6]. Nevertheless, the formal demonstration that pulpal resident stem cells are actually the reparative dentin-forming cells recruited in response to injury is still lacking. The hypothesis that a subset of stem cells carried by the vasculature replenishes the pulp after lesion can not be totally excluded. In the pulp, as in most tissues, the size of the pool of stem cells is very small (< 1%) and little is known about their anatomical sites within the pulp[12]. Moreover, the responsiveness of the pulp provides a dynamic system for tissue repair that may imply migration of stem cells from their resting places to the site of injury. Undifferentiated mesenchymal/mesectodermal cells present in the stroma, perivascular cells such as Rouget's pericytes or fibroblasts have all been proposed as potential progenitors mediating pulp repair after destruction of the odontoblasts and the *Hoehl's* sub-*odontoblastic* cell *layer*[13]. Advances in imaging technology and identification of stem cell markers are still needed to visualize stem/precursor cells *in situ*.

WHERE ARE THE DENTAL PULP STEM CELLS NICHES?

Stem cells are rare cells that are uniquely capable of both reproducing themselves and generating the differentiated cell types that are needed to carry out specialized functions. Stem cell behaviour is regulated by inputs from their local environment often referred as the "stem cell niche". Niches are defined as specific anatomic locations that provide structural support, trophic support, topographical informations and the appropriate physiological cues to control the maintenance, quiescence, self-renewal, recruitment towards differentiation and long-term regenerative capacity of stem cells. Hallmarks of a niche may include: the stem cell itself, stomal supporting cells that interact directly with the stem cells *via* secreted factors and cell surface molecules, extracellular matrix (ECM) that provides structure and mechanical signals, neuronal inputs and vascular network that carry systemic signals and represent a conduit for recruitment of inflammatory and circulating cells into the niche. In teeth, as in the adult blood system, multiple niches may exist and specific markers allowing the definitive identification of stem cells within the pulp are lacking.

Some data suggest that pericytes could differentiate into osteoblast-like cells, so odontogenic stem cells may reside in a perivascular niche[14]. In this context, it is interesting to mention that many haematopoetic stem cells (HSCs) and neuronal stem cells (NSCs) are localized close to the vascular network; this could be important to communicate "insult" and expose stem cells to signals activating their recruitment. Besides, alterations in ECM components and matrix elasticity related to damage or ageing may also provide mechanical signals that could have a profound impact on stem cell activity[15]. Thus, it appears that the distribution of tissue stem cells is not random and, within the dental pulp, there are potentially several distinct niches of stem/progenitor cells. Nevertheless, still little information is available regarding their topological organization and the inputs that recruit osteo-odontogenic stem cells to form reparative dentin[3]. In contrast to other tissues known to have a constant regeneration potential, such as intestine and bone marrow, dental pulp stem cells will react to form reparative dentin only after injury. This imply that signals ensure their survival and prevent their differentiation while maintaining their responsiveness following pulp damage. Whether an endogenous pool of stem cells associated with supportive stromal cells are mobilized at the site of injury and/or whether attraction of migrating stem cell is necessary to repopulate a niche and expand precursor cells at the appropriate site for dentin repair is unknown. In addition, the alteration of the dentin mineralized matrix promotes the release of bio-active molecules including high concentrations of Ca^{2+} which locally may also contribute to stem cells proliferation and differentiation in the post-injury pulpal environment.

DENTAL STEM CELLS-DIFFERENT TYPES, DIFFERENT LOCATIONS

In addition to DPSCs which were derived from the pulp of human permanent third molar, other stem cell populations have been isolated from exfoliated deciduous teeth (SHED), periodontal ligament (PDLCs), apical papilla (SCAP) and dental follicule (DFSCs). As for DPSCs, further studies are still needed to evaluate their potential of differentiation and their regenerative activity .

SHED, isolated from the pulp of human deciduous teeth appear distinct from DPSCs, having a higher proliferative rate and distinct gene expression profiles. SHED have osteoinductive capacity *in vivo*[16]. They can survive in mouse brain, expressing neural markers and possible application of SHED was even considered in alleviating Parkinson's disease[17]. As odontoblasts, they have a neural crest origin which may sustain their ability to adapt in a neuronal environment. Since children lose 20 deciduous teeth, SHED may be potentially used as an autologous stem cell source for dental pulp engineering once the children become adult. The commercial banking of these cells is becoming widespread but whether SHED maintain their stem cell properties after long-term storage (cryopreservation for more than 10 years) have not been assessed.

PDLSCs which derived from human periodontal ligament (PDL), a connective tissue between the cementum and the inner wall of the alveolar bone socket, represent a population of stem cells capable to differentiate in cementoblast-like cells and type 1 collagen-forming cells. Interestingly, transplantation of human PDLSCs in the periodontal defect of immunocompromissed mice, promotes the formation of a periodontal -like tissue, suggesting that PDLCs may be a potential tool for alveolar bone repair[18].

SCAP are derived from the apical part of the papilla of growing tooth roots[19,20]. It is important to note that the apical papilla tissue is present while the root apex is still open, before tooth eruption. *In vitro*, SCAP have been shown to exhibit dentinogenic and adipogenic properties, they also express neuronal markers. In clinical practice, they are easily accessible from extracted wisdom molars which develop later in life. Whether SCAP may represent a source of autologous stem cells for tooth repair remains an open question.

DFSCs derived from the dental follicle, a fibrous ectomesenchymal tissue that surrounds the developping tooth germ during the crown formation and disappears during the early stages of root development[21,22]. This tissue will form the periodontium, *i.e.*, cementum, periondontal ligament and alveolar bone. Thus, DFSCs may correspond to a heterogenous cell populations with different type of stem cells including cementoblasts, osteoblasts, stromal cells. In the adults, DFSCs can be easily accessible in impacted wisdom tooth during crown formation but not later (Table 1).

Finally, since 2009, several publications describe new populations of mesenchymal stem cells isolated from the human oral mucosa and gingiva (Zhang *et al*, 2012). Their differentiation and therapeutic potentials remain to be determined.

PERSPECTIVES AND OPEN QUESTIONS

Dental stem cells research is still confronted with the lack of precise knowledge related to the location and identity of the cells participating to reparative dentin formation. To this end, our laboratory developed the strategy and established stem cell lines from embryonic pulp of transgenic mouse[23] and Figure 1. One of the clones has the capacity after implantation in a rat molar, and in the ab-

Table 1 Types of dental pulp stem cells and their properties

Type of stem cells after birth	Dental stem cell properties	Signaling inputs for reparative dentin formation
Stem cells permanently present in the adult tooth: Dental pulp stem cell Periodontal ligament stem cells Apical papilla stem cells Stem cells present in deciduous tooth: Exfoliated deciduous teeth stem cells Stem cells present during crown formation: Dental follicule stem cells	Self-renewal Ability to enter in mitosis in response to appropriate signals and to differentiate towards odonto/osteogenic cells Long-term survival and maintenance of reparative capacity Distinct subpopulations expressing markers of mesenchymal stem cells of the bone marrow (STRO-1, CD44, CD 106, 3G5, CD146, CD90, Sca-1…)	Tooth injury may promotes stem cell recruitment by: Local secreted factors: bioactive extracellular matrix molecules Ca^{2+} release Mechanical inputs: changes in matrix elasticity Diffusible signals emanating from stromal, inflammatory, circulating… cells

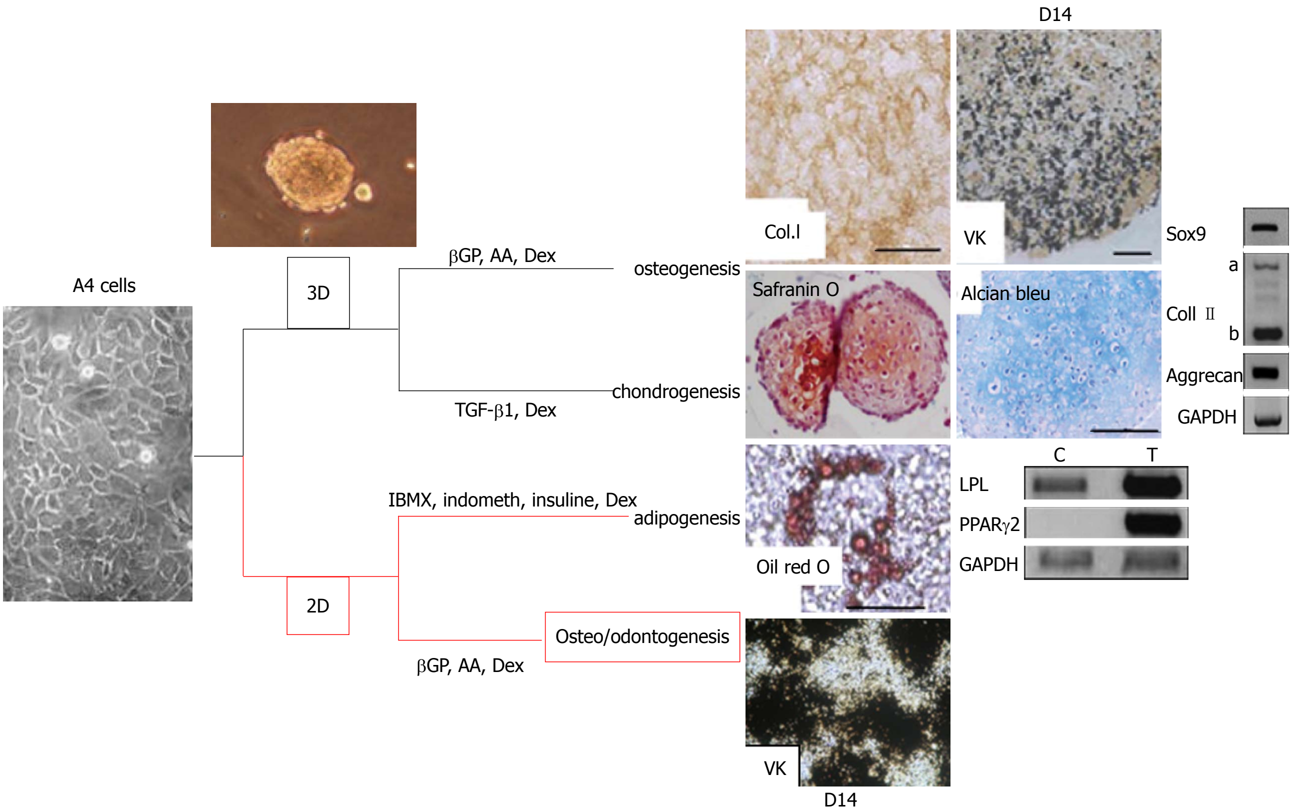

Figure 1 The A4 cells cultured in 2D or 3D, differently supplemented, give rise to different cell phenotypes, and consequently promote osteogenesis, chondrogenesis, adipogenesis or dentinogenesis. GAPDH: Glyceraldehyde phosphate dehydrogenase; TGF-β1: Transforming growth factor β1.

sence of any carrier or biomolecule, to promote efficient dentin repair[24,25]. Clonal cell lines derived from the dental sphere may represent valuable tool to answer several questions that are of fundamental importance to stem cell biology and clinical applications: Where are localized the presomptive stem cells niches? What are the markers allowing to visualize resident or migrating stem cells *in situ*? Which signals and molecular pathways sustain stem cells recruitment within the pulp and parodontium upon injury? By combining *in vitro* and *in vivo* experimental approaches, the answers to these questions will lead to a better understanding of stem cells potential for tooth repair and pave the way to develop new stem cell-based therapies.

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REVIEW

Basic properties and types of zirconia: An overview

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Abstract

This paper describes types and characteristics of zirconia materials in relation to their applications in dentistry. The zirconia material typically used today by most manufacturers is a tetragonal polycrystalline zirconia, partially stabilized with yttrium oxide. The mechanical properties of zirconia have been extensively investigated in the scientific literature and zirconia clearly measures up to any other equivalent manufactured material. The biocompatibility of zirconia has also been extensively evaluated and no local or systemic adverse reactions or cytotoxic effects have been found in relation to it. However, ceramic bonding, ageing, light transmission and manufacturing processes are all factors that need to be further evaluated in order to guide the successful use of zirconia as a prosthetic restorative material. Milling zirconia to full-contour might be an alternative to traditionally veneered restorations. A potential adhesion mechanism appears to be the combination of air abrasion with aluminum oxide particles (silanated or not), followed by sintering with materials containing special reactive monomers. Changes in zirconia properties before and after the sintering process have also been investigated. It was found that after sintering, surface roughness was greater, and micro hardness was slightly reduced; however, accurate precision of fit was not affected by the sintering process. Currently, zirconia restorations are manufactured by either soft or hard-milling processes, with the manufacturer of each claiming advantages over the other. Chipping of the veneering porcelain is reported as a common problem and has been labeled as its main clinical setback. As zirconia has demonstrated good mechanical and biological performance, future technology is attempting to improve esthetics and minimize veneer fracture, aiming to create confidence in the dental community towards this all-ceramic system. Milling zirconia to full-contour might be an alternative to traditionally veneered restorations. Finally, implications are drawn for manufacturing, machining, and widespread use of these materials.

Key words: Zirconia; Biocompatibility; Porcelain chipping; Mechanical properties

Core tip: Although all zirconia is chemically similar, the ultimate product can vary from manufacturer to manufacturer, with materials of varying density, uniformity homogeneity and crystalline transformation. This can be due to varying grain sizes of the powdered material ultimately affecting strength, with variations producing porosity. One type of restoration will not fit every clinical condition but today we have a range of options in zirconia ceramics, including monolithic full-contour type and conventional veneered type zirconia.

Saridag S, Tak O, Alniacik G. Basic properties and types of zirconia: An overview. *World J Stomatol* 2013; 2(3): 40-47 Available from: URL: http://www.wjgnet.com/2218-6263/full/v2/i3/40.htm DOI: http://dx.doi.org/10.5321/wjs.v2.i3.40

INTRODUCTION

Zirconium (Zr) is a metal with the atomic number 40. It was first discovered in 1789 by the chemist Martin

Klaproth[1-3]. The material has a density of 6.49 g/cm^3, a melting point of 1852 ℃ and a boiling point of 3580 ℃. It has a hexagonal crystal structure and is grayish in color. Zr does not occur in nature in a pure state. It can be found in conjunction with silicate oxide with the mineral name Zircon (ZrO_2 x SiO_2) or as a free oxide (Zirconia, ZrO_2) with the mineral name Baddeleyite[4]. These minerals cannot be used as primary materials in dentistry because of impurities of various metal elements that affect color and because of natural radionuclides like urania and thoria, which make them radioactive[5]. Complex and time-consuming processes that result in an effective separation of these elements are necessary in order to produce pure zirconia powders. After purification the material produced can be used as a ceramic biomaterial[4,6,7].

ZrO_2 is a polymorphic material and occurs in three forms: monoclinic, tetragonal and cubic. The monoclinic phase is stable at room temperatures up to 1170 ℃, the tetragonal at temperatures of 1170-2370 ℃ and the cubic at over 2370 ℃[8,9]. However, noticeable changes in volume are associated with these transformations: during the monoclinic to tetragonal transformation a 5% decrease in volume occurs when zirconium oxide is heated; conversely, a 3%-4% increase in volume is observed during the cooling process[4,10] (Figure 1).

STABILIZED ZIRCONIA

Several different oxides are added to zirconia to stabilize the tetragonal and/or cubic phases. Magnesia (MgO), Yttria (Y_2O_3), Calcia (CaO), and Ceria (CeO), amongst others, allow the generation of multiphase materials known as Partially Stabilized Zirconia (PSZ), whose microstructure at room temperature generally consists of cubic zirconia as the major phase, with monoclinic and tetragonal zirconia precipitates as the minor phase[4,11,12].

PSZ materials have been tested for their potential use as ceramic biomaterials. Mg-PSZ is one of the most commonly used zirconia-based engineering ceramics[13]. Residual porosity in the mass of the material, a rather coarse grain size (30-40 μm), and difficulties in obtaining Mg-PSZ precursors free of impurities, are all factors that have discouraged the interest of ceramic manufacturers in the development of Mg-PSZ for biomedical applications[4]. It has been reported that reinforcement by phase transformation toughening is less pronounced in Mg-PSZ than in Y-TZP (Yttrium-Tetragonal Zirconia Polycrystals), a finding that is discussed below[13]. Ceria (Ce)-doped zirconia ceramics have been very rarely considered, although they exhibit superior toughness (up to 20 MPa) and show no signs of ageing[14].

TRANSFORMATION/TOUGHENING MECHANISM

In the presence of a small amount of stabilizing oxides, and at room temperature, it is possible to obtain PSZ ceramics in the tetragonal phase only, known as Tetragonal Zirconia Polycrystals (TZP). The finely dispersed tetragonal ZrO_2 grains within the cubic matrix, provided that they are small enough, can be maintained in a metastable state that is able to transform into the monoclinic phase[11]. Tetragonal-to-monoclinic phase transformation in zirconia can be induced by stress, temperature and surface treatments[15,16]. Low temperature ageing *via* phase transformation of zirconia hip joint heads in normal atmospheric conditions has been reported after 10 years of incubation[10]. After the ageing of yttrium-stabilized zirconium dioxide in body fluid or water, some tetragonal-to-monoclinic phase transformation on the surface of zirconium dioxide has also been reported[17,18]. Even though some phase transition does occur, reports indicate that the effect on the material's mechanical properties is negligible[4,10].

Y-TZP (YTTRIUM-TETRAGONAL ZIRCONIA POLYCRYSTAL)

The addition of approximately 2%-3% of mol yttria (Y_2O_3) as a stabilizing agent in zirconia allows the sintering of fully tetragonal fine-grained zirconia ceramic materials made of 100% small metastable tetragonal grains and known as Y-TZP[11].

MECHANICAL PROPERTIES AND AGEING OF ZIRCONIA

Zirconia has mechanical properties similar to those of stainless steel. Its resistance to traction can be as high as 900-1200 MPa and its compression resistance is about 2000 MPa[4]. Cyclical load stresses are also tolerated well by this material. Applying an intermittent force of 28 kN to zirconia substrates, Cales and Stefani found that some 50 billion cycles were necessary to break the samples, but with a force in excess of 90 kN structural failure of the samples occurred after just 15 cycles[19]. Surface treatments can also modify the physical properties of zirconia. One property of zirconia that has not been well studied is the phenomenon of low-temperature degradation or "ageing". Water and nonaqueous solvents can induce the formation of zirconiahydroxides along a crack. This process accelerates expansion of the fracture and can result in reduced strength, toughness, and density, leading to failure of the restoration[14,20-22]. Surface grinding can also reduce strength[23,24]. Kosmac *et al*[15] confirmed this observation and reported reduced mean strength and reliability of zirconium oxide after grinding.

Zirconia is characterized by high flexural strength and fracture toughness as a result of a physical property known as transformation toughening[4,25,26]. The incidence of framework fracture was directly related to the design of the FPD, where inlay retained FPDs (IRFPD) showed the highest failure rate[27,28]. The most common complication observed in zirconia-based restorations was fracture of the veneering porcelain, manifesting clinically as chip-

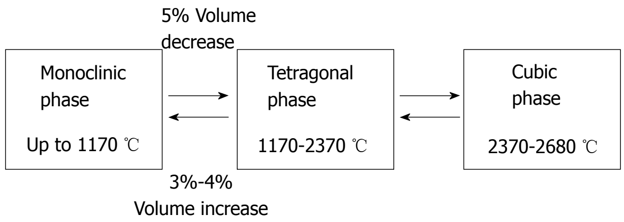

Figure 1 Temperature-related phase transformation of zirconia.

ping fractures of the veneering ceramic with or without exposing the underlying Y-TZP framework[27]. Several factors that may affect the rate of veneering fractures have been investigated. A loss of veneering material may result from an alteration of the crystal structure of the zirconia surface during airborne-particle abrasion of the framework before the veneering process. This may result in a change of the temperature expansion coefficients[15,25]. Other factors include the different surface treatments of the frameworks and the bond strength between the veneering ceramics and zirconia frameworks[29,30].

Sintering a CAD/CAM-milled lithium disilicate layering veneer cap onto the zirconia coping has significantly increased the mechanical strength of crown restorations and represents a cost effective way of fabricating all-ceramic restorations[31]. Milling of new generation full-contour zirconia might be an alternative approach to overcome chipping fractures of veneered zirconia restorations. Fabricating mono-block restorations from pure zirconia could increase the mechanical stability and expand the range of indications[32]. However, no clinical data is available yet.

BIOCOMPATIBILITY OF ZIRCONIA

The biocompatibility of zirconia has been extensively evaluated[4,21,33]. *In vitro* and *in vivo* studies have confirmed the high biocompatibility of Y-TZP with the use of very pure zirconia powders that have been purged of their radioactive content[34-39]. No local (cellular) or systemic adverse reactions to the material were reported[4,11,35,40,41]. Recent studies have demonstrated that fewer bacteria accumulate around Y-TZP than titanium[42-44]. This could possibly be explained by different protein adsorption properties[45]. In terms of periodontal health, none of the studies reported any difference or noted any changes in the biological health of the soft and hard tissues around the zirconia-based restorations. Although some data quantified and explored differences in the biocompatibility of zirconia, no instances of gingival inflammation or periodontitis could be shown[46]. These findings have led to the suggestion that zirconium oxide may be a suitable material for manufacturing implant abutments with a low bacterial colonization potential[44].

Zirconia as implant abutment material was first introduced in 1996[47]. A randomized controlled clinical trial comparing zirconia and titanium abutments supported by 40 single implants was published[48]. After being in function for three years, 18 zirconia and 10 titanium abutments were followed-up. Both abutment materials exhibited survival rates of 100%, as well as similar biological and esthetic outcomes. In an animal study, it was shown that the collagen fiber orientation was similar around zirconia and titanium implant necks. For both materials, the fibers run parallel-oblique and parallel to the implant surface[49]. In a clinical study, a similar degree of plaque accumulation was found at zirconia and titanium abutments at three years. In the same study, when zirconia abutments are used as restoration support, there were no significant differences in bone levels between zirconia and titanium abutments after 3-year follow-up[48].

ESTHETIC PROPERTIES AND LIGHT TRANSMISSION OF ZIRCONIA

All ceramic materials more satisfactorily address the demand for esthetic restorations than metal ceramic restorations with opaque cores[50,51]. However, the translucency of the most durable zirconia-based ceramic crowns is reported to be less than that of lithium disilicate glass ceramics, for which excellent esthetic results are documented[52-56]. In-Ceram Zirconia (VITA Zahnfabrik, Bad Säckingen, Germany), an aluminum oxide-based ceramic with 35% zirconium dioxide, has a relatively low translucency, equal to that of metal ceramic crowns when evaluated using the contrast ratio method[55]. This could be an obstacle to achieving an esthetically acceptable restoration. Among nonzirconia core materials, an optimal esthetic result has been reported with Procera AllCeram (Nobel Biocare AB, Göteborg, Sweden), which is a 99.9% aluminum oxide densely sintered ceramic[57], and IPS Empress (Ivoclar Vivadent AG, Schaan, Liechtenstein) lithium disilicate glass ceramic[58]. The latter evolved in 2005 to IPS e.max Press (Ivoclar Vivadent AG), with improved translucency and mechanical properties[59,60]. Alumina and glass ceramic have, respectively, fair to high relative translucency; nevertheless, their mechanical properties are lower than ZrO_2 ceramics[55,61].

Light transmission through Y-TZP varies as a function of: (1) the composition and thickness of the zirconia framework; and (2) the physical characteristics and degree of glazing of the veneering porcelain[62].

Based on this, the use of zirconia ceramics with different chemical compositions may be significant for clinicians. Additionally, measuring the degree of conversion of different resin luting agents beneath zirconia ceramic materials may produce better clinical outcomes[63]. Future studies should be expanded to include new generation full-contour zirconia[64]. Full-contour zirconia milling blanks are created through a unique patent-pending process. In one process the zirconium oxide powders are milled to further reduce the particle size of zirconium oxide, and mixed with a suitable binder to increase the compaction and density of the green state (compacted powders) and eliminate the closed porosity. The manufacturers claim that, unlike conventional high-pressure

Table 1 Three types of zirconia products and their milling/grinding technology (Information provided by manufacturers)

Milling at green stage (non-sintered)	Cercon base, Cercon (Degudent, Frankfurt, Germany) Lava Frame, Lava (3M ESPE, Seefeld, Germany) Hint-ELs Zirkon TPZ-G, DigiDent (Girrbach, Pforzheim, Germany) ZirkonZahn, Steger (Steger, Brunneck, Italy) Xavex G 100 Zirkon, Etkon (Etkon, Grafelfingen, Germany)
Grinding at pre-sintered stage	In-Ceram YZ Cubes, Cerec InLab (Sirona, Bensheim, Germany) ZS-Blanks, Everest (KaVo, Leutkirch, Germany) Hint-ELs Zirkon TZP-W, DigiDent (Girrbach, Pforzheim, Germany) DC-Shrink, Precident DCS (DCS, Allschwil, Switzerland) LAVA All-Ceramic System (3M ESPE, Seefeld, Germany) Cercon Smart Ceramics (DeguDent, Hanau, Germany) Procera Zirconia (Nobel Biocare, Göteborg, Sweden)
Grinding at completely sintered stage	DC-Zirkon, Precident DCS (DCS, Allschwil, Switzerland) Z-Blanks, Everest (KaVo, Leutkirch, Germany) Zirkon TM, Pro 50, Cynovad (Cynovad, Montreal, Canada) Hint-ELs Zirkon TZP-HIP, DigiDent (Girrbach, Pforzheim, Germany) HIP Zirkon, Etkon (Etkon, Grafelfingen, Germany)

milling blank manufacture, this processing gives full-contour zirconia improved light transmission, providing a lower, more natural shade value[65].

TYPES OF ZIRCONIA FOR MANUFACTURING PROCEDURE

Three main types of zirconia are available for use in clinical dentistry[66]. Although they are chemically identical, they have slightly different physical properties (*e.g.*, porosity, density, purity, strength), which may or may not be clinically relevant. Zirconia raw material (as previously mentioned) is not a natural product, but is chemically processed from minerals. With cold isostatic pressing, the powders are shaped into ceramic pre-forms. Cold isostatic pressing is the most accepted procedural technique for shaping Y-TZP and produces stable, chalk-like non-sintered green-stage objects with a very high primary density. The green objects are further stabilized and condensed up to about 95% of the theoretical density by means of sintering without pressure in the oxidized atmosphere of a special furnace, forming pre-sintered-type oxide-ceramic blanks[11,67]. Additional compression can be achieved with Hot Isostatic Postcompaction (HIP) performed at 1000 bar and 50 ℃ below the sintering temperature[67]. This procedure removes residual porosity and produces dense, fully-sintered-type oxide-ceramic blanks. Carrying out HIP on Y-TZP results in a gray-black material that usually requires subsequent heat treatment to oxidize and restore whiteness[68].

Zirconia ceramics are used in dentistry as materials for frameworks, generally fabricated by means of milling the zirconia block using a CAD/CAM machine system[69-74]. Blocks can be milled either at the green stage, the pre-sintered stage or the completely sintered stage. Green-stage zirconia blocks can be milled using dry carbide burs, pre-sintered zirconia blocks can be milled using carbide burs under cooling liquid, and milling of completely sintered zirconia blocks requires the use of diamonds under cooling liquid[75]. The three available types of zirconia products are shown in Table 1 together with the milling/grinding technology used in each case.

Frameworks made from green and pre-sintered zirconia are milled in an enlarged form to compensate for the shrinkage that occurs during sintering, usually 20%-25% for a partially-sintered framework[76]. The milling process is faster and the wear and tear on hardware is less than when milling from a fully-sintered blank. The framework is subsequently post-sintered in special furnaces (at about 1500 ℃) to reach the fully-sintered stage. The color of the zirconia can be individualized with the addition of oxides to the green-stage framework[68].

The question often arises as to which type of zirconia is best to use. It appears that each has advantages and disadvantages. Fully-sintered HIP zirconia has a denser polycrystalline structure with less porosity than non-HIP material, and this should translate clinically into increased resistance to fracture[77]. On the other hand, some investigators have questioned whether the amount of grinding needed during milling of fully sintered zirconia and the heat that is generated, cause surface and structural defects that can have adverse clinical implications[78]. The marginal fit of either type of material, however, is associated with very acceptable clinical results. Margin fitting of milled zirconia is as good as, if not superior to the fit of a restoration fabricated from a high noble alloy. Studies have measured the marginal gap of CAD/CAM-milled zirconia of both varieties and found it to be 40 to 70 μm[79]. However, compared to the alternative method, milling of fully sintered zirconia blocks is a time consuming process that causes greater wear of the diamond burs and is more expensive. Hence, from that point of view, green-stage zirconia could be regarded as more advantageous[67].

BONDING TO ZIRCONIA

The longevity of an indirect restoration is closely related to the integrity of the cement at the margin[80]. Although the use of zirconia ceramics for dental applications is ongoing, the best method to achieve a durable bond between the ceramic and the tooth structure is still unknown[81]. The only consensus found in the literature is that hydrofluoric acid etching and common silane agents are not effective with zirconia ceramics[81-83].

Several studies have investigated the bond strength and the durability of various bonding methods used to form high-strength zirconia ceramics. One technique commonly used to condition the ceramic surface is that of air abrasion[77,84-86]. Air abrasion with aliminium oxide particles is routinely performed to remove layers of contaminants, thus increasing micromechanical retention between the resin cement and the restoration[80,87,88]. These particles may or may not be silica-coated (with tribochemical treatment)[89-91].

Other techniques for the superficial treatment of zirconia ceramics which have been investigated are laser, plasma spraying and fusing glass pearls to the zirconia surface[92,93]. Higher laser power settings (400-600 mJ) cause excessive material deterioration, making them unsuitable as treatments for zirconia surfaces. Irradiation with 200 mJ provides mild surface alterations, with features intermediate between the effects of air abrasion and higher laser intensities[92]. Plasma spraying and glass pearl fusion treatments were found to improve the bond strength of resin cements to the surface. However, they were not compared with conventional methods of surface treatments for Y-TZP ceramics, such as air abrasion and tribochemical coating[93].

In other studies several coating agents were used to enhance the formation of chemical bonding with zirconia but only those agents that contain a phosphate monomer agent were effective in establishing a reliable bond with zirconia materials[84,94].

A recent study focusing on the long-term stability of zirconia resin bonding shows that it is directly related to the chemistry of the materials used, including primers. The authors suggest that a more hydrophobic compound is required to better resist the detrimental effect of hydrolysis in order to gain full benefit from the primers[95-97].

In a novel approach to enhance zirconia resin bond strength, selective infiltration-etching of zirconia-based materials has been tried. This method creates a retentive surface where the adhesive resin can infiltrate and interlock in order to establish a strong and a durable bond with zirconia[98-101].

CONCLUSION

Several positive characteristics of zirconia, such as biocompatibility, color and mechanical properties, make the material suitable for use in modern dentistry. However, ceramic bonding, ageing, light transmission and manufacturing processes are all factors that need to be further evaluated in order to guide the successful use of zirconia as a prosthetic restorative material. Milling zirconia to full-contour might be an alternative to traditionally veneered restorations.

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ORIGINAL ARTICLE

Clinical evaluation of implants in patients with maxillofacial defects

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Abstract

AIM: To show the efficacy of reconstruction and rehabilitation of large acquired maxillofacial defects due to tumor resections and firearm injuries.

METHODS: The study group comprised of 16 patients (10 men and 6 women) who were operated on because of their maxillofacial defects under local and general anesthesia between June 2007 and June 2011. Prosthetic treatment with the aid of dental implants was performed for all of the patients. Eight patients received an implant supported fixed prosthesis; six patients received implant supported overdentures and two patients received both. Patients were followed up postoperatively for 1 to 4 years. Implant success and survival rates were recorded. Panoramic radiographs were taken preoperatively, immediately after surgery, immediately after loading and at every recall session. Peri-implant and prosthetic complications were recorded. Subjects were asked to grade their oral health satisfaction after treatment according to 100 mm visual analog scale (VAS) and the oral health related quality of life of the patients was measured with the short-form Oral Health Impact Profile.

RESULTS: Five implants (3 in the mandible, 2 in the maxilla) in five patients were lost, while the other 53 survived, which brings an overall survival rate of 91.37% on the implant basis, but 68.75% on patient basis. All the failed implants were lost before abutment connection and were therefore regarded as early failures. For all failed implants, new implants were placed after a 2 mo period and the planning was maintained. The mean marginal bone loss (MBL) was 1.4 mm on the mesial side and 1.6 mm on the distal side of the implants. Five of the implants showed MBL > 2 mm (mean MBL = 2.3 mm) but less than 1/2 of the implant bodies and therefore were regarded as not successful but surviving implants. The VAS General Comfort mean score was 85.07, the VAS Speech mean score was 75.25 and the VAS Esthetics mean score was 82.74. No patient reported low scores (score lower than 50) of satisfaction in any of the evaluated factors. The mean of OHIP-14 scores was 5.5.

CONCLUSION: Although further follow up and larger case numbers will give more information about the success of dental implants as a treatment modality in maxillofacial defects patients, the actual results are encouraging and can be recommended for similar cases.

Key words: Dental implant; Maxillofacial defect; Overdenture; Prosthesis; Visual analog scale; Marginal bone loss

Core tip: Dental implant treatment is efficient in the reconstruction and rehabilitation of large acquired maxillofacial defects due to tumor resections and firearm injuries. Although further follow up and larger case numbers will give more information about the success of dental implants as a treatment modality in patients

with maxillofacial defects, the actual results are encouraging and can be recommended for similar cases.

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INTRODUCTION

Maxillofacial defects are initiated either by trauma or tumor resection. In both cases, the function and esthetics of the patients are impaired and a prosthetic rehabilitation is essential. Since removable prosthetic appliances function on soft tissues and the denture bearing areas are supposed to be composed of keratinized mucosa, defect cases create a challenge. Most of the acquired defects are surgically covered with thin mucosa which is not able to support denture bases. In this manner, dental implant treatment is a valuable aid to support the dentures, leaving the non-keratinized mucosa unloaded[1]. The use of dental implants in patients after trauma due to oral surgical resections, deformities, accidents or firearm injuries can give patients better function and self confidence by the achievement of retention and stability[1,2].

The structural and functional rehabilitation of maxillofacial defects, after oral tumor resection, maxillofacial trauma such as firearm injuries, avascular bone necrosis or large bone cysts, requires prosthetic reconstruction in most of the related patients. Local oral conditions, general health, as well as psychological, social and economic aspects, determine the final treatment outcome of the prosthetic rehabilitation[3]. The prosthodontic treatment in these patients creates a challenge due to several factors, such as bone volume deficiency, low quality of bone, altered anatomy, xerostomia, missing attached gingiva and associated fragile mucosa[4,5].

Maxillofacial defects caused by different reasons represent a challenging problem with regard to restoring optimal oral function and esthetics. These kinds of wounds exhibit a spectrum of complexity and mostly include extensive soft tissue trauma complicated by burns, foreign bodies, fractures and/or tissue loss. Since the clinician often faces situations with a remarkable tissue loss, dental implants are crucial to secure retention of the prosthetic appliances. Meanwhile, it is well known that dental implants enhance patient satisfaction and quality of life[6], provide improved retention and stability and enhanced chewing function and have the potential to preserve substantial bone[7-9].

The aim of this study was to report the treatment outcome of patients up to 4 years after reconstruction of oral and maxillofacial defects with a dental implant supported prosthesis and focus on prosthetic aspects, implant survival/success, patient satisfaction and quality of life.

MATERIAL AND METHODS

Patient recruitment, clinical and radiographic procedures

Fifty-eight implants placed in 16 patients with maxillofacial defects caused either by trauma, such as firearm injuries or accidents, or tumor resections of oral cancers at a university clinic between June 2007 and June 2011 were included in the present study. Informed written consent with regard to treatment and measurement procedures was given by all patients and approval from the university ethics commission was duly obtained. All the implants came from one manufacturer (Straumann®, Basel, Switzerland) and were placed by the same oral and maxillofacial surgeon.

All the patients suffered from alterations of the oral cavity (Table 1). Seven out of 16 patients (6 male, 1 female) had limitations in jaw opening (microstomia). The alterations were due to firearm injuries (3 patients: 2 male, 1 female) or ablative tumor surgery (13 patients: 8 male, 5 female) (Figures 1A-C). The details of the patients are presented in Table 1. For the patients with firearm injuries (n = 3; Figure 2A and B), the implant treatments were performed 1 year after reconstructive surgeries for the patients with firearm injuries and 2 years after the radiotherapy and/or chemotherapy for the patients who had undergone ablative tumor surgeries.

Surgery was performed as recommended by the manufacturer, using a one-stage surgical protocol in 10 patients (Figure 1D) and a two-stage surgical protocol in 6 patients. In all of the patients, large bony reconstructions were carried out by using free monocortico-cancellous iliac bone grafts or vascularized tissue flaps.

Prosthetic treatment of the defect patients was performed by 2 prosthodontists with 10 years of clinical experience. After implant surgery, 3 mo for the lower jaw and 6 mo for the upper jaw, osseointegration was waited for and then 8 patients received an implant supported fixed prosthesis (Figures 1E and 2A); six received implant supported overdentures (Figure 1B) and 2 received both (Table 1). The chosen prosthetic superstructures of the patients are presented in Table 1.

All participants received digital (Morita Veraview IC5®, J Morita MFG Corp, Kyoto, Japan) or analog panoramic radiographs (Planmeca®, Proline XC, Helsinki, Finland) using the imaging equipment before the surgery for treatment planning, immediately after and every year after loading of the implants for the evaluation of marginal bone levels of the implants.

Recalls were routinely performed 12, 24, 36 and 48 mo after loading. At each recall session, a clinical examination was performed by the same examiner. Implant success and survival rates were determined based on the following criteria: implants fulfilling all of the following criteria were regarded as successful[10]: no pain or tenderness upon function; 0 mobility (checked by manual manipulation); < 2 mm radiographic bone loss from initial surgery; no exudate history.

Figure 1 Intraoral view of a patient. A: Intraoral view of a patient after reconstruction of a gunshot wound; B: Delivered maxillary overdenture of the patient with the gunshot wound; C: Intraoral view of a patient after ablative tumor surgery; D: Insertion of dental implants using one-stage surgical protocol; E: Intraoral view of implant supported fixed prosthesis.

Table 1 Details of patients and implants

Patients (*n*)	16
Implants (*n*)	58
Patient age (mean, yr)	39
Patient gender	10 female, 6 male
Type of injury	firearm injuries (3 patients; 2 male, 1 female) or ablative tumor surgery (13 patients; 8 male, 5 female)
Insertion time of the implants	1 year after reconstructive surgeries for firearm injuries (n = 3) 2 years later for the patients who have undergone ablative tumor surgery (n = 13)
Loading time of the implants	3 mo after insertion for lower jaw and 6 mo after insertion for upper jaw for every patient
Location of implants	41 in the mandible, 17 in the maxilla
Type of prosthesis	8 patients received fixed prosthesis, 6 patients received overdentures, 2 patients received both

Implants with at least one of the following criteria but with no mobility (checked by manual manipulation) were regarded as surviving but not successful[10]: may have sensitivity on function; radiographic bone loss > 2 mm but less than 1/2 of implant body; may have exudate history.

Radiographic evaluation and bone level assessment

Panoramic radiographs were taken preoperatively (Figure 2B), immediately after surgery (Figure 2C), immediately after loading (Figure 2D) and at every recall session. In cases of insufficient quality, intraoral radiographs were taken as well. Mesial and distal marginal bone levels of all implants were determined at baseline and recall evaluations. The analog panoramic radiographs were scanned and digitized (Epson 1680 Pro®, Seiko Epson Cooperation, Nagano, Japan). Measurements were obtained from images of successive radiographs, which were analyzed at X20 magnification with the use of a software program (CorelDraw 11.0®, Corel Corp and Coral Ltd, Ottawa, Canada).

The known diameter of the implant at the collar region according to the manufacturer's dimensions of the respective implants was used as a reference point[11]. The distance from the supracrestal widest part of the implant to the crestal bone level was measured on the magnified images. To account for variability, the implant dimension (width) was measured and compared with the documentation dimensions; ratios were calculated to adjust for distortion. Bone levels were determined by applying a distortion coefficient (true bone height is equal to true implant width multiplied by bone height as measured on the radiograph, which is then divided by the implant diameter measured on the radiograph). The actual bone level measurement was performed independently by 2 examiners (a prosthodontist and an oral and maxillofacial surgeon) who were calibrated before the study.

The average from the 2 examiner calculations was used as the marginal bone level value. The level at which the marginal bone seemed to be attached was assessed by visual evaluation at the distal and mesial surfaces of all implants.

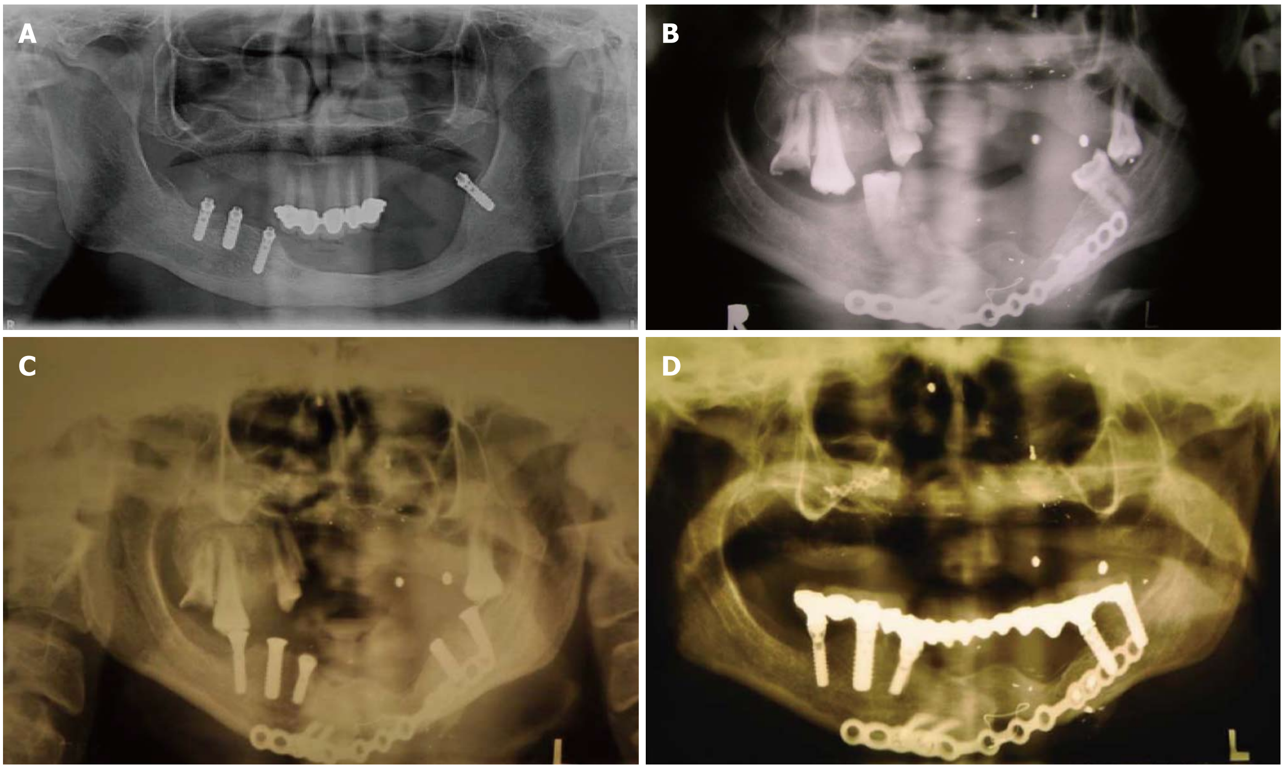

Figure 2 Panoramic radiograph. A: Panoramic radiograph taken after implant surgery; B: Panoramic radiograph taken before implant surgery; C: Panoramic radiograph taken after implant surgery; D: Panoramic radiograph taken after loading.

Figure 3 The visual analog scale form for general comfort, speech, esthetics and chewing.

Patient satisfaction and oral health related quality of life outcomes

Subjects were asked to grade their oral health satisfaction after treatment on a 0-100 mm visual analog scale (VAS) for 4 separate factors: general comfort, speech, esthetics and chewing (Figure 3). The scales were anchored by the extremes of potential responses (*e.g.*, completely satisfied-completely dissatisfied: the higher the score, the more satisfied the subject).

For the determination of quality of life of the patients, all subjects were asked to complete the Turkish version of the short-form Oral Health Impact Profile (OHIP-14), which has previously been determined to be valid and reliable[12]. Subjects rated each of the 14 items on a 5-point Likert scale from 0 = "never" to 4 = "very often". Items were added up to yield the total score. Achievable OHIP-14 score ranged from 0–56, with lower scores representing higher oral health-related quality of life[13].

RESULTS

Implant success, survival and failures

Five implants (3 in the mandible, 2 in the maxilla) in five patients were lost, while the other 53 survived, which brings an overall survival rate of 91.37% on the implant basis and 68.75% on a patient basis. Out of the 53 surviving implants, 48 were regarded as successful according to the criteria proposed by Misch *et al*[10] and thus the success rate was calculated as 82.75%. All the failed implants were lost before abutment connection and therefore regarded as early failures [14]. For all failed implants, new implants were placed after a 2 mo period and the planning was maintained.

Peri-implant complications and marginal bone loss

The mean marginal bone loss (MBL) was 1.4 mm on the mesial side and 1.6 mm on the distal side of the implants. 5 of the implants showed MBL > 2 mm (mean MBL = 2.3 mm) but less than 1/2 of implant bodies and were therefore regarded as not successful but surviving implants.

The MBL on the distal and mesial aspects of the implants up to 48 mo following loading did not exceed 2

Table 2 Oral HEALTH IMPACT PROFILE total and 7 domain mean scores

OHIP total	5.5 (range 0-56)
Functional limitation	0.31(range 0-8)
Physical pain	1.56 (range 0-8)
Psychological discomfort	1.37 (range 0-8)
Physical disability	1.06 (range 0-8)
Psychological disability	0.56 (range 0-8)
Social disability	0.18 (range 0-8)
Handicap	0.25 (range 0-8)

OHIP: Oral Health Impact Profile.

mm on average.

In two cases using fixed-detachable (hybrid type) restorations, excessive soft tissue under the prosthesis were observed at the 12 month recall appointment. For treatment, the hybrid dentures were unscrewed and removed and the large hyperplasic tissues were surgically excised. In order not to cause further trauma, the borders of the denture bases were adequately shortened in these areas and a week after surgical intervention, hybrid dentures were screwed to the abutments and tightened with the appropriate torque wrenches.

Prosthetic complications

During the observation period of up to 48 mo, the following prosthetic complications occurred: 1 fracture of a mandibular hybrid denture; 1 fracture of an abutment screw of a locator abutment; 1 fracture of the male part of a ball abutment; the requirement of rebasing in two overdentures (1 in the maxilla, 1 in the mandible); chipping of the veneering of a hybrid denture; and the requirement of substitution of the retention mechanism of 2 overdentures after an average service period of 21 mo (9-28 mo).

All prosthetic complications were eliminated and repaired; the fractured mandibular hybrid denture was redone on a new impression and model. Two overdentures were relined and the two fractured abutments were replaced. The chipped part of the hybrid denture was repaired and the retention mechanisms of the overdentures were replaced.

Patient satisfaction and oral health related quality of life scores

Patient satisfaction scores were as follows: VAS General Comfort mean score = 85.07 out of 100; VAS Speech mean score = 75.25 out of 100; VAS Esthetics mean score = 82.74 out of 100. No patient reported low scores (score lower than 50) of satisfaction in any of the evaluated factors. The mean of OHIP-14 scores was 5.5. The OHIP-14 total and the 7 domain scores of the patients are presented in Table 2.

DISCUSSION

Implant-supported prostheses for maxillofacial defect patients have become a reliable treatment modality[1,2]. It may be expected that in this kind of patients, implant failures increase since the conditions are tougher compared to conventionally placed and loaded dental implants. Often the implants are facing situations such as altered anatomy, xerostomia, missing attached gingiva around the implant neck or inconvenient bone[15-17]. It should be pointed out that maintenance of daily hygiene is very important for these patients, especially for patients suffering from xerostomia. With the absence or presence of small amounts of saliva, the oral cavity becomes more prone to oral infections; thus, the risk of implant failures may rise. As shown in one of our cases, the long edentulous span, which cannot be covered by a denture base because of grafted skin covering the reconstruction, had to be restored with a hybrid denture supported by a few implants (Figure 1C-E). Additionally, missing attached gingiva is known to be a disadvantageous condition for peri-implant health. In the present clinical study, the implant survival rate and success was lower compared to implants in conventional sites. In spite of a higher implant failure rate, this treatment gradually became a well-accepted option in the therapeutic spectrum of oral and maxillofacial deformities[18,19]. In spite of the improper implant positions in several cases, a success rate of 82.75% was obtained. Due to the need of malpositioning of the implants in the remaining tissue support, it could be expected that the survival and success rate of these implants would be impaired. There are studies reporting that implants had comparable success rates when they are placed angled or malpositioned[20]. The implant success and survival rates in the present study showed similarities to the studies illustrating the successful use of osseointegrated implants in the reconstruction of traumatic craniomaxillofacial injuries and in the rehabilitation of oral function in head and neck cancer patients[5,21-23]. However, the present study showed a higher rate of implant failure, peri-implant soft tissue complications and marginal bone loss than studies showing the implant data of patients without maxillofacial defects[6,8,11-14]. On the basis of clinical observations, bone loss ranging between 1 and 2.6 mm has been reported to occur around the margin of successfully osseointegrated dental implants[24,25]. In spite of a lack of consensus, the values generally accepted as a reasonable guideline for bone loss since the late 1980s is 1.5 mm for the first year after loading the implants and 0.2 mm of additional loss for each following year[10,26].

Regarding this guideline, the marginal bone loss rate reported here in the present study could be accepted as successful in spite of unfavorable conditions. On the other hand, it should be noted that the marginal bone loss rate presented in more recent studies lies much lower. The minimization of crestal bone loss was explained by surface roughness, evaluated as one of the key factors[27]. Nevertheless, the patients' clear judgment in favor of dental implant supported prosthetic rehabilitation in this study, which encourages this treatment modality. In the present study, a high level of patient satisfaction and quality of life were achieved (Table 2). The obtained

VAS and quality of life scores in this pilot study show similarities to the study of Schoen *et al*[21] which investigated the patient satisfaction and quality of life outcome of implant treatment in head and neck cancer patients[1]. Additionally, our results are comparable to other studies concerning treatment with dental implants[6,8,28-30].

In the present study, the patients were not asked to complete the VAS and OHIP-14 questionnaires before the treatment; thus, it was not possible to compare the pre and post treatment scores, which may be regarded as a limitation. All the patients were unable to function with the pre-treatment oral conditions; therefore, the authors did not consider it necessary and moral to constrain the patients in completing the questionnaires before treatment. Additionally, in the opinion of the authors, the OHIP-14 questionnaire is very hard to comprehend and could cause misleading results in these patients. The form could be modified for patients with maxillofacial defects just like the previously made modification for edentulous patients as OHIP-EDENT[31].

Early management of injured patients must focus on the basics of resuscitation. The secondary target in the treatment of these cases, however, should focus on tissue preservation, abstaining from unnecessary tissue resection, because the placement of dental implants can be problematic from time to time. The attention paid at the early stage of intervention can have an important impact on the quality of life of patients.

As a general approach at the dental school, the implant treatment has to be postponed for a certain period if a major resection and reconstruction has been performed. If radiotherapy and/or chemotherapy is administered, the patient has to wait at least 2 years for the implantation, as suggested previously[5]. The prosthetic complications recorded in the present study were slightly over the average of prosthetic patients treated in the related university clinic. Although complications, such as requirement of rebasing, chipping of veneering material and substitution of retention mechanism, are routinely encountered and well documented in the literature[32], the fracture of a hybrid denture, a locator abutment or of the male part of a ball attachment is not common. The misalignment or strategically disadvantageous numbers and positions of implants may be a factor that explains higher rates of complications in the present patient group.

Oral rehabilitation becomes even more complicated with the presence of microstomia[33], which can be encountered in this kind of patients. Microstomic patients experience considerable limitation in jaw opening and overall jaw mobility. This limitation in the oral opening makes gaining access to the oral cavity difficult, depending on the severity of microstomia. Therefore, traditional approaches for dental restoration should be modified to accommodate microstomia. Various treatment approaches have been proposed for microstomic patients, with or without endosseous implants. Reduced mouth opening may prevent instruments from safely entering the mouth for insertion of the implants. This is a critical factor in determining whether implant treatment can be provided and in deciding the number of inserts needed and the best places for insertion[34].

In the present study, 3 patients had a limited intraoral access, requiring modification of the approach. Also, there might be problems with the precision of dental laboratory work because of the inaccurate impressions which were hardly made with the modification methods[33]. Therefore, the precision of fit of the dental frameworks were very limited (Figure 2D). The strains due to the misfit of the denture can be a reason for the failures and prosthetic complications. In cases of firearm injuries, the severity of the defect resulting from facial firearm injuries varies according to the caliber of the weapon used, the distance from which the patient is shot and the part of the body involved[35]. Close range, high velocity firearm wounds can result in devastating functional and esthetic consequences. Maxillofacial traumas are mostly encountered in males (78%) and at a higher rate between the ages of 20-39 years. There are many reasons for maxillofacial trauma, such as fighting (48.2%), falling (26.2%), car accidents (4.2%) and firearm injury (1.2%)[36,37]. The epidemiology of facial fractures varies in type, severity and cause, depending on the population studied[38]. The differences between populations in the causes of maxillofacial fractures may be the result of risk factors and cultural differences between countries but are more likely to be influenced by the injury severity[39].

In situations with insufficient bone volume, invasive surgical procedures such as maxillary sinus floor elevation or the zygomatic implant placement[19], procedures mainly accomplished by maxillofacial surgeons, can be an alternative. However, individuals of the related patient group could appeal against additional complex surgical interventions after the long and griping procedures they have endured.

Meanwhile, it is a well known fact that the first year is critical for implant failure and for the largest portion of marginal bone loss around dental implants[34]. The results of an investigation showed that practically all implant losses occurred during the first 2 years, whereupon a steady state seemed to follow for up to 5 years after loading[40].

Despite disadvantageous loading conditions and poor bone quality and quantity, all the presented cases showed a stable situation around the implants after a period of 12-48 mo of loading time. Although further follow up and larger case numbers will give more information about the success of dental implants as a treatment modality in maxillofacial defect patients, the actual results are encouraging and can be recommended for similar cases. Even although the success and survival rate is slightly lower than conventionally loaded implants due to tougher conditions, dental implants seem to be a valuable aid in the maintenance of comfortable rehabilitation of maxillofacial defect patients.

COMMENTS

Background

In patients with maxillofacial defects, implant failures may increase, since the conditions are harder compared to conventionally placed dental implants. Often the implants are facing situations such as altered anatomy, xerostomia, missing attached gingiva around the implant neck or inconvenient bone.

Research frontiers

The treatment outcome of patients with maxillofacial defects up to 4 years after dental implant supported prosthesis should be investigated and prosthetic aspects, implant survival/success, patient satisfaction and quality of life of these patients should be demonstrated. In this study, the authors show that dental implants seem to be a valuable aid in the maintenance of comfortable rehabilitation of maxillofacial defect patients.

Innovations and breakthroughs

Studies of patients with maxillofacial defects are mostly case reports. This is one of the first studies to report the outcome of dental implant treatment in these patients.

Applications

The actual results are encouraging and dental implant treatment can be recommended for similar cases.

Peer review

The authors examined the prosthetic and peri-implant complications, patient satisfaction, marginal bone loss and success and survival of implants in patients with maxillofacial defects. The obtained positive results will be a valuable guide for clinicians facing the same difficulties in patients.

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BRIEF ARTICLE

Evaluation of factors affecting the success rate of orthodontic mini-implants by survival analysis

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Abstract

AIM: To investigate the success rate of mini-implants and its characteristics and risk factors by survival analyses.

METHODS: Three hundred and ninety-four mini-implants of the same type were placed by a single clinician. Age, gender, treatment duration, time of failure, side and jaw of implantation and the soft tissue at placement site were recorded. Odds ratio, survival curves, and Cox proportional hazard model were applied to evaluate the factors influencing the mini-implants' success rate.

RESULTS: The cumulative success rate was 88.1%. The maxilla had a significantly higher success rate than that of the mandible (91.7% *vs* 83.7%, respectively, *P* = 0.019). Placement of mini-implants in the attached gingiva (AG) showed a higher success rate than that of the mucogingival junction (MGJ) and mucous membrane (MM) (AG, 94.3%; MGJ, 85.8%; MM, 79.4%; *P* < 0.001). Significant association was found between the jaw and the gingival tissue type (*P* < 0.001). There were no significant differences between maxilla and mandible when compared within each placement site.

CONCLUSION: The gingival tissue type had the most significant effect on the success rate of the mini-implant with higher success rate in the attached gingiva.

Key words: Mini-implant; Success rate; Survival analysis; Gingival tissue; Treatment planning

Core tip: Anchorage reinforcement is a critical factor for successful orthodontic treatment outcome. Mini-implants are applied to achieve various dental movements such as anterior retraction, molar protraction and distalization, intrusion, extrusion, and correction of midline and occlusal canting. The gingival tissue type had the most significant effect on the success rate of the mini-implant with higher success rate in the attached gingiva.

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INTRODUCTION

Anchorage reinforcement is a critical factor for successful orthodontic treatment outcome. Mini-implants are applied to achieve various dental movements such as anterior retraction, molar protraction and distalization, intrusion, extrusion, and correction of midline and occlusal canting[1-4].

The factors affecting the success rate of mini-implants have been investigated extensively but not all of them are agreed upon regarding their significance by the investigators[5-10]. Type of mini-implant was suggested as a contributor to the success rate[11,12]. Age and gender of patients, the jaw and side receiving the mini-implant, and the type of gingival tissues were not significantly associated with the success rate[8,11,13,14].

However, Lee *et al*[15] reported a significant effect of age, and Manni *et al*[12] demonstrated the gender as a significant factor. In addition, peri-implant soft tissue characteristics may be a contributing factor[16]. Moon *et al*[13] also reported significant differences between placement sites between different teeth. Also, vertical skeletal pattern was reported to influence the success rate[10].

Recently, three or more types of mini-implants were placed by more than one operator[10,11,14,16]. However, Lee *et al*[15] inserted a single type of mini-implants and reported that there are no significant differences in the success rate according to clinicians. In Park *et al*[17] the mini-implants were placed by one clinician, but the sample size was relatively small for both reports.

However, a well-controlled study with larger sample size of a single type of mini-implants placed by one experienced clinician has not been conducted. This can minimize the effect of the operator- and mini-implant-related factors on the evaluation of success rate.

Therefore, the purpose of this study was to investigate the success rate of mini-implants and its characteristics and risk factors using the same type of mini-implants placed by single clinician by survival analyses.

MATERIALS AND METHODS

A hundred and sixty four patients (47 male, 117 female; mean age 24.0 ± 6.8 years) treated with fixed appliance from July, 2009 to March, 2010 in a private orthodontic clinic were included in this retrospective study. Those who had special medical history such as osteoporosis, thyroid problem, diabetes, and hypertension were excluded.

A total number of 394 mini-implants were placed for anchorage reinforcement by one right-handed experienced clinician using a single placement technique (30° to the surface of soft tissue and about 20 N•cm torque on the self drilling miniscrew) and were loaded 3 wk after placement with a similar amount of force. Only one type of mini-implants was used to exclude the effect of the screw material and design (6.0 mm in length and 1.5 mm in diameter, Biomaterials Korea, Seoul, Korea).

The records were examined to retrieve the following data: age, gender, date of mini-implant placement, date of failure (if occurred), date of removal at the end of treatment, location (upper, lower, right, left) and gingival tissue type at placement site [attached gingiva (AG), mucogingival junction (MGJ), mucous membrane (MM)]. The success of the mini-implant was defined as being functionally stable till the end of the treatment without signs of inflammation. Meanwhile, failure was recorded in case of removal of the mini-implant due to looseness.

Statistical analysis

SAS 9.2 (SAS Institute Inc. Cary, NC, United States) was used for the statistical analysis. The Fisher exact test significance and odds ratio statistics were calculated. A nonparametric life table method was used to easily visualize the hazard function over time. Association between significant variables was assessed by χ^2 test. Kaplan-Meier survival curves were generated, and the Gehan generalized Wilcoxon test was used to identify the variables associated with implant failure. Prognostic variables associated with implant failure were identified with the Cox proportional hazard model which is a survival model that relate the time passed before an event happens to one or more covariates (in our study: age, gender, jaw, side, and gingival tissue) that might be associated with that quantity of time. The level of statistical significance was set at 5%.

RESULTS

There was no significant difference in the success rates between implantation sides, gender, and age. However, there were significant differences between upper and lower implantation (91.7% *vs* 83.7%, respectively, $P = 0.019$) and according to the gingival tissue type at the placement site (AG, 94.3%; MGJ, 85.8%; MM, 79.4%; $P < 0.001$) (Table 1).

The hazard function of mini-implant survival time was regarded as the instantaneous failure rate[18]. As the latest failure event was at 27 wk, the function showed that the risk of failure was highest immediately after placement and then decreased to zero till the end of the treatment. The linear fit of the hazard function was $R^2 = 0.62$ with a negative slope over time (Figure 1).

The Kaplan-Meier survival curve according to jaw and gingival tissue type (Figure 2) demonstrated high success rates for all subgroups. The Gehan generalized Wilcoxon test revealed that the implants placed in the maxilla had a higher success rate than those placed in the mandible ($P = 0.014$). Also, those placed in the attached gingiva had a significantly higher survival rate than other subgroups ($P < 0.001$).

χ^2 test verified a significant association between the jaw and the gingival tissue type ($P < 0.001$) (Table 2). By Fisher's exact test and odds ratio analysis, there were no significant differences between maxilla and mandible when compared according to gingival tissue type, independently (Table 3). The Cox proportional hazard model also showed that the gender and gingival tissue type are significant factors for mini-implant survival (Table 4). The estimated probability of failure was lower for females ($P < 0.001$) and the attached gingiva ($P = 0.019$).

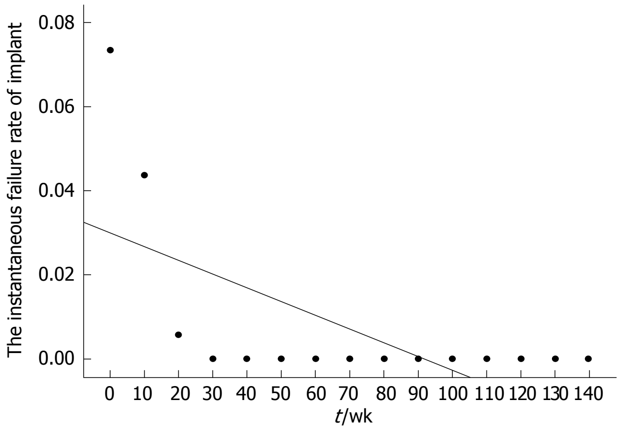

Figure 1 Instantaneous failure curve of mini-implant: The hazard function shows that the maximum risk is immediately after mini-implant placement and then it declines to zero by time. The linear fit of the hazard function was $R^2 = 0.623$.

DISCUSSION

With improvement of mini-implant materials, design and placement technique, recent studies have often reported mini-implant success rates higher than 90%[15,19]. On the other hand, since it is rare that a patient receives only one mini-implant during orthodontic treatment, the success rate faced by clinicians throughout treatment may be substantially lower due to presence of multiple mini-implants in each patient.

In our study, the success rate (88.1%) was slightly lower than that in Lee *et al*[15] (91.5%), higher than Manni *et al*[12] (81%) and similar to Cheng *et al*[16] (89%). Moreover, several studies evaluated numerous factors affecting the success rate of mini-implants[5,14,17,20]. However, most of them assessed many heterogenic variables using a small sample size that increase type Ⅱ errors and decrease statistical power. In our study, to eliminate the factors related to the clinician and the mini-implant, only one clinician placed 394 mini-implant of the same type following the same insertion technique.

Recently, Manni *et al*[12] evaluated 12 different factors affecting the stability of mini-implants. Although the mini-implants in their study were placed by the same clinician, they were of 3 different types. Furthermore, the evaluation of too many variables may lead to generation of higher-order interactions resulting in a complicated result interpretation[21]. Our research was limited to only five host variables to avoid such a complication.

Lee *et al*[15] also evaluated five variables affecting the success rate of the mini-implants. However, the anatomical location and the soft tissue of the insertion site were not included in their study. They found patient's age to be the only significant factor that affects the success rate of mini-implants. They recommended special caution when planning mini-implants for young patients. On the contrary, our results showed that the age was not a significant factor in determining the success of mini-implants.

Several reports demonstrated a significant effect for age on the success rate of mini-implants[15,20]. The higher risk of failure in younger patients could be attributed to their lower bone density[22,23]. However, in agreement with our results, other studies reported no significant differences among age-groups[13,14,17]. This inconsistency among results can be explained by the multifactorial nature of the mini-implant success rate. Moreover, it can be argued that Lee *et al*[15] and Chen *et al*[20] have overlooked the evaluation of the effect of gingival tissue type at the placement site.

In our study, the gingival tissue type at the placement site was the main factor affecting the success rate. In AG, the placement of mini-implant had a 2.7 times lower failure rate than in MGJ which in turn had a 1.6 times lower failure rate than in MM (Table 1). This was in accord with previous investigations[5,12,16]. Moreover, an animal study showed a significantly higher stability of mini-implants in keratinized gingiva. Within their limited sample size (22 mini-implants), all failed cases (n = 9) were placed in the non-keratinized gingiva[24]. The lower failure rate in the AG could be explained by the non-movable keratinized

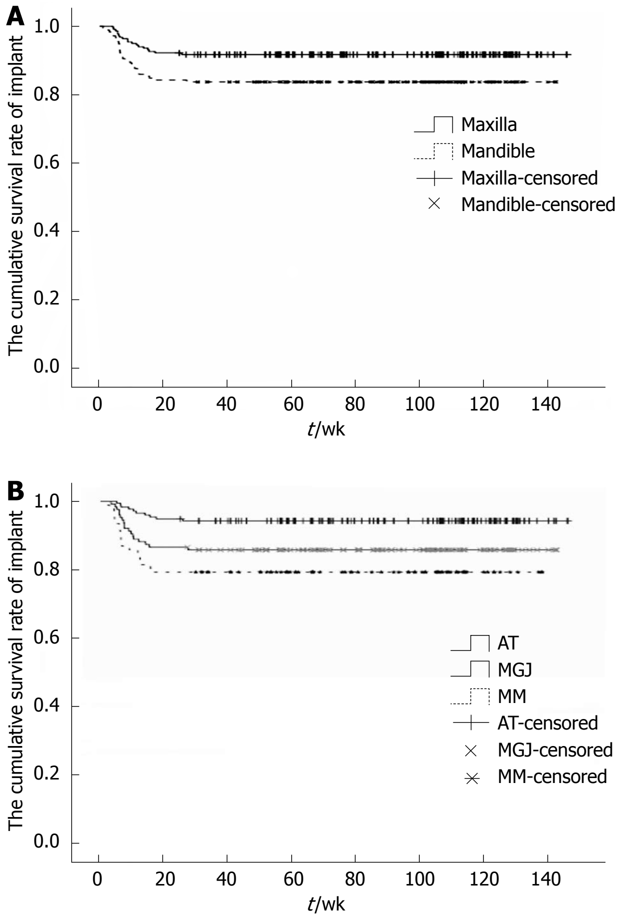

Figure 2 Kaplan-Meier survival analysis of mini-implant by jaw and gingival tissue. A: The survival rate of mini-implants placed in the maxilla was significantly higher than that of those placed in the mandible; B: The survival rate of mini-implants placed in the attached gingival (AG) was significantly higher than that of those placed in the mucogingival junction (MGJ) and mucous membrane (MM). The duration of survival in the censored cases was measured from mini-implant placement to completion of treatment.

Table 1 Mini-implants' success and failure rates, and ORs statistics by host variables *n* (%)

Variables	Success	Failure	Total	*P*-value	OR (95%CI)	
Gender				0.231		
Male	96 (84.96)	17 (15.04)	113			
Female	252 (89.36)	30 (10.64)	282		0.762 (0.354, 1.274)	
Jaw				0.019		
Maxilla	199 (91.71)	18 (8.29)	217			
Mandible	149 (83.71)	29 (16.29)	178		2.152 (1.151, 4.021)	
R/L side				0.877		
Left	117 (88.50)	23 (11.50)	200			
Right	171 (87.69)	24 (12.31)	195		1.080 (0.587, 1.986)	
Age				0.973		
< 20	106 (87.60)	15 (12.40)	121			
20-30	204 (88.31)	27 (11.69)	231		0.935 (0.477, 1.834)	
> 30	38 (88.37)	5 (11.63)	43		0.930 (0.316, 2.732)	
Gingival tissue				< 0.001		
AG	165 (94.29)	10 (5.71)	175			0.367 (0.163, 3.204)
MGJ	109 (85.83)	18 (14.17)	127		2.724 (1.212, 6.124)	
MM	73 (79.35)	19 (20.65)	92		4.294 (1.903, 9.689)	1.576 (0.775, 3.204)

Fisher's exact test. R/L: Right/left; AG: Attached gingiva; MGJ: Mucogingival junction; MM: Mucous membrane.

Table 2 Distribution of mini-implants according to gingival tissue type at the placement site in maxilla and mandible *n* (%)

	Mandible		Maxilla		*P*-value
	Total	Failed	Total	Failed	
Attached gingiva	34 (19.1)	4 (11.8)	141 (65.3)	6 (4.3)	
Mucogingival junction	78 (43.8)	11 (14.1)	49 (22.7)	7 (14.3)	< 0.001
Mucous membrane	66 (37.1)	14 (21.2)	26 (12.0)	5 (19.2)	

Table 3 Independent comparison of failure rate between maxilla and mandible according to gingival tissue type *n* (%)

Variables	Success	Failure	Total	*P*-value	OR (95%CI)
Attached gingiva				0.105	
Maxilla	135 (95.74)	6 (4.26)	141		
Mandible	30 (88.24)	4 (11.76)	34		3.000 (0.797, 11.293)
Mucogingival junction				1	
Maxilla	42 (85.71)	7 (14.29)	49		
Mandible	67 (85.90)	11 (14.10)	78		0.985 (0.354, 2.740)
Mucous membrane				1	
Maxilla	21 (80.77)	5 (19.23)	26		
Mandible	52 (78.79)	14 (21.21)	66		1.131 (0.362, 3.535)

tissue that decreases the susceptibility to irritation and infection. On the other hand, some authors reported no significant differences in the success rate according to soft tissue[14,17,25].

Several studies reported higher success rate of mini-implant placement in the maxilla than that for those placed in the mandible[12,16,20]. On the other hand, some authors reported no significant differences between the upper and lower jaws in mini-implant success rate[11,13,14,25]. In our study, the jaw, initially, was a significant factor affecting the success rate. However, with further analysis, a significant association (P < 0.001) was found between the jaw and the gingival tissue type. The mini-implants placed in the mandible were mainly placed in mucous membrane or MGJ, while those placed in the maxilla were mainly in the attached gingiva. No significant differences in the success rates were found between the mini-implants placed in upper and lower jaws when compared within each gingival tissue type.

This was in agreement with Moon *et al*[13] who placed all the mini-implants in the attached gingiva and showed no significant difference in the success rate between maxilla and mandible. In addition, in our results, Cox proportional hazard model showed no significant effect of the

Table 4 Regression analysis of factors affecting the failure rate of min-implants

	Beta	SE	Wald	*P*-value	Exp (B)	95%CI of Exp (B)
Gender	0.444	0.124	12.744	< 0.001	1.559	1.222-1.989
Jaw	0.107	0.109	0.956	0.358	1.113	0.898-1.378
R/L Side	-0.031	0.107	0.085	0.771	0.969	0.785-1.196
Age	-0.027	0.084	0.101	0.751	0.974	0.826-1.148
Gingival tissue	0.162	0.069	5.512	0.012	1.176	1.027-1.347

Cox proportional hazard model. Wald: Wald statistic; Exp (B): Exponential of Beta; R/L: Right/left.

jaw on the failure rate ($P = 0.358$). Therefore, the greater failure rate of mini-implants placed in the mandible can be explained by the lake of further analysis to examine any association between the jaw and other factors, such as inflammation, root proximity, and soft tissue mobility.

Similarly, gender was described as a significant factor in several studies. Moon *et al*[13] reported a higher success rate in male patients while in Antoszewska *et al*[5] study female subjects had a higher rate. Nevertheless, our results showed no significant difference in the rate according to gender. This was in accordance with several reports[14,17,20]. Interestingly, the Cox proportional hazard model in our study showed that gender was a significant factor. Therefore, future studies might be required to evaluate the influence of gender on the success rate with a larger sample size from both groups with uniform inclusion criteria that eliminate other confounding factors.

Time of loading has been evaluated in several reports but no consensus was reached. Trisi *et al*[26] demonstrated that immediate loading might undermine the stability of dental implants and increase the number of failures. On the contrary, other studies showed a positive influence for the immediate loading[12,27]. However, Miyawaki *et al*[11] found no correlation between the time of loading and success rate. In addition, Cheng *et al*[16] and Costa *et al*[28] achieved success rates of 89% and 87.5% with delayed and immediate loading, respectively. In our study, to minimize the effect of the loading time, all mini-implants were loaded three weeks after placement.

From our results, it is recommended that clinicians place mini-implant in the attached gingiva as long as possible to improve the success rate. However, further prospective controlled studies are required to evaluate the efficiency of different types of temporary anchorage devices used for various clinical situations.

In summary, with the single type of mini-implants used by the same clinician, survival analysis was performed to evaluate the success rate of mini-implant. The gender and gingival tissue type had significant effects on the success rate. Mini-implants placed in the attached gingiva had a higher success rate than that of those placed in the mucogingival junction and mucous membrane. However, no significant differences in the success rate were found according to age, gender, and implantation side and jaw. Therefore, it is recommended for clinician to consider the characteristics of gingival tissue prior to mini-implant insertion.

COMMENTS

Background

Anchorage reinforcement is a critical factor for successful orthodontic treatment outcome. Mini-implants are applied to achieve various dental movements such as anterior retraction, molar protraction and distalization, intrusion, extrusion, and correction of midline and occlusal canting.

Research frontiers

With improvement of mini-implant materials, design and placement technique, recent studies have often reported mini-implant success rates higher than 90%. On the other hand, since it is rare that a patient receives only one mini-implant during orthodontic treatment, the success rate faced by clinicians throughout treatment may be substantially lower due to presence of multiple mini-implants in each patient.

Innovations and breakthroughs

With the single type of mini-implants used by the same clinician, survival analysis was performed to evaluate the success rate of mini-implant. The gender and gingival tissue type had significant effects on the success rate. Mini-implants placed in the attached gingiva had a higher success rate than that of those placed in the mucogingival junction and mucous membrane.

Applications

From their results, it is recommended that clinicians place mini-implant in the attached gingiva as long as possible to improve the success rate. However, further prospective controlled studies are required to evaluate the efficiency of different types of temporary anchorage devices used for various clinical situations.

Peer review

This is a well-written and interesting article about mini-implants success rate. English grammar and language are good. The title reflects the major topic and contents of the study. The abstract clearly describes the research background, objectives, materials and methods, results and conclusions. The study design is appropriate, as well as the used statistical methods. The sample size and the statistical data are adequate for this clinical study.

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BRIEF ARTICLE

Management of missile injuries to the maxillofacial region: A case series

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Abstract

AIM: To assess our management of patients suffering from missile injuries to the maxillofacial region.

METHODS: From December 2009 to September 2012, 40 patients with missile injuries (high velocity gunshot and bullet wounds, explosive injuries and shrapnel *etc.*) affecting the maxillofacial region were treated. All except for 2 patients were males. All had soft tissue injuries with or without bone injuries. These patients were referred to the plastic and maxillofacial surgery ward of our hospital. The patients were 19 to 65 years of age (mean 45 years). In 19 cases, there were missile injuries to other parts of the body, especially the lower extremities. All of the patients were managed by early soft tissue debridement, comprehensive reconstruction and antibiotics. This retrospective study was approved by the IRB and ethical committees.

RESULTS: The majority of injuries were caused by high velocity projectiles (88%) and the remaining by car explosions or dynamite blasts (12%). 40 patients were treated surgically. Thirty patients had soft tissue loss (75%) and 20 patients (50%) had bone loss; there was combined soft tissue and bone loss in 10 (25%) patients. Facial fractures were in the orbital bones in 10 cases, maxillary in 7, nasal in 5 and the mandible in 3 cases. We used primary repair in the majority of soft tissue defects (25 of 40 cases). Bone repair was done primarily at the same stage using miniplates, titanium screws or wires. In some cases with a bone defect, iliac bone grafts were used simultaneously or in the later stages (mandibular defects). There was no failure of bone reconstruction in our cases. Infections occurred in two cases and were treated with systemic antibiotics and dressing changes, without any long term sequelae.

CONCLUSION: Our principles for soft tissue reconstructions were according to the reconstructive ladder and included primary repair, local flaps, skin grafts and regional flaps depending on the extent of damage. Primary repair in facial missile defects was not associated with increased morbidity or complications in this series. We recommend this approach when feasible.

Key words: Missile; Maxillofacial; Management; Primary; Surgery

Core tip: Exposure to missile injuries may result in unique and complex injury patterns from projectiles or fragments. Injuries to the face due to firearms are either high velocity or low energy; high velocity projectiles can result in devastating functional and aesthetic consequences, shattering the hard tissues. Early intervention in facial firearm injuries resulted in restoration of occlusion and continuity of the jaw, fixation of luxated or extruded teeth, early return of function, prevention of segment displacement and tissue contracture, less scarring and decreased need for major bone graft reconstruction later on.

Ebrahimi A, Motamedi MHK, Nejadsarvari N, Kazemi HM. Management of missile injuries to the maxillofacial region: A case series. *World J Stomatol* 2013; 2(3): 62-66 Available from: URL: http://www.wjgnet.com/2218-6263/full/v2/i3/62.htm DOI: http://dx.doi.org/10.5321/wjs.v2.i3.62

INTRODUCTION

Missile injuries to the maxillofacial region are important health issues, both in the military and civilian population. The range of damage of these injuries represents a continuum of severity from minor injuries to those resulting in lost workdays, long-term disability and fatalities [1].

We managed such patients after primary urgent management at our hospital. The principles of treating blunt trauma to the face are well established; however, missile injuries in this region have special features that provide the surgeon with multiple medical and surgical challenges when dealing with these injuries[2].

Severity

The severity of these injuries depends upon many factors, including the type of missile and type and site of the injury; damage to the tissue is much more a function of the velocity of the missile than of its mass[2].

Assessment and resuscitation

The most important factor in the care of patients with a missile injury is the initial assessment and resuscitation performed at the emergency department.

Management

The management of missile injuries of the maxillofacial region can be divided into three phases: immediate, intermediate and late[3]. Indeed, most plastic and maxillofacial surgeons manage patients in the intermediate and late phases but require cooperation between the emergency physician and maxillofacial surgeon for optimal and early management.

Controversy exists regarding early aggressive intervention or a more conservative approach[2]. In this article, we review facial reconstruction after missile injuries with early surgical intervention.

MATERIALS AND METHODS

Forty patients with missile injuries (high velocity gunshot wounds, explosive injuries) affecting the maxillofacial region were included in this retrospective study within the period from December 2009 to September 2012 consecutively. These patients were referred to the plastic and maxillofacial surgery ward of our hospital; 38 patients were men and 2 were women, with an age range of 19 to 65 years (mean 45 years). All patients had combined soft tissue with or without bone injuries in the facial region (Figure 1). In 19 cases, there were missile injuries to other parts of the body, especially the lower extremities. We managed all patients with early soft tissue debridement and reconstruction and placed them on antibiotics for one week after primary surgery. This study was approved by the IRB and ethical committee.

Soft tissue management

Our principles of reconstruction of the facial soft tissues were by primary intention, including primary repair, local flaps and regional flaps such as cervicofacial flaps. In periorbital wounds, the orbit and globe were examined carefully for detection of injuries and we requested an ophthalmologist consultation for such patients (Figures 2 and 3). In three cases of gunshot injury with unilateral blindness, globe enucleation was done.

Shell fragments

Shell fragments, bullets and shrapnel were removed if they were in the field of operation; otherwise they were left.

Bone management

For bone reconstruction, we restored shape, contour rigidity and stability to the facial skeleton with different devices, such as titanium screw and plate, wire and arch bar immobilization with or without bone grafts (Figure 1). Our method for bone grafting was in the early phase from the iliac crest.

Mandible

For treatment of gunshot wounds of the mandible, we used an intraoral or extraoral approach and open reduction and internal fixation with miniplates or reconstruction plates, with or without intermaxillary fixation. In one case, we used a reconstruction plate (Figure 1) and in a later stage iliac bone grafting was done.

Maxilla

For treatment of gunshot wounds of the maxilla, we used intraoral incision and open reduction and internal fixation with miniplates with or without intermaxillary fixation.

Frontal bone

For treatment of gunshot wounds of the frontal bone, we used an open approach from the laceration site or coronal incision and, after reduction, internal fixation with miniplates with or without bone graft was done.

Periorbital fractures

All periorbital fractures were operated on during the first week after injury. Upon admission of injured patients, examinations were done as indicated (radiography, axial and coronal facial CT scans, Doppler ultrasound for carotid artery damage).

Orbital fractures

For treatment of gunshot wounds of the orbit, we used

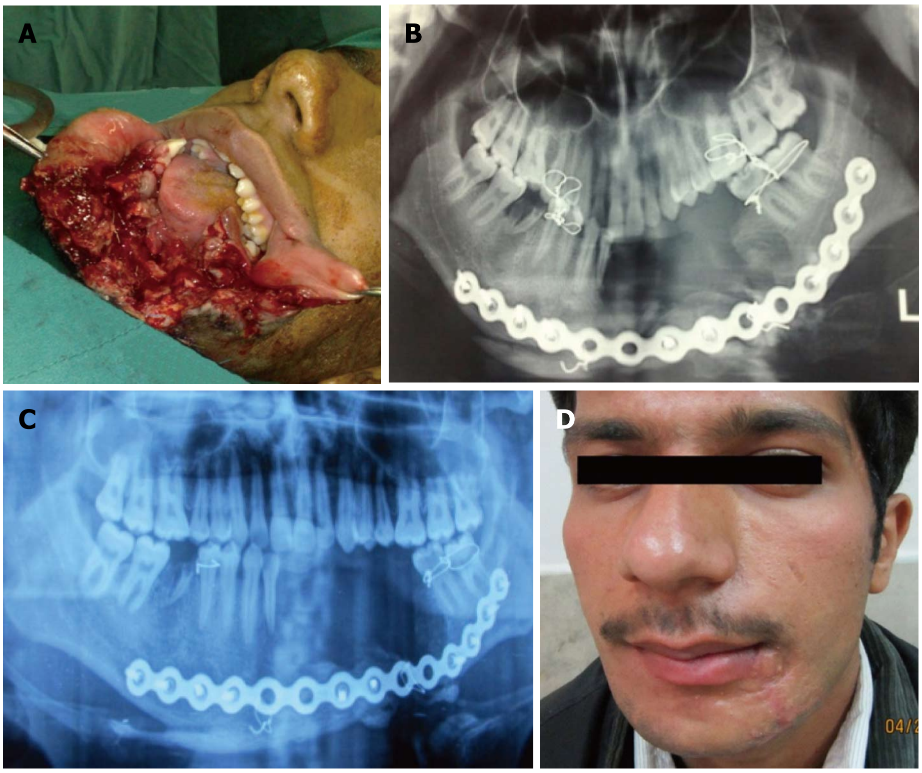

Figure 1 A 20 year old man with a gunshot wound to the lower face, with disruption of soft tissue and the mandible bone in body with bone defect. A: Before operation; B: Computed tomography scan before operation; C: Reconstruction with reconstructive plate; D: Three months post operation.

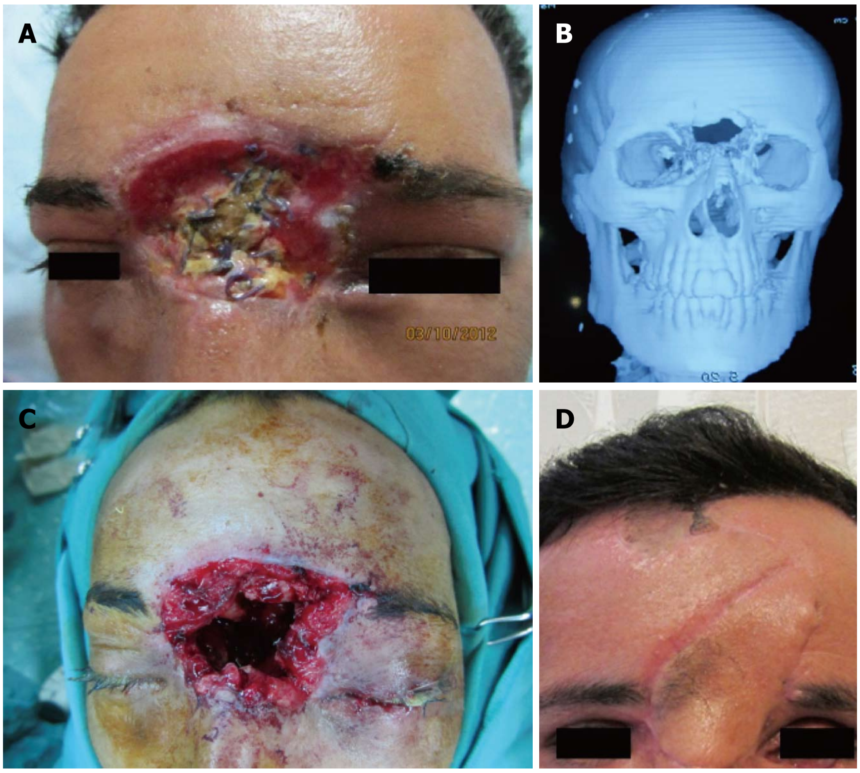

Figure 2 A 30 year old man with a gunshot wound to the upper face, with disruption of the forehead and frontal and ethmoid sinus and left eye to the base of the skull. A: Before operation; B: The patient was treated with abdominal fat to obliterate the frontal sinus elsewhere before referral. Computed tomography scan before reconstruction; C: Intra operative view; D: Reconstruction with forehead flap and iliac bone graft (one month post operation).

an open approach with reduction and internal fixation with miniplates and screws, with or without an implant.

Scars

All deformities and scar contractures were corrected after maturation of scars. Ophthalmic injuries were diagnosed in 10 patients (globe, eyelid and eyebrow). Enucleation of the unilateral eye was done in 3 cases by the ophthalmologist for severely damaged and complete blindness of the unilateral eye.

We used primary repair in the majority of soft tissue defects (25 of 40 cases). Bone repair was done primarily at the same stage using miniplates, titanium screws or wires. In some cases with a bone defect, iliac bone grafts were used

Figure 3 A 23 year old man with a gunshot wound defect of the eyebrow. A: Before operation; B: Early post operation; C: One year post operation.

Table 1 Distribution of facial soft tissue and bone damage in 40 gunshots and blast injured persons

	Site of injury	*n*	Bone	Soft tissue defect	Combined soft tissue-bone
1	Periorbital	12	10	6	4
2	Maxillary	17	7	16	6
3	Mandible	4	3	2	1
4	Nasal	5	3	4	3
5	Frontal	2	2	2	2
Total		40	25	30	16

simultaneously or in the later stages (mandibular defects).

RESULTS

A total of 40 patients were treated and followed from 5 months to 3 years. There were 38 male and 2 female patients, with an average age of 37 years (range 19-65 years). Most injuries were caused by high velocity projectiles (88%) and the remaining by car explosions or dynamite (12%). Thirty patients had soft tissue loss (75%) and 20 patients (50%) had bone loss; there was combined soft tissue and bone loss in 10 (25%) patients. Facial fractures were in the orbital bones in 10 cases, maxillary in 7, nasal in 5 and the mandible in 3 cases (Table 1).

There was no failure of bone reconstruction in our cases. Infections occurred in 2 cases and were treated with systemic antibiotics and dressing changes, without any long term sequelae.

DISCUSSION

Exposure to missile injuries may result in a unique and complex injury pattern, usually from fragments or bullet wounds which are often fatal if they involve the head. Blast overpressure is the abrupt, rapid rise in atmospheric pressure resulting from explosive detonation, firing of large caliber weapons and accident occupational explosions[4,5]. There are two schools of thought for the management of such patients subjected to missile injuries: early intervention and nonaggressive conservative intervention[2]. Injuries to the face due to firearms are either high velocity or low energy; high velocity projectiles can result in devastating functional and aesthetic consequences, shattering the hard tissues[6].

Our principles for soft tissue reconstructions were according to the reconstructive ladder, including primary repair, local flaps, skin grafts and regional flaps depending on the extent of damage (Figure 3). We used primary repair in the majority of soft tissue defects (25 of 30 cases) and recommend this approach for these injuries.

We used surgical intervention in all cases. Early intervention in facial firearm injuries resulted in restoration of occlusion and continuity of the jaw, fixation of luxated or extruded teeth, early return of function, prevention of segment displacement and tissue contracture, less scarring and decreased need for major bone graft reconstruction later in one study[6]. If continuity of the mandible can be obtained, in the subsequent operations there will be no need for maxillomandibular fixation. In this case series study, we had no major complications after early surgical interventions.

All facial wounds were under systemic antibiotic therapy for one week and local antibiotic ointment to prevent secondary infections. There was no failure of bone reconstruction; in our cases, maxillary defects were reconstructed with bicortical bone grafts in the same operation. We had facial wound infections postoperatively in 2 cases and treated them with systemic antibiotics and dressing changes, without any long term sequelae (these two patients had a mandible fracture with a through wound of the oral cavity without any medical immunocompromising factors).

The issue of when to treat maxillofacial firearm injuries remains controversial (early or delayed), although not all maxillofacial projectile injuries can be comprehensively treated at the onset[7]. Although all missile wounds are contaminated, the general consensus in the medical literature and textbooks consider these infections to be mostly of odontogenic origin[8]. In composite defects (soft tissue and bone), we used bone graft and soft tissue flaps simultaneously for coverage of bone and our results were free of any significant resorption or flap necrosis after early operative intervention.

In our study, the most common site of entrance and exit wounds was in the cheek (67%). In another study in Iraq by Kummona, the most common site was also in the cheek

Table 2 Associated injures in the face *n* (%)

Associated injures	
Facial nerve	2 (5)
Parotid duct	4 (10)
Globe	3 (7.5)
Oral mucosa	3 (7.5)
Lacrimal duct	2 (5)
Total	14 (35)

(54.8%). According to our results, the midface is a common site for gunshot injuries and a safe coverage for protection of the cheek in military and civilian people must be designed for combat. The face is the part of the body most subjected to injuries, either by road traffic accidents or missile war injuries[9]. In our experience, gunshot injuries of the craniofacial region are not a single site injury and often have associated injuries; thus, a complete evaluation of soft tissue and bones must be done for all patients. We used free bone grafting for 4 patients in our cases and the preferred site for bone graft harvesting was the iliac crest because of combined cortico-cancellous block of bone. For delayed reconstruction of the frontal cranium, we used titanium mesh and soft tissue flap with acceptable results (Figure 3) and without any complications. In our series, the most common associated injuries were ophthalmic injuries (Table 2), seen in 10 patients with unilateral blindness. In another study, the most common injured facial structure was the facial nerve and the second most common was ophthalmic injuries. An important problem in patients with gunshot injuries or blast damage is facial burn blast tattoos that must be managed early post damage by operative intervention. Application of silver sulfadiazine before the operative intervention helps to remove embedded particles better and decrease traumatic tattoos[10]. This procedure is also better to be done early. Advocates of primary management have supported this viewpoint[11-14].

In high velocity gunshot and blast injuries with facial damage to soft tissue and bone, early surgical intervention is beneficial and good results without significant complications can be obtained; we recommend this approach in these types of facial injuries.

COMMENTS

Background

Firearm projectiles can result in devastating functional and aesthetic consequences, shattering the hard tissues. Early intervention in facial firearm injuries is still in debate.

Research frontiers

Experience has shown that early management results in restoration of occlusion and continuity of the jaw, fixation of luxated or extruded teeth, early return of function, prevention of segment displacement and tissue contracture, less scarring and decreased need for major bone graft reconstruction later on.

Innovations and breakthroughs

Innovations in surgical instruments and hardware, plates and screws have enabled rigid fixation of fractures.

Applications

These advancements have enabled surgeons to better manage gunshot injuries.

Peer review

The manuscript is a result of good efforts on the part of the authors and may be useful to determine management of maxillofacial injuries secondary to missiles and gunshot wounds.

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Journals

English journal article (list all authors and include the PMID where applicable)

1 **Jung EM**, Clevert DA, Schreyer AG, Schmitt S, Rennert J, Kubale R, Feuerbach S, Jung F. Evaluation of quantitative contrast harmonic imaging to assess malignancy of liver tumors: A prospective controlled two-center study. *World J Gastroenterol* 2007; **13**: 6356-6364 [PMID: 18081224 DOI: 10.3748/wjg.13.6356]

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2 **Lin GZ**, Wang XZ, Wang P, Lin J, Yang FD. Immunologic effect of Jianpi Yishen decoction in treatment of Pixu-diarrhoea. *Shijie Huaren Xiaohua Zazhi* 1999; **7**: 285-287

In press

3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

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4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

Both personal authors and an organization as author

5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

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8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

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Personal author(s)

10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

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11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

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12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

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13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

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14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic

programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

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15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

Statistical data

Write as mean ± SD or mean ± SE.

Statistical expression

Express *t* test as *t* (in italics), *F* test as *F* (in italics), chi square test as χ^2 (in Greek), related coefficient as *r* (in italics), degree of freedom as υ (in Greek), sample number as *n* (in italics), and probability as *P* (in italics).

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