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RESEARCH ARTICLES

REVIEW ARTICLE

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RESEARCH ARTICLE

Histomorphometric Comparison of Resorbable Collagen Sponges with Xenogen Grafts in Terms of New Bone Formation in Sinus Floor Elevations: An Experimental Study in the Rabbits

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ABSTRACT

Due to a number of complicated factors, implanting the edentulous posterior maxilla is often a difficult procedure. It is stated that maxillary sinus floor elevation is a predictable treatment option to obtain sufficient bone height and volume for implant placement. In this study, it was aimed to compare the resorbable collagen sponges which are thought to be used in maxillary sinus floor elevation with xenogen graft particles, histopathologically and histomorphometrically in terms of new bone formation. For this purpose; In 16 New Zealand white rabbits, bilateral sinus floor elevation was performed, the cavities formed under the sinus membrane were augmented by placing a collagen sponge on the right side and an equal volume of xenogen grafts on the left side. In the postoperative period, the rabbits were sacrificed at the end of the 4th and 8th weeks, 8 each time. The obtained samples were divided into 4 groups and evaluated histopathologically and histomorphometrically. Results: Histopathological evaluation revealed that the two materials were biocompatible materials and formed a suitable environment for the transfer of osteogenic cells. Histomorphometric evaluations showed that there was no difference between the materials in terms of percentage of new bone formation. ($p \leq 0.05$) However, the newly formed bone area and osteoid area were found to be much larger in the areas where xenogen grafts were used ($p \leq 0.05$). Collagen sponge was unable to maintain its volume during the test period and resorbed. Minimal resorption was observed in xenogen graft particles.

Keywords: Sinus floor elevation, resorbable collagen sponge, xenograft, histomorphometry

INTRODUCTION

Today, implant-supported prostheses have revolutionized dentistry by offering a predictable and functional fixed treatment option for missing teeth. The posterior maxilla has been shown to be one of the most challenging areas for implant survival.[1, 2]

Several treatment options have been proposed for fixed prosthetic rehabilitation of the edentulous posterior maxilla. Sinus floor elevation is applied using graft materials to direct bone augmentation and create new bone tissue for the future implant placement site.[3-10]

If the cavity created under the sinus membrane is preserved for a sufficient period of time without inserting autogenous bone or graft materials, new bone is expected to form in this space. Histomorphometic evaluation is the gold standard for evaluating bone healing in augmented sinuses.

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MATERIALS AND METHODS

A total of sixteen adult New Zealand white rabbits (eight females and eight males) weighing between 3–4 kg was used in the study.

In the study, control groups used xenogenic graft material, Bio-Oss® (Geistlich Pharma AG, Wolhusen, Switzerland), while test groups used CollaPlug® (Zimmer Dental, Carlsbad, California, America), a sponge wound dressing material containing resorbable collagen. Bio-Gide® (Geistlich Pharma AG, Wolhusen, Switzerland) collagen membrane was used to cover the bone windows opened to reach the maxillary sinus.

S1 Group: Samples that were taken in the fourth week and using resorbable sponges for augmentation.

G1 Group: Samples that were taken in the fourth week and using xenogenic graft particles for augmentation.

S2 Group: Samples that were taken in the eighth week and using resorbable sponges for augmentation.

G2 Group: Samples that were taken in the eighth week and where xenogenic graft particles were used for augmentation.

1. Surgical Method

Under veterinary control, general anesthesia was given to the sixteen rabbits included in the study by the intramuscular administration of 50 mg/kg Ketamine HCl (Ketasol 10%, Richter Pharma, Austria) and 7 mg/kg Xylazine HCL (Rompun 2%, Bayer, Istanbul).

Following the midline of the nasal bone, a 5 cm long incision was made, including skin and subcutaneous tissues. The full-thickness flap was elevated and the nasal bone, and nasoincisal suture were exposed. In order for the windows on both sides of the nasoincisal suture to be of equal size, a 6 mm diameter marking was first made with a trephine bur. Then, the osteotomy was completed with steel and diamond burs, and the maxillary sinus membrane was reached. The sinus membrane was elevated in all directions with the help of special elevators to create the necessary space for graft placement (Figure 1.A)

CollaPlug® collagen sponge and Bio-Oss® xenogenic graft particles are prepared with a volume of 0.5 ccs.

CollaPlug® was placed in the space created in the right maxillary sinuses of all the rabbits, while Bio-Oss® xenogenic graft particles were placed in the space created in the left maxillary sinuses (Figure 1.A, 1.B). The bone windows were covered with Bio-Gide® resorbable membrane (Figure 1.B). Flaps were sutured in the original position with 3.0 vicryl (Coated Vicryl, Doğsan, Istanbul, Turkey).

As planned in the study, eight of the subjects were euthanized by administering 150 mg/kg ketamine intramuscularly following general anesthesia on the fourth week. The remaining eight subjects were euthanized on the eighth week.

After removing the surrounding soft tissues, the maxilla of the subjects was excised under the orbital floor with appropriate discs and burs. The samples obtained were fixed in 10%

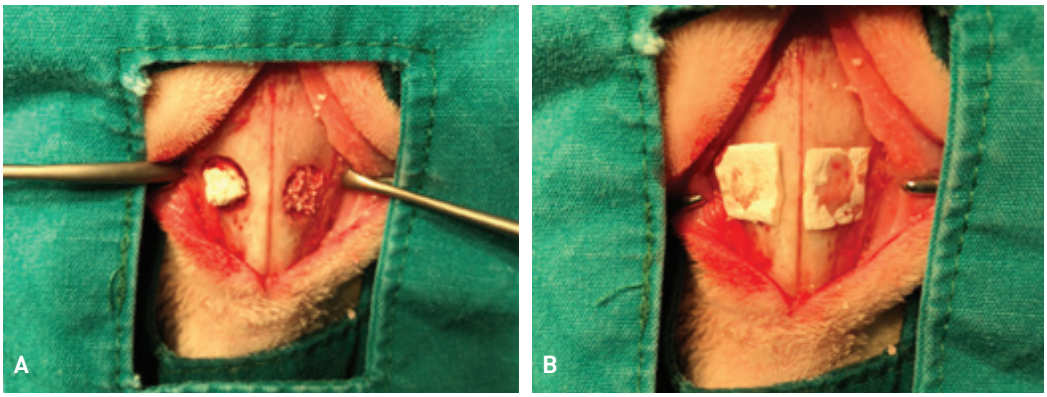

Figure 1. A. CollaPlug® was placed in the space created in the right maxillary sinuses of all the rabbits, while Bio-Oss® xenogenic graft particles were placed in the space created in the left maxillary sinuses, B. The bone windows were covered with Bio-Gide® resorbable membrane.

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formaldehyde solution for histopathological examination and labeled by group name.

2. Histological Examination

Histopathological and histomorphometric evaluations were performed in Başkent University Faculty of Medicine, Department of Pathology.

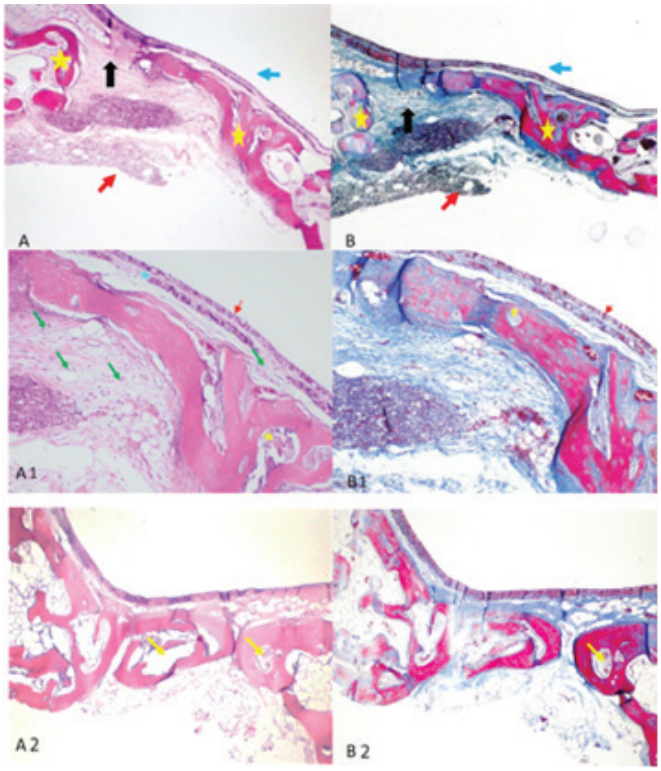

Figure 2. A, 2.B. Week four collagen sponge group (S1). H&Ex40 (2.A), MTKx40 (2.B). New bone formations formed between the maxillary wall and the Schneiderian membrane. No bone formation (black arrow). (Blue arrow: sinus mucosa, yellow star: newly formed bone trabeculae, red arrow: maxillary sinus wall osteotomy area.), 2.A.1, 2.B.1. Red arrow: surface lined with ciliated single-layer columnar epithelium, green arrow: vessel sections in the stroma, yellow arrow: bone marrow distance in newly formed bone, 2.A.2, 2.B.2. Week eight collagen sponge group (S2). Loose connective tissue without inflammation under the surface epithelium and new bone formation, including bone marrow space. (Yellow arrows: bone marrow areas.)

3. Histomorphometric Evaluation

Histomorphometric evaluations were done with OsteoidHisto (Insitute of Ageing and Chronic Diseases, University of Liverpool, Liverpool, UK), which is an Open-Source Software program. For this purpose, microscopic photographs were taken at x20 magnification in MTK stained sections with ROI via microscope imaging program (Olympus, U-TV1XC, Tokyo, Japan) and loaded into OsteoidHisto for measurements to be taken semi-automatically.

4. Statistical Method

The Mann Whitney U test was used to determine the mean of the first and second measurements of each group and whether the differences between these averages were significant. The Wilcoxon Sign Test was conducted to determine whether the difference between the first and second measurement average and the difference between the average was significant for the CollaPlug® and Bio-Oss® groups. Analyses were made with SPSS 20.0 software at a 95% confidence level.

RESULTS

1. S1 Group

After week four, the sponge group was observed to have loose connective tissue, minor salivary glands and vascular structures and bone trabeculae surrounded by an osteoblastic rim under the sinus mucosa epithelium lined with a single row of ciliated cubic-columnar epithelium. While full-thickness bone formation was not observed in some areas, fibrous connective tissue, including vascular structures, was observed, and osteoid formation was seen in the local bone adjacent to central areas. No residual material was found in this group. Rare inflammatory cells and vascular proliferation were observed, especially in the osteotomy area of the maxillary wall. (Figure 2.A, 2.B, 2.A.1, 2.B.1)

2. G1 Group

Osteoid formation surrounding the residual graft material was observed in all subjects in the xenogenic graft group at week four. While the newly formed osteoid was mostly observed in areas from the adjacent local bone to the center, there were osteoblastic cell lines around it, but osteoclasts were detected very rarely. There were osteocyte lacunae in the osteoid. The newly formed bone volume was measured as 23 ± 6.5%, and the newly formed bone area as 577287 ± 193011 μm². The osteoid

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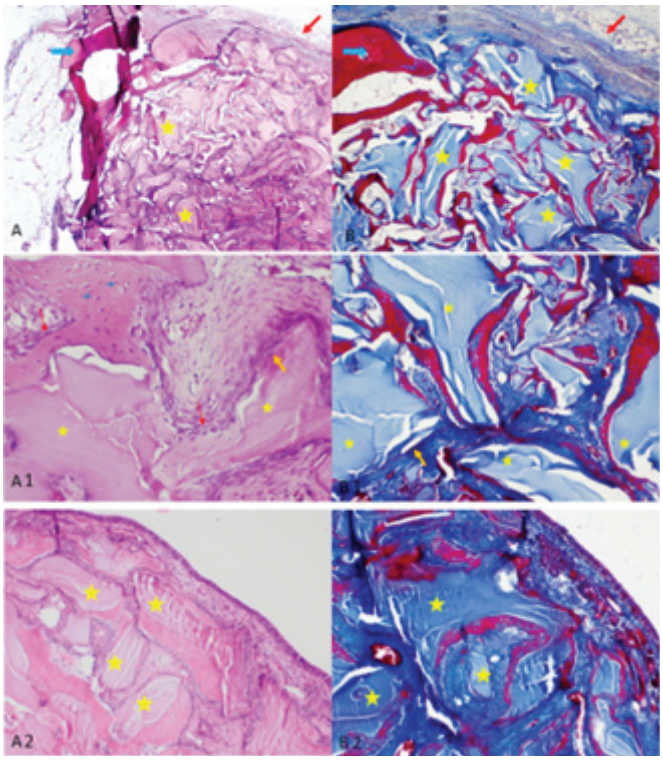
area was measured as 256953 ± 102380 µm². In areas where osteoid was not formed, fibrous connective tissue, including vascular structures, was seen in between (Figure 3.A, 3.B, 3.A.1, 3.B.1) The connective tissue percentage was determined to be 42.23 ± 13.60% on average. In this group, the mean residual graft volume was measured as 34.79 ± 11.80%. Rare chronic inflammatory cells were detected in the osteotomy site of the maxilla wall. The total ROI area was measured as an average of 3664094.4 ± 731074.5 µm².



Figures 3. A, 3.B. Week four xenogenic graft group (G1). H&Ex20 (3.A), MTKx40 (3.B). Residual graft material filling the augmented area and surrounding osteoid, fibrous connective tissue. (Yellow star: residual graft material, red arrow: maxillary wall osteotomy area, blue arrow: local bone tissue.) 3.A.1, 3.B.1. New bone formations surrounded by osteoblastic cells formed around residual graft material. In some areas, fibrous connective tissue is observed around and between the graft material. (Yellow star: graft material, orange arrow: non-osteoid transitional areas around the graft, blue arrows: osteocytes, red arrow: osteoblastic rim.) 3.A.2, 3.B.2. Week eight xenogenic graft group (G2). Mucosal epithelium lined by ciliated single-layer epithelium and bone tissue surrounded by an osteoblastic rim underlying denser connective tissue and residual graft materials. In the MTC stained section, the newly formed bone is red, the connective tissue is blue, and the residual graft is pale blue. (Yellow star: graft material.)

3. S2 Group

After week eight, new bone formations were seen in all subjects in the collagen sponge group. The percentage of newly formed bone volume was measured as 39.5 ± 9.5%, and the newly formed bone area was measured as 280446 ± 146950 µm². While full-thickness bone was usually formed in the augmented area, there was occasional connective tissue interruption. The connective tissue percentage was found to be 60.52 ± 9.55% on average. Similar to week four, no residual material was found in this group. Inflammatory cells were not seen in this group. The total ROI was measured as 967726.6 ± 387179.4 µm². (Figure 2.A.2, 2.B.2)

4. G2 Group

After week eight, residual graft material and new bone formations were detected around graft particles, which was slightly more than after week four. This newly formed bone was in the spaces between and in close contact with the graft particles. The newly formed bone volume was measured as 41.4 ± 9.5% and the newly formed bone area as 791391 ± 257161 µm². Sparse osteoclasts were observed around the bones lined with osteoblastic cells. The connective tissue observed in between was denser than in the other groups (Figure 3.A.2, 3.B.2). The connective tissue percentage was determined as 28.42 ± 15.67% on average. In this group, the residual graft volume decreased slightly compared to the fourth week and was measured as 30.19 ± 8.46% on average. Inflammatory cells were not seen in this group. The total ROI was determined as 3073085.2 ± 637331.1 µm².

5. Statistical Results

When the variation between the first and second measurements of each group's new bone formation volume was examined, no significant difference was found between the groups at four weeks and eight weeks (Table 1).

When the variation between the first and second measurements of each group's new bone area (B. Ar) is examined, the measurements differ significantly between the collagen sponge and xenogenic graft groups. In both measurements, the average of the xenogenic graft group was significantly higher than the average of the collagen sponge group (Table 1).

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When the variation between the first and second measurements of each group's osteoid area (Os. Ar) was examined, the measurements showed a significant difference between the collagen sponge and xenogenic graft groups. In both measurements, the average of the xenogenic graft group(G1-G2) was significantly higher than the average of the collagen sponge group (S1-S2) (Table 1).

When the collagen sponge group (S1-S2) was examined for the parameters of new bone volume (BV/TV), new bone area (Os. Ar), and soft tissue volume (STV/TV), a significant difference was observed between the first and second measurements (p←0.05). While a significant decrease was observed in the second measurement of the soft tissue volume (STV/TV) compared to the first measurement, a significant increase was observed from the first measurement to the second measurement for new bone volume (BV/TV) and new bone area (Os. Ar) (Table 2).

Table 1: The variation between the first and second measurements of each group's for the parameters of new bone volume (BV/TV), new bone area (B. Ar), and osteoid area (Os. Ar)

		N	Average	Standard Deviation	t	p
New Bone Volume (%) BV/TV	S1	8	27,0	9,9	0,968	0,350
	G1	8	23,0	6,5		
	S2	8	39,5	9,5	-0,401	0,695
	G2	8	41,4	9,5		
New Bone Area (µm2) B. Ar	S1	8	284496	94817	-6,199	0,002*
	G1	8	577287	193011		
	S2	8	146950	146950	-9,543	0,000*
	G2	8	257161	257161		
Osteoid Area (µm2) Os. Ar	S1	8	61956	24615		0,000*
	G1	8	256953	102380		
	S2	8	114458	58861		0,000*
	G2	8	524009	286233		

Table 2: The collagen sponge group examination for the parameters of new bone volume (BV/TV), new bone area (B. Ar), and soft tissue volume (STV/TV)

Collagen Sponge Group		N	Average	Standard Deviation	p
Vascular Proliferation	1.	8	14,75	5,26	0,004*
	2.	8	6,88	1,81	
New Bone	B. Ar (1)	8	284496	94817	0,091
	B. Ar (2)	8	280446	146950	
	Os. Ar (1)	8	61956,3	24614,8	0,020*
	Os. Ar (2)	8	114458,2	58861,1	
	BV/TV (1)	8	27,03	9,93	0,015*
	BV/TV (2)	8	39,48	9,55	
Soft Tissue Volume	STV/TV (1)	8	72,97	9,93	0,015*
	STV/TV (2)	8	60,52	9,55	

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When the variation between the first and second measurements in the xenogenic graft group(G1-G2) was examined for the parameters of new bone area (B. Ar), osteoid area (Os. Ar), new bone volume (BV/TV), and soft tissue volume (STV/TV), there was a significant difference between the first and second measurements. (Table 3)

A significant increase from the first measurement to the second measurement was observed in new bone area (B. Ar), osteoid area (Os. Ar), and new bone volume (BV/TV). A significant decrease in soft tissue volume (STV/TV) was observed.

Table 3: The xenogenic graft group examination for the parameters of new bone volume (BV/TV), new bone area (B. Ar), and soft tissue volume (STV/TV)

Xenogenic Graft Group		N	Average	Standard Deviation	p
Vascular Proliferation	1.	8	13,38	2,56	0,000*
	2.	8	6,50	1,60	
New Bone	B. Ar (1)	8	577287	193011	0,027*
	B. Ar (2)	8	791391	257161	
	Os. Ar (1)	8	256953	102380	0,009*
	Os. Ar (2)	8	524009	286233	
	BV/TV (1)	8	22,98	6,50	0,002*
	BV/TV (2)	8	41,38	9,47	
Residual Graft	GV/TV (1)	8	34,79	11,80	0,246
	GV/TV (2)	8	30,19	8,46	
Soft Tissue Volume	STV/TV (1)	8	42,23	13,60	0,019*
	STV/TV (2)	8	28,42	15,67	

DISCUSSION

Sinus floor elevation is performed with the use of graft materials to guide bone augmentation and create new bone tissue at the site of future implant placement.[3-10]

In our study, while high volumetric stability was observed in the regions where we used xenogenic grafts, serious volume loss was observed in the regions where we used collagen sponge.

Yıldırım et al. performed a total of fifteen sinus floor elevations in eleven patients and used xenogenic graft particles (Bio-Oss®) as augmentation material. As a result of histomorphometric measurements, an average of 14.7% of new bone formation and 29.7% of residual grafts were observed.[11] In our study, when the results from week eight were taken into account, the presence of residual grafts was found at a rate of 30.19%, similar to their study. However, when evaluated in terms of new bone formation, in our study, unlike their study, new bone formation was observed at a rate of 41.38%. The reason for this difference could be the use of different living materials in the studies and different surgical techniques.

Data from animal experiments and reports from clinical studies in humans have clearly demonstrated that new bone formation occurs under the elevated Schneiderian membrane (SM) without the use of graft material.[12-15] Elevation of the Schneiderian membrane creates a cavity that is immediately filled with a blood clot. If the formed clot can be preserved for a sufficient time without resorption, it will be replaced by newly formed bone. However, if there is no structure protecting the formed space, the blood clot will be rapidly absorbed, the elevated sinus membrane will collapse, and new bone formation will not occur.[16]

Berberi et al. used resorbed sponge containing type 1 collagen as sinus augmentation material in their prospective clinical study. In their study, in which they showed histologically new bone formation with the biopsies they obtained after a six-month recovery period, they also stated that they provided an average of 8 mm bone gain in all regions in the radiological examination.[17]

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Smith et al. performed sinus floor elevations in sheep in their study and used Bio-Oss® particles as augmentation material. They found no signs of inflammation in any of the biopsies they took at four, six, and twelve weeks.[18] In our study, unlike Smith et al.'s study, mild inflammation was observed in the osteotomy area at the fourth week, while no signs of inflammation were found at the eighth week, similar to their study.

This suggests that both xenogenic graft particles (Bio-oss®) and collagen sponges (Collaplug®) are biocompatible materials and do not cause any foreign body reaction.[19] In the groups measured at four weeks (S1 and G1), the mild inflammation observed in the osteotomy area was thought to be due to the degradation of the barrier membrane placed in this area.

In sinus floor elevation applications, implants and/or various biomaterials are placed in the space created after the elevation of the Schneiderian membrane, thus protecting this space and forming new bone in this area. Histological and histomorphometric examinations can be performed on biopsies obtained after the required waiting time. The BV/TV values of the new bone formed after the histomorphometric examinations show the percentage of the new bone formation volume in the total tissue in the area of interest.[20] This value can also be considered as the ability of the placed material to form new bone. In order to compare the new bone formation abilities of the graft materials used in our study, histomorphometric examination was performed on the biopsies obtained at four and eight weeks, and the BV/TV values of the newly formed bone were compared.

Statistical analyses based on the data we obtained showed that there was no significant difference between the BV/TV values of the two materials compared at four and eight weeks. This suggests that the new bone formation abilities of the two materials are similar. When the results of both materials at four and eight weeks were compared, new bone formation increased significantly. This increase suggests that bone remodeling continues throughout the study and, considering that the eight-week period in rabbits corresponds to six to eight months in humans, a six-month waiting period is required to place implants in the augmented sinus areas.

In an experimental animal study, Choi et al. stated that the structural strength of collagen sponges is insufficient to protect the augmented volume in the sinus.[21]

When the osteoid area values obtained in our study were compared statistically, it was found that the regions where xenogenic graft was used were significantly higher than the regions where collagen was used. This situation makes us think that the prepared samples contain less osteoid area due to the rapid resorptions and volume losses of collagen sponges.

The exact origin of osteogenic cells in bone repair of the maxilla is unknown. They can migrate to the area by blood or reproduce from existing stem cells in the area, or both can occur at the same time. The Schneiderian membrane (SM) may also contain osteoprogenitor cells. In a series of in vitro and in vivo studies in human subjects, Srouji et al. successfully demonstrated osteoprogenitor cells in sinus membrane samples. These cells formed histologically prominent bone in ectopic regions following transplantation into mice.[22] However, it is unclear whether osteoprogenitor cells originating from the sinus membrane play an important role in new bone formation after sinus floor elevation.

Scala et al., in another study, applied sinus floor elevation and simultaneous implantation with the lateral window method without using graft material and determined that new bone formation occurs from the maxillary sinus walls and septum.[23]

In our study, new bone formations were mostly seen from the maxillary sinus walls toward the central regions. Although the contribution of the Schneiderian membrane to new bone formation in the later stages of healing or when more stable conditions are provided, this contribution could not be demonstrated in the early results of our study.

Choi et al., in their study examining the structural strength of collagen sponges impregnated with bone morphogenic protein, determined that the collagen sponges were completely resorbed in the histological examination of the biopsies taken from the rabbits after eight weeks.[24]

In our study, complete resorption was observed in the areas where collagen sponge was used in the samples taken at both four and eight weeks, similar to the other studies using this material, and no residual structure was encountered.[24]

In a study conducted by Lambert et al., they examined the impact of different materials on sinus floor elevation. They created spaces in the maxillary sinuses of rabbits and filled them with either clot, autogenous bone, or xenogenic graft. After six months, they found that 77.6% of subjects with blood

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clots, 81.3% with autogenous bone, and 49.2% with xenogenic grafts exhibited a soft tissue component.[25]

In our study, we investigated the rate of soft tissue formation in areas treated with a collagen sponge. At week four, the measurement showed a rate of 72.9±9.9%, which decreased to 60.52±9.55% at week eight. This decline between the two time points was attributed to ongoing new bone formation during the regeneration process.

In this study, the effects of sponges containing type 1 atecollagen (CollaPlug®) and xenogen grafts (Bio-Oss®) on new bone formation in sinus floor elevation applications were examined histologically and histomorphometrically. No significant inflammation and foreign body reaction were observed in the areas where both materials were used. Both materials provided new bone formation in the areas where they were used. No histomorphometric difference was found between the two materials when evaluated in terms of their ability to form new bone.

CONCLUSION

Both materials provided a similar amount of vascular proliferation in the areas where they were used, creating a suitable environment for the transfer of osteogenic cells. The collagen sponge could not maintain its initial volume throughout the experiment and the augmented area collapsed to a large extent. The xenogen graft showed superior volumetric stability and maintained its volume throughout the study, acting as a framework for the newly formed bone. While the collagen sponge was completely resorbed during the experiment, a very low tendency to resorption was observed in the xenogen graft particles. When the newly formed bone and osteoid areas were evaluated, it was seen that the xenogen graft created much more new bone and osteoid areas than the atecollagen sponge. While the new bone formed in the areas where atecollagen sponge was used showed lower density, the bone-graft complex was observed in a denser structure in the areas where xenogen graft was used. A denser trabecular bone network was formed in the areas where atecollagen sponge was used compared to the xenogen graft.

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DATA SHARING STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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RESEARCH ARTICLE

Retrospective Investigation of Maxillofacial Fractures in Antalya Region

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ABSTRACT

Objective: The aim of this study was to investigate the relationship between fractures and mechanism of injury, age, gender, regional analysis of trauma patterns and to compare these findings with the existing literature in patients with maxillofacial fractures admitted to Antalya Training and Research Hospital.

Materials and Methods: For this study, a comprehensive review was conducted on the records of 209 patients diagnosed with maxillofacial fractures at Antalya Training and Research Hospital between 2017 and 2021. The analysis included various facets, such as gender distribution, age demographics, underlying causes of fractures, monthly distribution of fracture incidents, specific sites of fractures, and the classification of fracture types.

Results: The study involved 209 patients—142 males and 67 females—ranging in age from 5 to 79 years, with an average age of 33.75 years. The highest fracture incidence occurred in the 21-30 age group. Motor vehicle accidents, falls, and assaults were the primary causes of maxillofacial fractures across all ages. Notably, motor vehicle accidents led to the most hospital admissions, except for the 0-10 age group, where falls took precedence. Among patients aged 0-10, falls were the primary reason for admission; in all other age groups, they ranked second. Monthly analysis revealed subtle fluctuations in fracture incidence.

Conclusion: Our study effectively highlights the connection between maxillofacial fractures and several factors as injury mechanisms, age, and gender. Within our diverse society, regional trauma analysis enables the creation of tailored regulations for protective measures that align with our social structure.

Keywords: maxillofacial fracture, epidemiology, trauma

INTRODUCTION

A maxillofacial fracture involves the fractures of bones within the central region of the face. This type of injury commonly results from a powerful, blunt impact directed at the mid-facial area. Fractures occurring in these bones can impede functions such as breathing, eyesight, chewing, and speech. Maxillofacial injuries are prevalent among trauma patients, often occurring either as isolated incidents or with other severe injuries like cranial, spinal, upper, and lower body trauma.[1] Maxillofacial fractures have the potential to be exceedingly serious. The causes behind maxillofacial fractures vary based on age, gender, socioeconomic status, cultural norms, and geographic location. Although traffic accidents, falls, and assaults consistently rank as the top etiological factors worldwide, their order of prevalence may differ. Occupational accidents, sports-related injuries, and gunshot wounds contribute to the range of causes.[2–5]

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In the realm of maxillofacial trauma, mandibular fractures are the second most common type, succeeding nasal fractures. Other affected bones include the maxilla and zygomatic bone.

The method of treating maxillofacial fractures depends on the severity and location of the fracture. Initiation of treatment may occur within the emergency department to ensure that blood clotting or swelling do not obstruct the breathing process.[6]

The current literature contains several studies that investigate the demographic distribution of patients with maxillofacial trauma through different criteria. This study undertakes a retrospective analysis of patient data, specifically focusing on those diagnosed with maxillofacial fractures (excluding isolated nasal fractures). The analysis includes patients who sought treatment at Antalya Education and Research Hospital from 2017 to 2021. By comparing these findings with existing literature, the study aims to contribute valuable insights into the field.

MATERIALS AND METHODS

The ethics committee approval of the study was obtained with the decision of the Health Sciences University Antalya Training and Research Hospital Clinical Research Ethics Committee dated 30/06/2022 and numbered 13/10. For this study, a thorough examination of records was performed on 209 patients who had been diagnosed with maxillofacial fractures and had been admitted to Antalya Training and Research Hospital between the years 2017 and 2021. A comprehensive analysis was conducted, focusing on parameters such as gender, age, etiological causes of fractures, distribution of fracture cases across different months and fracture types among the patients. The scope of the study encompassed fractures occurring in the mandible, maxilla, and zygomatic complex. However, isolated nasal fractures were excluded from consideration. The investigation delved into several aspects, including gender distribution, age demographics, underlying causes of fractures, monthly distribution of fracture incidents, specific sites of fractures, and the classification of fracture types. The findings were then visually presented as graphs and charts.

RESULTS

During the period spanning from January 2017 to November 2021, a total of 209 patients who were admitted to the hospital due to maxillofacial fracture were included in the study. The age range of the patients was 5 to 79 years, with an average age of 33.75 years. Among these individuals, 142 were male, while 67 were female. Within this patient cohort, 32 fell into the pediatric category, specifically those under 18 years of age. The male-to-female ratio within the pediatric patient group was 2.55:1, whereas in the adult patient group, it stood at 2.05:1. Overall, the male-to-female ratio in the entire patient cohort was 2.11:1 (Table 1).

Table 1. Breakdown of patients by gender and age period

	Pediatric patients (%)	Adult patients (%)	Total patients (%)
Female	9 (4)	58 (28)	67 (32)
Male	23 (11)	119 (57)	142 (68)
Total	32 (15)	177 (85)	209 (100)

Age groups were segmented into eight distinct blocks. An in-depth examination of these age groups unveiled that the highest incidence of fractures was observed in the 21-30 age group, accounting for 58 cases, followed closely by the 11-20 age group, which documented 46 cases. On the other end of the spectrum, the 0-10 age group exhibited the lowest number of fractures, with only 2 cases recorded. Notably, the age group that displayed the most balanced female-to-male ratio was the 41-50 age group, presenting a ratio of 1.38. (Figure 1)

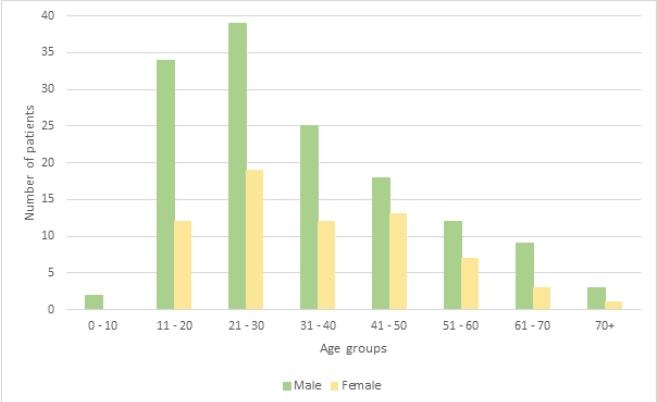

Figure 1. Distribution of male and female patients across each age group

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In terms of age groups, motor vehicle accidents, falls, and assaults emerged as the three predominant causes of maxillofacial fractures across all age ranges. Notably, research underscores that motor vehicle accidents constitute the leading cause of hospital admissions. This trend remains consistent across all age cohorts, except for individuals aged 0-10 years, where falls take precedence as the primary reason for admission. Interestingly, among patients aged 0-10 years, falls are the primary admission factor, while for all other age groups, they rank as the second most prevalent cause. (Figure 2)

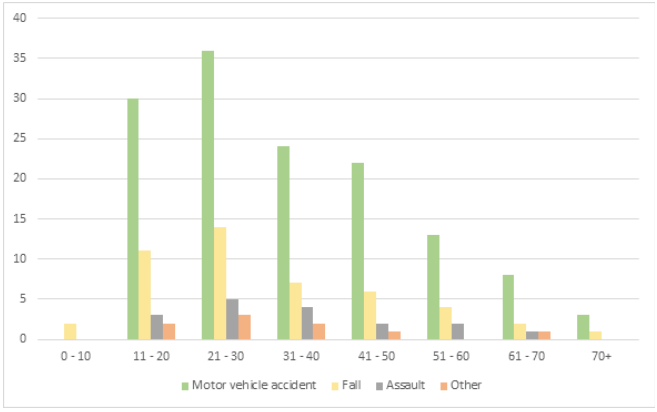

Figure 2. Breakdown of maxillofacial fracture causes within each age group

Upon closer examination of the monthly distribution, a subtle fluctuation in the incidence of maxillofacial fractures became apparent. March exhibited the highest incidence with 31 cases, closely trailed by May with 21 cases, and January with 19 cases. Conversely, November displayed the lowest frequency of fractures, recording only 11 cases. (Figure 3)

When examining the distribution of fracture sites based on different causes, it becomes evident that mandibular fractures consistently occupy the top spot across all etiologies—motor vehicle accidents, falls, and assaults—that lead to fractures. Following closely in the second position are zygoma fractures, with maxilla fractures securing the third position in this ranking. Among the 209 patients under study, mandibular fractures were noteworthy, emerging as the most prevalent facial fracture site, accounting for 128 cases of maxillofacial injury. (Figure 4)

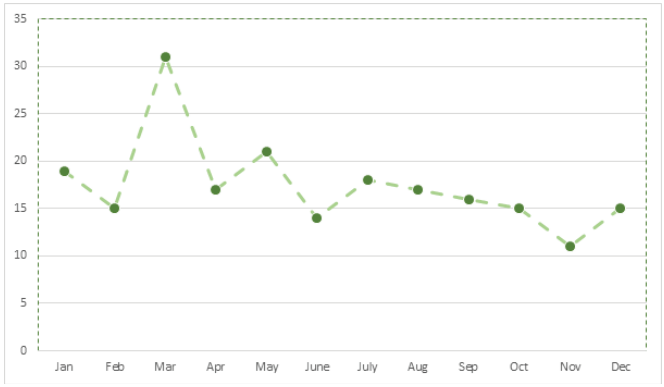

Figure 3. Patient distribution based on months

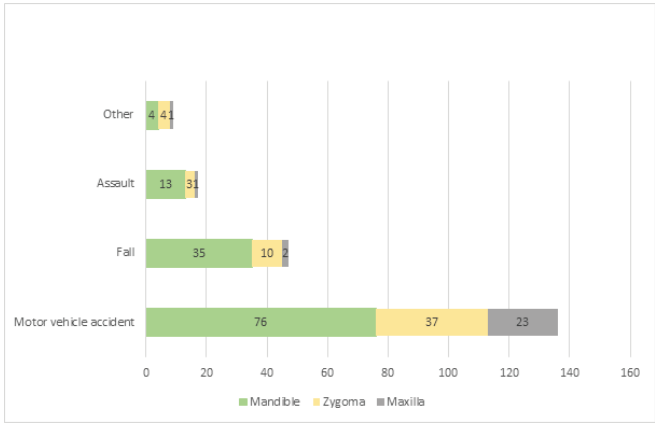

Figure 4. Notable fracture site prevalence within each etiology

DISCUSSION

Numerous studies have been conducted investigating injuries stemming from maxillofacial traumas. The majority of epidemiological studies focused on maxillofacial fractures have been conducted retrospectively. These studies have unveiled that the causes and occurrences of maxillofacial trauma vary depending on geographical location, socioeconomic status, cultural norms, and environmental factors. It is worth noting that there can be disparities in the outcomes of epidemiological studies on fractures across countries and even within different regions of the same country. These differences often reflect the impact of local conditions. Epidemiological studies play a pivotal role in documenting population variations over time, highlighting pressing issues, and implementing necessary preventive measures to avert accidents. Broadening the

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scope of trauma studies aids in developing databases that can define distinct case characteristics. This information assists in devising public health initiatives encompassing preventive strategies, treatment protocols, and legal procedures.[4,7–12]

While previous years have seen studies in this field, the current study was designed because of the absence of such research in the Antalya region. The study's primary goal is to retrospectively assess epidemiological data from patients diagnosed with maxillofacial fractures, specifically those who sought treatment at Antalya Education and Research Hospital between 2017-2022 and compare it with existing literature.

Despite significant advancements in automobile technology, transportation infrastructure, and economic growth, the prevalence of road traffic accidents as the primary cause of maxillofacial injuries remains substantial. This is notable given the increased utilization and development of protective mechanisms for vehicle occupants. Extensive research spanning various regions supports that motor vehicle accidents stand as the primary etiological factor for maxillofacial fractures.[13] A systematic review conducted by Boffano P et al., which analyzed articles on maxillofacial trauma epidemiology between January 1980 and December 2013, identified 69 studies across Africa, North America and Brazil, Asia, Europe, and Oceania. The findings revealed that motor vehicle accidents predominated in studies from America, Africa, and Asia. In European studies, a more varied etiological landscape emerged, where assaults and traffic accidents played vital roles. In Oceania, assaults are the dominant factor.14 In an epidemiological analysis of maxillofacial fractures in Italy by Bonavolont P et al., the leading etiological factor was traffic accidents (57.1%), followed by assaults (21.7%), falls (14.2%), occupational accidents (3.5%), sports accidents (3.3%), and other causes (0.2%).[15] In a retrospective study by Erol B et al., focusing on maxillofacial fractures, it was observed that motor vehicle accidents and falls shared the top position with similar frequencies.[16] In developing countries, inadequate traffic infrastructure, lax enforcement of traffic regulations, and insufficient adoption of protective measures such as seat belts and helmets contribute to motor vehicle accidents ranking as a leading etiological factor. Additionally, falls, occupational accidents, and sports injuries hold significant roles in the etiology of maxillofacial fractures.[17] Over time, shifts in the occurrence and causes of maxillofacial fractures reflect transformations in societal structures and variations across different societies.[18] Aligning with existing literature, our study also established motor vehicle accidents as the foremost cause among the examined etiological factors.

In a retrospective epidemiological study focused on mandibular fractures, Er Y et al. noted noteworthy trends in the male-to-female ratio among patients. Between 1980 and 1995, this ratio stood at 3.9, decreased to 2.78 during 1995-2001, and further declined to 2.28 for the years 2005-2009, indicating a gradual reduction over the years.[19] Numerous studies conducted both domestically and internationally have consistently revealed a higher incidence of maxillofacial fractures in male patients compared to female patients across all age groups.4,20 Al-Habbab RY et al. highlighted that recent reports indicate a shift towards a more balanced male-to-female ratio. This change could be attributed to evolving workforce dynamics, with an increasing number of women engaged in higher-risk outdoor occupations that expose them to the causes of maxillofacial fractures.[21] In another study, male-to-female ratio was 1.8, and significant variations in etiology were observed between Italians and individuals of other nationalities.[15] In our study, although the proportion of males was higher than the proportion of females in accordance with the literature, it was proportionally lower than many studies in the literature.

Mandibular fractures were the most frequently occurring (36%), followed by zygoma fractures (20.4%), orbital wall fractures (16.1%), and maxilla fractures (11.8%).15 Kanala S et al. noted that the mandible exhibited the highest susceptibility to fractures among facial skeleton regions (47%). Among midface fractures, the zygomatic complex fracture accounted for the predominant subtype (17%), while fractures of the maxillary bone comprised 12% of the cases. Similar findings have been reported by other researchers, with zygomatic fractures consistently emerging as the primary subtype of midface fractures across various age groups, encompassing both pediatric and adult populations.[6] Similar to the literature, the mandible had the highest fracture rate among the facial bones in our study.

Erol B et al. found that the highest frequency of fractures occurred during the summer, followed by fall, spring, and winter.[16] Er Y et al.'s study indicated that patient admissions did not exhibit significant variations across different months of trauma.[19] In regions like Egypt, where there's minimal change in weather conditions between seasons, it has been noted that the number of mandibular fracture cases remains

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consistent throughout the year.[22] When analyzing the monthly distribution of maxillofacial fractures in our study, there is a slight fluctuation in the incidence of fractures.

Limitations: Due to the retrospective design of our study, we could not draw conclusions regarding the influence of social background on maxillofacial fractures.

CONCLUSION

Our study has effectively highlighted the correlation between maxillofacial fractures and a diverse range of factors, including the mechanism of injury, age, and gender. Within our multicultural society, a regional analysis of trauma studies paves the way for the enactment of regulations that encompass tailored protective measures aligned with the prevailing social structure. Moreover, it stimulates the advancement of preventive medical research. The realm of Public Health emerges as a pivotal player in tackling the challenges highlighted by our study.

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RESEARCH ARTICLE

Clinical Findings of Temporomandibular Joint Disc Displacement with Reduction in Children and Adolescents

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ABSTRACT

Objective: Recent studies have shown that temporomandibular joint (TMJ) disc displacement with reduction (DDwR) frequently affects children and adolescents. Although it is noted that the incidence of TMJ disorders increases with age in young individuals, there is no study comparing symptoms across different age groups. This study aims to evaluate whether there is a difference in symptoms observed in the childhood and adolescent periods in terms of TMJ DDwR.

Materials and Methods: The study included 43 individuals with TMJ DDwR aged 9-16 . Patients were divided into two groups, consisting of ages 9-12 (n:14) and 13-16 (n:29). The diagnosis of DDwR was made using a combination of clinical examination and, when necessary, imaging methods. Demographic data, diseased joints, sleep bruxism (SB), pain (Visual analog scale (VAS), and maximum mouth opening (MMO) were assessed in clinical examination findings.

Results: Between the groups; the gender distribution is similar, and there is no statistical difference (p= 0.058). There is no difference in terms of the DDwR side (p= 0.287) and SB between the groups (p= 0.058). No relationship was found between age and pain scores (r= 0.083). When VAS and MMO values were compared between the groups, no statistically significant difference was found (p=0.127 and p=0.062)

Conclusion: TMJ DDwR symptoms appear to be similar in children and adolescents. Early diagnosis of symptoms in children and adolescents will help prevent the progression of the condition.

Keywords: Adolescents, children, prevalence, temporomandibular disorders.

INTRODUCTION

The term temporomandibular disorder (TMD) is used to describe pathological conditions affecting the temporomandibular joint (TMJ), masticatory muscles, and associated structures. Common clinical signs of TMD are joint and/or muscle pain, joint noises, and limited or irregular jaw functions.[1] One of the most debated topics in clinical dentistry is the etiology of TMD, as these disorders are considered a heterogeneous group of psycho-physiological disorders.[2] Although TMD has traditionally been considered a condition that primarily affects adults, epidemiological studies have reported its occurrence in children and adolescents.[3]

Among the several types of TMD, disc displacement with reduction (DDwR) is the most common type encountered in adults, with prevalence rates up to 35 %.3 It has also been reported in the young population, with prevalence rates around 26%.4 For the differential diagnosis of DDwR, it is essential

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to accurately identify signs and symptoms. To ensure an early diagnosis, routine dental examinations in all age groups should always include the evaluation of TMJ and surrounding tissues.

Childhood spans the time from birth to approximately 11-12 years of age, while the period between 12 and 18 years of age is defined as adolescence. Adolescence encompasses a developmental period during which many biological, cognitive, social, and personality characteristics transition from childhood to adulthood.[5] TMD-related pain has previously been reported as the main non-dental cause of orofacial pain in children and adolescents. Pain is often localized in the masticatory muscles and preauricular region. In addition, TMJ sounds have been reported as a common TMD symptom in children.[6] In children, TMJ sounds may result from disc displacement, structural changes in the disc and joint surfaces, coordination disorders of muscles, or joint subluxation, similar to adults. Studies also indicate that TMD symptoms vary during childhood and adolescence, with pain symptoms becoming more pronounced, especially in later stages of life.[7] This study aims to evaluate whether there are differences in signs and symptoms among TMD patients in childhood and adolescence.

MATERIALS AND METHODS

Participants: A retrospective study was made of a series of 75 TMD patients aged 9 to 16 years between the years 2020-2022. Fifteen patients were excluded due to an incomplete registry of the clinical data. Among the 60 patients, 43 patients with a diagnosis of TMJ DDwR were included in the study. The study was approved by the Ondokuz Mayıs University Faculty of Medicine Ethics Committee (OMÜ TAEK 2021/430) and conducted following the principles of the Helsinki Declaration. Diagnosis of TMJ DDwR was based on the criteria of the international DC/TMD consortium.[8]

-Inclusion Criteria:

- Patients aged 9-16 years with a diagnosis of TMJ DDwR at least on one side.

-Exclusion Criteria: Individuals with;

- a history of trauma to the TMJ region,
- a history of TMJ-related surgery,
- neurological or psychiatric disorders,
- dental or orofacial pain.

Two groups were then created according to the ages of the patients:

Group 1 (n=14): Patients aged 9-12 years diagnosed with TMJ DDwR.

Group 2 (n=29): Patients aged 13-16 years diagnosed with TMJ DDwR

Clinical examination: Demographic data, the presence of pain, and limitations in jaw functions were assessed for all individuals included in the study. Evaluated parameters included:

Maximum Mouth Opening (MMO): After ensuring that patients opened their mouths as wide as possible, measurements in millimeters were made with a ruler between the incisal edges of the central incisors in the upper and lower jaws.

Joint Sounds: The presence of joint sounds during palpation in the preauricular region and during mouth movements was noted.

Pain intensity: The Visual Analog Scale (VAS) was assessed to evaluate patients' complaints. The scale features a line ranging from 0 to 10, with a patient who has no pain rated at 0 degrees, and a patient with the most severe pain they have ever experienced rated at 10 degrees.

Sleep bruxism (SB): The diagnosis of SB depended upon the respondent's awareness, according to the Oral Behavior Checklist 8 and the dentoalveolar level.

Statistical Analysis: Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software package. Continuous variables were expressed as mean ± standard deviation and categorical variables were presented as numbers and percentages. The normal distribution of variables was assessed using the Shapiro-Wilk test. The Spearman Correlation Test was used to assess the strength and direction of association between variables.

RESULTS

This study included a total of 43 TMJ DDwR patients aged between 9 and 16 years. The demographic data of the patients is given in Table 1. All patients in both groups have a TMJ clicking sound. The mean age of the patients was calculated as 13, 65±2, 14. The participants in the study consisted of 18 (41.9%) females and 25 (58.1%) males. In terms of gender, there was no statistically significant difference among the

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groups (p= 0.058) TMD was unilateral in 76% of cases and bilateral in 24% of cases. There is no difference in terms of the TMD side between the groups (p= 0.287). When the presence of bruxism was assessed, it was observed to be present in 64% of patients in the first group and 65% in the second group. The difference between the groups was not found to be statistically significant (p= 0.598). When VAS and MMO values were compared between the groups, no statistically significant difference was found (p=0.127 and p=0.062, respectively) (Table 2). No statistical relationship was found between age and VAS score (r= 0.083).

Table 1. Statistical comparison of groups in terms of SB, TMD side, and gender.

	n	SB	TMD side		Gender	
			Unilateral	Bilateral	Girl	Boy
Group 1	14 (%32,6)	9 (%64)	12	2	3	11
Group 2	29 (%67,4)	19 (%65)	21	8	15	14
Total	43	28 (%65)	33	10	18	25
p		0,598	0,287		0,058	

Abbreviations: SB: Sleep bruxism; TMD: Temporomandibular disorder.

Table 2. Assessment of groups Based on MMO and VAS findings

	VAS Mean±SS	MMO Mean±SS
Group 1	5,14±2,21	33,64±5,73
Group 2	6,03±3,02	36,72±5,20
p	0,127	0,062

Abbreviations: VAS: Visual Analog Scale, MMO: Maximum mouth opening

DISCUSSION

In the past, TMD has been widely believed to be more common in adults. Nevertheless, an increasing number of clinicians have affirmed that TMD exhibits a high prevalence among adolescents.[9] Recent studies reported that the prevalence rate of DDwR was around 26% in the young population.[10] Despite the similarities in the masticatory systems of adults and children, some notable differences exist. The most significant distinction lies in the growth and development process in children, and another significant difference is a child's capacity to tolerate changes in their masticatory system. Unlike adults, who can readily perceive even minor alterations in occlusion, such as elevated restorations, and may experience discomfort, children may struggle to discern sudden occlusal changes and can easily adapt to resultant pathological conditions. Over time, this adaptation can transform into permanent pathological changes in adulthood.[11]

Children with TMJ DDwR may experience a range of symptoms, including jaw pain, clicking or popping sounds during jaw movement, limited mouth opening, and discomfort while chewing. The prevalence of the signs and symptoms typically increases with age.[12] In a study conducted by Marpaung et al., TMD prevalence was compared between children and adolescent age groups, revealing a higher prevalence among adolescents (13-18 years; 36.9%) compared to children (7-12 years; 23.4%).[13] Furthermore, Bonjardim and colleagues' study[14] suggested that adolescent girls are probably more affected than boys, likely due to biological variables, as girls typically undergo early maturation compared to boys. This situation can be attributed to the characterization of most symptoms as mild in young children, the higher adaptability of children compared to adults, and therefore the challenges in detecting TMD in children. This often results in research predominantly focusing on patient samples actively seeking

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treatment.[15] In our study, unlike the literature, no relationship was detected between age and clinical symptoms. The reason for this difference may be the examination of a more specific TMD subgroup in our study. The term TMD is used to describe a range of conditions involving the TMJ and its related structures. Clinically and radiologically, numerous diseases that are distinct from one another are categorized under the TMD umbrella. This situation can lead to confusion in the literature. It was argued that defining study populations solely based on the presence of TMD made it impossible to identify specific treated conditions. Clarifying a specific TMD subgroup allows for more realistic results. In our study, patients diagnosed with TMJ DDwR were evaluated for this purpose.

Studies have shown that children with TMD rarely present with complaints of pain to healthcare professionals. In a study conducted by Al-Khotani and colleagues, it was determined that over 75% of children with TMD had not sought any medical or dental care for their pain.[16] Nonetheless, pain in children and adolescents can have serious consequences because orofacial pain can impact their quality of life, particularly their physical and learning abilities. Additionally, it can affect their sleep patterns, influencing growth and development.[17] Therefore, early diagnosis is crucial as it can prevent disease progression and irreversible damage to structures. Especially in children, there is a higher potential for muscle recovery, and their physiological adaptability can help reduce TMD symptoms.[18]

Temporomandibular joint sounds are categorized as cardinal symptoms of TMD. According to a systematic review, 14.0% of the children or adolescents had clinical TMJ sounds, while a current investigation detected an even higher percentage up to 31.9% for German adolescents.[19] Farsi et al. reported joint sounds as the most common TMD symptom in children.6 In our study, all patients had TMJ sounds. This is attributed to the fact that the patient population consisted of individuals with TMJ DDwrR. Joint sounds are quite common in childhood and often resolve on their own without the need for treatment. However, it should be noted that these patients may be more susceptible to TMD disorders in later life.[20]

There is a debated association between SB and TMD. Some studies suggest that individuals with SB may have a higher risk of developing TMD, while others do not find a significant link. In our study, SB was found in %65 of the patients. No difference was found in terms of SB presence between the child and adolescent groups. In our study, SB was assessed using both OBCL (Oral Behaviors Checklist) and dentoalveolar examination. Polysomnography (PSG) is the gold standard for SB assessment, but it can only be performed in specific centers and is challenging to implement. In children and adolescents whose growth and development are still ongoing, the accurate assessment of factors causing TMD is crucial for jaw function and facial development. Early diagnosis and treatment of TMD can prevent future problems for the individual. Maintaining healthy lifestyle habits is important for pain management, but psychological interventions that help adolescents develop pain-coping skills, such as relaxation training and cognitive restructuring, can make a significant difference.[21] Furthermore, studies have shown that parafunctional habits observed in child patients can act as predictors of the same habits 20 years later.[22]

The main limitation of this study is the young age group under evaluation, which tends to conceal their existing symptoms and has low cooperation. The other limitation is that it is an associational type of research and not a cause-effect investigation. Based on this fact, it is not possible to establish a causal link among the variables. In addition, no control group was used for comparison with the study group. However, this is the first study in the literature that solely evaluated children and adolescents with TMJ DDwR.

There is no approved TMD management specifically for children and adolescents, but non-invasive and reversible care should be preferred. Therefore, examining the chewing system should be included as part of routine dental check-ups to prevent TMD. A clinical examination (muscle and joint) is necessary to identify the most common symptoms, including facial pain and/or joint sounds palpated. If there are TMD symptoms, behavioral retraining should begin as soon as possible, and the patient should be reevaluated.

In conclusion, TMJ DDwR in childhood is a multifaceted condition that requires careful evaluation, accurate diagnosis, and appropriate management. Early intervention and a comprehensive approach that considers both physical and emotional aspects can help children lead healthier, pain-free lives while minimizing potential long-term consequences. Regular follow-up and collaboration between healthcare providers are essential to achieving the best outcomes for affected children.

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Conflict of Interest

The authors and/or their family members have no potential conflicts of interest related to this study, including scientific and medical committee memberships or affiliations, consultancy, expert witness involvement, employment in any company, shareholding, or similar situations.

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RESEARCH ARTICLE

Evaluation of the Relationship Between Marginal Bone Loss and Implant Angulation in All-on-Four System

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ABSTRACT

Purpose: The All-on-four concept is a reliable treatment modality for severely atrophic jaws. The aim of this study is to investigate the correlation between the marginal bone loss, length, and angulation of tilted implants inserted for full-arch rehabilitation according to the All-on-four concept using cone-beam computer tomography (CBCT) images.

Material and Methods: A retrospective study was conducted based on medical records including clinical and radiographical data of dental implant patients treated between September 2017 and September 2023. The patients were treated with dental implants according to the All-on-four concept with the same dental implant brand. Patients without any systemic conditions, non-smokers, and patients who received immediate prosthetic rehabilitation were included in this study. From the CBCT images, the average marginal bone loss was compared between implants according to their angle-length measurement.

Results: The mean follow-up time was 32.7±16.9 months. The angulation of the axial implants was between 73.07 to 98.41 degrees and lateral implants were tilted 50.45 to 86.46 degrees. The marginal bone loss increased as the angle of the implant increased. The resorption rate was not affected by gender, age, and follow-up duration.

Conclusion: Regarding this study's findings, it can be stated that the wide range of different implant angulations in the All-on-four concept is well tolerated in physiologic limits regarding marginal bone loss, thus it is a successful procedure for rehabilitation of edentulous patients. However, care must be taken for follow-ups and the cooperation of the patient is crucial for the prognosis.

Keywords: All-on-four, Implant agulation, Marginal Bone Loss, Marginal Bone Loss

INTRODUCTION

Implant treatment is one of the most common treatment options for partial or total edentulism. However, the outcome of implant therapy is determined by the length and width of residual bone level. Implants are suggested to ideally be positioned parallel to one another, to neighboring teeth, and vertically aligned with axial stresses.[1] The constraints of anatomical structures such as the maxillary sinus and inferior alveolar nerve often preclude implants from being placed axially. Although bone augmentation is a common surgical procedure aimed to increase bone height prior to or concurrently with the placement of dental implants, this procedure has limitations such as increased morbidity, possible surgical difficulties, high expense, and a longer healing period.[2] Alternative fixed restoration options for the atrophic jaw without augmentation procedure include implant-supported fixed partial dentures with a distal cantilever, the use of short implants or the zygomatic implants, implant placement in the pterygoid region, and the use of subperiosteal implants. Another option is the use of a distally tilted posterior implant anteriorly to avoid the maxillary sinus or mental foramina.[3,4]

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The all-on-four concept allows for the use of longer implants, enhances the greater implant-to-bone contact area and implant stability; creates distance between the anterior and posterior implants, resulting in greater load distribution; and significantly reduces the distal cantilever size or eliminates it.[5] Also, the patient satisfaction rate for All-on-four implants was reported to be very high.[6]

In clinical studies, the effect of implant angle on peri-implant bone resorption in the all-on-four concept has been controversial. In the studies in the literature to date, most authors divided the implants into two groups tilted and axial without considering the angulation degrees and reported their data comparing these two groups.[3,4,7,8,9,10,11,12] Also, the general tendency was toward evaluating the marginal bone loss (MBL) among tilted and axial implants with plain radiographs.[13] However, we used CBCT to accurately measure implant angulation and MBL and aimed to evaluate the correlation between the angulation degree of the implants and marginal bone loss for full-arch rehabilitation according to the All-on-four concept.

MATERIAL AND METHOD

Patient Selection:

Clinical and radiographic records of patients admitted to the hospital between 2017-2023 were evaluated and patients who underwent the procedure of the All-on-four concept either maxilla, mandible, or both in Baskent University, Department of Oral and Maxillofacial Surgery, Ankara, Turkey were included in this retrospective study. Inclusion criteria were having preoperative and postoperative CBCT images, having the same brand of dental implants (Nobel Biocare, Swiss), having operations carried out by the same surgical team with over 15 years of experience, patients who received immediate provisional prosthetic rehabilitation, not having any systemic conditions, and not smoking. Implants without sufficient primary stability for prosthetic rehabilitation, patients who need major grafting, and lack clinical and radiological data were excluded from the study.

This study was approved by Baskent University Institutional review board (Project no: D-KA23/27) and Baskent University Research Committee.

Data collection:

Preoperative, postoperative and post-prosthetic panoramic graphs of the patient rehabilitated with the "all on four" technique are given in Figures 1, 2 and 3. The CBCT (Morita 3D Accuitomo 170 (J Morita, Kyoto, Japan)) images from all patients were taken by the same operator and analyzed by one examiner. The same software program was used to measure the implant angulation and the marginal bone loss. To measure the implant angulation each image of tilted implants was adjusted to the sagittal section and each image of axial implants was adjusted to the frontal section. Anterior implants were considered as axial implants and posterior implants were considered as tilted implants. The angle created by the line tracing the alveolar bone ridge and a parallel line superimposed with the long axis of the implant is considered as angulation of the implant. The angles were measured between distal and mesial aspects from the long axis of the

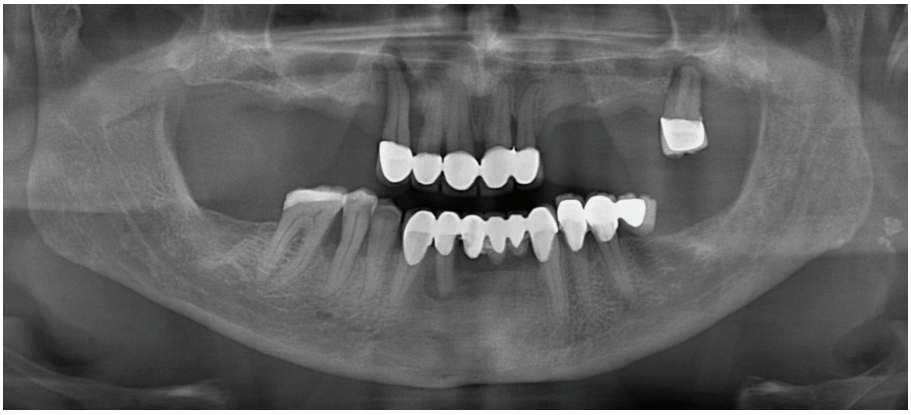

Figure 1. Representative pre-operative orthopantomography of a patient.

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implant and the crossing horizontal line, which indicates the alveolar bone level. To assess the marginal bone loss on the CBCT sagittal section, the interval between the implant neck to the most apical point of the alveolar bone around the implant neck was measured on both sides in millimeters. Distal and mesial measurements were averaged to obtain the mean marginal bone loss. (Figure 4)

To adjust for radiographic distortion, the actual length and width of the implants were compared to the measured implant dimensions on the CBCT sagittal sections.

Statistical Analyses:

All statistical data analyses were processed with the Statistical Package for the Social Sciences (SPSS) version 28.0 (IBM Corp., Armonk, NY, USA). The partial correlation analysis was carried out to evaluate the association between marginal bone loss on the distal and mesial side of the implant with explanatory variables such as gender, age, and follow-up controlled. The Pearson correlation coefficient analysis was performed to evaluate the correlating relation between mesial, distal, and mean marginal bone loss and implant angulation separately. Anterior implants are considered axial implants and posterior implants are considered tilted implants; the 2 groups of implants were equated on marginal bone loss level using a paired samples t-test. The resulting measurement p-value equal to or less than 0.05 was considered statistically significant.

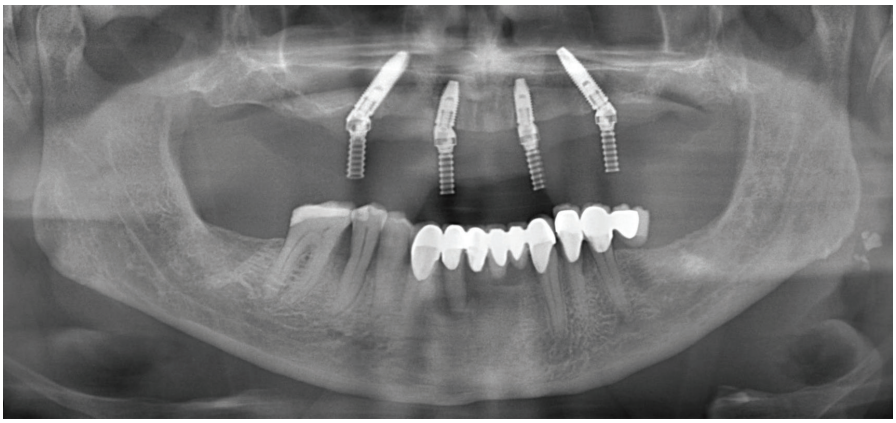

Figure 2. Representative post-operative orthopantomography of the same patient rehabilitated with a maxillary All-on-four.

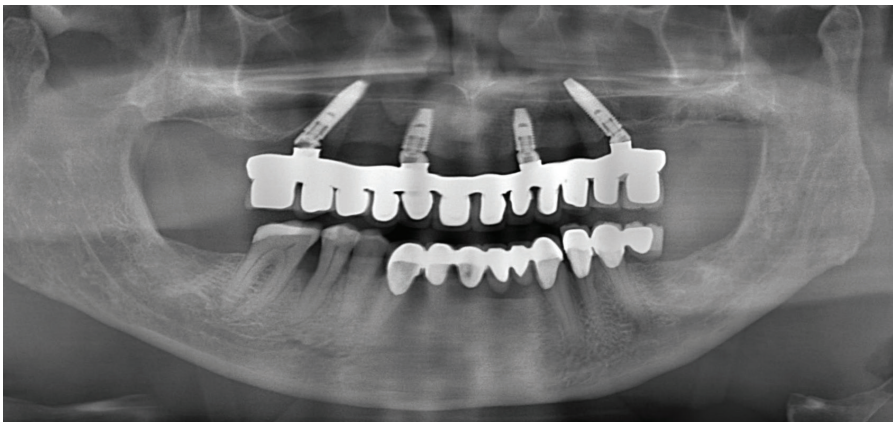

Figure 3. Representative post-loading of orthopantomography of the same patient rehabilitated with a maxillary All-on-four.

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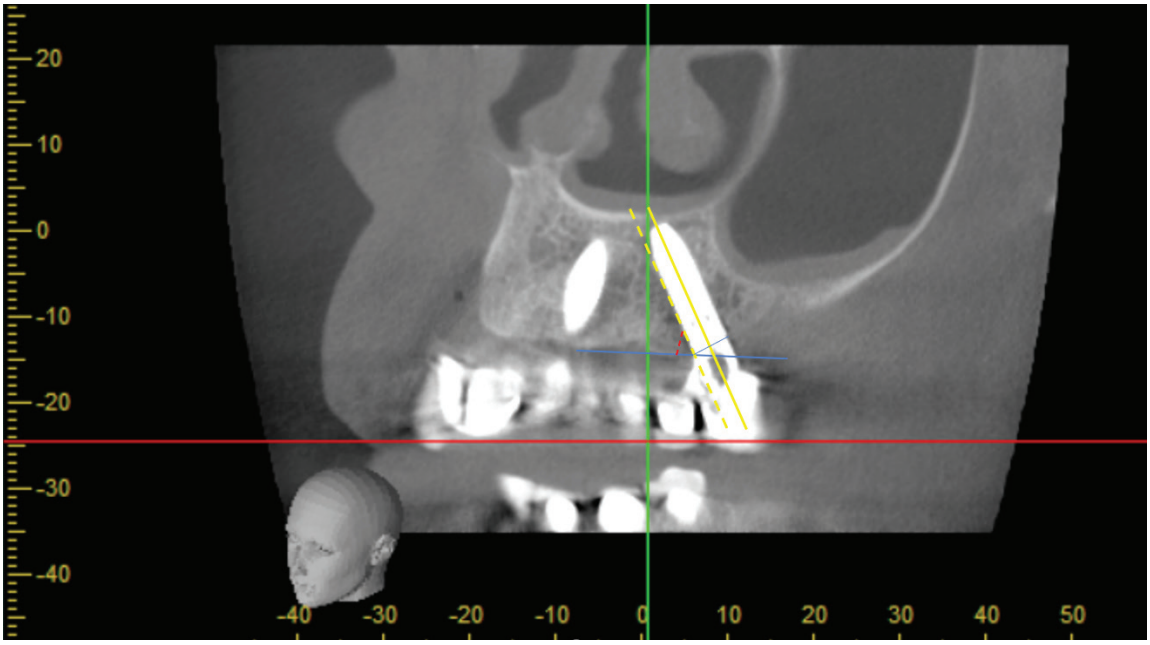

Figure 4. Measurement of angulation of implants on CBCT.

RESULTS

Nine out of 20 patients were eligible for inclusion in this study. Five females and four males with a mean age of 59 years (range 36-71 years). A total of 36 implants were placed, 28 implants were in the maxilla while 8 implants were in the mandible. The mean follow-up was 32.7 months (range 25-67 months). Maximum mean marginal bone resorption in the tilted implants was measured as 1.83 mm and implant angulation differed between 50.45° to 86.46°, and maximum mean marginal bone resorption in the axial implants was measured as 1.96 mm and implant angulation differed from 73.07° to 98.41°. The length of the distal implants differs between 13 to 16 mm and the axial implants differ between 10 to 13 mm (Table 1).

There was no correlation between angulation and distal marginal bone loss (r=-0.019) (Table 2) (Figure 5), with no significant correlation (P →0.966) when gender, age, and follow-up duration were controlled separately with the partial correlation test (Table 3).

Table 1. Data of implants regarding position, diameter, length, follow-up, and angulation.

Gender	Age	Follow up \month\	Jaw	Implants																	
				1. Implant					2. Implant					3. Implant					4. Implant				
				Diameter /mm/	Length /mm/	Implant angulation	MBL		Diameter /mm/	Length /mm/	Implant angulation	MBL		Diameter /mm/	Length /mm/	Implant angulation	MBL		Diameter /mm/	Length /mm/	Implant angulation	MBL	
							Mesial \mm\	Distal \mm\				Mesial \mm\	Distal \mm\				Mesial \mm\	Distal \mm\				Mesial \mm\	Distal \mm\
Female	63	25	Maxilla	4.3	16	85	0.4	0.35	3.5	13	91	0.3	0.1	3.5	13	89	0.2	0.25	4.3	16	62	0.1	0
Male	71	27	Maxilla	4.3	16	61.43	0.3	0.37	4.3	13	81.12	0.4	0	4.3	13	78.69	0.17	0.27	4.3	15	59.9	0.09	0.06
Male	48	67	Maxilla	4.3	15	81	1.5	1.4	4.3	13	94	1.2	1	4.3	11.5	90	0.5	0.5	4.3	15	79	0.8	0.1
Female	60	50	Maxilla	3.5	16	86.46	1.33	0.64	3.5	11.5	73.07	1.22	0.98	3.5	13	98.41	0.52	1	3.5	16	59.34	1.49	0.97
Male	61	21	Maxilla	4.3	16	50.45	1.39	1.09	4.3	11.5	96.05	0	0.1	4.3	11.5	88.23	0	0	4.3	16	66.26	1.65	0.97
Male	61	21	Mandibula	4.3	13	59.38	1.83	0.43	4.3	11.5	90	0.8	0	4.3	11.5	90	1.59	1.96	4.3	13	50.47	1.06	1.39
Female	36	22	Maxilla	4.3	13	61.19	0.5	0	3.75	11.5	79.26	0.4	0	3.75	11.5	90	0.4	0	4.3	13	54.84	0.3	0
Female	36	22	Mandibula	4.3	13	79.99	0.3	0.2	3.75	11.5	89.24	0.4	0.5	3.75	11.5	88.75	0.4	0.28	4.3	13	58.45	0.4	0.2
Female	67	46	Maxilla	4.3	13	68	0.3	0	4.3	10	94	0.4	0.1	4.3	11.5	89	0.5	0.1	4.3	16	69	0.2	0.5
Male	67	12	Maxilla	4.3	15	59.46	1.41	0.45	4.3	10	77.13	0.2	0	4.3	10	78.02	0	0	4.3	15	64.9	0.3	0
Female	60	47	Maxilla	4.3	13	73	0.4	0.45	4.3	13	90	0.3	0.8	4.3	13	83	0.2	0.8	4.3	13	67	0.8	0.2

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Table 2. The Pearson correlation coefficient test between implant angulation and distal marginal bone loss of implants.

		Distal MBL /mm/	Implant angulation
Distal MBL /mm/	**Pearson Correlation**	1	-.019
	Sig. (2-tailed)		.901
Implant angulation	**Pearson Correlation**	-.019	1
	Sig. (2-tailed)	.901	

Table 3. Partial correlation test between implant angulation and distal marginal bone loss of implant when gender, age, and follow-up are controlled separately.

Control Variables			**Distal MBL /mm/**	**Implant angulation**
Gender, Age, Follow-up	**Distal MBL /mm/**	**Correlation**	1.000	-.007
		Sig. (2-tailed)	.	.966
		df	0	39
	Implant angulation	**Correlation**	-.007	1.000
		Sig. (2-tailed)	.966	.
		df	39	0

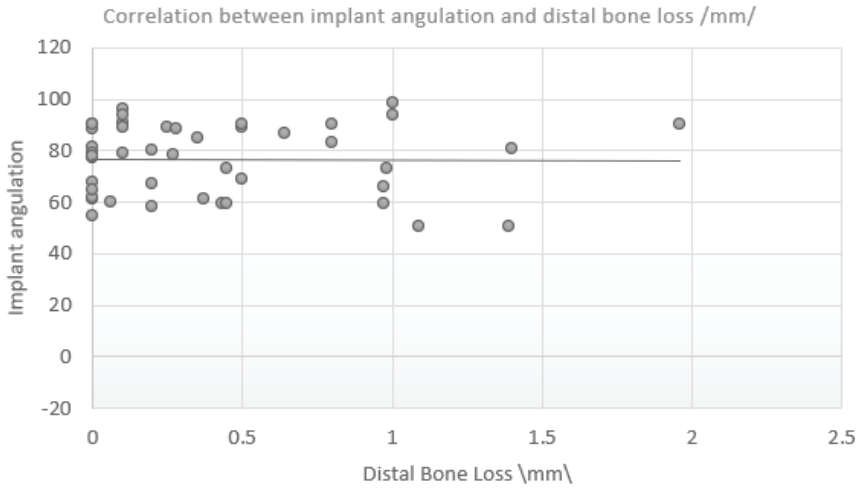

Figure 5. Correlation between implant angulation and distal bone loss.

There was a very weak negative correlation between angulation and mesial marginal bone loss (r=-0.243) (Table 4) (Figure 6) with no significant correlation (P →0.129) in the partial correlation test when gender, age, and follow-up were controlled (Table 5).

The statistical analysis showed a very weak negative correlation between the angulation and the mean marginal bone loss (r=-0.148) (Table 6) (Figure 7) meaning the mean marginal bone loss decreases very slightly when the implant angulation increases or becomes closer to 900 to the alveolar bone ridge. In the partial correlation test, these results were not significant (P →0.386) when gender, age, and follow-up were considered (Table 7).

In the Paired Sample t-test mean-marginal bone loss in axial implants was 0.42+0.42 mm and in tilted implants it was 0.60+0.47 mm. The difference between axial and tilted implants in mean marginal bone loss was not statistically significant (P →0.086) (Table 8) (Figure 8).

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Table 4. The Pearson correlation coefficient test between implant angulation and mesial marginal bone loss of the implants.

		Mesial MBL /mm/	Implant angulation
Mesial MBL /mm/	Pearson Correlation	1	-.243
	Sig. (2-tailed)		.112
Implant angulation	Pearson Correlation	-.243	1
	Sig. (2-tailed)	.112	

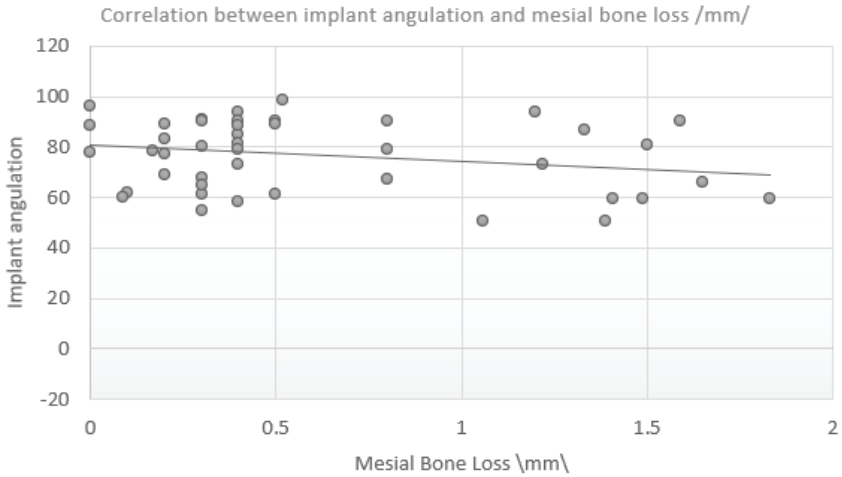

Figure 6. Correlation between implant angulation and mesial bone loss.

Table 5. Partial correlation test between implant angulation and mesial marginal bone loss of implant when gender, age, and follow-up are controlled separately.

Control Variables			**Mesial MBL /mm/**	**Implant angulation**
Gender, Age, Follow-up	**Mesial MBL /mm/**	Correlation	1.000	-.241
		Sig. (2-tailed)	.	.129
		df	0	39
	Implant angulation	Correlation	-.241	1.000
		Sig. (2-tailed)	.129	.
		df	39	0

Table 6. The Pearson correlation coefficient test between implant angulation and mean marginal bone loss of the implants.

		Mean MBL /mm/	**Implant angulation**
Mean MBL /mm/	**Pearson Correlation**	1	-.148
	Sig. (2-tailed)		.337
Implant angulation	**Pearson Correlation**	-.148	1
	Sig. (2-tailed)	.337	

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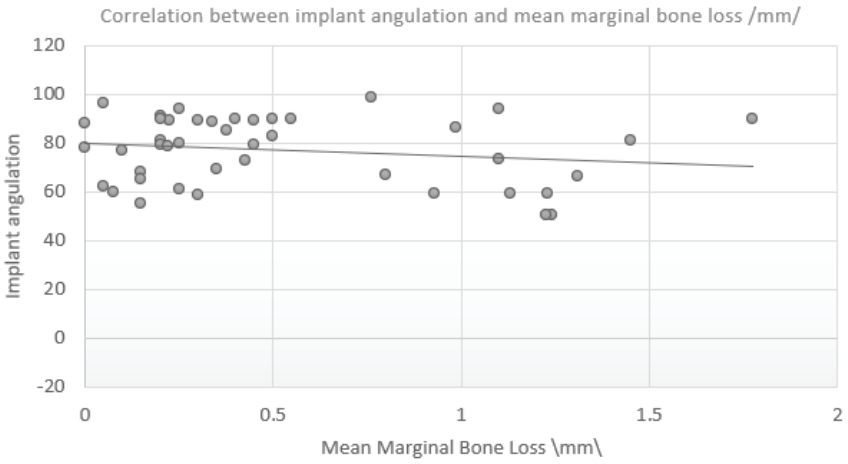

Figure 7. Correlation between implant angulation and mean marginal bone loss.

Table 7. Partial correlation test between implant angulation and the mean marginal bone loss of implant when gender, age, and follow-up are controlled separately.

Control Variables			Mean MBL /mm/	Implant angulation
Gender, Age, Follow-up	**Mean MBL /mm/**	**Correlation**	1.000	-.139
		Sig. (2-tailed)	.	.386
		df	0	39
	Implant angulation	**Correlation**	-.139	1.000
		Sig. (2-tailed)	.386	.
		df	39	0

Table 8. Paired Sample t-test between axial and tilted implants in mean marginal bone loss.

		Paired Differences							Significance	
					95% Confidence Interval of the Difference					
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	One-Sided p	Two-sided p
Pair 1	**Axial implant – Tilted implant**	-.177727	.462747	.098658	-.382898	.027443	-1.801	21	.043	.086

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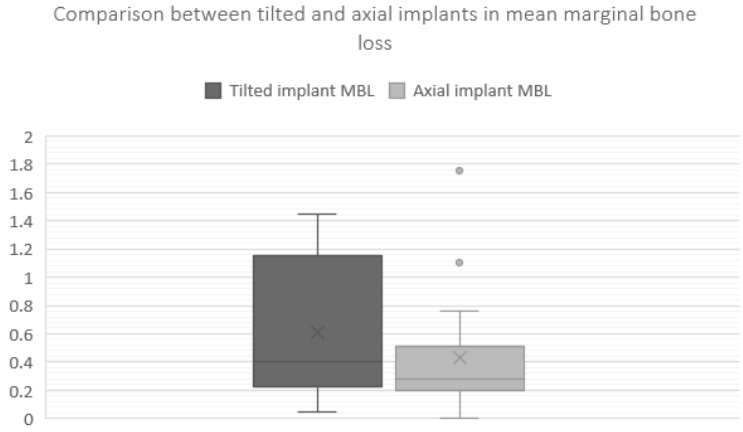

Figure 8. Comparison between tilted and axial implants in mean marginal bone loss.

DISCUSSION

Bone augmentation operations are one of the best options for implant-supported prosthesis of the atrophic jaws. However, the augmentation procedure may not be convenient for many patients due to medical or socioeconomic conditions as well as a patient who avoids multiple surgical procedures. The all-on-four concept provides surgical and prosthetic advantages such as increasing the contact area between the bone and implant by using longer implants and reducing cantilever length. In the literature, it is still a controversial topic whether tilted implants cause more marginal bone loss compared to axial implants.

In this study, there was no statistically significant difference in marginal bone loss between tilted and axial implants which is consistent with the literature.[7,14,15,13,8,9] Malo et al.[12] evaluated the average marginal bone loss with periapical radiographs, the bone loss of 5- and 10-year evaluations were stable with an average annual bone loss under 0.1 mm. However, the present study used CBCT images to measure the bone level, for more accurate data on mean marginal bone loss, which was 0.6 mm and 0.4 mm for tilted and axial implants respectively.

A recent systematic review and meta-analysis evaluated 8 papers consisting of a total of the 2036 axial implants and 1951 tilted implants with ranged follow-up periods from 5-17 years[13]. They found that there was no significant difference in marginal bone loss between tilted and axial implants. However, the paper was not conclusive about the effect of angulation degree, and all the studies measured bone loss using periapical radiographs.

Studies evaluating the inclination degree of tilted implants' effect on marginal bone loss are very limited and mostly designed to divide the study groups according to a specific reference angulation degree. Luciano et al[16], studied the placement of posterior implants at an angle greater than 450. The study showed that tilting angulation of posterior implants did not significantly influenced peri-implant bone loss, while the peri-implant bone loss was greater for those distally tilted implants consistent with our results. When the analysis was performed independently for the maxilla and mandible, no significant differences in the marginal bone loss were found between tilted and straight implants.

In literature, studies described a wide variety of prosthetic restorations. Paolo Malo et al. reported a 98.8% prosthetic success rate in the mandible with 10-18 years follow-up[11] and a 99.2% in the maxilla with 5-13 years follow-up[12]. There is a very limited number of studies that reported the correlation between marginal bone loss and prosthetic complications. It was suggested that the condition of the alveolar ridge, the antagonist dentition type, the implant brand/model, and using a temporary prosthesis during the osseointegration period significantly affect the MBL of axial and tilted implants as they were considered parts of the same supporting compound for a

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fixed dental prosthesis.[17] In the present study, all the patients used provisional prosthesis, and fixed prosthesis as a final restoration and all the implants were the same brand. Hence the effect of the prosthetic rehabilitation can be eliminated, however, the antagonist dentition was different for all the patients and statistical analysis was not performed due to the small sample size. The limitations of this study are the difference of the antagonist prosthetic restoration sand not standardizing the macroscopic structures like diameter and length due to the retrospective nature of the study along with small sample size.

Hopp et al.[3] evaluated the effect of gender on marginal bone loss in 891 (364 male, 527 female) patients in their study. They revealed that the female gender was associated with marginal bone loss →2.8 mm at 5 years of controls showing a 2-fold increased risk compared to males. Another study evaluated the influence of patient-dependent variables like age and gender on the MBL of axial and tilted implants. The results showed that the patient-dependent variables assessed did not significantly affect the MBL for the tilted implant group[17] similar to our results.

CONCLUSION

It is important to evaluate the prospect of marginal bone loss and survival of the tilted implants as these implants are exposed to higher lateral forces compared to axial implants. CBCT evaluation and correlation of the angle and the bone loss of the All-on-four concepts were not studied previously as far as our knowledge. Regarding the result of this study, there is a slight correlation between the inclination degree of the implants and marginal bone loss which suggests that a variety of different implant angulations can be well tolerated within physiologic limits. However, this finding was not significant, which may be due to the small sample size. In conclusion, it is safe to use tilted implants in the All-on-four concept for successful results, but studies with larger sample sizes and evaluating the superimposition of the pre-and post-operative CBCT images of the marginal bone would also be beneficial.

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REVIEW ARTICLE

Mandibular Distraksiyon Osteogenezinde Adjuvan Tedaviler: Hormonal ve Farmakolojik Ajanlar

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ÖZET

Distraksiyon osteogenezi traksiyon uygulanarak birbirinden uzaklaştırılan kemik segmentlerinin arasında oluşan kallusun yeni kemik formasyonuna dönüştüğü bir tekniktir ve maksillofasiyal bölgedeki çeşitli defektlerin tedavisinde kullanılır. Distraksiyon tekniğinin yumuşak dokular üzerinde önemli avantajlara sahiptir. Ancak tedavi süresinin uzun olması önemli bir dezavantajdır. Son yıllarda distraksiyon sürecini kısaltabilecek pek çok materyal ve metot üzerinde çalışmalar yapılmış, çeşitli hormonal proteinler, farmakolojik ajanların distraksiyon osteogenezinde başarılı olabileceği gösterilmiştir. Bu derlemede mandibular distraksiyon osteogenezinde araştırılan hormonal proteinlerin ve farmakolojik ajanların kapsamlı bir incelemesini sunduk. [tr]

Anahtar Kelimeler: distraksiyon, adjuvan tedavi, mandibular distraksiyon osteogenezi

GİRİŞ

Distraksiyon Osteogenezi (DO); traksiyon uygulanarak birbirinden uzaklaştırılan kemik segmentlerinin arasında oluşan kallusun yeni kemik formasyonuna dönüştüğü bir tekniktir[1]. Bu teknik osteotomi dönemi, latent dönem, distraksiyon dönemi ve konsolidasyon dönemi olmak üzere birbirini takip eden dört aşamadan oluşmaktadır. Osteotomi döneminde kemikte ilgili bölgede segmentler arasında cerrahi osteotomi oluşturulmakta ve distraktör yerleştirilmektedir. Latent dönemde distraktör aktive edilene kadar primer kallus oluşumu için latent sürenin geçmesine izin verilmektedir. Distraksiyon döneminde distraktör cihazı aktive edilerek kemik fragmanlarının kademeli olarak ayrılması sağlanmaktadır. Konsolidasyon dönemi ise distraktörlerin yeni oluşan kemiğin olgunlaşması için bölgede tutulduğu son dönemdir. Distraksiyon boşluğunda bulunan olgunlaşmamış kemik zamanla mineralize olmakta ve sonunda olgun kemiğe dönüşmektedir[2,3].

DO tekniği ilk kez 1989'da Ilizarov tarafından geliştirilmiştir. Daha sonra, 1992'de MacCarthy, ekstraoral tek yönlü bir distraktör kullanarak mandibula üzerinde DO tekniğini uygulamıştır [4–7]. DO yöntemi, post-travmatik yaralanmalarda, konjenital malformasyonlarda, tümör nedeniyle rezeksiyon uygulanan vakalarda ve kazanılmış kemik kaybı vakaları dahil olmak üzere maksillofasiyal bölgedeki çeşitli defektlerin tedavisinde kullanılabilmektedir[8].

Distraksiyon tekniğinin en önemli avantajı çevredeki yumuşak dokularda adaptif değişikliklerin oluşmasıdır[7]. Ancak tedavi süresinin uzun olması uygulanabilirliğini kısıtlamaktadır. Uzun süreli konsolidasyon aşaması boyunca lokal enfeksiyonlar, distraktör cihazı veya vidanın gevşemesi ve kırılmalar dahil olmak üzere birçok komplikasyon meydana gelebilmektedir [9,10]. Son yıllarda DO sürecini tamamlamak için gereken uzun süreyi azaltmak ve yenilenen kemiğin olgunlaşmasını geliştirmek için hormonlar, büyüme faktörleri, elektronik ve ultrasonik stimülasyon yöntemleri, farmakolojik ajanlar dahil olmak üzere çok sayıda teknik, yöntem ve malzeme araştırılmıştır [11,12]. Bu çalışmanın amacı, deneysel mandibular distraksiyon osteogenezi (MDO) modellerinde araştırılan çeşitli hormonal ve farmakolojik tedavilerin kapsamlı bir incelemesini sunmaktır.

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1.Hormonal Proteinlerin Distraksiyon Osteogenezine Etkileri

Kemik formasyonu ve rezorpsiyonunun bir arada görüldüğü durum kemiğin yeniden şekillenmesi olarak bilinir. Bu süreç, fizyolojik olarak osteoblastlar ve osteoklastlar birlikte çalıştıklarında gerçekleşir ve DO tekniğinde bu hücreler çok önemli bir role sahiptir [11–13]. Kemik dokusunun yeniden şekillenme mekanizmasının aktivitesinin düzenlenmesinde sistemik hormonlar (melatonin, östradiol, paratiroid ve büyüme hormonları) önemli bir etkendir[14]. Melatonin, oksitosin, paratiroid hormonu, büyüme hormonu, adiponektin ve eritropoietinin distraksiyon osteogenezi üzerindeki etkisi, farklı hayvan çalışmalarında incelenmiştir (Tablo1).

1.1. Melatonin

Melatonin, epifiz bezi tarafından salınan triptofan türevli bir indolamin hormonudur. Yapılan araştırmalar, melatoninin antioksidan özelliklere sahip olduğunu ve osteoklastogenezi baskıladığı için kemik dokusu rezorpsiyonunu inhibe ettiğini göstermiştir. Ayrıca osteoblast diferansiasyonunu ve proliferasyonunu arttırmaktadır[13,15,16]. Bir rat modeli üzerinde yapılan çalışmada DO ile birlikte farklı dozlarda sistemik melatonin uygulanmış ve melatoninin yeni kemik rejenerasyonunu doza bağlı arttırdığı bulunmuştur[14].

1.2. Oksitosin

Oksitosin hipotalamusta üretilen ve başlıca uterus kasılmalarını sağlayarak doğum ve laktasyon olaylarında rol oynayan bir hormondur[17]. Hipotalamusta üretilen oksitosinin ayrıca sosyal bellek, öğrenme, cinsel davranış ve ağrı algısında rol almaktadır[18]. Son zamanlarda yapılan araştırmalar, oksitosinin kemik metabolizmasında yer alan çeşitli mekanizmaları etkileyerek anabolik bir etki yarattığını göstermiştir[19–22]. Tavşanlarla yapılan bir çalışma modelinde DO sırasında uygulanan oksitosinin yeni kemik oluşumunu ve kemik iyileşmesini arttırdığı görülmüştür. Oksitosinin, distraksiyon oranını arttırarak 1 mm/gün standart distraksiyon yerine, 2mm/ gün distraksiyon oranını sağlayabileceği bulunmuştur.[23]

1.3. Büyüme Hormonu

Büyüme hormonu, dokular üzerinde doğrudan ve insülin benzeri büyüme faktörü-1 (IGF-I) aracılığı ile dolaylı olarak stimülasyon oluşturan sistemik etkili bir hormondur. Büyüme hormonunun sistemik uygulaması, kemiğin prekürsör hücrelerinin proliferasyonunu ve farklılaşmasını düzenlemekle birlikte osteoblastik aktiviteyi hızlandırmaktadır [24]. Köpeklerde yapılan bir çalışmada büyüme hormonu uygulanmış gruplarda daha fazla yeni kemik oluşumu ve mekanik güç, daha yüksek

Tablo 1. Mandibular distraksiyon osteogenezinde araştırılan hormonal proteinler

Referans	Yıl	Model	Adjuvan	Sonuçlar
[14]	2018	Rat	Melatonin	Daha fazla osteoklast, osteoblast, osteopontin (OPN) ve vasküler endotelyal büyüme faktörü (VEGF) seviyeleri
[23]	2020	Rat	Okistosin	Artmış yeni kemik oluşumu ve kemik iyileşmesi
[24]	2003	Köpek	Rekombinat insan büyüme hormonu	Daha yüksek kemik mineral yoğunluğu (BMD), mekanik güç ve yeni kemik oluşumu
[24]	2004	Köpek	Büyüme Hormonu (Kitosan Mikroküre Kapsül)	Yeni kemik oluşumunda aktif minerilizasyonun uyarılması
[29]	2016	Tavşan	Paratiroid hormonu	Osteoblast sayısı, trabeküler kemik alanı ve kemik mineral yoğunluğu
[34]	2012	Rat	Paratiroid hormonu	Daha fazla kemik hacmi
[30]	2017	Tavşan	Paratiroid hormonu	Daha matur ve fazla kemik oluşumu, daha fazla kemik hacmi fraksiyonu, trabekül sayısı ve trabeküler kalınlık ve mekanik özellikler
[31]	2011	Tavşan	Adiponektin	Daha fazla kemik oluşumu ve daha yüksek kemik mineral yoğunluğu (BMD) ve kemik mineral içeriği (BMC)
[33]	2009	Tavşan	Rekombinant insan eritropoietini	Daha fazla sayıda osteoblast ve kan damarı, önemli ölçüde daha büyük kemik oluşumu alanı

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Tablo 2: Mandibular distraksiyon osteogenezinde araştırılan farmakolojik ajanlar

Referans	Yıl	Model	Adjuvan	Sonuçlar
[40]	2008	Tavşan modeli	Alendronat	Alendronat uygulanmış gruplarda daha yoğun osteojenik oluşum, ortalama kemik mineral yoğunluğunda artış ve daha hızlı kemik iyileşmesi
[41]	2011	Tavşan modeli	Sistemik-Lokal Alendronat	Sistemik ve lokal alendronat gruplarında kontrol grubuna göre kemik iyileşme parametrelerinde artış, rejenerasyon yoğunluğunda anlamlı bir farklılık ve ortalama kemik mineral yoğunluğunda anlamlı bir artış saptanmıştır.
[42]	2017	Tavşan modeli	Alendronat	1mm/gün distraksiyon oranında alendronat uygulanmış grupta artmış kemik iyileşmesi saptanmıştır.
[43]	2017	Rat modeli	Sistemik- Lokal Zoledronik asit	Yeni kemik oluşum miktarı, osteoblast ve osteoklast hücreleri, osteopontin ve vasküler endotelyal büyüme faktörü sistemik ve lokal zoledronik asit gruplarında kontrol grubuna göre ve sistemik zoledronik asit grubunda lokal zoledronik asit grubuna göre daha yüksek
[44]bone segments were maintained in a neutral position by distractor for 7 days then distraction was initiated at a rate of 0.5 mm twice a day for 10 days to achieve a total distraction of 10 mm, followed by a consolidation period. Animals were divided into 3 equal groups according to the injected drug (saline solution [control], zoledronic acid, alendronate	2014	Köpek modeli	Zoledronik asit-Alendronat	Deney gruplarında kemik oluşumu ve olgunlaşması kontrol grubundan daha hızlı Zoledronik asit, konsolidasyon süresini kısaltmada alendronattan daha etkili
[45]	2006	Tavşan modeli	Zoledronik asit	Zoledronik asit gruplarında kemik mineral yoğunluğu ve kemik mineral içeriğinde anlamlı farklılık saptanmıştır.
[12]	2008	Tavşan modeli	Zoledronik asit	Deney gruplarında ossifikasyon alanlarında, osteoblast, osteoklast sayılarında, kollagen miktarı ve fibroblast sayısında anlamlı farklılık saptanmıştır.
[49]	2008	Tavşan modeli	Simvastatin	Radyografik değerlendirmede sistemik simvastatin grubunda lokal ve simvastatin grubuna ve kontrol grubuna göre rejenerasyon alanının arttığı gözlenmiştir. Histomorfometrik değerlendirmede ise anlamlı bir farklılık görülmemiştir.
[47]	2015	Tavşan modeli	Simvastatin	Histomorfometrik incelemede deney grubunda yeni kemik oluşumunda artış gözlenmiştir. Diğer parametrelerde önemli farklılık olmamıştır.

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[50]an iron chelator that has been shown to increase angiogenesis, will improve bone regeneration by means of augmentations in quality and quantity of bone and bone-producing cells. Methods: Two groups of rats (n = 12	2014	Rat modeli	Deforaksamin	Deney grubunda daha yoğun kemik alanları, osteosit proliferasyonunda artış
[51]	2012	Rat modeli	Deforaksamin	Deney grubunda distrakasiyon boşluğunda vaskülaritede artış
[52]as well as a prolonged return to activities of normal daily living. Developing innovative techniques to abridge consolidation periods could be immensely effective in preventing these problematic morbidities. Deferoxamine (DFO	2013	Rat modeli	Deforaksamin	Deney gruplarında kemik hacim fraksiyonunda, kemik mineral yoğunluğunda ve nihai yükte önemli artış
[53]	2011	Tavşan modeli	İcariin	Deney gruplarında kemik mineral yoğunluğnda artış, daha yüksek trabeküler sayı ve daha az trabeküler ayrılma
[54]	2016	Tavşan modeli	Osteoformin	Deney gruplarında hızlanmış kemik iyileşmesi
[55]	2009	Tavşan modeli	Osteoformin	Deney grubunda kemik mineral yoğunluğu ve kemik mineral içeriği değerleri, yeni oluşan kemik alanları, damar sayısı ve osteoblastlar anlamlı olarak daha fazla
[56]	2014	Tavşan modeli	Propolis	Deney gruplarında kemik mineral içeriği ve kemik mineral yoğunluğu daha yüksek, daha hızlı kemik iyileşmesi
[57]	2002	Köpek modeli	Kalsiyum sülfat	Kalsiyum sülfat ve kombine materyallerinin distraksiyon osteogenezinde erken kemik konsolidasyonunda etkili bulunmuştur.
[58]	2005	Köpek modeli	Kalsiyum sülfat	Kalsiyum sülfat ve kombine materyallerinin yeni kemik oluşumunda kontrol grubuna göre artış sağlamıştır.
[59]	2001	Tavşan modeli	Kalsiyum sülfat	Deney gruplarında kontrol gruplarına göre yeni oluşan kemiğin kalsifikasyonu daha yüksek.
[60]	2009	Tavşan modeli	Kalsiyum hidroksit	Deney gruplarında rejenerasyon ve yeni kemik hacmi artmıştır.
[61]	2017	Tavşan modeli	Stronsiyum Sitrat	Çalışma gruplarında daha fazla olgun kemik, daha yüksek kemik yoğunluğu, daha fazla maksimum yük
[62]	2021	Tavşan modeli	Stronsiyum Sitrat	Çalışma gruplarında daha yüksek yeni kemik yüzdesi, daha kalın kemik trabekülleri
[66]	2019	Tavşan modeli	E vitamini	Deney grubundaki tavşanlarda kemik mineral yoğunluğu ve kemik mineral içeriği daha fazla, osteoblast, osteoklast, damar sayıları ve yeni oluşan kemik alanı daha fazla

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kemik mineral yoğunluğu olduğu bulunmuş olup büyüme hormonunun DO'da erken kemik konsolidasyonunda etkili olduğu sonucuna varılmıştır[24]. Köpekler üzerinde yapılan başka bir çalışmada ise kitosan mikroküre lerine enkapsüle edilmiş büyüme hormonunun DO'da yeni kemik gelişiminin aktif mineralizasyonunu uyardığı ve DO'da erken kemik konsolidasyonunda oldukça etkili olduğu sonucuna varılmıştır.[25]

1.4. Paratiroid Hormonu

Paratiroid hormonu, paratiroid bezinin ana hücreleri tarafından salgılanan kalsiyum düzenleyici önemli bir hormondur. Bu hormon vücuttaki kalsiyum ve fosfor metabolizmasının dengesini korumakta, kemiklerin anabolik ve katabolik metabolizmasını düzenlemektedir. Çalışmalar, paratiroid hormonunun kemik metabolizması üzerindeki etkilerinin öncelikle bu hormonun dozuna ve uygulama yöntemine bağlı olduğunu göstermiştir. Özellikle, yüksek dozda paratiroid hormonunun sürekli uygulanması kemik rezorpsiyonunu artırabilirken, küçük dozlarda paratiroid hormonunun aralıklı olarak verilmesi osteojenik etkilere sahiptir[26–28]. Tavşanlar üzerinde yapılan bir çalışmada rekombinant insan paratiroid hormonu DO sırasında uygulanmış olup paratiroid hormonu uygulanmış gruplarda yeni kemik oluşumunun ve mineralizasyonun hızlandığı gösterilmiştir. Bu çalışmada aynı zamanda paratiroid hormonu 10, 20, 30 ve 40 µg/kg gibi farklı dozajlarda uygulanmış olup günlük 30 µg / kg rekombinant insan paratiroid hormonunun en etkili sonucu sağladığı bildirilmiştir [29]. Paratiroid hormomunun etkilerinin araştırıldığı başka bir çalışmada ise hızlı distraksiyon oranının yeni kemik oluşumu üzerinde neden olduğu zararlı etkinin paratiroid hormonu ile telafi edilebileceği belirtilmiştir[30].

1.5. Adiponektin

Adipositler tarafından üretilen, salgılanan ve protein yapılı hormon olan adiponektinin, osteoblastogenezi aktive ederek ve osteoklastogenezi baskılayarak kemik hacmini arttırdığı ve anjiyogenezi uyardığı bildirilmiştir. Tavşanlarla yapılan bir çalışmada adiponektin uygulanan gruplarda daha fazla kemik oluşumu, daha yüksek kemik mineral yoğunluğu ve kemik mineral içeriği oluştuğu gözlenmiştir[31].

1.6. Eritropoietin

Eritropoietin (EPO) temel rolü eritrosit üretimi olan fizyolojik bir hormondur ve EPO'nun kemik onarımı sırasında kondrojenik ve anjiyojenik yanıtları arttırdığı ve iskelet rejenerasyonunu kolaylaştırmak için tedavi edici bir ajan olarak hizmet verdiği bulunmuştur[32]. Bir tavşan modelinde yapılan çalışmada eritropoietinin yeni oluşan kemik miktarında, osteoblast ve kan damarlarının sayısında önemli bir artışa neden olduğu bildirilmiştir[33].

2. Farmakolojik Ajanların Distraksiyon Osteogenezine Etkileri

Kemik metabolizmasında rol oynayan ilaçlar özellikle osteoporoz hastalarının tedavisinde günümüzde sıklıkla kullanılmaktadır. Kemik metabolizmasına etki eden ilaçların kullanılması mandibular distraksiyon osteogenezinde de konsolidasyon süresini kontrol etmek ve azaltmak amacıyla kullanılabilir ve bu ilaçların etkinlikleri deneysel çalışmalarla değerlendirilmiştir (Tablo 2).

2.1. Bifosfonatlar

Bifosfonatlar, kemik mineralizasyonunu düzenleyen endojen inorganik pirofosfatların analoglarıdır. Nitrojen içermeyen bifosfonatlar, kemik dokusunda osteoklastlar tarafından yakalanarak hücre içinde adenozin trifosfat (ATP) toksik analoglarına dönüştürülerek etki gösterirler. Vücutta çok hızlı metabolize edilirler. Nitrojen içeren bifosfonatlar antirezorptif etkilerini mevalonat yolu üzerinden gösterirler[34]. Kemikte hidroksiapatit kristallerine bağlanırlar ve buradan salınıp osteoklastlar tarafından absorbe edilirler. Osteoklastın hücre içinde kolesterol üreten mevalonat yolunun enzimlerinden biri olan farnesildifosfatın sentezini inhibe ederler. Bu sebeple osteoklastın kemik rezorbsiyonunu oluşturabilmesi için gereken yüzey özellikleri oluşamaz, osteoklastik aktivite baskılanır ve razorptif aktivitede azalma olur [35]. Bifosfonatlar olgunlaşmamış ve öncü osteoklast hücrelerine de etki gösterebilirler[36]. Nitrojen içeren bifosfonatlar nitrojen içermeyen bifosfonatlardan 100–2000 kat daha güçlü etki gösterirler[37] Kemik rezorpsiyonunu inhibe etmede en güçlü BP'lerden birkaçı alendronat, pamidronat, risedronat ve zoledronik asittir[38].

Tekin ve ark.'nın çalışmasında sistemik olarak uygulanan alendronatın distraksiyon boşluğunda yeni kemik oluşumunu hızlandırmada etkili olduğu ve tavşan mandibulasında 1 mm / gün yerine, 2 mm / gün distraksiyon hızına izin verebileceği gösterilmiştir [39]. Küçük ve ark.'nın yaptığı çalışmada sistemik ve lokal alendronat gruplarının kontrol gruplarından üstün olduğunu gösterilmiştir. Sistemik alendronatın yeni kemik oluşumunu hızlandırmada lokal alendronata göre daha etkili olduğu, ancak istatistiksel olarak anlamlı olmadığı

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gösterilmiştir[40]. Alp ve ark.'nın çalışmasında lokal olarak uygulanan düşük dozlu alendronat enjeksiyonlarının yeni kemik oluşumunda başarılı olduğu sonucuna varılmıştır[41].

Dündar ve ark.'nın sıçanlarda yaptığı çalışmada lokal ve sistemik olarak uygulanan zoledronik asidin mandibular DO'ya etkisi değerlendirilmiş, sistemik ve lokal uygulama gruplarında kontrol grubuna göre yeni kemik oluşumu, osteoblast, osteoklast, osteopontin ve VEGF (vasküler endotelyal büyüme faktörü) miktarı daha yüksek; sistemik uygulama grubunda ise lokal uygulama grubuna göre bu değerler daha daha yüksek bulunmuştur[42]. Baiomy ve ark'nın köpeklerde yaptıkları çalışmada, lokal alendronat ve zoledronik asit uygulaması karşılaştırılmıştır. Histolojik ve radyografik analizler, zoledronik asidin alendronattan ve salin enjeksiyonundan daha güçlü olduğunu, deney gruplarında kemik rejenerasyonunun ve kemik mineral yoğunluğu değerlerinin daha fazla olduğunu kanıtlamıştır[43]. Pampu ve ark.'nın 2006'da yaptıkları çalışmada, tavşanlara MDO sırasında sistemik zoledronik asit uygulanmıştır ve zoledronik asitin konsolidasyon süresini kısaltarak, pinlerin etrafında oluşabilecek enfeksiyon insidansını azaltabileceği ve eksternal fiksatörün çıkarılmasının ardından kırılmalarla ilişkili komplikasyon riskini azalabileceği belirtilmiştir[44]. Pampu ve ark 2008 yılında ise, sistemik zoledronik asit uygulamasının yeni oluşan kemiğin mineralizasyonu üzerindeki etkisini değerlendirmek ve immatür tavşan mandibulasının uzaması sırasında çevreleyen kemik üzerindeki gerilime bağlı osteoporozu belirlemek amaçlı bir çalışma yapmışlar; iki grup arasında osteoblast, osteoklast ve kollajen miktarları açısından önemli bir fark görülmüş, ayrıca yeni oluşan kemik alanları ve fibroblast sayısı deney grubunda daha yüksek olarak bulunmuştur [12]. Bifosfonatların sistemik uygulaması DO'da kemik rejenerasyonu üzerinde olumlu etkiler göstermesine karşılık osteonekroz riski önemli bir faktördür. Bu nedenler bifosfonatların DO'da lokal olarak uygulanması kemik oluşumunun hızlanmasında daha güvenli olarak değerlendirilmiştir[45].

2.2. Statinler

Statinler, 3-hidroksi-3-metilglutaril koenzimini inhibe ederek lipit düzeyini azaltan ve kardiyovasküler hastalıkların tedavisinde kullanılan ilaçlardır. Çeşitli çalışmalar, statinler içerisinde yer alan simvastatinin hem lokal hem de sistemik uygulamalarının kemik rejenerasyonuna katkıda bulunduğunu göstermiştir[46]. Statinler osteoklastogenezisi ve kemik rezorpsiyonu azaltıp osteogenezisi arttırmaktadır[47]. Kılıç ve ark'nın simvastatini sistemik ve lokal olarak tavşanlara uyguladıkları çalışmada radyografik değerlendirme ile, rejenerasyon alanının kontrol grubuna göre lokal simvastatin grubunda %9,6 ve sistemik simvastatin grubunda %19,3 arttığını göstermiş, her iki deney grubunda da rejenerasyon yoğunluğu kontrol grubuna göre arttığı bildirilmiştir[48]. Kahraman ve ark'nın 2015 yılında tavşanlar üzerinde yaptığı çalışmada, MDO sırasında distraksiyon boşluğuna simvastatin ve salinden oluşan çözelti jelatin süngerle lokal olarak uygulanmıştır. Histolojik olarak deney grubunda daha çok kemik oluşumu gösterilmiş ancak diğer analizlerde gruplar arasında önemli ölçüde farklılık bulunmamıştır[46].

2.3. Deforaksamin

İskelet onarımında anjiogenez oldukça önemli bir basamaktır ve son zamanlardaki çalışmalarda iyileşme sırasında kan akışını arttırmak için farmakolojik ajanlara odaklanılmıştır. Deferoksamin bir demir şelatörü olup, ABD Gıda ve İlaç İdaresi onaylı bir ilaçtır. Deforaksamin, hipoksiye yanıtın bir düzenleyicisi olarak anjiyogenezi aktive eden HIF (hipoksi ile indüklenebilir faktör) yolu ile anjiyogenezi artırır. Farberg ve ark. 2014 yılında, Donneys ve ark. ise 2012 ve 2013 yıllarında deforaksaminin ratlardaki MDO üzerine etkisi ile ilgili çalışmalar yapmışlardır [49–51]. Farberg ve ark. deforaksaminin MDO'da rejenerasyon oluşumunun miktarını ve kalitesini iyileştirebileceğini belirtmişlerdir [49]. Donneys ve ark. 2012 yılında yaptıkları çalışmada deney grubunda damar sayısında %40 artış olduğunu ve bu durumun rejenerasyonu arttırdığını göstermişler, 2013 yılında yaptıkları çalışmada ise deney gruplarında, kontrol gruplarına kıyasla kemik hacmi fraksiyonunda, kemik mineral yoğunluğunda ve nihai yükte artış olduğunu göstermişlerdir. Yazarlar lokalize deforaksamin enjeksiyonu ile vasküler yoğunluğun arttırılmasının, kemik kalitesini veya gücünü önemli ölçüde etkilemeden kemik rejenerasyonunu hızlandırmak için etkili bir yol sağladığını belirtmişlerdir[50,51].

2.4. İcariin

İcariin içeren ilaçlar, kemik oluşumunun uyarılması ve kemik rezorpsiyonunun önlenmesi yoluyla osteoporoz tedavisinde ve osteonekrozun önlenmesinde yararlı etkiler sergiler. Wei ve ark'nın tavşanlarla yaptıkları çalışmada, deney grubundaki hayvanlara icariin uygulanmış ve kontrol grubuna kıyasla deney grubunda yeni kemik hacminin, trabekül sayısı ve kalınlığının arttığı görülmüştür [52].

2.5. Osteoformin

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Osteoformin, bir polimer poliaspartat olup negatif yüklü reçinelerden biridir. Daha önceki in vitro çalışmalarda, osteoforminin osteoblast benzeri hücreleri uyardığı, alkalin fosfataz aktivasyonunu ve tip I kollajen salınımını artırdığı gözlenmiştir. Dayısoylu ve ark. yaptıkları çalışmada tavşanlara uygulanan MDO'da osteoforminin etkilerini araştırmışlar, osteoforminin kemik iyileşmesini hızlandırdığını bulmuşlar ancak insanlarda osteoforminin kullanılmadan önce daha fazla deneysel çalışma yapılması gerektiğini önermişlerdir [53]. Pampu ve ark.'nın çalışmasında distraksiyon alanına osteoformin uygulanmış ve osteoforminin DO sırasında yeni oluşan kemiğin olgunlaşmasını ve iyileşme oranını arttırdığı ve konsolidasyon süresini kısaltabileceği bildirilmiştir[54].

2.6. Propolis

Propolis, bal arılarının topladığı reçine içerikli bir malzemedir. Propolis amino asitler, fenolik asitler, fenolik asit esterleri, flavonoidler, sinnamik asit gibi birçok doğal bileşeni içermektedir. Bereket ve ark.'nın tavşanlarla yaptığı çalışmada deney grubuna DO boyunca oral olarak propolis uygulanmıştır ve çalışma grubunda yeni kemik oluşumunun hızlandığı bildirilmiştir[55].

2.7. Kalsiyum Sülfat

Kalsiyum sülfat, osteokondüktif etkisi nedeniyle ortopedik ve dentoalveolar uygulamalarda kemik grefti olarak kullanılan biyouyumlu bir materyaldir. Cho ve ark. yaptıkları çalışmalarda köpeklere uygulanan MDO'da kalsiyum sülftala kombine kitosan ve hiyalaronik asit uygulamışlar ve kalsiyum sülfat ile kombine materyallerinin distraksiyon osteogenezinde erken kemik konsolidasyonunda oldukça etkili olduğu sonucuna varmışlardır[56,57]. Al ruhami ve ark.'nın yaptığı çalışmada, tavşanların distrakte kemiğine kalsiyum sülfat hemihidrat tozu uygulanmış ve çalışma grubunda daha fazla matur kemik oluşumu ve daha erken kalsifikasyon görülmüş olup bu durumun fiksasyon süresini kısaltabileceği belirtilmiştir[58].

2.8. Kalsiyum Hidroksit

Kalsiyum hidroksit (KH), periapikal lezyonlar için yaygın olarak kullanılan, antimikrobiyal, antiinflamatuar ve sert doku onarımını indükleme etkisi bulunan antijenik olmayan bir ilaçtır. KH'nin alkali etkisi enflame dokulardaki asidik ortamı nötralize ederek ve osteoklast oluşumunu azaltarak kemik rezorpsiyonunun durmasına neden olur. Polat ve ark.'nın yaptığı bir çalışmada DO sırasında tavşanlara KH solüsyonu uygulanmış ve yeni oluşan kemik hacminde çalışma ve kontrol gruplarında farklılık olduğu gösterilmiştir. Ancak yazarlar KH'nin etkilerinin değerlendirilmesi için daha fazla çalışmaya ihtiyaç olduğunu belirtmiştir[59].

2.9. Stronsiyum

Stronsiyum, kalsiyuma benzer bir element olup stronsiyum ranelat ve stronsiyum sitrat olmak üzere iki ana formu bulunmaktadır. Stronsiyum ranelat, osteoklast aktivitesini inhibe etmesi ve osteoblast proliferasyonunu uyarması nedeniyle osteoporoz tedavisinde kullanılmaktadır. Ancak pediyatrik popülasyonda onaylanmış bir ilaç değildir. Stronsiyum sitrat ise, Kuzey Amerika'da yaygın olarak bulunan, reçetesiz satılan bir kemik sağlığı takviyesidir. Taylor ve ark'nın tavşanlarla yaptığı çalışmada deney grubundaki hayvanlara oral stronsiyum sitrat uygulanmış ve çalışma grubundaki tavşanlarının daha olgun kemiğe ve daha yüksek kemik yoğunluğu sahip olduğu, üç noktalı eğilme testi sonuçlarına göre maksimum yükünün, kontrol grubuna göre daha fazla olduğu gösterilmiştir[60]. Alansi ve ark. da 2021 yılında tavşanlarda MDO sırasında çalışma gruplarına sitronsiyum sitrat uygulamışlar ve stronsiyum sitratın kontrol grubuyla karşılaştırıldığında çalışma grubunda yeni kemik oluşumunu ve olgunlaşmasını arttırdığını ortaya koymuşlardır[61].

2.10. E Vitamini

Antioksidanlar yeni kemik oluşumu sırasında serbest radikallerin olumsuz etkilerini baskılayarak osteoblastik aktiviteyi arttırırken osteoklastik aktiviteyi azaltmaktadır. E vitamini (α-tokoferol), köklü antioksidan özelliği ile bilinmektedir ve distraksiyon osteogenezine etkileri yapılan çalışmalarla değerlendirilmiştir [62–65]. Akçay ve ark.'nın 2019 yılında tavşanlarla yaptıkları çalışmada, deney grubundaki hayvanlara α-tokoferol uygulanmış ve deney grubunda, yeni oluşan kemik alanının daha fazla olduğu, kemik mineral yoğunluğu ve kemik mineral içeriği değerlerinin daha yüksek olduğu, osteoblast, osteoklast sayısının daha fazla olduğu gösterilmiştir. DO'nun osteogenezini hızlandırmak için yararlı bir protokol olabileceği bildirilmiştir[65].

SONUÇ

Maksillofasiyal bölgenin deformiteleri rekonstrüktif yöntemler ve ortognatik cerrahi işlemler ile tedavi edilebilmektedir. Ancak bu yöntemlerdeki büyük kemik segmentlerinin hareketi esnasında, yumuşak dokular yeni oluşan pozisyona adapte

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olamamakta, bu durumda fonksiyonel ve estetik problemler oluşturabilmektedir. Bu nedenle zaman içinde pek çok alternatif tedavi yöntemi araştırılmıştır. Bu alternatif metotların bir tanesi de distraksiyon osteogenezidir. Bu teknikte, yeni kemik oluşumu ile birlikte yumuşak dokularda da hacimsel değişiklikler sağlanabilmektedir[66]. DO kemiklere uygulanan osteotomi ya da kortikotominin ardından, distraktörün yerleştirilmesi, oluşan kallusa traksiyon uygulanması sonucunda kemik segmentlerinin birbirine bakan yüzeylerinde yeni kemik oluşumu ve komşu bölgelerde yumuşak doku formasyonunun meydana geldiği biyolojik bir olaydır[67]. DO'nun tedavi süresinin uzun olması sebebi ile son yıllarda daha hızlı bir iyileşme sağlanabilmesi için pek çok araştırma yapılmış, birçok materyal ve metod deneysel olarak DO ile uygulanmıştır.

Hormonal proteinlerden olan oksitosin, melatonin, adiponektin ve eritropoietinin distraksiyon osteogenezinde adjuvan olarak uygulanması ile başarılı sonuçlar elde edilmiştir. Aynı zamanda literatürde bu hormonların kullanımı ile ciddi yan etkiler belirtilmemiştir. Güvenirliklerinin saptanmasının ardından bu hormonların DO'da uygulanacağı dozajlarla ilgili klinik çalışmalar yapılmalıdır. Paratiroid hormon uygulamalarında ise doza bağlı ikili etkilerin saptanması ve paratiroid hormonun güvenirliği ile ilişkili literatürde çelişkili ifadelerin yer alması, uygulanabilirliği konusunda endişe oluşturmaktadır[68]. Büyüme hormonunun da çocuklarda kullanımına ilişkin çeşitli yan etkiler bildirilmiş, kanser insidansı ve mortalite oranı dahil olmak üzere uzun süreli kullanımda oluşan etkilerin değerlendirilmesi gerektiği belirtilmiştir[69]. Bu nedenle paratirod hormonu ve büyüme hormonunun etkilerinin daha iyi anlaşılabilmesi için daha fazla çalışmasının yapılması gerektiği düşünülmektedir.

Bifosfonatların MDO'da kemik oluşumunu arttırabileceği yapılan çalışmalarda gösterilmiştir. Ancak bifosfonat kullanımı ve osteonekroz arasında bir korelasyon olduğu düşünülmekte ve bifosfonatların DO'da uygulanabilirliği konusu belirsizliğini korumaktadır[10]. Bifosfonatların lokal uygulamalarının güvenirliğinin belirlenebilmesi için daha fazla çalışma yapılmalıdır. Statinlerin mandibular DO'ya etkisi araştırılmıştır ancak deney gruplarında kontrol gruplarına göre önemli bir farklılık bulunmadığını belirten yayınlar mevcuttur[46]. Deforaksamin, icariin ve osteoforminin kemik rejenerasyonunu arttırdığı düşünülmektedir[50,52,53]. Kalsiyum sülfatın hyalaronik asit ya da kitosan ile kombine uygulamalarının ve vitamin E'nin konsolidasyon süresini kısaltabileceği gösterilmiştir[57,65]. Stronsiyum sitratın da konsolidasyon süresini kısaltabileceği ve kemik yoğunluğunu arttırabileceği gösterilmiştir. Bu farmokolijik ajanların bilinen ciddi bir yan etkisinin olmaması nedeni ile etkinliklerinin klinik çalışmalar ile desteklenmesi gerektiği düşünülmektedir[60].

DO'da tedavi süresini kısaltabilecek ve kemik oluşumunu, iyileşmesini hızlandırabilecek çok sayıda materyal ve yöntem olmasına karşın bu uygulamaların çeşitli avantaj ve dezavantajları söz konusudur. Büyüme hormonu, paratiroid hormunu ve bifosfonatların DO'da güvenle uygulanıp uygulanamayacağının belirlenebilmesi amacıyla daha fazla çalışması yapılması gerektiğini; oksitosin, melatonin, adiponektin, eritropoietin deforaksamin, icariin, kalsiyum sülfat, vitamin E gibi adjuvanların DO'da yeterli etkiye sahip olup olmayacağının belirlenebilmesi ve uygun dozajların belirlenebilmesi için klinik çalışmalar yapılması gerektiğini düşünmekteyiz. Bu derlemede distraksiyon osteogenezinde uygulanabilecek adjuvan ajanların avantaj ve dezavantajları geniş bir şekilde değerlendirilmiş olup klinik uygulanabilirlik açısından tartışılmıştır. Distraksiyon osteogenezinde kemik oluşumunu, iyileşmesini hızlandıracak ve tedavi süresini kısaltacak ajanlardaki gelişmeler ile gelecek yıllarda DO'nun kliniklerde uygulanabilirliğinin artacağı görüşündeyiz.

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REVIEW ARTICLE

Fixation Methods Used in Sagittal Split Ramus Osteotomy

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ABSTRACT

The sagittal split ramus osteotomy (SSRO) is a technique frequently used in orthognathic surgery for the treatment of congenital or acquired mandibular irregularities. Congenital or acquired deformities of the mandible, such as hypoplasia, hyperplasia, and asymmetry, can be corrected with this method. The SSRO procedure creates a broad bone contact surface in the mandible, supporting both post-operative stability and the early healing process. Additionally, this technique prepares a suitable foundation for the application of various fixation methods. The correct fixation of the segments after osteotomy directly affects the success of the procedure. Ensuring immobility between the bone fragments is of critical importance to the success of the surgery. Among the fixation materials and techniques used after SSRO are wire osteosynthesis, intermaxillary fixation, bicortical screw systems, mini plate-screw systems, hybrid systems using bicortical screws and plates, and resorbable mini plate-screw systems. An ideal fixation system should promote rapid bone healing, the commencement of early mandibular function post-operatively, and a reduction in the amount of relapse. However, despite many studies on this topic, an universally accepted ideal fixation method has yet to be determined. In our review, various fixation types and methods used for the frequently applied SSRO method in orthognathic surgery have been examined in detail. Information on the advantages, disadvantages, and effectiveness in clinical application of these techniques has been provided. The selection of the correct fixation method, which plays a critical role in the success of SSRO, is believed to directly impact both patient outcomes and the healing process. In this context, our review aims to provide clinicians with information and guidance in determining the most suitable fixation method for potential clinical scenarios they may encounter.

Keywords: fixation, stabilization, sagittal split ramus osteotomy

SSRO is a mandibular orthognathic surgical procedure that allows the correction of dentofacial deformities. The first mandibular osteotomy surgery was performed in 1849 by Hullihen. Since then, many different mandibular osteotomy methods have been developed; however, the sagittal osteotomy design of the ramus described by Trauner and Obwegeser in 1955 has become the most popular method. This osteotomy design has undergone various modifications over time. The original osteotomy design by Trauner and Obwegeser has evolved over time with various improvements by Dal Pont, Hunsuck, and Epker to its present form.[1,2]

Today, SSRO is the most frequently used method among mandibular orthognathic surgical techniques. Various movements can be achieved in the mandible with SSRO. The main indications for this method are:

1. Cases of mandibular retrognathia where the mandible needs to be moved forward.
2. Cases of mandibular prognathia where the mandible needs to be moved backward.
3. Cases of mandibular asymmetry.

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In addition to these indications, there are some contraindications:

1. Situations where the height of the ramus is significantly insufficient.
2. Cases where the mediolateral dimension of the ramus is thin.
3. Patients with advanced ramus hypoplasia.[1,3]

While this technique offers a series of advantages, it also harbors potential disadvantages and risks. A comprehensive evaluation of SSRO will help determine the potential benefits and complications of using this method.

Advantages of SSRO include:

1. Allows movement of the distal segment in all three planes.
2. The post-surgical healing process occurs rapidly.
3. Enables positioning of the segments in the desired position during the operation.
4. Causes minimal changes in the muscles. As a result, the risk of relapse is low.
5. Allows for the preservation of the natural position of the temporomandibular joint.
6. The operation duration is short and the complication rate is low.[4,5]

Disadvantages of SSRO include:

1. There is a risk of temporary or permanent nerve damage in the inferior alveolar nerve.
2. Malocclusion can occur as a result of incorrect condyle positioning.
3. Unwanted fractures and separations can occur during the operation.[6,7]

The SSRO procedure is a technique that allows for the repositioning of the mandible and is performed with bone cuts in the sagittal plane. This procedure is done with the aim of bringing the mandible to a more aesthetically and functionally ideal position. However, this procedure requires the repositioning of the mandible in a precise and accurate manner while preserving anatomical and neural structures. For this reason, high surgical skill and detailed planning are necessary. It is essential for surgeons to conduct a comprehensive evaluation to determine the most appropriate treatment method for each patient.[3]

WHAT IS FIXATION?

During orthognathic surgery, the immobility of the created segments is ensured by fixation methods until the healing process is completed in the post-operative period. Ensuring the fixation of the segments in the correct anatomical position is extremely important.[1,8]

After SSRO fixation, rotation can occur in the segments. The proximal segment undergoes counterclockwise rotation because it is pulled anterior-superiorly by the masseter and temporal muscle fibers. The distal segment undergoes counterclockwise rotation as well, due to being pulled posterior-inferiorly by the mylohyoid, geniohyoid, genioglossus, and suprahyoid muscles. As a result of these rotation movements, relapse occurs. Relapse is a multifactorial outcome. Relapse occurring within the first 6 months post-operation is termed early-period relapse, while that occurring after 6 months is termed late-period relapse. Among the causes of relapse after SSRO, the chosen fixation technique, insufficient stabilization of fragments, and muscle and soft tissue tensions play a significant role. Currently, it is known that relapse occurs and ramus height decreases due to the inability to position the condyle ideally.8,9 It is reported that the highest rate of relapse in orthognathic surgery occurs in the 2nd postoperative month. Therefore, the impact of different fixation methods on skeletal stability has pushed many clinicians and researchers to search for the ideal fixation system.[1,8]

An ideal fixation system should allow the patient to move their jaw in the early postoperative period, maintain facial ratios and occlusion, be easy to apply, be cost-effective, be compatible with facial tissues, and minimize the risk of infection. In addition, it should provide maximum resistance to masticatory forces and induce minimal stress in surrounding tissues. However, to this day, there is no fixation system that fully conforms to these criteria. When selecting a fixation system, a choice should be made taking into consideration the patient's general health, age, gender, bone quality, treatment objectives, anatomical structure, desired level of stability, postoperative relapse risk, and the surgeon's experience and preferences.[1,3]

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FIXATION RIGIDITY

Non-Rigid Fixation

It's a type of fixation that is not rigid enough to completely prevent movement between fragments while the skeletal structure is actively in use. This movement constitutes the primary difference between rigid and non-rigid fixation.

Wire fixation is an example of non-rigid fixation applied in mandibular fractures. This type of fixation can provide stability by preventing the expansion of the gap, but it cannot neutralize torsional and shearing forces. Additional fixation methods, such as maxillomandibular fixation (MMF), are needed to neutralize such forces.

As a result of the application of non-rigid fixation, there is slight mobility between fragments, hence healing occurs as secondary bone healing. In secondary bone healing, a tissue called periosteal callus forms. This process involves tissue differentiation that goes through various stages, including resorption and fibrous healing around the bone fragment.[1,10]

Semi-Rigid Fixation

It's a type of fixation that is strong enough to allow active movement of the skeletal structure during the healing period but not stable enough to prevent movement between fragments. Such fixations are referred to as functional stabilization. Although they might not provide enough stability for direct bone healing, they offer a level of stability that permits functional movement. The application of a single mini-plate in fractures of the mandibular angle or mandibular body can serve as an example of semi-rigid fixation. Even though there's movement between fragments in this type of fixation, clinical outcomes have been observed to be extremely successful. In an area where semi-rigid fixation is applied, secondary bone healing occurs.[1,10]

Rigid Fixation

Rigid fixation can be defined as a type of fixation that allows active use of the skeletal structure, is strong enough to prevent the movement of mobile fragments, and is applied directly to the bones. This definition encompasses the anatomically correct positioning of bone fragments through surgical intervention and their stable fixation. Examples of rigid fixation applications in the mandible include the combined use of plates and screws, and the application of 2 lag screws.

During rigid fixation, there is no callus formation during bone healing. The bone healing that occurs as a result of rigid fixation is referred to as primary (direct) bone healing. For primary bone healing to commence, perfect immobilization between bone fragments must be ensured, and there should be minimal gap between the fragments.[1,10]

FIXATION METHODS USED AFTER SSRO:

1. Rigid Intermaxillary Fixation
2. Osteosuture (Fixation with wire)
3. Osteosynthesis (Bicortical screw, use of Plates and Monocortical screws, Hybrid Systems)
4. Resorbable Systems

Rigid Intermaxillary Fixation

Rigid intermaxillary fixation is currently used in conjunction with wire fixation. In the past, although rigid intermaxillary fixation was used after SSRO surgeries, a relapse rate of 90% was observed. The bone segments were not stable after fixation, leading to movements in the proximal and distal segments exposed to muscle and soft tissue tension during the postoperative period. As a result, adequate stabilization could not be achieved. Moreover, rigid intermaxillary fixation, which is done by taking force from natural teeth, led to the extrusion of the teeth and encountered relapse. The inability to achieve sufficient stabilization and the resulting relapse suggested that rigid intermaxillary fixation was not adequate for fixation after SSRO, pushing surgeons to seek new methods.[11,12]

Osteosuture (Wire Fixation)

The initial wire fixation was done to support maxillomandibular fixation by passing the wire through the priform rim and circummandibularly binding it to the premolar and molar teeth. Subsequently, wire fixation applications have been performed in various regions and configurations. Wire fixation has generally been used in surgical operations where the mandible is moved backward.[1,10]

Osteosynthesis (Bicortical screw, Use of plates and monocortical screws, Hybrid Systems)

The inability of rigid intermaxillary fixation and wire fixation to provide adequate stability has pushed surgeons to seek more stable, rigid, and reliable fixation systems. In 1974, Spiessel

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described a fixation method using lag screws to accelerate healing and enhance stability. In 1978, the use of positional screws began due to concerns that lag screws generated torque in the condylar segment and caused damage to the inferior alveolar nerve. From the 1980s onwards, the use of monocortical screw and plate fixation has started.[11,13,14]

Screws

Screws used in orthognathic surgery are employed for the fixation of plates to the bone or for keeping bone fragments together. Monocortical screws and bicortical screws are frequently used in orthognathic surgery. Screws are typically named based on the external diameter of the thread. The diameter of screws used in orthognathic surgery usually ranges between 1.0 mm and 2.7 mm. In the event of fixation failure, there are emergency screws available that are larger than the screw previously used. Based on their placement into the bone, screws are classified as self-drilling and self-tapping.[14] (Figure 1)

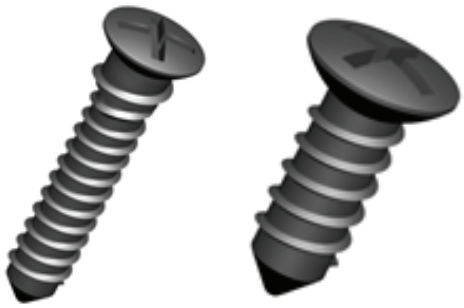

Figure 1. Bicortical Screw Monocortical Screw

Bicortical Screws

In orthognathic surgery, the application of bicortical screws initially began with the use of lag screws. Lag screws work on the principle of pulling bone fragments towards each other, hence they are also referred to as pull screws. Lag screws have threads only at their distal end, and when fixation is applied, they cause compression in both proximal and distal segments. The use of lag screws ensures rigid fixation of bone fragments and, due to the high level of bone contact, they also initiate primary bone healing. For lag screws to be used, both bone segments need to have a thick cortical structure. For the screw to fulfill its lag function, it needs to transition from a wider groove to a narrower one, resulting in pressure between bone segments upon fixation. Among the advantages of lag screws are that they provide an extremely rigid fixation, have a relatively low cost, and require minimal equipment.[1,15]

However, there are also several disadvantages to using lag screws. In cases where there is a gap between bone segments, displacement can occur in both the proximal and distal segments as a result of lag screw application. Since lag screws operate on the principle of compression, damage can occur in the inferior alveolar nerve that lies between bone segments.[3,16] Moreover, studies have shown that the use of lag screws in mandibular advancement can lead to temporomandibular joint dysfunction and condylar displacement due to their compressive effects.[11]

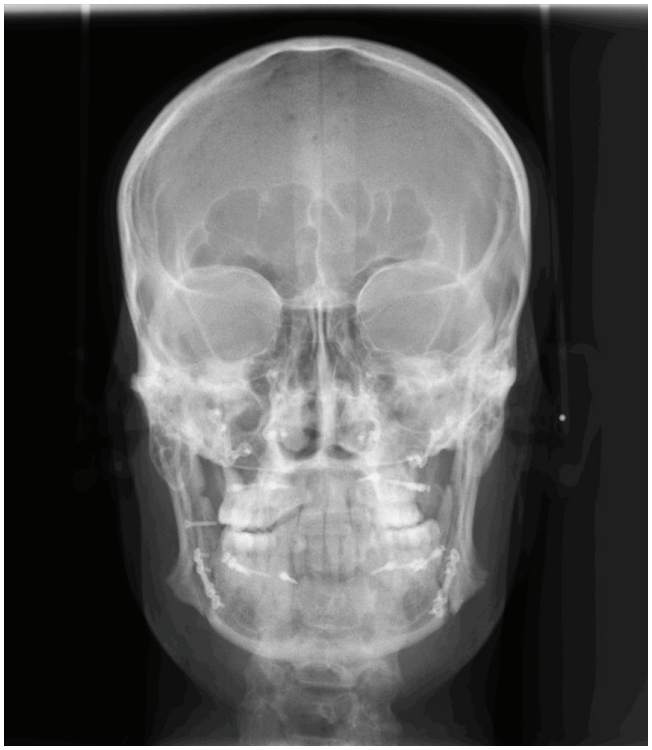

Figure2. Bicortical screw application after SSRO surgery

To avoid the drawbacks of lag screws, the use of positional screws came into play in subsequent years. Positional screws anchor to both the distal and proximal segments. The screw hole is prepared with an equal diameter in both segments. Unlike lag screws, positional screws do not cause compression in the distal and proximal segments during fixation. Since no

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compression occurs in positional screw fixation, no torque is generated in the segments or condyle. Additionally, it has been observed that the risk of nerve damage due to positional screw fixation is significantly reduced compared to lag screw fixation. However, in positional screw applications, if the segments are not aligned properly, they can drift apart. Because there's no pulling force resulting from fixation, it's extremely difficult to determine if the screw has anchored to the medial segment. Even if the screw doesn't attach to the medial segment, it can still lodge in the lateral cortex.[3,17] (Figure 2)

After SSRO, 2 or 3 bicortical screws are typically used for fixation. Bicortical screws can be placed in linear, reverse L, and L positions.(Figure3,4)

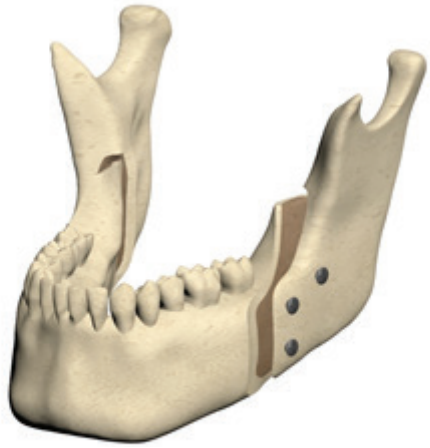

Figure 3. Application of 3 bicortical screws in inverted L position after SSRO

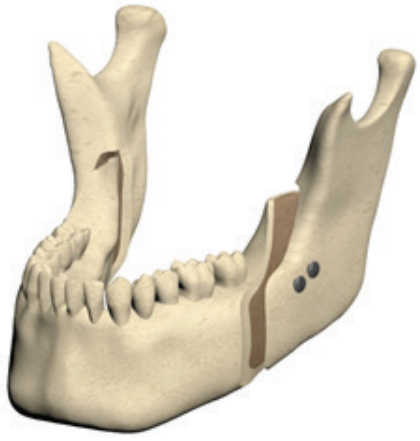

Figure 4. Application of 2 bicortical screws in linear position after SSRO

Plates

Due to anatomical restrictions, the challenge of applying bicortical screws over time has led to the use of plates in orthognathic surgery. The plates used in orthognathic surgery differ in terms of size, shape, and purpose of use. In craniofacial regions, plates are used in flat, X, Y, double Y, H, and L configurations. The thickness of these plates typically varies between 0.5 mm and 0.9 mm. Plates used in mandibular orthognathic surgery are designed as 1-1.5 mm thick microplates and 2.0 mm thick mini plates.(Figure 5) Plates used in mandibular orthognathic surgery provide functionally stable fixation that allows bone compatibility and bone healing.[3,14]

Figure 5. 4-hole conventional miniplate

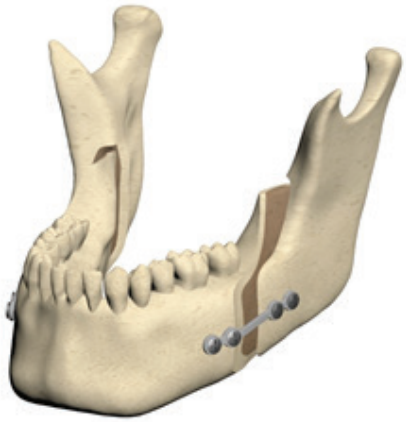

Figure 6. 4-hole conventional miniplate application after SSRO surgery

In 1973, Michelet and colleagues first recommended mini plate and monocortical screw fixation after SSRO.[18]

Mini plates are a routinely used fixation system in mandibular orthognathic surgery. Mini plates used in mandibular orthognathic surgery are available as 2-hole, 3-hole, 4-hole, 6-hole, and 8-hole.[10] (Figure 6) They can be categorized

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as conventional mini plates and locked mini plates. In conventional mini plate systems, the plate is pressed towards the bone as a result of the fixation with a monocortical screw. Primary stability is provided by this pressure. The plates must be positioned correctly onto the bone. Incorrect positioning of plates results in a loss of stability. Due to their design, stability loss is more frequent in conventional plates compared to locked plate systems. In locked plate systems, screws hold onto both the plate and the bone. In this type of fixation, the plate does not exert pressure on the bone. Therefore, bone nutrition is higher and the likelihood of screw loosening is lower.[14]

The advantages of using mini plates after SSRO include the ability to place them intraorally, the ability to adjust the position of the distal and proximal segment in the early period, the low risk of damage to the inferior alveolar nerve, the ability to remove the plate and monocortical screw under local anesthesia, and causing minimal displacement in the condyle. On the other hand, disadvantages include plates showing less stability compared to bicortical screws, susceptibility to infection, inability to withstand chewing forces leading to breakage, and thermal sensitivity.[1]

Hybrid Systems

Hybrid fixation is a fixation method that involves the combined use of plates, monocortical screws, and bicortical screws. In this method, the aim is to increase the existing stability by utilizing the advantages of plates and bicortical screws and to distribute the resulting stresses homogeneously. The hybrid fixation technique was first introduced by Schwartz and Relle in 1996. In their study, the researchers suggested stabilizing the segments with a mini plate after bringing the segments to the correct anatomical position and then providing rigid fixation with bicortical screws. According to the results of the study, they reported that hybrid fixation increased stability and reduced the risk of postoperative recurrence.[19] (Figure 7)

Resorbable Systems

In the face of infections, inflammations, and toxic reactions seen in fixation systems made of titanium and stainless steel, the use of resorbable materials in orthognathic surgery has come to the fore. These materials are derived from Polyglycolic Acid (PGA) and Poly-L Lactic Acid (PLLA). It was believed that plates and screws made of these materials could successfully stabilize the segments 6-8 weeks after surgery. Resorbable materials dissolve into water and carbon dioxide, eliminating the need for a second surgery to remove the materials. In addition, there are disadvantages of resorbable materials such as being palpable from tissues due to their thickness, high cost, and thermal sensitivity.[4,20,21]

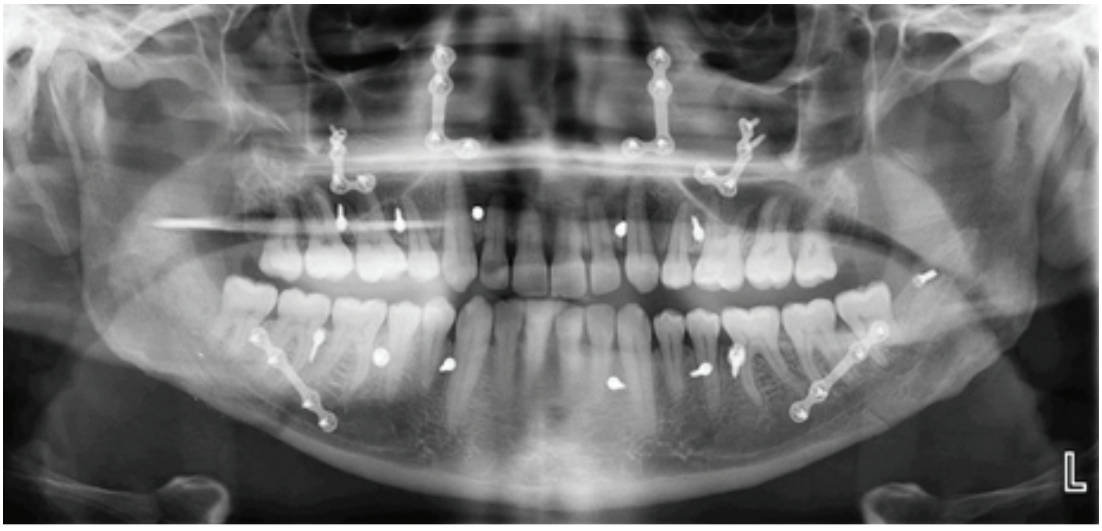

Figure 7. Hybrid fixation application after SSRO surgery

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DISCUSSION

Since its description by SSRO, Trauner, and Obwegeser in 1955, the SSRO technique has become a significant method in correcting mandibular deformities. This technique is widely preferred among surgeons for correcting various mandibular deformities such as congenital or acquired hypoplasia, hyperplasia, and asymmetry. Despite its advantages like high healing potential and ease of use, ongoing debates persist regarding the choice of fixation method. Stability plays a critical role in the success of repositioning mandibular segments after osteotomy. Despite extensive research on the ideal fixation technique, a general consensus has not yet been reached. Traditionally, fixed orthodontic appliances, modified splints, and occlusal splints have been used, but the development of rigid internal fixation systems like bicortical screws and miniplates has surpassed these practices.[1,3]

In 1974, the rigid internal fixation method described by Spiessl and Tschopp improved the reliability and stability of SSRO. During this period, various fixation techniques were used, such as screws placed in a reverse L shape and linearly on the upper border to maintain the new skeletal position. However, complications associated with bicortical screw usage have led surgeons to explore alternative techniques. Since the 1980s, new fixation systems like miniplates and monocortical screws have been introduced to avoid these complications.[13,22]

In a study conducted by Dolce et al. in which they compared wire fixation and bicortical screw fixation in patients undergoing mandibular advancement with SSRO, it was reported that wire fixation resulted in a 42% recurrence rate after 5 years. Researchers believed that wire fixation did not provide adequate stability after mandibular advancement.[23]

Watzke et al. compared bicortical screw and wire fixation for stability in patients undergoing mandibular advancement with SSRO at postoperative 6 weeks and 1 year. The study found that bicortical screw fixation was more stable, with a 15% recurrence rate associated with wire fixation.[11]

In a study by Maurer et al. in 2003, they compared the placement of three bicortical screws in a reverse L position with conventional miniplate fixation using finite element analysis after SSRO. The study concluded that bicortical screw fixation provided more stable results against chewing forces.[24]

Peira Filho et al. compared three different fixation methods after SSRO in a 2013 study. They applied force to polyurethane mandible models until a 10 mm displacement occurred. The study concluded that the placement of three bicortical screws in a reverse L position was more stable than a 4-hole conventional miniplate and a sagittal split sliding plate.[25]

In a study conducted by Sindel and colleagues in 2014, they compared the effects of bicortical screw configurations on stability after SSRO. According to the results of the study, it was reported that the configuration with 3 bicortical screws placed in a reverse L position was the most stable, followed by 3 bicortical screws placed in an L position and 3 bicortical screws placed linearly.[26]

The use of bicortical screws has limitations due to the need for extraoral access, the risk of nerve damage, the possibility of bone resorption caused by stress, and the potential to increase temporomandibular joint disorders. However, in vitro and clinical studies have reported no statistically significant difference in postoperative changes between bicortical screw and miniplate fixation techniques.

In a study by Olivera et al. in 2012, they compared the biomechanical results of three fixation methods (three bicortical screws in a reverse L position, hybrid fixation, and two 4-hole conventional miniplates) in a sheep mandibular model undergoing 5 mm mandibular advancement with SSRO. The study found that all three fixation systems provided similar biomechanical results until a bone fracture occurred in the second molar region.[13]

Furthermore, a prospective multicenter study by Borstlap et al. reported that miniplate fixation after SSRO provided sufficient stability and high patient satisfaction, making it a reliable method.[27]

In the future, it has been suggested that the use of bicortical screws in addition to the miniplate system may have a positive effect on stability, and the use of hybrid fixation is recommended to take advantage of the benefits of both systems. With hybrid fixation, the goal is to achieve more effective stability in orthognathic surgery by combining the high stability provided by bicortical screw fixation with the minimal invasiveness and ease of use of miniplates.[19]

In a study by Oğuz et al. in 2015, they compared six different fixation methods in mandible models undergoing 5 mm advancement after SSRO. Hybrid fixation was used in one group, while various types of plate fixation were used in five groups. The study concluded that hybrid fixation provided

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better stabilization values compared to plate fixation.[28]

The use of resorbable materials has increased in fixation systems due to complications such as infection, inflammation, and toxic reactions associated with titanium and stainless steel fixation systems.[21,29]

Ueki et al. evaluated the stability of titanium plate and resorbable plate fixation after SSRO in a sheep mandibular model. The study found no recurrence in either group at the end of the first year.[30]

Despite numerous experimental and clinical studies on fixation systems after SSRO, there is still no consensus on the most ideal method among the fixation techniques. This indicates that the effort to determine the most suitable method among existing methods continues.

RESULTS

Since the time SSRO was defined, the choice of fixation type and its rigidity post-operation has remained a subject of debate. Despite clinical applications and experimental/mechanical studies on various fixation systems, an ideal fixation system has not yet been determined.

While immediate stability may provide insights into long-term stability, the applicability and success of a fixation system should be evaluated on a case-by-case basis. In the past, the cause of relapse occurring either early or late was often attributed to the rigidity of the fixation system. Today, condylar resorption can occur due to the inability to correctly position the condyle, leading to relapse. It is believed that maintaining condylar position in cases where the mandible is set back and using semi-rigid fixation can prevent relapse. However, in cases where the mandible is advanced, especially in severe cases, the rigidity of fixation remains important. Various systems are used to increase fixation rigidity, and fixation with three bicortical screws placed in a reverse L configuration, which is the most rigid stabilization method, may not always yield ideal results. This is because of the challenges posed by bicortical screw fixation in clinical practice and the difficulty in positioning the condyle in the ideal position. Therefore, fixation with monocortical screws and miniplate fixation or hybrid systems have become more popular alternatives.

As a general conclusion from these studies, it is evident that the selection of a fixation system tailored to the specific case is critical for the success of the operation. When choosing a fixation system after SSRO, factors such as fixation rigidity, relapse, cost, surgical experience, ease of application, and aesthetic concerns should be taken into consideration.

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