CASE SERIES STUDY

https://doi.org/10.5125/jkaoms.2024.50.6.350
pISSN 2234-7550 · eISSN 2234-5930

Delayed inflammation after biodegradable and osteoconductive osteofixation in orthognathic surgery

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Abstract (J Korean Assoc Oral Maxillofac Surg 2024;50:350-355)

Objectives: This study aims to identify patterns and to describe the clinical course of delayed adverse tissue responses in patients who underwent orthognathic osteotomy with biodegradable osteofixation.

Patients and Methods: Through a retrospective review of cases between 2013 and 2020, we identified three patients who underwent bimaxillary osteotomy and fixation with unsintered-hydroxyapatite/poly-L lactic acid (u-HA/PLLA) devices, after which they developed delayed inflammation. These lesions were treated with drainage and/or removal of the devices. Histological evaluations were conducted using H&E staining, and structural changes in the u-HA/PLLA devices were assessed by scanning electron microscopy (SEM).

Results: Inflammatory lesions developed only in the mandible, with onset ranging from 12 to 35 months postoperation. Histological studies identified foreign-body granulomas or secondarily infected lesions. SEM analysis indicated biodegradation and tissue integration.

Conclusion: Orthognathic patients treated using u-HA/PLLA devices should be informed about the potential for delayed inflammation and monitored for at least 3 years.

Key words: Biodegradable osteofixation, Delayed inflammation, Foreign-body reaction

[paper submitted 2024. 9. 3 / accepted 2024. 10. 3]

I. Introduction

Orthognathic surgery requires stable osteofixation for effective bone healing and remodeling. Traditionally, titanium plates and screws have been considered the “Gold Standard” for rigid fixation. However, problems associated with titanium plating systems include thermal sensitivity, growth restriction of surrounding bony tissues, interference with radiographic imaging, and screw migration[1]. Additionally, a report indicated that titanium miniplates are a risk factor for bisphosphonate-related osteonecrosis of the jaw[2]. As a result, titanium internal fixators often must be removed in a secondary operation.

Biodegradable plates have been introduced as an effective alternative to titanium devices, addressing many of these issues. Since 2000, innovative biodegradable materials have been increasingly utilized in orthognathic surgery[3,4] with the advantage of no need for device removal. However, drawbacks of biodegradable plates include weaker mechanical properties compared to titanium alloys and a delayed inflammatory response. Numerous clinical studies have demonstrated comparable stability between biodegradable and titanium osteofixation in orthognathic surgery[5,6].

Nevertheless, descriptive information on delayed inflammation following biodegradable osteofixation in orthognathic surgery patients is sparse. This study reviews three patients who underwent biodegradable and osteoconductive osteofixation after orthognathic osteotomy and exhibited delayed inflammatory responses.

II. Patients and Methods

A retrospective review of patients with dentofacial deformities operated on by a single surgeon between 2013 and 2020, was conducted. Three patients were identified who

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underwent bimaxillary orthognathic osteotomy and fixation with unsintered-hydroxyapatite/poly-L lactic acid (u-HA/PLLA) devices, subsequently developing adverse tissue reactions. These lesions were treated with debridement and/or removal of the fixation devices. Histological evaluations were performed using H&E staining, and structural changes of the devices were assessed using scanning electron microscopy (SEM). Written informed consent was obtained from all patients, and this study was approved by the Institutional Review Board (IRB) of Gangneung-Wonju National University Dental Hospital (IRB No. GWNUDH-IRB2024-A007).

III. Results

1. Case 1

A 23-year-old male patient was referred to our department for a surgery-first orthognathic procedure due to bimaxillary protrusion. Maxillomandibular osteotomies were performed for maxillary posterior movement, mandibular setback, and advancement genioplasty. Mini-sized u-HA/PLLA plates were used for maxillary fixation, and u-HA/PLLA mesh (Osteotrans MX; Takiron) was used for mandibular fixation. Twenty months later, a well-defined, painless swelling was noted on both sides of the mandibular vestibules.(Fig. 1. A, 1. D) Debridement and device removal were performed under local anesthesia (Fig. 1. B, 1. E) and prophylactic antibiotics were prescribed. H&E staining demonstrated multi-nucleated giant cells phagocytosing foreign granular materials with inflammatory cell infiltration, indicative of a foreign-body reaction.(Fig. 1. C, 1. F) SEM imaging of the explanted u-HA/PLLA mesh revealed that the device surface was disintegrating and pores had formed.(Fig. 2. A-2. C) At higher magnification, fibroblasts and exosomes were attached to the surface (Fig. 2. D) and fibrin coagulation materials formed bundles, indicating that the organization process was in progress.(Fig. 2. E, 2. F) However, osteoconductive changes were not detected. This patient experienced a second episode of chronic inflammation 34 months after the operation, and a second debridement was performed.(Fig. 3)

2. Case 2

A 29-year-old male was referred to our department due to mandibular prognathism. Maxillomandibular osteotomy was performed for maxillary posterior impaction and mandibular setback. Osteofixation was completed using u-HA/PLLA devices according to our protocol[6]. Twelve months later, a well-defined, painless swelling was observed on the left-side sagittal spliting ramus osteotomy (SSRO) site.(Fig. 4. A) The inflammation was resolved with drainage and anti-inflammatory medication without device removal. H&E staining

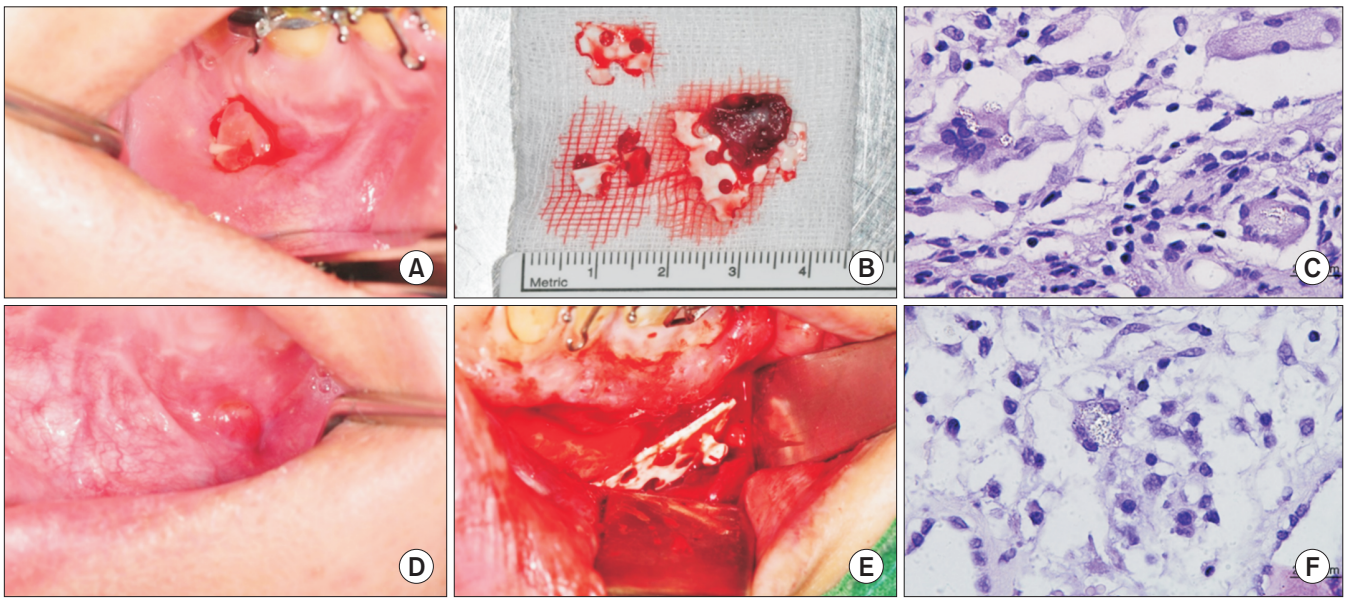

Fig. 1. A, D. A localized mucosal swelling was observed on both sides of the mandibular vestibule. B, E. Removal of the fixation devices was performed. Multi-nucleated giant cells were observed phagocytosing granular-shaped foreign materials, accompanied by inflammatory cell infiltration (H&E staining; C, F: ×100).
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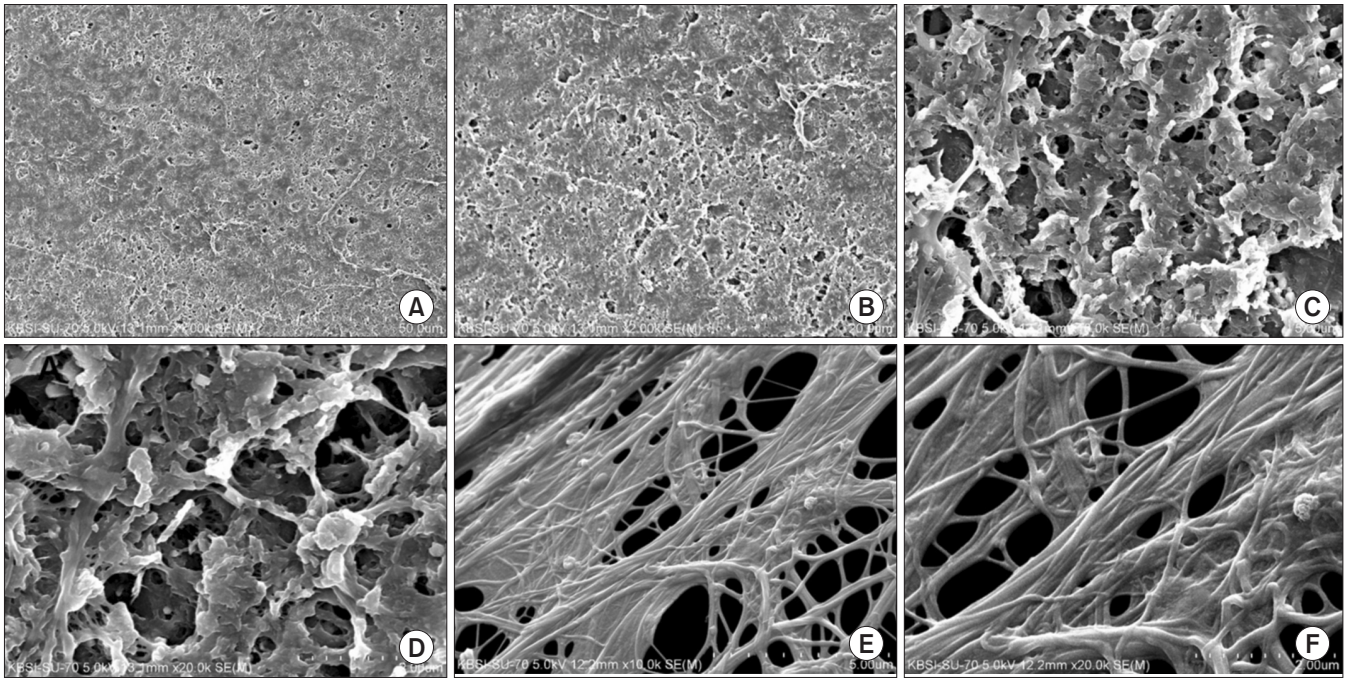

Fig. 2. Scanning electron microscopy images of the explanted unsintered-hydroxyapatite/poly-L lactic acid (u-HA/PLLA) nanocomposite at increasing magnifications 20 months after surgical implantation. At lower magnification (A-C), the surface of the device appears roughened with pores. At higher magnification, cells and exosomes are observed attached to the surface (D), and fibrous fibers have formed bundles and adhered to the surface of the u-HA/PLLA nanocomposite (E, F).
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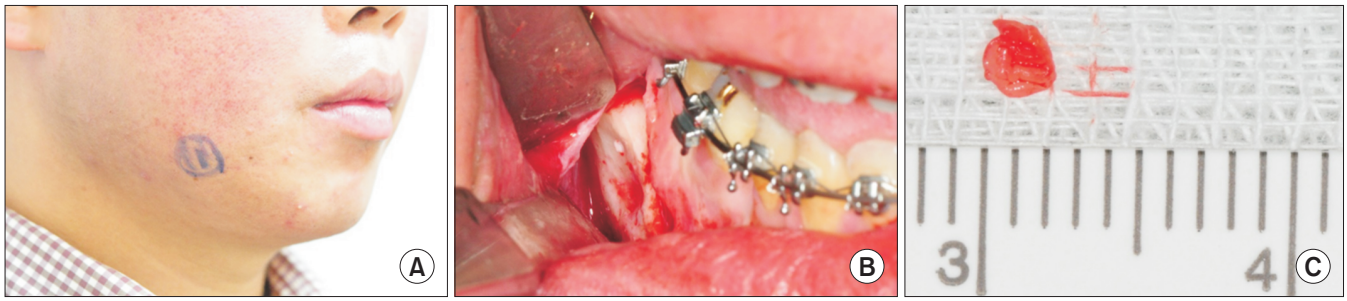

Fig. 3. A. Thirty-four months after the operation, the patient in Case 1 complained of a palpable swelling in the right-side lower chin area (marked area). B. A piece of the remaining u-HA/PLLA screw was observed. C. A second debridement was performed.
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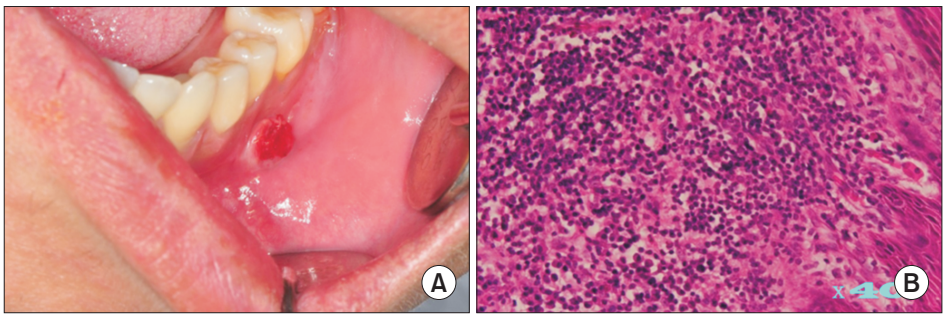

Fig. 4. A. A papule-like mucosal swelling was observed in the left-side mandibular vestibule. B. The lesion exhibited a granuloma with proliferation of plasma cells and lymphocytes (H&E staining, ×40).
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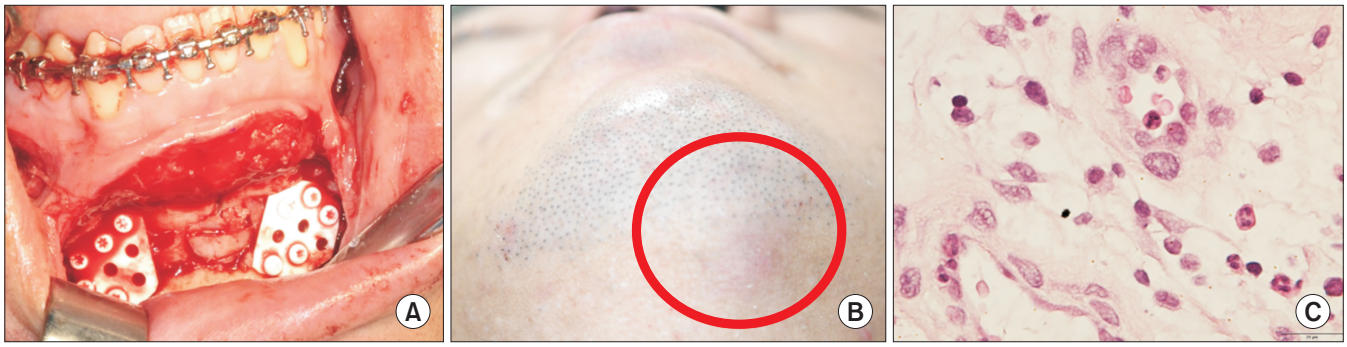

Fig. 5. A. Unsintered-hydroxyapatite/poly-L lactic acid meshes were applied for fixation of the genial osteotomy. B. Thirty-five months after the operation, a diffuse swelling was detected in the left lower chin area (red circle). Initially, partial debridement was performed through an intraoral vestibular incision. However, the symptoms persisted, and a second debridement was carried out. C. The specimens from the second debridement revealed a suppurative lesion with proliferation of polymorphonuclear leukocytes, plasma cells, and small capillaries (H&E staining, ×100).
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revealed a chronic inflammatory lesion with plasma cell and small lymphocyte infiltration.(Fig. 4. B)

3. Case 3

A 23-year-old male patient visited our department for correction of secondary maxillary hypoplasia due to a unilateral cleft deformity. Cleft orthognathic surgery was performed with maxillary advancement, mandibular setback, and reduction genioplasty. Osteofixation was completed using u-HA/PLLA devices.(Fig. 5. A) Thirty-five months later, the patient complained of diffuse swelling on the left side of the lower chin area.(Fig. 5. B) The lesion was initially treated with repeated drainage and later with removal of the u-HA/PLLA mesh under conscious sedation. H&E staining revealed a pus-discharge lesion with loose stroma and proliferation of polymorphonuclear leukocytes and small capillaries.(Fig. 5. C) The symptoms resolved after removal of the partially resorbed devices on the left side of the chin, with no recurrence over 14 months of follow-up.

IV. Discussion

This study aimed to evaluate the inflammatory complications of biodegradable osteofixation devices, particularly u-HA/PLLA, in orthognathic surgery. The results indicate that, while u-HA/PLLA fixation devices offer the advantage of avoiding secondary surgery for removal, they are associated with delayed inflammatory reactions, especially in the mandible. This study also explores potential mechanisms and provides clinical recommendations based on the findings.

In 1966, polylactic acid was first proposed for surgical implants in an animal experiment[7]. Subsequently, three biodegradable materials, polyglycolic acid (PGA), PLLA, and poly-D-lactic acid (PDLA), have been widely used in clinical settings. These materials are metabolized via hydrolysis and are excreted by the lungs as carbon dioxide and water following the citric acid cycle. The rate of biodegradation depends on the crystallinity and hydrophobicity of the hydrolyzed products[8]. PDLA, an isomeric form of PLLA, shares the same molecular formula but has different spatial orientations of optically active carbon atoms, resulting in different biomechanical and degradation properties. Degradation of PLLA releases crystalline particles that are highly hydrophobic and more resistant to degradation compared to PDLA[9]. As a result, foreign-body reactions, although not highly irritable to host cells, are frequently reported with the use of PLLA due to its prolonged degradation period[10,11].

Over the decades, biodegradable devices have evolved, exhibiting improved degradation rates and decreased adverse tissue reactions by altering the constituent ratios. The polymer ratio scan affects the host's immunological response to biodegradable implants. Between 2002 and 2012, the author used second-generation bioresorbable poly-L/D-lactide plates consisting of 70% PLLA and 30% PDLA without observing delayed inflammatory responses. This could be attributed to the amorphous structure of the copolymer, which does not release crystalline particles[12].

In 1999, hydroxyapatite was physically incorporated into PLLA due to its documented osteoconductive properties. The material used in the study was au-HA/PLLA nanocomposite[13]. Clinically, the degradation period of u-HA/PLLA is longer than 5.5 years[14], potentially leading to foreign-body reactions as a low degradation rate is related with increased

metabolite accumulation. At a later stage of u-HA/PLLA biodegradation, the disintegrated PLLA undergoes enzymolysis. In this decomposition stage, the host tissue's clearance capacity may be overloaded, increasing the risk of adverse tissue reactions[15]. The remaining crystalline PLLA particles may trigger a foreign-body tissue reaction, and the uneven release of PLLA fragments can provoke a physical inflammatory response.

An ideal biodegradable fixation device should fully resorb once the bone healing process is complete, with resulting metabolites causing no local or systemic reactions. A delayed foreign-body reaction is defined as inflammatory symptoms occurring 6 months after implantation and typically does not involve infection[16]. In present study, the onset of inflammation occurred 20, 12, and 35 months after the operations, with the spectrum of adverse tissue responses ranging from localized nonspecific inflammation (Case 2) to severe foreign-body reactions necessitating device removal (Cases 1 and 3). The timing of the tissue reaction and the clinical findings of fragmented u-HA/PLLA devices in Cases 1 and 3 indicate a foreign-body reaction during the late degradation process, while the relatively early-stage reaction in Case 2 is notable.

The management of delayed inflammation varied according to the clinical manifestations. Mild-to-moderate inflammation (Case 2) may be treated with drainage and anti-inflammatory drugs. However, severe or recurrent inflammation (Case 1) and/or secondary infections (Case 3) require device removal. In this study, histological findings in Case 1 were consistent with those typically observed in aseptic foreign-body reactions, demonstrating foreign particles surrounded by multinucleated giant cells with inflammatory cell infiltration. The lesion in Case 2 developed 12 months after implantation, likely due to acidic metabolites such as fragmented lactic acid, which can evoke inflammation and recruit inflammatory cells, as seen in the histologic specimen. This phenomenon can lead to the accumulation of sterile fluid, necessitating surgical drainage. The histological findings in Case 3 revealed a suppurative lesion, likely due to secondary inoculation of intraoral pathogens through an intraoral incision. SEM images from Case 1 revealed that the implant was undergoing biodegradation and was well-integrated with the surrounding host tissues.

Factors such as the degradation rate of polymers, implant volume and shape, and recipient environment may affect the occurrence of foreign-body reactions[17]. A low degradation rate is associated with increased accumulation of metabolites, which can increase the risk of adverse reactions, as described above. If the volume and shape of the devices allow accumulation of sterile fluid from an immunological reaction, the clearance capacity of the host tissue may decrease, leading to clinical symptoms. Considering the shape of the device, the mesh plate used in this study may be more advantageous than other forms of u-HA/PLLA devices due to its even release of metabolites. Most studies reported a less than 5% occurrence rate of delayed inflammation in patients with biodegradable plates. However, no adverse tissue reactions occurred in 44 pediatric patients with facial fractures[18], reflecting more favorable recipient environments.

In this study, delayed inflammation occurred only in the mandible and did not occur in the maxillary fixation site, which was fixed with four u-HA/PLLA plates in the standard position. The author suggests that the coarse structure and high vascularity of the maxillary bone may prevent the accumulation of exudate from a foreign-body reaction. However, the rate of delayed foreign-body reactions caused by biodegradable PLLA/PGA or PLDLA/trimethylene carbonate plates is 3.4% among 234 patients with zygomaticomaxillary fractures[19]. We also suggest that there are differences in the characteristics of patient groups between those undergoing orthognathic surgery and trauma patients. In general, the orthognathic surgery patient group is within an age range that has a stronger immune system compared to the trauma patient group. In this study, the incidence of delayed inflammatory reactions at the SSRO site is less than 1%.

Additionally, the risk of foreign-body reactions appears to be independent of gender[20] even though all three patients in this study were male. However, it has been reported that smokers have a higher rate of delayed inflammatory reactions compared to nonsmokers[21]. The severity of inflammatory responses varies among individuals, likely due to the differences in immune status, including hyper-reaction and sensitivity to degradation products. The patient in Case 1 exhibited bilateral and repeated occurrences of delayed inflammation, and the source of the second inflammation was possibly a residual u-HA/PLLA screw, as seen in Fig. 3. B. It is possible that this patient had a genetic predisposition to sensitivity to PLLA metabolites, which warrants further study.

V. Conclusion

The author encountered three cases of delayed inflammation following orthognathic osteotomy and u-HA/PLLA osteofixation. The lesions occurred only in the mandible and were treated uneventfully with routine drainage and/or de-

vice removal without further complications. It is important to inform orthognathic patients undergoing u-HA/PLLA osteofixation about the possibility of delayed inflammation, and long-term follow-up is recommended.

Author's Contributions

Y.W.P. performed the operation and wrote the manuscript.

Funding

No funding to declare.

Ethics Approval and Consent to Participate

Written informed consent was obtained from all patients, and this study was approved by the Institutional Review Board (IRB) of Gangneung-Wonju National University Dental Hospital (IRB No. GWNUDH-IRB2024-A007).

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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How to cite this article: Park YW. Delayed inflammation after biodegradable and osteoconductive osteofixation in orthognathic surgery. J Korean Assoc Oral Maxillofac Surg 2024;50:350-355. https://doi.org/10.5125/jkaoms.2024.50.6.350