

Unexpected Bone Resorption in Mentum Induced by the Soft-Tissue Filler Hyaluronic Acid: A Preliminary Retrospective Cohort Study of Asian Patients

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Background: As one of the most commonly used soft-tissue fillers, hyaluronic acid is generally considered safe and efficacious. However, evident bone resorption in mentum was observed. In this study, the authors analyzed the impact of hyaluronic acid on bone resorption in mentum and the influencing factors.

Methods: The authors retrospectively compared the computed tomographic scans of patients with or without mentum augmentation using hyaluronic acid. The body mass index- and sex-matched control group was selected randomly. Semimandibular bone resorption index was calculated as the ratio of bone thickness in the incisive fossa to that in the mandibular symphysis. Injection volume, injection interval, the number of injections, product, complication were also recorded.

Results: From January of 2014 to June of 2019, 80 patients (160 cases) and 80 controls were recruited. The bone resorption index in the hyaluronic acid injection cohort was significantly lower than in the controls (75.25 ± 10.02 versus 82.86 ± 6.38 ; $p = 0.000$). Patients injected with greater than or equal to 1 ml per time were more susceptible to bone erosion compared with patients injected with less (68.89 ± 10.84 versus 76.49 ± 9.42 ; $p = 0.000$). There was no significant difference between one- versus multiple-injection groups and short-injection-interval versus long-injection-interval (≥ 6 months) groups. Furthermore, no reduced aesthetics were realized.

Conclusions: Hyaluronic acid injection could induce bone resorption in the mentum; nevertheless, the aesthetics were not impaired. The severity of the bone loss was positively correlated with the injection volume per time; therefore, large-volume injection of hyaluronic acid should be performed with caution. The patients should be fully informed about this complication pre-operatively. (*Plast. Reconstr. Surg.* 146: 147e, 2020.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Use of soft-tissue fillers has become an essential plastic procedure around the world. The advantages of soft-tissue fillers to correct age-related disharmonies, restore skin firmness and volume, and adjust facial contour have led to their widespread use. Different from Western societies, in which soft-tissue augmentation is

commonly considered as a useful procedure for facial rejuvenation among Caucasian patients,¹⁻³ facial contouring is the priority for Asian patients.⁴ Asian cephalometric studies have suggested decreased chin projection compared with Caucasians, which is considered an unattractive trait in Asian culture.^{5,6} Asian women desire an inverted triangle contour and a more projected,

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three-dimensional profile.⁷ Because of the anatomical difference and cultural disparity, chin augmentation is conventionally performed for a younger population and is regarded as an important and indispensable procedure in lower face aesthetic contouring.^{8,9}

Compared with sliding genioplasty and implants, injectable fillers offer a safe and efficacious method of three-dimensional chin shaping for patients with mild and moderate microgenia.^{10,11} In 2018, we first reported nine cases of mental bone erosion after hyaluronic acid injection.¹² With time, we found that this phenomenon was not sporadic. Therefore, a retrospective, comparative study was conducted to shed light on this complication and the possible pathogenesis, and to highlight the need for awareness and change in clinical practice.

PATIENTS AND METHODS

We retrospectively reviewed the computed tomography database of patients with a medical history of chin augmentation with hyaluronic acid from January of 2014 to October of 2019 at the Maxillofacial Department of the Chinese Academy of Medical Science and Plastic Surgery Hospital. Patients hospitalized for other operations, including liposuction, breast augmentation, or rhinoplasty, were excluded because of the lack of computed tomographic scans. (See Figure, Supplemental Digital Content 1, which displays a flow-chart of the conduct of the cohort study. *CAMS & PSH*, Chinese Academy of Medical Sciences and Plastic Surgery Hospital; *CT*, computed tomographic; *HA*, hyaluronic acid; *BMI*, body mass index, <http://links.lww.com/PRS/E116>.) All of the computed tomographic scans were from patients who were hospitalized for facial contouring operations, including osseous genioplasty, en bloc mandibular angle-body-chin curved osteotomy, and reduction malarplasty. For the control group, patients from the same database without hyaluronic acid injection were randomly chosen and matched according to sex and body mass index. This constitutes a mixture of recessive chin and normal chin-lip relationship populations in both cohorts, because patients hospitalized for osseous genioplasty and en bloc mandibular angle-body-chin curved osteotomy had recessive chin and patients hospitalized for malarplasty were normal chin-lip relationship populations. Patients were excluded if they had undergone chin augmentation except for hyaluronic acid injection, such as autologous fat, alloplastic implants,

polyacrylamide gel, and genioplasty. Information regarding demographics, complications, injection volume, injection interval, number of injections, and product brand was collected for analysis.

Methods

The semimandibular bone resorption index was calculated as the ratio of bone thickness in the incisive fossa compared with bone thickness in the mandibular symphysis (Figs. 1 through 3). Computed tomographic scans were analyzed using Mimics software 17.0 (Materialise, Leuven, Belgium). The bone thickness was measured three times by three independent authors (X.G., G.S., and D.Z.), and the values were averaged.

Patients were phoned and asked to rate their satisfaction with previous hyaluronic acid injection procedure (i.e., not satisfied, satisfied, or very satisfied) and the influence of bone erosion on aesthetics (i.e., does not realize, feels influenced, largely influenced) using a three-level scale. This study was approved by and conducted under the guidelines of the Institutional Review Board of the Chinese Academy of Medical Sciences and Plastic Surgery Hospital.

Statistical Analysis

Data analyses were conducted using SPSS Version 16.0 (SPSS, Inc., Chicago, Ill.). The independent t test was used to compare the bone resorption index between cohorts and across subgroups. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Eighty patients (160 semimandibular cases) met our inclusion criteria, and 80 controls were sex and body mass index matched. All patient demographics are listed in Supplemental Digital Content 2. [See Table, Supplemental Digital Content 2, which provides the demographics of all the enrolled patients. NA, not available (the patients cannot remember the detailed information about their injection history); F, female; M, male. *The patient had regional infection after the injection, <http://links.lww.com/PRS/E117>.] There were 77 women (96.25 percent) and three men (3.75 percent). Average ages were 25.90 ± 4.09 years (range, 19 to 36 years) in the hyaluronic acid injection group and 25.29 ± 4.51 years (range, 15 to 36 years) in the controls. All patients had a medical history of hyaluronic acid injection in the mentum 6 months before the hospitalization and had preoperative computed

F1-F3

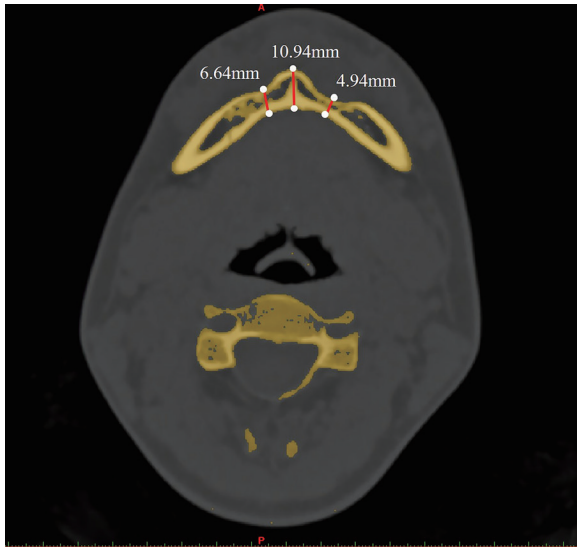


Fig. 1. Sectional view computed tomographic scan of mandible and mentum for calculation of bone resorption index. This figure illustrates how to measure the bone thickness in the incisive fossa and in the middle line.

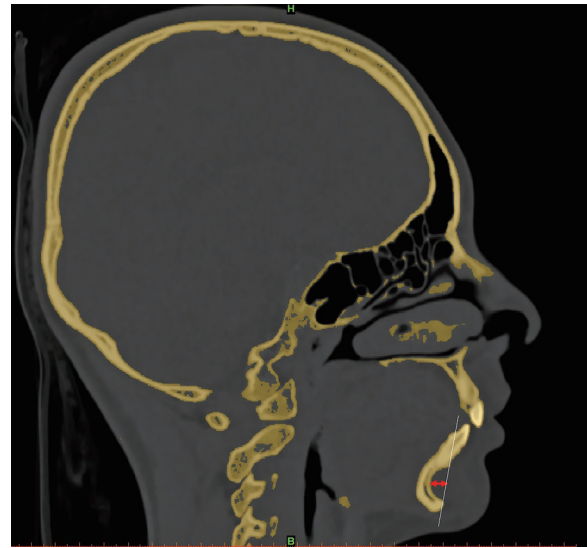


Fig. 2. Sagittal view computed tomographic scan of the skull. The red arrow indicates the bone erosion in the mentum.

tomographic scans for facial contouring surgery. All patients received hyaluronic acid injection in cosmetic clinics, and 33 patients could provide partial medical records. Fillers were generally placed at the pogonion and were more central than tapered. The bone resorption index in the hyaluronic acid injection cohort was significantly smaller than the controls (75.25 ± 10.02 versus 82.86 ± 6.38 ; $p = 0.000$) (Table 1 and Fig. 4). (See Table, Supplemental Digital Content 3, which provides the bone resorption index result of every individual in the hyaluronic acid injection cohort, <http://links.lww.com/PRS/E118>. See Table, Supplemental Digital Content 4, which provides the bone resorption index result of controls, <http://links.lww.com/PRS/E119>.)

Thirty-three patients could recall partial details of hyaluronic acid injection, including injection volume, injection interval, the number of injections, and product brand. Multiple products, including Restylane (Q-Med, Uppsala, Sweden), Biohyalux (Bloomage BioTechnology, Shandong, People's Republic of China), Neuramis (VEL.KOREA Co., Inc., Seoul, Republic of Korea), Yvoire (LG Life Sciences, Seoul, Republic of Korea), Juvederm (Allergan, Inc., Irvine, Calif.), and Elravie (Beauzen Co., Ltd, Seoul, Republic of Korea), were used; thus, product brand was not adopted for subgroup analysis.

Twenty-one patients (42 cases) had hyaluronic acid injected multiple times; thus, hemimandibular data for 42 cases were compared with

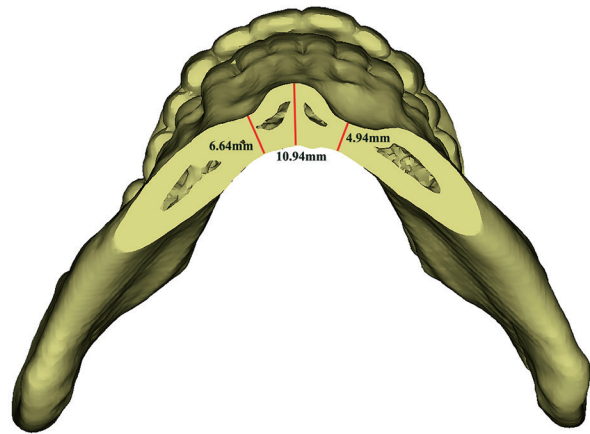


Fig. 3. Bottom-frontal view of the three-dimensional reconstruction of the mandible and mentum. This figure depicts the concavities in bilateral incisive fossa, with the middle symphysis less affected.

the remaining data (59 patients; 118 cases) were compared using an independent *t* test, and no significant difference was revealed. However, the bone resorption index in the multiple-injection group was smaller (72.80 ± 8.24 versus 76.11 ± 10.54 ; $p = 0.068$) (Table 2 and Fig. 5).

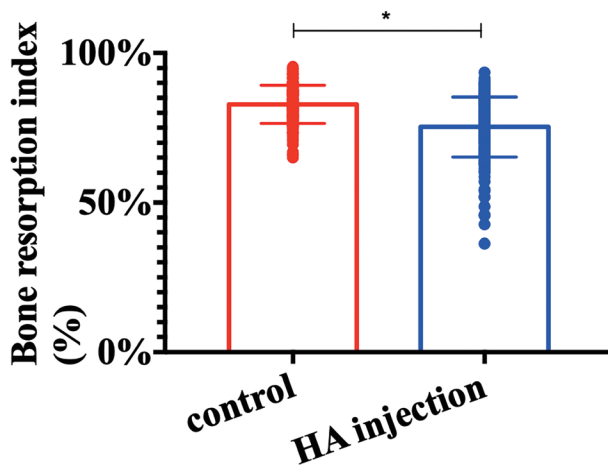
Thirteen patients (26 cases) reported large-volume injection per time; 10 of these patients received multiple injections. When compared with leftover data (67 patients; 134 cases), patients injected greater than or equal to 1 ml per time were more susceptible to bone erosion (68.89 ± 10.84 versus 76.49 ± 9.42 ; $p = 0.000$) (Table 2 and Fig. 6).

Table 1. Patient Demographics

Characteristic	Total	HA Injection*	Matched Cohort*	<i>p</i>
Mean age ± SD, yr		25.90 ± 4.09	25.29 ± 4.51	0.370
Mean BMI ± SD, kg/m ²		19.90 ± 2.34	19.38 ± 2.01	0.168
Sex				Not applied
Female	77			
Male	3			
BRI, %		75.25 ± 10.02	82.86 ± 6.38	0.000

HA, hyaluronic acid; BMI, body mass index; BRI, bone resorption index.

*160 semimandibular cases.

**Fig. 4.** Comparison of bone resorption index between hyaluronic acid (HA) injection cohort and controls. A significant difference was detected.

Six patients (12 cases) reported a short injection interval within 6 months, whereas 11 patients (22 cases) indicated a longer injection interval of greater than or equal to 6 months. Compared with the long-injection-interval group, although the bone resorption index in the short-injection-interval group was less (69.57 ± 9.34 versus 72.95 ± 7.78 ; $p = 0.267$), there was no significant difference between these two groups (Table 2 and Fig. 7).

Furthermore, 70 patients (87.50 percent) in the hyaluronic acid injection group responded to the satisfaction survey: 32 patients (45.71 percent)

felt very satisfied, 37 patients (52.86 percent) selected satisfied, and one patient (1.43 percent) reported being dissatisfied because of infection after the injection that was addressed by hyaluronidase injection. All patients stated that they did not realize any reduced aesthetic outcomes caused by bone erosion.

CASE REPORT

A 21-year-old woman who had undergone chin augmentation using hyaluronic acid (the patient could not recall the brand) three times was admitted to our department. The patient was asymptomatic, and she decided to undergo genioplasty for permanent change because of the satisfying aesthetic outcome. The injection volume was more than 1 ml each time, and the injection interval was approximately 3 months. Preoperative computed tomographic scans showed the evident bone erosion in the bilateral mandibular incisive fossa with the symphysis less affected (Fig. 8). Intraoperative photography confirmed deep concavities in the incisive fossa, without any periapical lesions (Fig. 9). A sliding genioplasty was performed, and she recovered uneventfully. The aesthetic result was satisfactory. Several other classic preoperative computed tomographic scans and intraoperative photographs are also illustrated in Figures 10 through 14.

DISCUSSION

Chin augmentation with injectable soft-tissue fillers is a less-invasive, quick-recovery procedure for a large subset of patients with microgenia or for patients with the normal chin-lip relationship but who desire a more pointed chin.^{1,13} With the increasing popularity of hyaluronic acid, the incidence of complications was also increased. Bone

Table 2. Patient Demographic and Subgroup Analysis

Characteristic	Multiple-Injection Group	Single-Injection Group	Large-Volume Injection Group	Small-Volume Injection Group	Short-Injection-Interval Group (<6 mo)	Long-Injection-Interval Group (≥6 mo)
No. of cases	42	118	26	134	12	22
Mean age ± SD, yr	25.14 ± 3.98	26.17 ± 4.13	25.54 ± 5.08	27.34 ± 9.72	23.00 ± 4.19	26.36 ± 4.25
<i>p</i>	0.327		0.517		0.138	
Mean BMI ± SD, kg/m ²	19.55 ± 2.71	20.05 ± 2.18	19.59 ± 2.81	20.00 ± 2.20	19.36 ± 2.00	19.35 ± 3.06
<i>p</i>	0.459		0.583		0.996	
Mean BRI ± SD, %	72.80 ± 8.24	76.11 ± 10.54	68.89 ± 10.84	76.49 ± 9.42	69.57 ± 9.34	72.95 ± 7.78
<i>p</i>	0.068		0.000		0.267	

BMI, body mass index; BRI, bone resorption index.

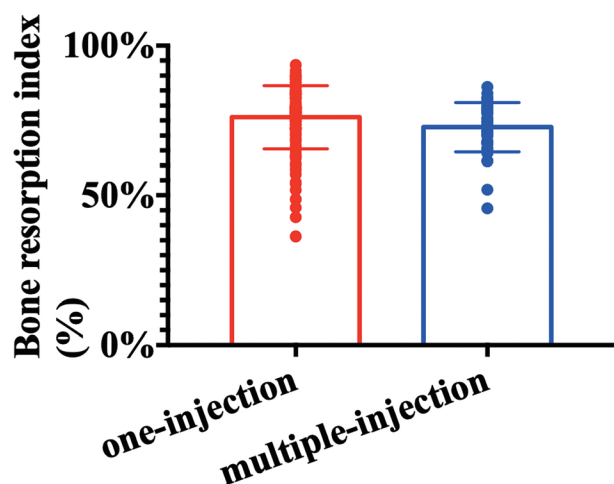


Fig. 5. Comparison of bone resorption index between single-injection versus multiple-injection subgroups. Although the average bone resorption index in the multiple-injection group was smaller, there was no significant difference.

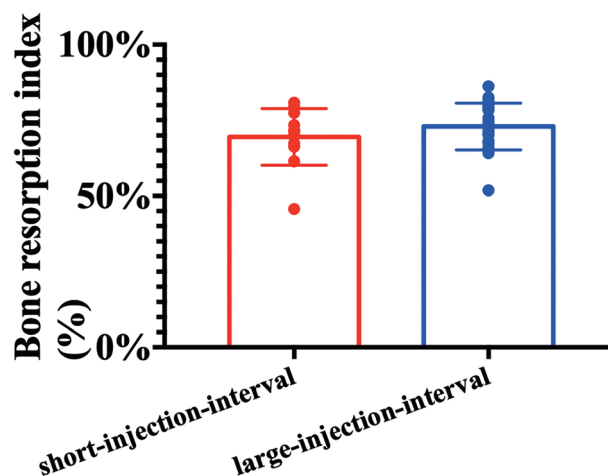


Fig. 7. Comparison of bone resorption index between short-injection-interval versus long-injection-interval (≥ 6 months) subgroups. Although the average bone resorption index in the short-injection-interval group was smaller, there was no significant difference.

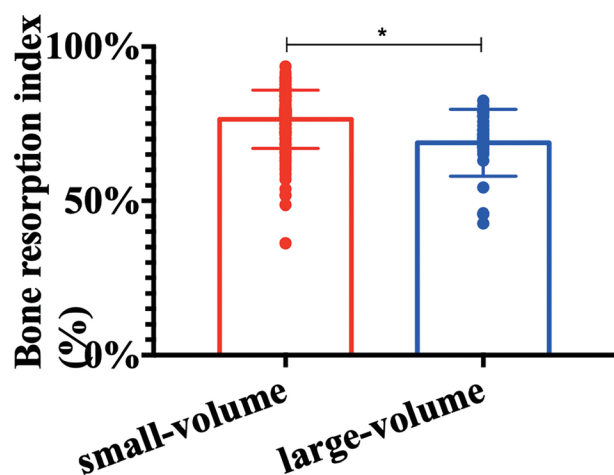


Fig. 6. Comparison of bone resorption index between small-volume (≤ 1 ml) versus large-volume injection subgroups. A significant difference was detected.

resorption in mentum, first found by Robinson and Shuken,¹⁴ is a common phenomenon related to chin augmentation using implants in patients in their middle twenties.¹⁵ However, bone resorption associated with hyaluronic acid injection was seldom reported. In 2018, we first reported nine cases of mental bone absorption after chin augmentation using hyaluronic acid. With time, we realized that this phenomenon was not sporadic and was associated with several injection-related factors. Thus, we retrospectively compared 80 patients with a medical history of mental hyaluronic acid injection with 80 sex- and body mass index-matched patients without previous chin

augmentation. Our results confirmed the contribution of hyaluronic acid injection to mental bone loss.

Subgroup analysis indicated that patients receiving large-volume injection per time were more susceptible to bony absorption. Furthermore, although there was no significant difference in bone resorption index when one-injection versus multiple-injection groups and short-injection-interval versus long-injection-interval groups were compared, the multiple-injection and short-injection-interval groups had a lower level of bone resorption index. In the subgroup analysis, we compared patients injected multiple times with the leftover data and compared patients injected with a large volume with the leftover data. As many patients involuntarily do not report on detailed information about injection history, designating patients with incomplete information as the one-injection and low-volume group inevitably increased the level of bone resorption index in the one-injection and low-volume group. Therefore, the exact difference could be higher than the analyzed result.

Based on our clinical experiences, we realize that all mental bone erosion cases share several similar characteristics. These are as follows. First, although hyaluronic acid was conventionally injected in the midline of the mentum, bone erosion mainly appeared in bilateral mandibular incisive fossa, with the mandibular symphysis less affected. The outer cortex in incisive fossa is thinner than that in the midline, which may be a

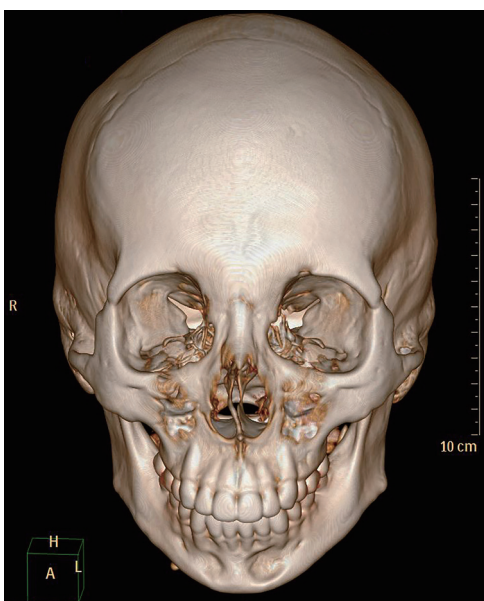


Fig. 8. Classic case. Three-dimensional reconstruction of the computed tomographic scans of a 30-year-old woman. She underwent hyaluronic acid injection three times, with more than 1 ml each time. Evident concavities could be found in bilateral incisive fossa.



Fig. 9. Classic case. Intraoperative photograph of a 30-year-old woman. The toothpick assisted in displaying the deep hole in the mentum.

possible reason for this phenomenon. Two injections at superolateral sites on either side of the chin may be the second possible reason. Second, patients with mental bone loss were asymptomatic, and no apical lesions were found intraoperatively. Third, all patients stated that they did not notice any impaired cosmetic outcomes caused by bone erosion. There is still no definitive conclusion. In our opinion, the possible causes may be as follows:

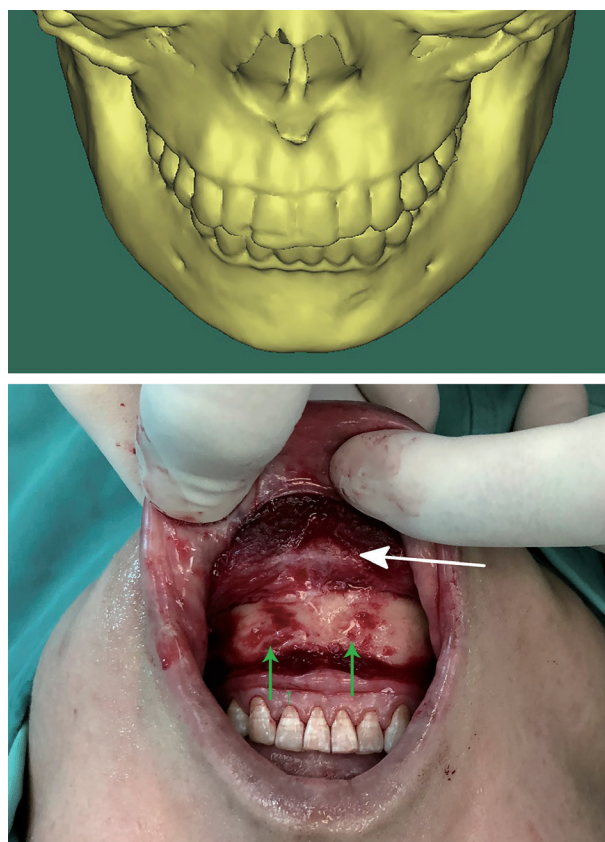


Fig. 10. Additional case 1. (Above) Three-dimensional reconstruction of the computed tomographic scans from a 27-year-old woman. She had injection of hyaluronic acid two times (Restylane). The injection volumes were 1.5 and 0.6 ml, and the injection interval was longer than 6 months. Bony resorption could be found in bilateral incisive fossa. (Below) Intraoperative photograph of the same patient. Green arrows indicate the bone loss, and white arrow indicates the remaining hyaluronic acid.

1. Pressure-related phenomenon. Bone erosion is a common phenomenon in implant-related mentum augmentation, and although soft-tissue filler could only exist temporarily, intermittent, frequent injection may also mimic a similar pressure effect.
2. The equilibrium between osteoclasts and osteoblasts was impaired by the affinity of hyaluronic acid to osteoclasts.¹⁶
3. Labial incompetence and hyperactivity of mentalis.¹⁷

The clinical value of this study is critical because it is time for us to rethink previous consensus on chin augmentation with hyaluronic acid, especially for Asians. According to the Asia-Pacific Consensus group, the recommended injection volume for chin apex augmentation



Fig. 11. Additional case 2. (Above) Three-dimensional reconstruction of the computed tomographic scans of a 26-year-old woman. She could not remember the exact injection-related information. Bony resorption could be found in bilateral incisive fossa. (Below) Intraoperative photograph of the same patient. Green arrow indicates the remaining hyaluronic acid.



Fig. 12. (Above) Additional case 3. Three-dimensional reconstruction of the computed tomographic scans of a 30-year-old woman. She had chin augmentation with hyaluronic acid one time (Yvoire). The injection volume was 1.5 ml. Bony resorption could be found in bilateral incisive fossa. (Below) Intraoperative photograph of the same patient. Bone loss could be seen in bilateral incisive fossa.

was 1 to 3 ml in Asians,⁷ whereas it was only 0.4 to 0.9 ml in Caucasians (0.2 to 0.3 ml per site, and the product was delivered to two to three injection sites).¹⁸ This not only uncovered the different anatomical characteristics among different ethnicities but also revealed the distant sense of beauty influenced by the culture. As a pointed “elfin” chin was considered attractive, hyaluronic acid was considered as a finer sculpturing tool for an increasing number of patients with a normal chin-lip relationship. Our finding suggests that a small volume rather than a large volume was less susceptible to bone erosion (bone resorption index, 67.74 ± 11.22 percent versus 76.49 ± 9.74 percent; $p = 0.000$); thus, a smaller volume might be safer. Furthermore, different from subdermal injection for facial rejuvenation, the most recommended injection planes for mental augmentation were suprapariosteum and subdermis. In our opinion, placing hyaluronic acid directly onto the suprapariosteum may exert an aggregation effect

of osteoclasts, and also cause direct and indirect pressure effects by the product and the mentalis above.

However, the results of the present study should be interpreted with caution. Suprapariosteum and subdermis are comparatively safe from devastating vascular complications.¹⁹ Suprapariosteum is relatively avascular and could provide the desired projection from the bone. Two cases of vascular occlusion after hyaluronic acid augmentation of the mentum have been reported.²⁰ Surgeons should always keep in mind that in the “no-risk-free-area” face, safety takes precedence over aesthetic outcome. Further studies on the efficacy and safety of deep versus superficial injections in the mentum need to be performed to draw further conclusion.

Moreover, because radiologic follow-up does not seem to be a regular recommended examination, affected patients might be overlooked.

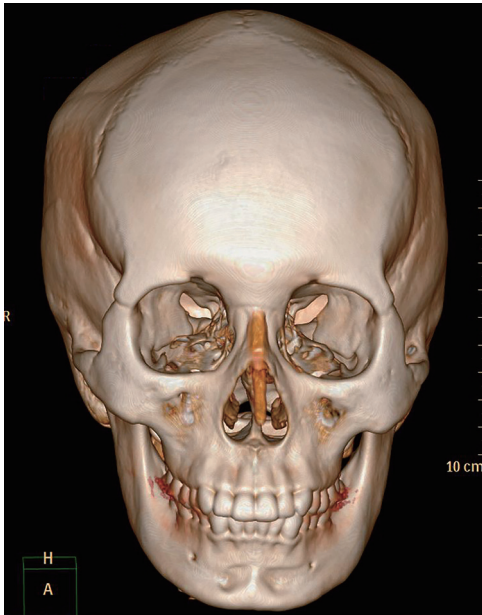


Fig. 13. Additional case 4. Three-dimensional reconstruction of the computed tomographic scans from a 23-year-old woman. She could not remember the exact injection-related information. Evident bony resorption could be found in bilateral incisive fossa.

Whether radiographic examination should be a routine after several rounds of hyaluronic acid injection still warrants further study. The depth of concavity in [Figures 1](#) through [3](#) was nearly half of the bone thickness; therefore, gliding genioplasty was generally considered as a treatment option for such cases.

This study has several intrinsic limitations. First, there was a lack of preoperative computed tomographic scans. However, because the radiologic examination was not a regular preinjection and postinjection examination, this limitation could hardly be improved. Second, the recruited patients were hospitalized for facial contouring operations, and had comparatively flatter and wider profiles and were thus less effective at representing normal Asian patients. A large-scale study could be conducted to ameliorate this limitation.

CONCLUSIONS

Hyaluronic acid injection can induce bone resorption in the mentum, and the severity is correlated with the injection volume per time; however, the aesthetic result is not impaired. It is time for us to rethink previous consensuses on chin augmentation. Our finding suggests that smaller volume injection might be safer. Short-interval injection within 6 months should be avoided.

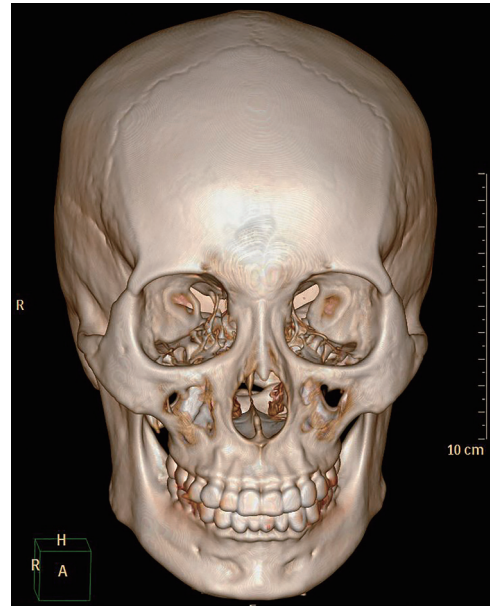


Fig. 14. Additional case 5. Three-dimensional reconstruction of the computed tomographic scans from a 31-year-old woman. She could not remember the exact injection-related information. Evident bony resorption could be found in bilateral incisive fossa.

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