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Cephalometric analysis following combined Sub-SMAS hyaluronic acid injection and subdermal and supraperiosteal poly-L-lactic acid injections in Asian women

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Abstract

Background: The aging face is characterized by skin laxity and volume loss. Attenuation of facial retaining ligaments significantly contributes to skin sagginess and soft tissue volume loss.

Aims: We designed a prospective cohort study to quantitatively assess the efficacy of hyaluronic acid (HA) with adjunct poly-L-lactic acid (PLLA) injections in strengthening the retaining ligaments.

Patients/Methods: A total of 12 Asian women were treated with HA injections to the orbital, zygomatic, buccal-maxillary, and mandibular retaining ligaments with adjunct supraperiosteal and subdermal PLLA injections to the temporal region, midface, and lower face. Cephalometric measurements were done before treatment and 2, 4, 12, and 24 weeks post-procedurally.

Results: Eyebrow peak and tail angles increased 20.0° ± 3.8° to 21.0° ± 3.8° ($p < 0.05$) and −2.9° ± 4.2° to −1.3° ± 3.3° ($p < 0.001$) at week 12. Eyebrow-to-orbital-rim distance increased 1.9 ± 2.0 mm to 3.9 ± 1.5 mm ($p < 0.001$) at week 12. Eyebrow-to-upper-eyelid distance increased 11.6 ± 3.0 mm to 12.7 ± 3.2 mm ($p < 0.001$) at week 24. Eyebrow-peak-to-lateral-limbus distance decreased 6.1 ± 3.1 mm to 5.3 ± 2.4 mm ($p < 0.05$) at week 4. Tragus-oral-commissure length and lower-facial-contouring length decreased 281 ± 11 mm to 275 ± 10 mm ($p < 0.01$) and 297 ± 14 to 292 ± 11 mm ($p < 0.05$) at week 12, respectively.

Conclusion: Hyaluronic acid injection for strengthening of facial retaining ligaments with adjunct PLLA is viable, safe, and effective in facial rejuvenation as supported by quantitative data.

KEYWORDS
cephalometric analysis, facial rejuvenation, facial retaining ligaments, hyaluronic acid, poly-L-lactic acid

1 | INTRODUCTION

The aging face has been the focus of numerous studies due to the inevitability of the condition. The associated overlying skin laxity, underlying soft tissue volume loss, and changes in facial topography and bony structures are the results of an assortment of intrinsic and environmental factors.[1-4] The effects of the aging process on the soft tissue components of the face are mostly defined by a decrease in volume and skin elasticity. While the former is the results of a combined effect of senescent facial lipoatrophy and changes in the underlying skeletal topography, the latter is caused by the decrease in elastin and collagen content of the skin and the compromised integrity of the retaining ligaments of the face.[2,3,5-7]

The retaining ligaments of the face are fibrous tissue that acts as the tether that anchors the overlying dermis and soft tissue of the face to the underlying denser connective tissue and bone, maintaining their normal anatomic position.[8,9] They can be divided into the true osteocutaneous retaining ligaments (originating from the periosteum and extending to the dermis) and fascial retaining ligaments (securing the intervening layers of facial tissue).[10-12] It is believed that the loosening of the true ligaments with age and repetitive muscular movement of the face, coupled with the force of gravity, leads to the sagging of soft tissue and increase of unwanted epidermal folds associated with the aging face.[10,11,13,14]

Currently, there are surgical (eg, rhytidoplasty and rhytidectomy) and non-surgical (eg, thread lifts, thermage, and dermal fillers) options for treatment of the aging face. The attenuation and elongation of the retaining ligaments of the face and the accompanying downward migration of the interwoven SMAS result in undesired changes of fat distribution in the face, leading to the appearance of facial aging. Buttressing and retightening the retaining ligaments would theoretically lead to the secondary lifting of the SMAS and other overlying tissue of the face. The True Lift™ technique is marked by the identification and injection of hyaluronic acid at the base of the osteocutaneous facial retaining ligaments, tightening them via a cantilever effect.[15] Theoretically, the hyaluronic acid will act as a buttress for the retaining ligaments, effectively leading to the indirect lifting of the overlying soft tissue and improve the sagginess and laxity of skin.

The collagen-stimulating agent poly-L-lactic acid (PLLA) achieves its effect by eliciting an inflammatory response in the injected region. Such a response would eventually lead to granulomatous reactions by the host's immune system, ultimately resulting in formation of fibrous connective tissue and dermal fibroplasia.[16] This phenomenon could technically lead to the perceived tightening of the overlying skin in addition to its widely reported volumizing effect. By combining such an effect with the strengthening of the facial retaining ligaments provided by discrete injections of hyaluronic acid, a synergistic effect could be achieved. Hence, in this study, we will quantitatively assess the efficacy of sub-SMAS injection of hyaluronic acid in conjunction with PLLA using various parametric anatomical measurements.

2 | MATERIALS AND METHOD

2.1 | Patient selection

Subjects were recruited and followed up at a single medical center between June 2019 and May 2020. Consenting female patients above the age of 20 are assessed by a board-certified plastic surgeon and assessed for signs of facial aging. Those with downward sloping of the lateral eyebrows, laxity of the malar fat pads, or jowling who would potentially benefit from non-invasive facial rejuvenation were included. Patients with previous allergic reaction to hyaluronic acid, PLLA, or any other dermal fillers are excluded. Patients who have received surgery or are currently receiving treatment for facial rejuvenation within the past 6 months are also excluded from the study.

2.2 | Materials

Hyaluronic acid (Restylane® LYFT™ Lidocaine) and poly-L-lactic acid (SCULPTRA® Aesthetic) were obtained from Galderma S.A. (Uppsala, Sweden). Facial and cephalometric analytical system (Morpheus 3D® Scanner) was obtained from Morpheus Co., Ltd. (Gyeonggi, Korea).

2.3 | Method

Recruited patients are given injections of hyaluronic acid according to the True Lift™ technique of retightening facial retaining ligaments (as described by Huang 2018) with an adjunct dose of SCULPTRA® Aesthetic dermal filler at key locations on the face as described in the technique section.[15] Angular and linear measurements of various facial landmarks are assessed by Morpheus 3D® before treatment and during subsequent follow-ups at 2, 4, 12, and 24 weeks post-treatment. The facial and cephalometric measurements are done as described by Tsai et al. (2021), with focus on the angular measurements of eyebrow peak, eyebrow tail, pupil-eyebrow peak, and the linear measurements of eyebrow-orbital, orbital-eyelid, eyebrow-iris, tragus-oral, and lower facial contouring lengths (Figure 1).[17] High-resolution photographs were also taken concurrent to the assessment with Morpheus 3D®.

Statistical analyses of the data are done on SPSS (version 25; IBM SPSS Inc., Chicago, Illinois). The results are reported as mean ± standard deviation. Shapiro-Wilk test was used to determine the normality of each sample group; normally distributed samples were analyzed with the student's paired *t* test while non-normally distributed samples were analyzed with Wilcoxon signed-rank test. A *p*-value of less than 0.05 compared with the baseline measurement was considered a significant difference.

All patients gave informed consent for participation in this study prior to enrollment. This study was reviewed and approved by the institutional review board of China Medical University Hospital (IRB No. CMUH108-REC2-074).

2.4 | Technique

For the True Lift™ technique (starred locations on the left side of Figure 2), 1.0 ml of Restylane® LYFT™ Lidocaine will be injected on each side of the face at the orbital retaining ligament (0.1 ml), zygomatic retaining ligament (0.2 ml), one centimeter medial to the zygomatic retaining ligament along the zygomatic arch (0.2 ml), buccal-maxillary retaining ligament (0.4 ml), and mandibular retaining ligament (0.1 ml). Upward force is applied with the non-dominant hand to relieve the tension in the retaining ligaments by restoring the overlying soft tissue to its original position. Restylane® LYFT™ is then injected just superficial to the periosteum and deep into the SMAS layer.

For SCULPTRA® Aesthetic (right side of Figure 2), a total of 8.0 ml of filler will be injected on each side of the face. Injections will be made subdermally in a retrograde fanning manner using the threading technique and supraperiosteally in boluses. For the first group of supraperiosteal injections (dark blue, solid), six injections are done in pairs along two parallel lines between the eyebrow and the excanthion lateral to the palpebral fissure into the retro-orbicularis fat. Each injection is 0.5 ml each in volume. For the tear trough (light blue, crossed), subdermal injections are done in two divisions of 0.5 ml each, with the entry point of the first injection at the zygomatic arch directly inferior to the excanthion and the second injection approximately 1 cm below the first. Injections here are directed medially, keeping the needle inferior to the orbital rim. In the malar region (purple, solid), three supraperiosteal injections of 0.5 ml each are done around the infraorbital foramen. The first two injections are done at the level of the infraorbital foramen at 0.5 cm on either side of a vertical line drawn from the pupil. The third injection is done 0.5 cm inferior to the previous entry point lateral to the infraorbital foramen. In the cheek region (red, crossed), three subdermal injections of 0.5 ml each are done in a retrograde fanning manner and directed posteriorly. The injections are done along the anterior border of the masseter muscle starting at 1 cm inferior to the zygomatic arch, with each subsequent injection being 1 cm inferior to the previous one. Finally, two more subdermal injections of 0.5 ml each are done in the buccal region directed superoposteriorly (green, crossed). The first injection is located on a line drawn between the oral commissure and the tragus at 1 cm anterior to the anterior border of the masseter muscle, while the second injection located 1 cm inferior to the first.

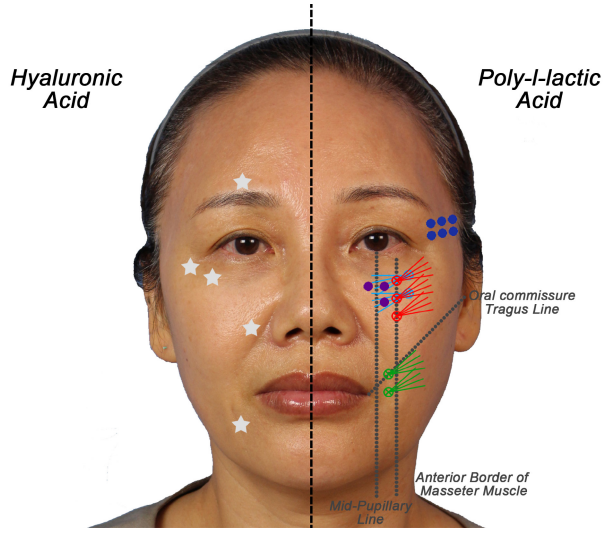

FIGURE 1 Angular and linear cephalometric measurements measured at baseline and follow-ups at weeks 2, 4, 12, and 24. Measurements are done in three-dimensional imaging taken by Morpheus 3D®

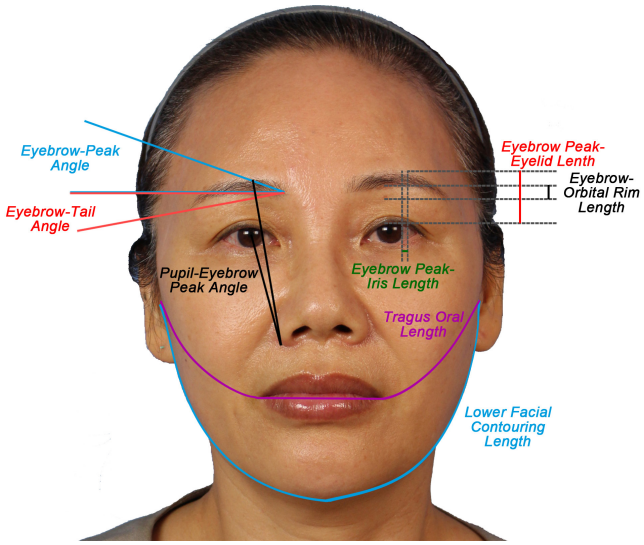

FIGURE 2 Injection locations and patterns for hyaluronic acid (left side) and poly-l-lactic acid (right side). The hyaluronic acid injections are done superficial to the periosteum and deep to the superficial musculoaponeurotic system, while poly-l-lactic acid injections are done in micro-bolus injections or in a fanning pattern as indicated

3 | RESULTS

A total of 12 female patients were recruited, with a mean age of 42.7 years. There were no adverse effects reported, and none of the patients were lost to follow-up.

3.1 | Angular measurements

Eyebrow peak angle increased steadily from 20.0 ± 3.8 degree, reaching 21.0 ± 3.8 degree at week 12, with statistical significance compared with baseline levels ($p < 0.05$). The angle dropped off at week 24 to 19.5 ± 4.2 degrees, but without significant difference compared with baseline levels. Eyebrow tail angle also increased from −2.9 ± 4.2 degrees at baseline to −1.7 ± 3.6 degree by week 4 ($p < 0.05$) and −1.3 ± 3.3 at week 12 ($p < 0.001$), tapering off to −2.0 ± 3.7 degree at week 24 ($p < 0.05$). Pupil-eyebrow peak angle

decreased from 2.5 ± 1.7 degree at baseline to 1.8 ± 1.3 degree at week 4 ($p < 0.05$) but did not show significant changes thereafter.

3.2 | Linear measurements

Eyebrow-orbital length increased significantly from 1.9 ± 2.0 mm at baseline to 3.3 ± 1.2 mm at week 2 ($p < 0.001$), steadily increasing to 3.9 ± 1.5 mm at week 12 ($p < 0.001$) and tapering off to 3.1 ± 1.9 mm at week 24 ($p < 0.01$). Eyebrow-eyelid length increased significantly from 11.6 ± 3.0 mm at baseline to 12.2 ± 2.7 mm at week 4 ($p < 0.05$) and continued to increase until it reached 12.7 ± 3.2 mm at week 24 ($p < 0.001$). Eyebrow peak-iris length showed a decreasing trend from a baseline of 6.1 ± 3.1 mm, bottoming out at 5.3 ± 2.4 mm at week 4. Tragus-oral length decreased steadily from a baseline of 281 ± 11 mm until it reached statistical significance by week 12 at 275 ± 10 mm ($p < 0.01$). Lower facial contouring length also decreased from a baseline of 297 ± 14 mm at baseline with a statistically significant decrease by week 12 at 292 ± 11 mm ($p < 0.05$).

4 | DISCUSSION

In our study, we have provided quantitative data to support the positive effects of using hyaluronic acid and adjunct poly-l-lactic acid as support for facial retaining ligaments. Injection of hyaluronic acid to the orbital retaining ligaments had resulted in significant lifting effects on the eyebrows, reflected in the increased eyebrow peak angles, eyebrow tail angles, and the distance between the inferior border of the eyebrow and the orbital rim. (Table 1). Eyebrow peak-iris length, described as being ideally as small as possible by Westmore in 1974, also showed a decreasing trend in our study with statistically significant findings (Table 1).[18] These measurements are reflected as an up-lifting and up-turning effect on the eyebrows (Figure 3). As for the injections of hyaluronic acid to the bucco-maxillary retaining ligaments and lateral mandibular retaining ligaments, lifting of the jawline and midface is observed (Figure 4). Qualitatively, this can be observed as a decrease in the nasolabial folds and jowling with a quantitative decrease in tragus-oral length and lower facial contouring length, respectively.

The choice of biphasic hyaluronic acid is the obvious choice for the True Lift™ technique, as its time-proven durability and tenacity are ideal for support of the retaining ligaments.[19] For this study, a 1,4-butane-diol diglycidyl ether (BDDE) cross-linked biphasic filler (Restylane LYFT™; Galderma S.A., Uppsala, Sweden) was chosen for its more resilient and persistent nature compared with their monophasic counterparts.[19–21] Compared with the other members of the Restylane™ family, the biphasic hyaluronic acid of Restylane LYFT™ has a larger particle size, translating into a greater firmness and ability for the filler to resist gravity and other external forces while retaining its shape.[22] The large particle size of Restylane LYFT™ is also ideal for the deep dermis injections required of the True Lift™ technique.[20,21]

TABLE 1 Various angular and linear cephalometric measurements taken before the treatment and during follow-ups

	Eyebrow-peak (°)	Eyebrow-tail (°)	Pupil-eyebrow peak (°)	Eyebrow-orbit (mm)	Eyebrow-eyelid (mm)	Eyebrow peak-iris (mm)	Tragus-oral (mm)	Lower facial contouring (mm)
Before treatment	20.0 ± 3.8	−2.9 ± 4.2	2.5 ± 1.7	1.9 ± 2.0	11.6 ± 3.0	6.1 ± 3.1	281 ± 11	297 ± 14
Week 2	20.0 ± 3.6	−2.6 ± 4.5	2.3 ± 1.7	3.3 ± 1.2***	11.6 ± 2.6	5.9 ± 2.9	282 ± 11	295 ± 13
Week 4	20.2 ± 3.3	−1.7 ± 3.6*	1.8 ± 1.3	3.8 ± 1.7***	12.2 ± 2.7*	5.3 ± 2.4	278 ± 12	294 ± 12
Week 12	21.0 ± 3.8*	−1.3 ± 3.3***	2.0 ± 1.1	3.9 ± 1.5***	12.6 ± 3.2**	5.4 ± 2.5	275 ± 10**	292 ± 11*
Week 24	19.5 ± 4.2	−2.0 ± 3.7	2.2 ± 1.3	3.1 ± 1.9**	12.7 ± 3.2***	6.1 ± 2.6	276 ± 11*	290 ± 12**

*Indicates a statistically significant difference ($p < 0.05$) between follow-up measurements and baseline measurements; **Indicates a statistically significant difference ($p < 0.01$) between follow-up measurements and baseline measurements; ***Indicates a statistically significant difference ($p < 0.001$) between follow-up measurements and baseline measurements.

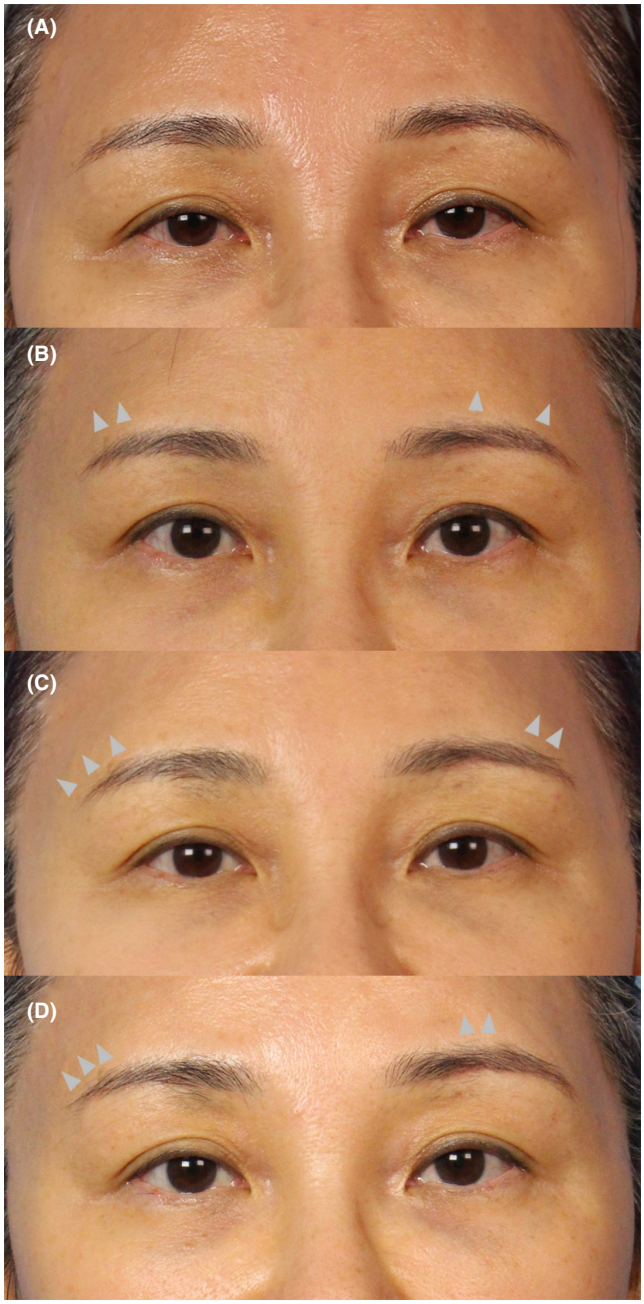

FIGURE 3 High-resolution photographs of the forehead and eyebrows of a subject at (A) baseline, (B) week 4, (C) week 12, and (D) week 24. Note the increasing eyebrow-eyelid distance due to the up-lifting effects on the eyebrow (arrows)

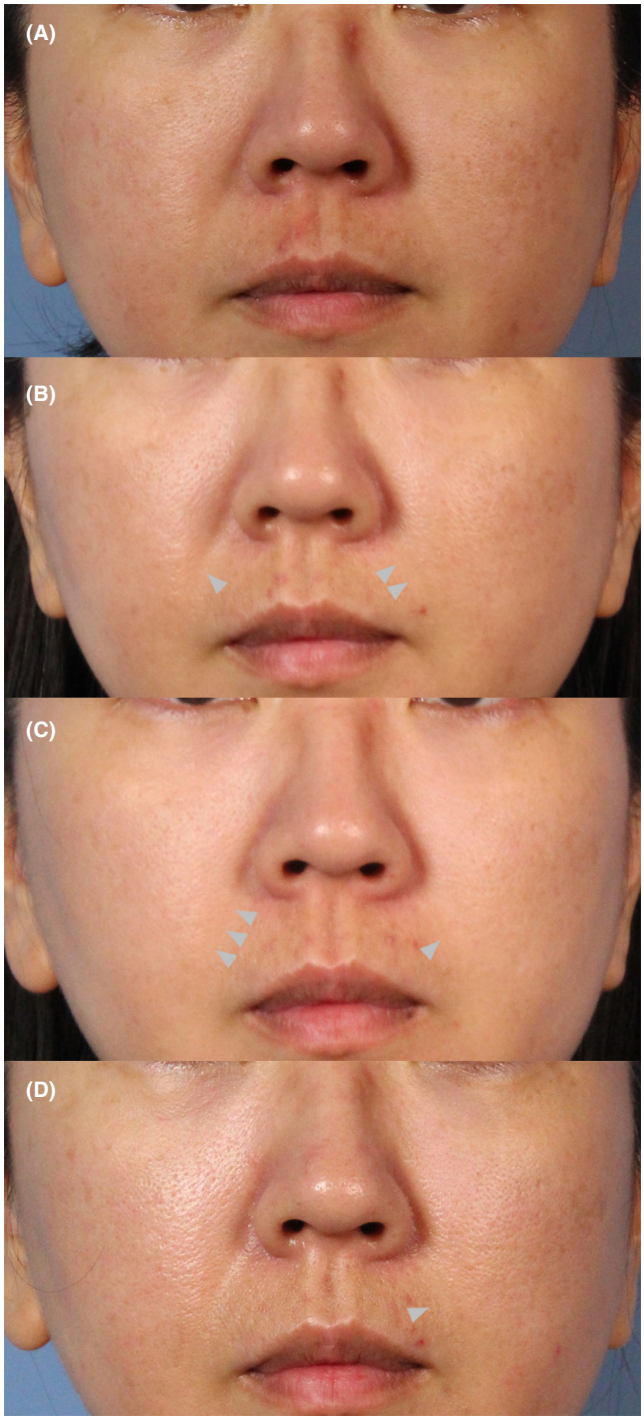

FIGURE 4 High-resolution photographs of the midface of a subject at (A) baseline, (B) week 4, (C) week 12, and (D) week 24. Note augmented medial cheek fat and decreased nasolabial folds (arrows)

In addition to the injections of hyaluronic acid for buttressing the retaining ligaments, we have added adjunct injections of PLLA for its collagen-stimulating and granulomatous reaction-inducing effects. PLLA is a biodegradable and biocompatible agent that acts as a collagen stimulator by inducing localized inflammatory response in the surrounding tissue after injection.[23] The production and deposition of collagen by the recruited fibroblasts during the inflammatory response result in the tightening of the dermis and volumizing effect perceived after PLLA injection via granuloma formation and dermal thickening. The location and direction of the subdermal and supraperiosteal injections of the technique described in our study reflect similar tracts used in traditional thread lifting techniques. By inducing granuloma formation and fibroplasia in these areas, we believe that a combined lifting and volumizing effect could be achieved with the host response to the injected PLLA as injections of PLLA targeting the vicinity of various superficial and deep fat

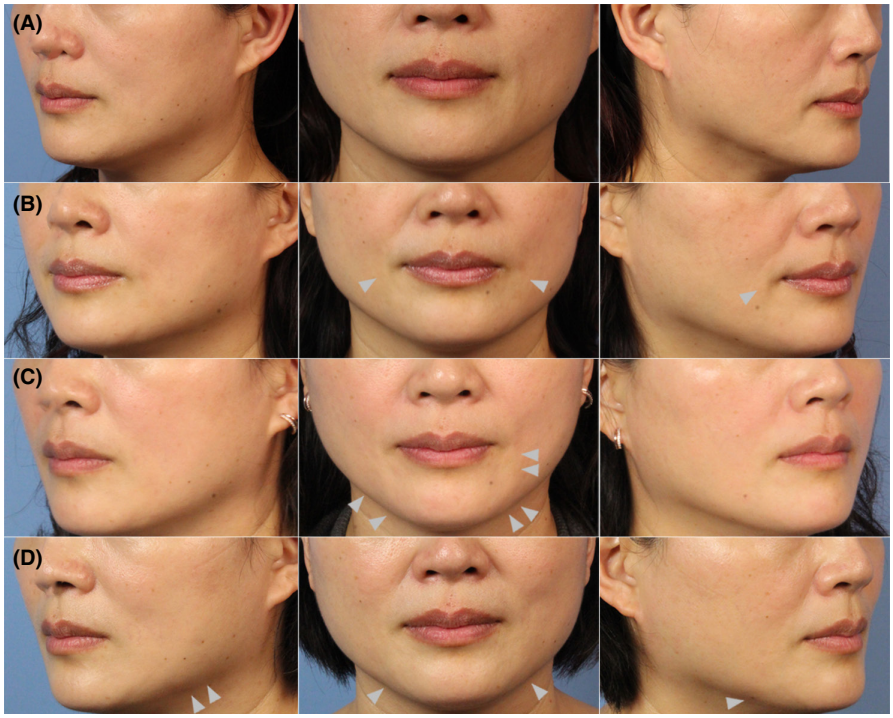

FIGURE 5 High-resolution photographs of the lower face and jawline of a subject at (A) baseline, (B) week 4, (C) week 12, and (D) week 24. Note the perceivable improvement in the jowls and decrease in the lower facial contouring line (arrows)

compartments based on their anatomical locations have reported lifting effects in certain areas of the face.[24]

The rationale behind combining the True Lift™ injection technique of HA with adjunct PLLA injections can be elucidated by considering the *in vivo* dynamics of the respective filler. The effects of the HA injections can be immediately observed post-injection, lasting for up to 6–8 months.[25,26] Conversely, the empty space left behind during the degradation of the PLLA fillers has been found to be filled by type I collagen fibers starting at 1 month and up to 24 months after injection.[27] By having HA hold the facial retaining ligaments in the preferred positions during early recovery phase, the regions treated with PLLA would be progressively converted into type I collagen as the HA degrades, holding the overlying soft tissues in the desired dispositions despite the gradual loss in integrity of the HA buttress. By combining the relatively shorter-lasting effects of HA and the longer-lasting effects of PLLA, we believe that a synergistic outcome can be achieved (Figure 5).

Other complementary effects using combinations of hyaluronic acid, PLLA, and other facial rejuvenation procedures have been reported.[28,29] In the recommendations regarding combined therapy proposed by de Melo et al. 2020 though, volume adjustment (both reduction and augmentation) was to precede tissue repositioning.[29] In our study, the skin tightening effect induced by the inflammatory response to PLLA was done concurrently with physical repositioning and support by HA. Despite this, no adverse effects were observed while satisfactory results were reported both qualitatively and quantitatively.

No volumetric measurements were done in this study as the volumizing effects of PLLA have been widely reported and confirmed quantitatively with 3-dimensional analytical systems.[30–34] However, further studies with various cephalometric measurements may be warranted comparing the effects of hyaluronic acid injections to the retaining ligaments alone against the combined effects of hyaluronic acid and adjunct PLLA injections.

5 | CONCLUSION

The facial retaining ligaments are an integral part of the facial anatomical architecture and are a key target in facial rejuvenation. In this study, we have confirmed their significance by quantitatively confirming the efficacy of injecting hyaluronic acid into the sub-SMAS layer with adjunct doses of PLLA. By lifting the overlying fat, fascia, and skin through supporting the facial retaining ligaments, effective facial rejuvenation through brow-lifting, midface support, and jawline contouring can be achieved.

CONFLICT OF INTEREST

All authors denied any competing interest and/or personal/financial relationships that may inappropriately influence their actions.

AUTHOR CONTRIBUTIONS

This study was designed, directed, and coordinated by C.C.C. as the primary investigator; Y.H.H. and P.H. provided the conceptual guidance; A.D.C. and C.C.C. conceived and designed the analysis; C.C.C. and Y.H.H. performed the medical procedures described; C.K.Y. and E.T.L. collected and arranged the data; H.M.C. and B.S.L. contributed the data analysis tools; C.K.Y., L.C.T., and A.D.C. performed the data analysis; A.D.C. wrote the manuscript. All the authors reviewed and commented on the manuscript and agreed to its contents.

ETHICAL APPROVAL

All patients gave informed consent for participation in this study prior to enrollment. This study was reviewed and approved by the institutional review board of China Medical University Hospital (IRB No. CMUH108-REC2-074).

EMPLOYMENT

All authors denied recent (within the past 5 years), current, or anticipated employment by an organization that may gain or lose financially from publication of the article.

OTHER COMPETING INTERESTS

All authors denied any personal relationship which may inappropriately affect the integrity of the research reported (by an author) or the objectivity of the review of the manuscript (by a reviewer or Editor).

PERSONAL FINANCIAL INTERESTS

All authors denied any stocks or shares in a company that may gain or lose financially from publication of the article; consulting fees or other remuneration from an organization that may gain or lose financially from publication of the article; patents or patent applications that are owned by or licensed to companies/institutions that may gain or lose value from publication of the article.

PHOTO CONSENT

The patients whose photographs are included in this study gave the author(s) and any affiliated third parties full consent on the use and/or distribution of all photographs and digital images for printed publication, electronic publication, online access, and/or promotional use.

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