



COMPARISON OF LOW MOLECULAR WEIGHT AND HIGH MOLECULAR WEIGHT HYALURONIC ACIDS USED IN LIP AUGMENTATION

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ABSTRACT

Objectives: The current study is designed to compare between low molecular weight and high molecular weight hyaluronic acids used in lip augmentation. **Subjects and method:** thirty-six patients with average age (18:35) years old were randomly divided into two groups: Group (A): Lip rejuvenation was performed with Juvéderm Vollbella with Lidocaine. Group (B): Lip rejuvenation was performed with Restylane-L. Follow up: done at 1 and 14 days after each treatment and at 1 and 6 Months also. Lip fullness assessed from 3D facial images using Allergan lip Fullness Scale, the Linear measurements in the form of Vermilion show and lip projection, the symmetry and aesthetic features of the lip analyzed also from 3D facial images. **Results:** According to the post injection lip fullness scale when compared to the base line, the change in group (A) injected with Juvéderm Vollbella with Lidocaine were (88.89%) compared to group (B) injected with Restylane-L were (83.33%), this indicates very high improvement in the each group, the total change improvement were ≥ 1 point improvement in both groups, however improvement in group (A) were more than group (B) but this is statistically insignificant. **Conclusion:** Regarding the effectiveness and duration of Lip augmentation there was no significant difference between Juvéderm vollbella and Restylane-L.

KEYWORDS: Lip rejuvenation, HA dermal fillers, Juvéderm vollbella, Restylane-L

INTRODUCTION

Lips and the perioral area are of outstanding importance in beauty appearance, attractiveness, and youthfulness. Lips are a central part of facial aesthetics due to their color, surface texture, and shape. Well defined lips with proper fullness are often portrayed as a symbol of youth and in the same time especially in females associated with romance and sex appeal. The lips due to several factors like loss of teeth, smoking, ultraviolet exposure, anatomical and congenital defects like cleft may

contribute to bone resorption and loss of volume, elasticity of subcutaneous soft tissue, retraction of lip red which directly results in lips with aging or unaesthetic appearance, loss of attractiveness, and fragility ⁽¹⁾.

Aging of the lips and perioral area is characterized by perioral fine lines, marionette lines, and flattening of the cupid's bow. The philtrum becomes longer and ill defined, indirectly contributing to a thinner upper lip. Furthermore The smile, for instance, gets narrower vertically and wider transversely ⁽²⁾.

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Dentistry and maxillofacial surgery play a significant role in restoring oral, lip and perioral aesthetics as lip care by Lip augmentation and enhancement may help to preserve a youthful and healthy appearance and enhance the aesthetic outcome of aesthetic restorative dentistry⁽³⁻⁶⁾.

The goal of a lip augmentation procedure is to create smooth lips with adequate volume and a well-defined vermilion border, there is no single way to achieve the intended results. However, anatomical knowledge and the use of appropriate products and techniques are essential for a natural appearance⁽⁷⁻⁹⁾.

Lip enhancement techniques are classified into surgical and nonsurgical procedures, surgical procedures like, V-Y mucosal advancement technique and aims to advance the labial mucosa forward. Other options for surgical lip augmentation include Surgical lip implants and autologous fat transfer and direct lip lift and sub-nasal lip lift procedures which are used only rarely⁽¹⁰⁻¹²⁾.

The injection of dermal fillers is the most popular nonsurgical procedure performed to increase the volume and improve the shape of the lips, Semi-permanent dermal fillers—such as calcium hydroxyapatite and poly-L-lactic acid and permanent fillers are not preferred for lip augmentation because they have an increased risk of irregularity and nodule formation. Hyaluronic acid fillers are the most used products for lip enhancement^(12,13).

Hyaluronic acid fillers are particularly popular because they have a low potential for allergic reaction and require no skin testing. Although they are not permanent, most of these agents have a significant length of duration. These numbers are expected to rise in the future as there is currently no other class of filling agent that rivals the popularity of hyaluronic acid⁽¹⁴⁾.

Juvéderm Volbella with Lidocaine is the newest member of Juvéderm family, Volbella contains a lower HA concentration (15 mg/mL) than does

Restylane, Perlane (20mg /mL), would result in a less hydrophilic gel that absorbs less water from surrounding tissues after injection. Juvéderm Volbella filler uses according to the manufacturing company the Vycross technology; this proprietary process creates highly efficient cross-linkage of a mix of low and high molecular weight HA, imparting greater gel hardness (a higher G prime value) and increased resistance to endogenous hyaluronidase degradation of the product, this physiochemical property accounts for longevity, superior cohesivity, and notable lifting capacity which increases product duration of action and produces a higher-viscosity gel with greater lift capacity⁽¹⁵⁻¹⁷⁾.

The present study evaluated the safety and effectiveness of Juvéderm Volbella with Lidocaine for lip volume enhancement versus Restylane.

SUBJECTS AND METHODS

Study design:

It is prospective, randomized clinical study. The study was conducted on patients in need for lip augmentation. Patients were selected from the outpatient maxillofacial surgery clinic at faculty of dental medicine, Cairo, Boys, Al-Azhar University.

Inclusion criteria:

Inclusion criteria included patients in need of lip augmentation with score of 1 (minimal) or 2 (mild) on the validated 5-point Allergan lip fullness Scale⁽¹¹⁾. Also, the patients selected was at Age over than 18 years and Non-smoker's with good oral hygiene.

Exclusion criteria:

Exclusion criteria included patients with Presence of medical contraindications for the surgical procedures, History of multiple severe allergies, autoimmune disease, or skin cancer, Presence of semi-permanent fillers or permanent implants in the lip, Allergy to Lidocaine, Hyaluronic acid, or streptococcal proteins, Sever psychological problems.

In addition to patients unable to sign the informed consent, Pregnant patient and patients who planned for orthognathic surgery.

Ethical consideration:

The research was approved by the ethical committee at Faculty of Dental Medicine (Boys- Cairo(Al-Azhar University with ethical code 749/2042

Sample size calculation:

According to a previous study by Bosniak et al (2004), that after 3 months, 15% of cases showed mild improvement, and 75% showed moderate improvement and 10% showed complete improvement of lip commissure, in comparison to 51% mild improvement and 34% moderate improvement and 15% no improvement after 6 months. Regarding lip fullness, at 3 months, 0% showed no improvement, 3.5% mild improvement, 20% moderate improvement and 76.5% complete improvement, in comparison to 25%, 35%, 35% and 6% respectively after 6 months. A medium effect size of approximately 0.43 is expected A total sample size of 36 patients (18 in each group) will be sufficient to detect an effect size of 0.43 at a power of 0.8 ($1-\beta$ error =0.8) and using a two-sided hypothesis test and a significance level 0.05 (α error= 0.05) for data

Intervention

The patients were divided randomly into two groups: Group (A): were received Juvéderm Volbella with Lidocaine. Group (B): were received Restylane-L.

Preoperative 3D facial and regular photographs was taken after the patient approval. We used standardized method 1:1 proportion for photo documentation to have a baseline photograph for comparison post treatment. The rejuvenation done under local anesthesia and the filler was injected by 30-gauge needle. The injection sites vary according to the patients' needs but generally in most patients the injection done first at vermilion border where

the insertion point of the needle was just little below the vermilion border The full length of the needle was inserted to create channel and the filler is injected while withdrawing the needle from the tissue. the injection was done in a systemic manner where the lip is divided into right and left halves and inject into one half (often left side) and compare it to the other side and then The vermilion body which approached from the mucosal side of the lip nearly in the center of the half of the lip and midway between the wet dry line and the vermilion border the needle is inserted laterally at 45 degree angle and then directed toward the center at 20 degree angle. Retrograde threading of the gel was done in a medial to lateral direction then the philtral columns injection was achieved by inserting the full length of the needle at the G-K point toward the nasal septum, and injection was done by using the retrograde threading small uniform thread of the product is deposited with the end of the retrograde threading of philtral column a small amount of gel was deposited to create ant post strut and produce a lift of the cupids bow, this provide support to the projection of the center of the upper lip and also help to shorten the appearance of elongated cutaneous upper lip then the peri oral lines approached where nasolabial fold was rejuvenated by insertion the needle from the lip to the nose direction and the injection is done by the retrograde threading and finally injection of the filler in the oral commissure achieved by insertion and directing the needle toward the commissures but stopped at least 1mm before the mucosa, it is recommended to inject below the commissures to produce an upward lift (smile lift).

Follow up visits done at 1 and 14 days after each treatment and at 1 and 6 Months also to assess the changes of the lip fullness by Allergan lip fullness scale and change in the linear measurements of vermilion show and lip projection by using facial 3d images by (Bellus 3D app) which processed by (3Dmatics software). (Figure 1-3)



FIG (1) Showing the clinical changes in the lip fullness after injected with Juvéderm vollella; (A) Showing the lip before the injection with Juvéderm vollella; (B) The lip fullness at the 1st day after the injection; (C) The lip fullness at the day 14 after the injection; (D) The lip fullness after 1 month of the injection; (E) The lip fullness after 6 months of the injection.

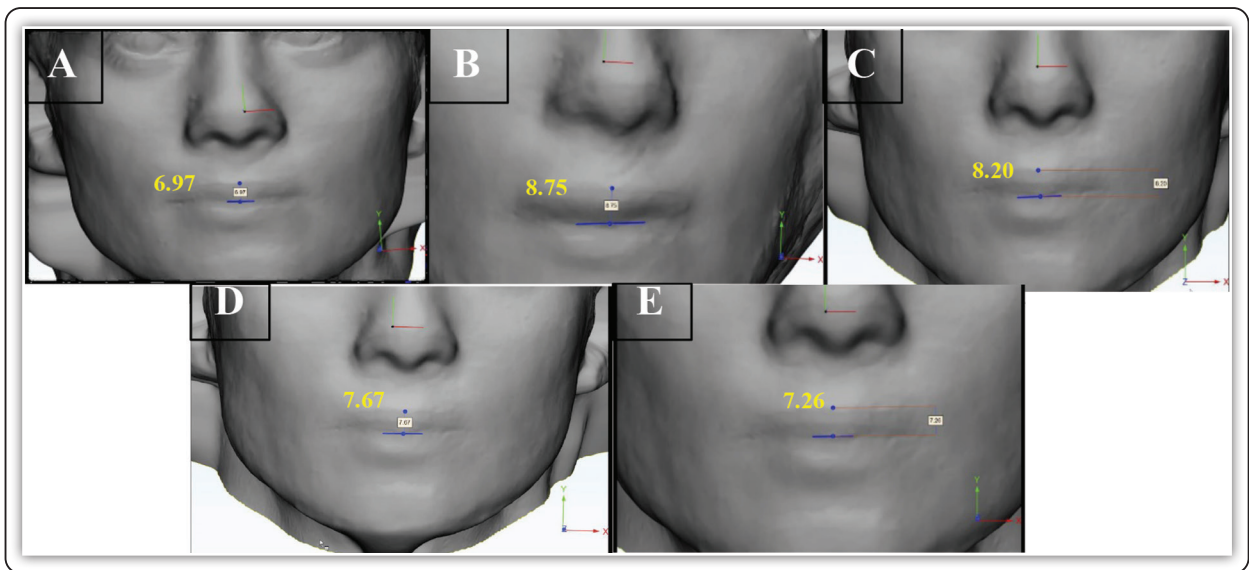


FIG (2) Facial 3D images showing the changes of the lip fullness after injected with Juvéderm vollella; (A) Showing facial 3D image of the lip before the injection with Juvéderm vollella; (B) Facial 3D image of the lip fullness at the 1st day after the injection; (C) Facial 3D image of the lip fullness at the day 14 after the injection; (D) Facial 3D image of the lip fullness after 1 month of the injection; (E) Facial 3D image of the lip fullness after 6 months of the injection.

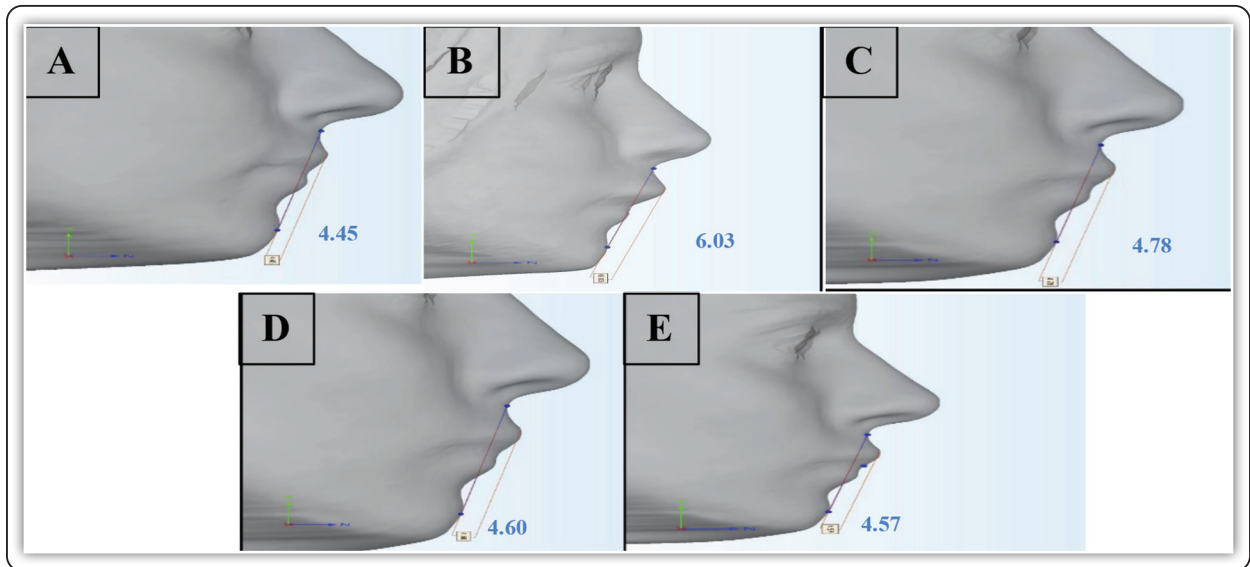


FIG (3) Facial 3D images showing the change in of the linear measurements of lip projection after injected with Juvéderm vollella; (A) Showing facial 3D image of linear measurement of the lip projection before the injection with Juvéderm vollella; (B) Showing changes in the measurements of the lip projection at the 1st day after the injection; (C) Showing changes in the measurements of the lip projection at the day 14 after the injection; (D) Showing changes in the measurements of the lip projection after 1 month of the injection; (E) Showing Changes in the measurements of the lip projection after 6 months of the injection.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage

RESULTS

Post-operative change of the lip fullness compared to the base line .According to the post injection lip fullness scale when compared to the pre injection scale, the change in group (A) injected with Juvéderm Volbella with Lidocaine were (88.89%) compared to group injected with Restylane-L were (83.33%), this indicates very high improvement in the each group, the total change improvement were ≥1 point improvement in both groups, however improvement in group (A) were more than group (B) but this is statistically insignificant. Figure (4)

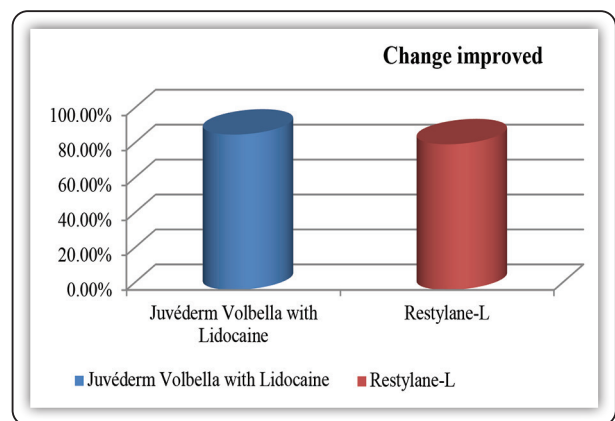


FIG (1) Bar chart showing the change improvement of the lip fullness compared to the base line in both groups.

Post injection Allergan lip fullness scale were comparable in each, as in group (A) when compared to the base line scale where no one patient was 0 (0.0%), 7 patients (38.9%), 8 patients (44.4%) and 3 patients (16.7%) were minimal, mild, moderate and marked, respectively compared to group (B) where no one patient was 0 (0.0%), 10 patients (55.6%),

6 patients (33.3%) and 2 patients (11.1%) were minimal, mild, moderate and marked respectively, there is no statistically significant difference between the two groups with p-value ($p=0.602$), as presented in table (2) compared to table (1).

TABLE (1) Comparison between the two groups according to their pre injection Allergan lip fullness scale.

Allergan Lip fullness scale (pre injection)	Group (A) (n=18)	Group (B) (n=18)	Test value	p-value
Minimal (1)	5 (27.8%)	7 (38.9%)	0.125	0.724
Mild (2)	13 (72.2%)	11 (61.1%)		

Using: χ^2 : Chi-square test; $p\text{-value} > 0.05$ NS

TABLE (2) Comparison between the two groups according to their Allergan lip fullness scale (post injection).

Allergan Lip fullness scale (Post injection)	Group (A) (n=18)	Group (B) (n=18)	Test value	p-value
Minimal (1)	0 (0.0%)	0 (0.0%)	1.015	0.602
Mild (2)	7 (38.9%)	10 (55.6%)		
Moderate (3)	8 (44.4%)	6 (33.3%)		
Marked (4)	3 (16.7%)	2 (11.1%)		
#Change improved	88.89%	83.33%		

Using: Fisher's Exact; $p\text{-value} > 0.05$ NS

Improvement was assessed by a favorable change of the score from a high value

DISCUSSION

Injection of dermal fillers is the second most frequent nonsurgical cosmetic procedure performed in the world. Dermal fillers are an option in the treatment of volume deficiency, scars, and rhytids; facial sculpting; facial contouring; and augmentation of specific anatomical sites such as the lips⁽¹⁸⁾.

This study targeted the augmentation of lips and perioral region because the Full lips have long been considered aesthetically attractive, sensual, and youthful. Patients often seek volumization of their lips, which may be thin as a baseline genetic trait or may progressively thin as part of the well-described aging process.

The study used the nonsurgical cosmetic (HA dermal fillers) in treatment of the unaesthetic lip because Hyaluronic acid fillers have a low potential for allergic reaction and require no skin testing. Although they are not permanent, most of these agents have a significant length of duration. The procedure is relatively quick to perform, and the patient feels little discomfort if the appropriate pain management techniques are used.

The present study selected to evaluate the safety and effectiveness of Juvéderm Volbella versus Restylane-L, as Juvéderm Volbella is the newest member of Juvéderm family and uses a new cross-linking technology Vycross (Allergan, Irvine, Calif.) technology platform, which combines low- and high-molecular-weight hyaluronic acid with a novel cross-linking process. These properties increase cross-linking efficiency, resulting in a tightly cross-linked hyaluronic acid network, which increases product duration of action and produces a higher-viscosity gel with greater lift capacity while Restylane is the first FDA approved HA dermal filler.

This comparison helps the operators to choose the right filler for the indicated patients as the study is well controlled study as it done by the same operator on nearly the same age, attitude and the social level patients, the age average was (18-35) narrow range to restrict the age impact factor on the comparison.

This study gave its main end result: the effectiveness of Juvéderm Volbella with Lidocaine for lip augmentation and enhancement was comparable to the treatment with Restylane- L.

The result was based on an assessment by lip fullness from 3D facial images using the LFS. Results also were supported by assessments made by the investigators.

The photographic (3d facial images) and investigator assessments of LFS at baseline differed considerably; the photographic assessment found a higher mean LFS score and rated high percentage of the subjects as having moderate or marked lip fullness at baseline. Accordingly, these cases difficult to show the 1-point improvement in overall lip fullness. Differences were also observed between assessors for oral commissures and perioral lines. Therefore, the photographic assessment regarding the LFS is less sensitive for measuring observable changes compared with in-person assessment.

The next result of the study was due to the instability of the assessment by LFS based on 3D images we use the dimensional analysis by linear measurements based on lip vermilion show in the frontal view and the lip projection in lateral view and it was better than using LFS because the availability of stable measurements in millimeters and at the same time uses the same 1:1 proportion 3D facial image.

By these objective measurements of lip from the dimensional analysis of the 3D images Juvéderm Volbella with Lidocaine was effective as Restylane-L These results agree with Previous comparative study conducted by Wolters Kluwer Health which published in 2015 on the American society of plastic surgeons and also with studies using other injectable gels from the Juvéderm family, including Juvéderm Volbella (without lidocaine) and Juvéderm Ultra, which were effective in augmenting lip fullness and reducing perioral lines and oral commissures ^(15,19).

One of the most important point to be discussed is absence of clinical impact of the difference between the Juvéderm Volbella and Restylane-L regarding the molecular weight, degree and method

of crosslinking, HA concentration and the type of the gel (monophasic versus biphasic) and the pattern of the distribution in the dermal layer, we concluded that the effect after injection and the durability of both types was comparable with no big differences although the recommendation of using Mono phasic HA in addition to the high cost of Juvéderm, this agree with study that published on august 2016 by Dr costa in aesthetic surgery journal in title Durability of Three Different Types of Hyaluronic Acid Fillers in Skin: Are There Differences Among Biphasic, Monophasic Monodensified, and Monophasic Polydensified Products? and agree with that published by K.Y. Park, H.K. Kim, B.J. Kim in title Comparative study of hyaluronic acid fillers in vitro and in vivo testing ^(20, 21).

The coast / benefit ratio of the Juvéderm Volbella is a critical point to be discussed and should be considered because the very important fact; the HA based fillers are temporary and the patients may need to be re injected every (6:9) months to maintain the result of filler.

Finally, regarding the technique in this study, we used the conventional filler injection techniques which are not standardized and predictable in their results because the injection depend on the clinical sense of the operators and patients point of views so we recommend to the new technology of 3D photographs and simulation like the MD Codes™ approach ⁽²²⁾.

The MD Codes™ approach which provides a practical, structured method that helps to facilitate treatment choices. The MD Codes, or medical codes, represent specific anatomical subunits for injection of HA fillers. Each MD Code includes information regarding the target depth of injection, the proper delivery tool (needle or cannula) and delivery technique), and the minimum product volume recommended to achieve visible, reproducible results. In addition, during treatment planning, the appropriate MD Codes are selected using algorithms

focused on lessening unfavorable facial attributes (a saggy, tired, sad, or angry look) and enhancing positive attributes (an attractive, younger, more contoured, or feminine [soft] or masculine look⁽²²⁾.

CONCLUSION

Injection of HA dermal fillers is a reliable technique for improvement of the patient aesthetic, there were very low complications or adverse injection site reaction associated with injection of Juvéderm Volbella and Rystelane-L. Regarding the effectiveness and duration there was no significant difference between Juvéderm Volbella and Restylane-L.

REFERENCES

1. Klein A. In search of the perfect lip: 2005. *Dermatol Surg.* 2005; 31:1599–1603.
2. Leveque J, Goubanova E. Influence of age on the lips and perioral skin. *Dermatology.* 2004; 208:307–313.
3. Trookman N, Rizer R, Ford R, Mehta R, Gotz V. Clinical assessment of a combination lip treatment to restore moisturization and fullness. *J Clin Aesthet Dermatol.* 2009; 2:44–48.
4. Trookman N, Rizer R, Ford R, Ho E, Gotz V. Immediate and long-term clinical benefits of a topical treatment for facial lines and wrinkles. *J Clin Aesthet Dermatol.* 2009; 2:38–43.
5. Frese C, Staehle H, Wolff D. The assessment of dentofacial esthetics in restorative dentistry: a review of the literature. *J Am Dent Assoc.* 2012; 143:461–466.
6. Niamtu J. Perioral soft-tissue rejuvenation techniques to enhance esthetic restorative dentistry. *Compend Contin Educ Dent.* 2003; 24: 811–818.
7. Byrne P, Hilger P. Lip augmentation. *Facial Plast Surg.* 2004; 20:31–8.
8. Clymer M. Evolution in techniques: lip augmentation. *Facial Plast Surg.* 2007; 23:21–26.
9. Sarnoff D, Saini R, Gotkin R. Comparison of filling agents for lip augmentation. *Aesthet Surg J.* 2008; 28:556–563.
10. Obradovic B, Obradovic M. Triple V-Y vermilion augmentation of the upper lip. *J Craniofac Surg.* 2015;26: 736–738.
11. Maloney B, Truswell W, Waldman S. Lip augmentation: discussion and debate. *Facial Plast Surg Clin North Am.* 2012; 20:327–346.
12. Mannino G, Lipner S. Current concepts in lip augmentation. *Cutis.* 2016; 98: 325–329.
13. Landau M. Lip augmentation and rejuvenation using Dermicol-P35 30G: personal experiences from my clinic. *Aesthet Surg J.* 2009; 29: 12–15.
14. Karen L, Beasley S, Margaret A, Weiss M. Hyaluronic Acid Fillers: A Comprehensive Review. *Facial Plastic Surgery.* 2009; 25:86-93.
15. Eccleston D, Murphy D. Juvéderm® Volbella™ in the perioral area: a 12-month prospective, multicenter, open-label study. *Clin Cosmet Investig Dermatol.* 2012; 5:167–172.
16. Jones D, Murphy D. Volumizing hyaluronic acid filler for midface volume deficit: 2-year results from a pivotal single-blind randomized controlled study. *Dermatol Surg.* 2013; 39:1602–1612.
17. Carruthers J, Carruthers A, Tezel A, Kraemer J, Craik L. Volumizing with a 20-mg/mL smooth, highly cohesive, viscous hyaluronic acid filler and its role in facial rejuvenation therapy.
18. Rohrich R, Ghavami A, Crosby M. The role of hyaluronic acid fillers (Restylane) in facial cosmetic surgery: review and technical considerations. *Plast Reconstr Surg.* 2007; 120:41-54.
19. Fagien S, Maas C, Murphy D. Juvéderm Lips Study Group. Juvederm ultra for lip enhancement: an openlabel, multicenter study. *Aesthet Surg J.* 2013; 33:414–420.
20. Park K, Kim H, Kim B. Comparative study of hyaluronic acid fillers by in vitro and in vivo testing. *J Eur Acad Dermatol Venereol.* 2014; 28:565-568.
21. Da Costa A, Biccigo D, De Souza W. Durability of Three Different Types of Hyaluronic Acid Fillers in Skin: Are There Differences Among Biphasic, Monophasic Monodensified, and Monophasic Polydensified Products? *Aesthet Surg J.* 2017; 37:573-581.
22. De Maio M. MD Codes™: A Methodological Approach to Facial Aesthetic Treatment with Injectable Hyaluronic Acid Fillers. *Aesthetic Plast Surg.* 2021; 45:690-709.