COSMETIC

Distribution Pattern of the Superior and Inferior Labial Arteries: Impact for Safe Upper and Lower Lip Augmentation Procedures

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Roseau, Commonwealth of Dominica; Salzburg and Vienna, Austria; and Kiel, Munich, Tuebingen, and Luebeck, Germany **Background:** Understanding the precise position and course of the superior and inferior labial arteries within the upper lip and the lower lip is crucial for safe and complication-free applications of volumizing materials.

Methods: One hundred ninety-three anatomical head specimens (56.5 percent female cadavers) of Caucasian ethnicity were investigated in this large multicenter anatomical study. In total, six 3-cm-long vertical incisions were performed on each lip (midline and 1 cm medial to the angles of the mouth) to identify the position of the superior and inferior labial arteries in relation to the orbicularis oris muscle.

Results: Three different positions of the superior and inferior labial arteries were identified: submucosal (i.e., between the oral mucosa and the orbicularis oris muscle in 78.1 percent of the cases), intramuscular (i.e., between the superficial and deep layers of the orbicularis oris muscle in 17.5 percent of the cases), and subcutaneous (i.e., between the skin and the orbicularis oris muscle in 2.1 percent of the cases). The variability in changing the respective position along the labial course was 29 percent for the total upper and 32 percent for the total lower lip. The midline location was identified in both the upper and lower lips to be the most variable.

Conclusions: Based on the results of this investigation, a safer location for the application of volumizing material is the subcutaneous plane in the paramedian location of both the upper lip and the lower lip. Care has to be taken when aiming to inject in the midline, as the artery can be identified more frequently in superficial positions. (*Plast. Reconstr. Surg.* 139: 1075, 2017.)

A ccording to the annual statistical report of the American Society of Plastic Surgeons, the application of soft-tissue fillers has gained considerable interest in our society. The use of soft-tissue fillers has increased between 2000 and 2015 by 274 percent and from 2014 to 2015 by 6 percent.¹ Most products are based on hyaluronic acid, and the most frequent locations for facial

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volumizing procedures are the lips.^{2–5} Enhancement of lip volume, reformation of the Cupid's bow, and restoration of the vermillion border are frequent indications for the application of materials into the upper and lower lips.⁶ Interestingly, the inability to conceal these signs of aging has been associated with increased anxiety and depression.⁷

Frequent application of volumizing materials in the head and neck region has led to multiple complications, including pain, bruising, inflammation, and necrosis,⁸ but also hemiplegia, aphasia, and blindness.⁹ The latter, however, has also been reported to result from application of volumizing materials into the lips, which suggests a potential involvement of the arterial vascular system.^{10–12}

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Previous reports have focused on the anatomy of the upper and lower lips and have revealed that the superior and inferior labial arteries show a high variability in presence and course.^{13–16} The results of these studies, however, lack the information of the precise position of both labial arteries in relation to the different layers of the lips. This information is of essential interest for manufacturers and health care professionals when applying volumizing materials.

Therefore, the aim of the present study was to investigate the precise position and course of the superior and inferior labial arteries within the upper and lower lips to provide guidance for manufacturers and health care professionals concerning the application of volumizing materials into the lips. We specifically designed a large multicenter anatomical study based on data from six different anatomical departments to provide reliable and valid results to answer this clinically relevant question. In addition, we included a computed tomographic imaging part in our analyses to show the well-developed vascularization of the lips.

MATERIALS AND METHODS

Study Sample

One hundred ninety-three human anatomical head specimens were included in this multicenter study, with 56.5 percent of those being female cadavers. All specimens were taken from Caucasian body donors from the body donation programs of the universities participating in this study. While alive, all body donors gave informed consent for participation in medical education and in scientific investigations with a medical background. The procedures applied in this study complied with the laws of the country in which they were performed.

Anatomical Dissection

Anatomical dissection was performed according to a standardized central protocol in six different anatomical departments, without significant difference in sex distribution between the six participating anatomical sites (p = 0.67): Institute of Anatomy, Paracelsus Medical University Salzburg & Nuremberg, Salzburg, Austria; Center of Anatomy and Cell Biology, Division of Anatomy, Medical University of Vienna, Vienna, Austria; Institute of Anatomy, Christian-Albrechts-University of Kiel, Kiel, Germany; Institute of Anatomy, Department of Clinical Anatomy and Cell Analysis, University of Tuebingen, Tuebingen, Germany; Institute of Anatomy, University of Luebeck, Luebeck, Germany; and Department of Anatomy, Ross University School of Medicine, Roseau, Commonwealth of Dominica. The standardized central protocol provided information on the dissection procedure, and all participating sites followed this protocol during dissections, which were carried out by two investigators at each site.

Anatomical dissection was based on vertical 3-cm-long incisions of the upper and lower lips in each three defined locations: midline, 1 cm medial to the left angle (paramedian left), and 1 cm medial to the right angle of the mouth (paramedian right) (Fig. 1). The position of the main trunk of the superior/inferior labial artery in relation to the orbicularis oris muscle was documented.

Computed Tomographic Imaging

To show the well-developed vascularization of the upper and lower lips, a computed tomographic imaging series was obtained in 10 fresh frozen cephalic specimens originating from six female and four male cadavers, with a mean ± SD age of 72.6 ± 8.2 years. Bilateral access to the facial artery was made introducing an intravenous port for the application of contrast agent. Arterial contrasting was performed by injecting radiopaque dye (Lipidiol Ultra-Fluide Iohexol, Omnipaque; Amersham, Princeton, N.J.). Multiple computed tomographic scans were obtained to achieve maximal contrasting of the labial vasculature. The following parameters were applied to each of the computed tomographic scans: field of view, 200 mm; slice thickness, 0.6 mm; increment, 0.4 mm; voltage, 120 kV; and current, 400 mA/ second.

Statistical Analysis

The Manhattan metric was used to count the number of jumps (i.e., the change of position of the measured artery along its course within the upper or lower lip from paramedian right to midline to paramedian left). Generalized linear models were used to identify whether the measured location or the sex had an influence on the position of the superior and inferior labial arteries. All reported tests were two-sided, and values of p < 0.05 were considered as statistically significant. All statistical analyses in this report were performed by use of Mathematica, Version 7.0 (Wolfram Research, Inc., Champaign, Ill.) and Statistica 13 (StatSoft, Tulsa, Okla.).



Fig. 1. Schematic of the dissection procedure, provided in the central study design protocol. Three incisions were made in the upper lip and in the lower lip: 1 cm medial to the right angle of the mouth, midline, and 1 cm medial to the left angle of the mouth.

RESULTS

In all of the 193 investigated anatomical head specimens, the superior and inferior labial arteries were identified within the respective lip. The superior labial artery was identified to run at the level of the vermillion border, whereas the inferior labial artery was found in general inferior to the vermillion border in the lower lip. The overall distribution of the position of the superior and inferior labial arteries was 78.1 percent submucosal, 17.5 percent intramuscular, and 2.1 percent subcutaneous (Table 1 and Figs. 2 and 3). In 0.6 percent of the cases, two arteries were found in the same lip to run in the submucosal and intramuscular position, 1.3 percent in the submucosal and subcutaneous position, and 0.2 percent in the intramuscular and subcutaneous position. No statistical significant differences were detected when investigating the influence of sex on these distributions.

The distribution for the upper lip was 78.1, 17.6, and 2.6 percent, whereas the distribution for the lower lip was 78.1, 17.3, and 1.7 percent for the respective arterial position. The calculated variation (i.e., the change between the layers) was 29 percent for the total upper lip and 32 percent for the total lower lip. When calculating the number of jumps (i.e., how often one artery changes its plane during its course within the upper/lower lip), it was identified that 71 percent in the upper lip and 67 percent in the lower lip of the cases did not change the plane, whereas 16 percent and 9 percent changed one time and 13 percent and 23 percent changed two times, respectively (Fig. 4).

Looking at the position of the arteries in the midline location, it was observed that in 70.5 percent (77.2 percent upper lip versus 63.7 percent lower lip) of the cases the artery was identified in the submucosal position, in 23.6 percent (18.7 percent upper lip versus 28.5 percent lower lip) it

	Anatomical Position					
Labial Location	Submucosal (%)	Intramuscular (%)	Subcutaneous (%)	Submucosal and Intramuscular (%)	Submucosal and Subcutaneous (%)	Intramuscular and Subcutaneous (%)
Upper lip						
Paramedian right	150 (77.7)	36(18.7)	5(2.6)	1(0.5)	1(0.5)	0
Midline	149 (77.2)	36 (18.7)	4(2.1)	2(1)	1(0.5)	1(0.5)
Paramedian left	153 (79.3)	30 (15.5)	6(3.1)	2(1)	2 (1)	O Í
Lower lip	× /					
Paramedian right	166 (86)	23(11.9)	2(1)	0	3(1.6)	0
Midline	123 (63.7)	55 (28.5)	6(3.1)	2(1)	6(3.1)	1(0.5)
Paramedian left	163 (84.5)	22 (11.4)	2 (1)	Ô,	6 (3.1)	0

*Three anatomical positions and their combinations in relation to the orbicularis oris muscle were identified: submucosal, intramuscular, and subcutaneous. Data are given as absolute values and percentages of the total sample (n = 193).

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Fig. 2. Schematic drawings (exemplified for the lower lip) of the three identified positions of the superior and inferior labial arteries in the upper and lower lips: (*right*) submucosal (i.e., between the oral mucosa and the orbicularis oris muscle); (*center*) intramuscular (i.e., between the superficial and the deep layer of the orbicularis oris muscle); (*left*) subcutaneous (i.e., between the skin and the orbicularis oris muscle).



Fig. 3. Anatomical dissection of the position of the superior and inferior labial arteries within the lips: (*left*) subcutaneous (i.e., between the skin and the orbicularis oris muscle); (*center*) intramuscular (i.e., between the superficial and deep layer of the orbicularis oris muscle); (*right*) submucosal (i.e., between the oral mucosa and the orbicularis oris muscle.

was identified in the intramuscular position, and in 2.6 percent (2.1 percent upper lip versus 3.1 percent lower lip) it was identified in the subcutaneous position (Table 1).

The probability of the superior and inferior labial arteries to change planes along their courses was significantly higher when compared to the submucosal position, if the arteries were once identified in the midline in the intramuscular (upper lip, p < 0.001; lower lip, p < 0.001) or in the subcutaneous (and combinations) position (upper lip, p < 0.001; lower lip, p < 0.001) (Fig. 5). On the contrary, arteries in the submucosal position in the midline of both the upper and lower lips indicate a significantly more stable course with significantly less change in planes



Fig. 4. Bar graph showing the frequencies of the superior and inferior labial arteries within the upper (*blue bars*) and lower (*orange bars*) lips to change planes, calculated by the number of jumps of each artery along its course in the lip. The *y* axis represents the number of investigated cases and the *x* axis represents the number of jumps of the respective arteries.

along the course in the respective lip (Fig. 5). The results of the computed tomographic scans revealed a well-vascularized capillary network of lips, with small arteries reaching until the surface of the lips and thus leading to a complete contrasting of the outer morphology of the lips (Fig. 6).

DISCUSSION

The results presented in this large multicenter anatomical investigation including 193 specimens reveal a variable coursing pattern of both the superior and inferior labial arteries. The position of each respective artery varies between three different positions (and their



Fig. 5. Whisker plots showing the number of jumps (i.e., the frequency of the superior labial artery within the upper lip and of the inferior labial artery within the lower lip to change planes when identified in the midline location). Data are presented as means with 95 percent confidence intervals.

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Fig. 6. Three-dimensional reconstruction of a computed tomographic scan of the head after the application of contrast agent into the right facial artery. Please consider that the facial veins have also been partially filled as the contrast agent passed the capillary network and partially entered the venous system.

combinations). The most frequent position identified was the submucosal position, followed in frequency by the intramuscular position and the subcutaneous position.

The strength of the present study is its sample size, with 193 human anatomical specimens of Caucasian ethnicity, which was only accomplished by the collaboration of six anatomical departments from different countries. Moreover, the investigated anatomical specimens were not hemisected as reported previously^{13,14} but were used in completeness to follow the complete course of the arteries.

The results presented in this study are partially in line with previous reports about the arterial distribution of the superior and inferior labial arteries.^{13–15,17} Recently, Lee et al.¹⁴ studied 36 body donors of Asian ethnicity, and reported that the superior labial artery followed a constant course along the vermillion border at a depth of 3 mm, without providing any information regarding variability in position.¹⁴ Our results are partially in line with these findings, as we likewise identified the superior labial artery at the level of the vermillion border. However, we found a high variability in the position of the artery in relation to the orbicularis oris muscle and thus in the depth of the artery. Our results reveal that the artery is mostly found in the submucosal position (78.1 percent) but varies especially within the upper lip. Thereby, it showed a variation of 29 percent, and predominantly in the midline the superior labial artery was found to lie more superficial. This is of great interest, as aesthetic procedures aiming to increase the volume of the upper lip or to contour the Cupid's bow are applied in this delicate region of the upper lip. Therefore, awareness of the anatomical variations is a crucial concept, and is mandatory when injecting superficially in the midline.

In another publication by Lee et al.¹³ investigating the distribution pattern of the inferior labial artery, the authors identified its position in 46 percent of the cases in the periosteal layer and in 15.9 percent of the cases in the intramuscular layer.¹³ However, the authors did not specify the location (midline versus paramedian) in which the arteries were investigated or whether a change of planes occurred during their course. Our results showed that, similar to the upper lip, the artery can be identified more superficially in the midline, with 28.5 percent in the intramuscular position. In addition, we found an overall variability to change planes of 32 percent within the lower lip. These results are unique in their presented form because, for the first time, a study provides reliable data based on large-sample analysis to estimate the risk of injecting volumizing materials into the respective planes of the upper and lower lips. Future guidelines of scientific societies and industrial partners can be coordinated with regard to the respective position of the artery to minimize the risk of adverse effects when applying specific products into the respective layers of the lip.

The variation in the distribution pattern of the labial arteries is explainable when focusing on facial embryogenesis.^{18–21} In the embryo, the formation of the superior and the inferior labial arteries precedes the formation of the orbicularis oris muscle, and thus the muscle precursor cells have to form around preexisting vessels. This implies that a high variability in the migratory pathway of the muscle precursor cells is given and that this fact is responsible for the three definite positions the labial artery is able to occupy (i.e., submucosal, intramuscular, and subcutaneous). In addition, the muscle precursor cells form a thicker layer in the upper lip compared with the lower lip, with fewer cells being present in the midline in both lips.¹⁹ This explains the relative thinness of both the upper and lower lips in the midline and the different pattern of the superior and inferior labial arteries in the midline compared with paramedian locations.

In postnatal life, the orbicularis oris muscle complex is a two-layer muscular sphincter arranged in fibers running circular and perpendicular to the oral commissure. The deep layer of this muscle is formed by a continuation of the buccinator muscle, and the superficial layer is established by the irradiating muscle fibers derived from the muscles of facial expression.

The facial artery can be identified superficial to the buccinator muscle but deep to the muscles of facial expression within the buccal space in the midface.²² The modiolus represents the location where the aforementioned muscles fuse and form a perpendicular muscular pillar with an extension of 1.0×1.5 cm.²³ The facial artery is attached to the modiolus by means of a ligamentous structure²³ and can be identified in most cases within 1 to 2 cm posterior to the angle of the mouth in the horizontal plane. Both the superior and inferior arteries (if present) travel in relation to the two layers of the orbicularis oris muscle complex toward the midline and anastomose with the respective vessels from the contralateral side.¹⁵ As the labial arteries were previously shown to display high variability with regard to course, presence, and location,^{13,14,17} it is plausible that they can be found in different positions in relation to the orbicularis oris muscle. In our study, three different position of the arteries were identified (i.e., submucosal, intramuscular, and subcutaneous), and these results are contradictory to the previously established "rule" that, within the lips, the labial arteries follow a constant course in the submucosal plane. The results presented provide robust evidence that a change in the current paradigm has to occur to account for the anatomical variation in the arterial vascular pattern and to limit the risk for vascular complications, of which irreversible blindness is the most severe⁹ and that can occur even in the hands of experienced injectors when applying volumizing materials.

Given the amount of labial augmentation procedures, it is remarkable that the severity and amount of complications are limited compared with the number of injections in the perioral region.⁹ This could be because the capillary network of the upper and lower lips is well developed and vascular complications are "well" tolerated and potentially occur more frequently than clinically observed but with less clinical or aesthetic impact. This fact has been demonstrated by the imaging part of our study, which supports this assumption when revealing the total contrasting of the lips as compared to other facial regions where only the vessel itself was contrasted (Fig. 6). The position of the arteries within the upper and lower lips could be ensured by using imaging techniques or by means of clinical examination to estimate safer locations for the volumizing procedures. Based on the results of our investigation, a safer location for the application of volumizing material is the subcutaneous plane in paramedian locations both in the upper lip and in the lower lip. In the midline, however, injectors have to be aware of the anatomical variations reported when aiming to inject into more superficial planes.

CONCLUSIONS

Here, we present data from a large multicenter anatomical study investigating 193 head specimens revealing the distribution pattern of the superior and inferior labial arteries in the upper and lower lips. We identified three different positions of the arteries in relation to the orbicularis oris muscle: submucosal (78.1 percent), intramuscular (17.5 percent), and subcutaneous (2.1 percent). The variability in the position of the superior labial artery to change the plane is 29 percent, whereas it is 32 percent for the inferior labial artery. Profound anatomical knowledge of the precise position of the superior and inferior labial arteries can reduce the risk of adverse effect and increase the probability of safe and long-lasting results.

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REFERENCES

- American Society of Plastic Surgeons. 2015 cosmetic plastic surgery statistics. Available at: https://d2wirczt3b6wjm.cloudfront.net/News/Statistics/2015/plastic-surgery-statistics-fullreport-2015.pdf. Accessed June 25, 2016.
- 2. Brandt FS, Cazzaniga A. Hyaluronic acid gel fillers in the management of facial aging. *Clin Interv Aging* 2008;3:153–159.
- 3. Bogdan Allemann I, Baumann L. Hyaluronic acid gel (Juvéderm) preparations in the treatment of facial wrinkles and folds. *Clin Interv Aging* 2008;3:629–634.

- Bergeret-Galley C. Choosing injectable implants according to treatment area: The European experience. *Facial Plast Surg.* 2009;25:135–142.
- 5. Sarnoff DS, Saini R, Gotkin RH. Comparison of filling agents for lip augmentation. *Aesthet Surg J.* 2008;28:556–563.
- Philipp-Dormston WG, Hilton S, Nathan M. A prospective, open-label, multicenter, observational, postmarket study of the use of a 15 mg/mL hyaluronic acid dermal filler in the lips. J Cosmet Dermatol. 2014;13:125–134.
- Gupta MA, Gilchrest BA. Psychosocial aspects of aging skin. Dermatol Clin. 2005;23:643–648.
- 8. Grunebaum LD, Bogdan Allemann I, Dayan S, Mandy S, Baumann L. The risk of alar necrosis associated with dermal filler injection. *Dermatol Surg.* 2009;35(Suppl 2):1635–1640.
- 9. Beleznay K, Carruthers JD, Humphrey S, Jones D. Avoiding and treating blindness from fillers: A review of the world literature. *Dermatol Surg.* 2015;41:1097–1117.
- Danesh-Meyer HV, Savino PJ, Sergott RC. Ocular and cerebral ischemia following facial injection of autologous fat. *Arch Ophthalmol.* 2001;119:777–778.
- Chen Y, Wang W, Li J, Yu Y, Li L, Lu N. Fundus artery occlusion caused by cosmetic facial injections. *Chin Med J (Engl.)* 2014;127:1434–1437.
- Feinendegen DL, Baumgartner RW, Schroth G, Mattle HP, Tschopp H. Middle cerebral artery occlusion AND ocular fat embolism after autologous fat injection in the face. *J Neurol.* 1998;245:53–54.
- 13. Lee SH, Lee HJ, Kim YS, Kim HJ, Hu KS. What is the difference between the inferior labial artery and the horizontal labiomental artery? *Surg Radiol Anat.* 2015;37:947–953.

- Lee SH, Gil YC, Choi YJ, Tansatit T, Kim HJ, Hu KS. Topographic anatomy of the superior labial artery for dermal filler injection. *Plast Reconstr Surg.* 2015;135:445–450.
- Loukas M, Hullett J, Louis RG Jr, et al. A detailed observation of variations of the facial artery, with emphasis on the superior labial artery. *Surg Radiol Anat.* 2006;28:316–324.
- Turan A, Kostakoğlu N, Tuncel U. Reverse superior labial artery flap in reconstruction of nose and medial cheek defects. *Ann Plast Surg.* 2015;74:418–425.
- 17. Tansatit T, Apinuntrum P, Phetudom T. A typical pattern of the labial arteries with implication for lip augmentation with injectable fillers. *Aesthetic Plast Surg.* 2014;38:1083–1089.
- Tandler J. Zur Entwicklungsgeschichte der Kopfarterien bei den Mammalia. Morphol Jahrb. 1902;30:275–274.
- Gasser RF. The development of the facial muscles in man. AmJ Anat. 1967;120:357–376.
- 20. De la Cuadra-Blanco C, Peces-Peña MD, Carvallo-de Moraes LO, Herrera-Lara ME, Mérida-Velasco JR. Development of the platysma muscle and the superficial musculoaponeurotic system (human specimens at 8–17 weeks of development). *Scientific World Journal* 2013;2013:716962.
- 21. O'Rahilly R, Müller F. *Human Embryology and Teratology*. 2nd ed. New York: Wiley-Liss; 1996.
- 22. Cotofana S, Schenck TL, Trevidic P, et al. Midface: Clinical anatomy and regional approaches with injectable fillers. *Plast Reconstr Surg.* 2015;136(Suppl):219S–234S.
- 23. Al-Hoqail RA, Abdel Meguid EM. An anatomical and analytical study of the modiolus: Enlightening its relevance to plastic surgery. *Aesthetic Plast Surg*. 2009;33:147–152.