



Safe Glabellar Wrinkle Correction With Soft Tissue Filler Using Doppler Ultrasound

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Aesthetic Surgery Journal
2020, 1–9
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DOI: 10.1093/asj/sjaa197
www.aestheticsurgeryjournal.com

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Abstract

Background: Glabellar wrinkle corrections are usually performed by injecting botulinum toxin and hyaluronic acid fillers. The glabella is one of the most dangerous locations for filler injection because of possible visual complications.

Objectives: The aim of this study was to use Doppler ultrasound to determine the anatomic relation between glabellar wrinkles and the supratrochlear artery pathway, perform safe hyaluronic acid filler injection to correct glabellar wrinkles, and determine the efficacy of the procedure.

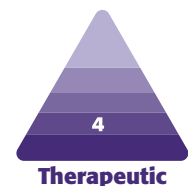
Methods: From January 2019 to July 2019, 42 patients (74 glabellar wrinkle lines; 32 bilateral and 10 unilateral wrinkles) were evaluated. Glabellar wrinkle lines were corrected with hyaluronic acid filler. Doppler ultrasound was used to avoid the supratrochlear artery.

Results: Among the 74 wrinkle lines, the supratrochlear arteries were located either at the glabellar wrinkle lines (30/74, 41%) or lateral to the glabellar wrinkle lines (44/74, 59%). In the latter 44 wrinkles, fillers were injected into the subdermal layer of the glabellar wrinkle lines. In the 30 wrinkles where supratrochlear artery was located at the glabellar wrinkle lines, the artery was located at the deep subcutaneous layer in 24 and at the subdermal layer in 6; thus, filler injection was not performed.

Conclusions: The supratrochlear artery may be located either at or lateral to the glabellar wrinkle lines. When performing glabellar wrinkle correction, Doppler ultrasound can be used to confirm the location of the supratrochlear artery before filler injection, which helps in avoiding vascular complications.

Level of Evidence: 4

Editorial Decision date: June 29, 2020; online publish-ahead-of-print July 9, 2020.



Soft tissue filler injection is one of the commonest aesthetic procedures because it is relatively easy to perform.¹ However, it brings the risk of serious complications, including skin necrosis and blindness.² The arteries of the face can be classified as internal and external carotid branches. The supratrochlear artery, a well-studied branch of the internal carotid artery, is located near the glabellar wrinkle lines. Embolism caused by filler particles in the internal carotid artery is a dangerous complication that brings the risk of blindness;^{3–5} thus, correction of glabellar

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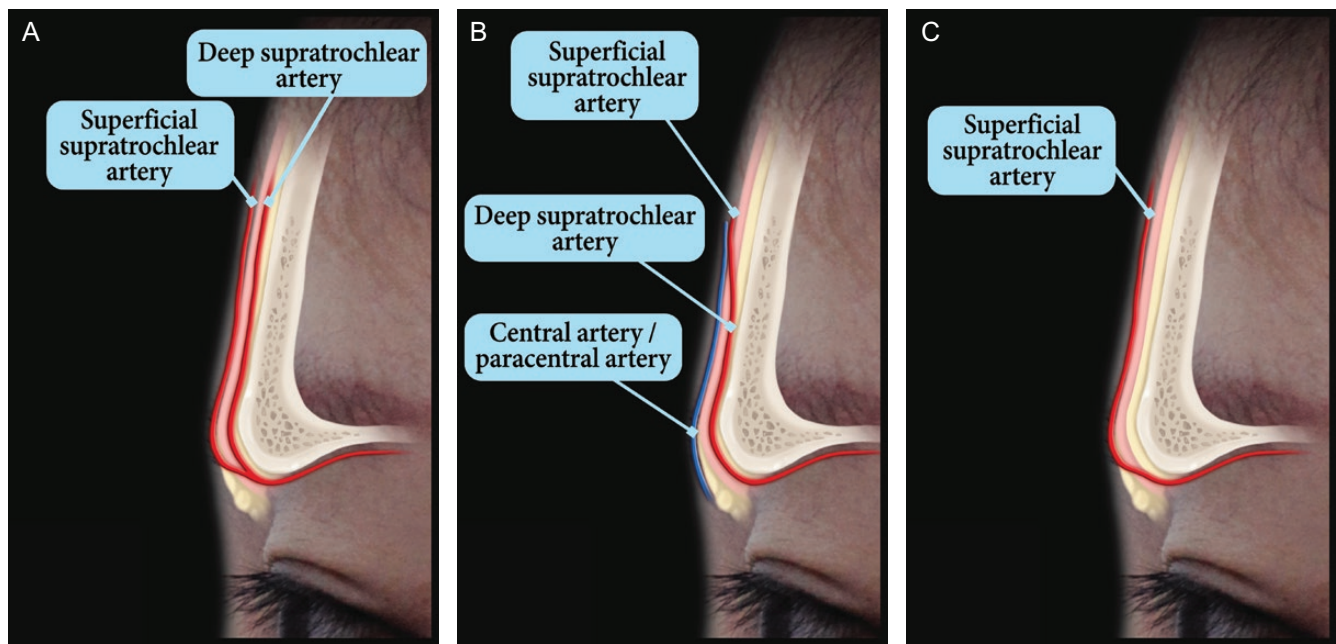


Figure 1. Supratrochlear artery pathways are superimposed on the face of a representative 28-year-old female subject. The supratrochlear and supraorbital arteries are branches of the ophthalmic artery. The supratrochlear artery perforates the medial orbital septum and runs to the glabellar area. The pathway of the supratrochlear artery in the glabella can be classified as type I, which includes the superficial and deep branches, which are further subdivided into (A) type Ia (superficial and deep branches), (B) type Ib (superficial branch anastomosis with the central artery), and (C) type II (superficial branch only).

wrinkle lines by soft tissue filler injection is among the commonest filler procedures that can cause blindness.⁶

Injection guidelines for this procedure were formulated based on a cadaveric study, but are of limited value because the long needles used to establish the topography might in practice encounter arteries.⁷ Another approach to administering glabellar filler involves dermal injection of fillers with a low storage modulus (G') into the target rhytides,⁸ although this can also result in an encounter with the superficial branch of the supratrochlear artery. Because glabellar wrinkles are caused by repetitive movements of the corrugator supercilii and procerus muscles, the first choice would be injecting botulinum toxin into the target muscle.⁹ However, once the wrinkle becomes a prominent groove, botulinum toxin injection is no longer sufficient for correction, thus necessitating concomitant filler injection.

As described in a previous report, the pathway of the supratrochlear artery can be divided into superficial and deep branches (Figure 1).⁷ Clinically, we can predict the approximate path of glabellar wrinkles and the supratrochlear artery, but the anatomic relation between the two is difficult to confirm. The objective of this study was to use Doppler ultrasound to determine the anatomic relation between glabellar wrinkles and the supratrochlear artery pathway to enable us to perform safe hyaluronic acid filler injection to correct glabellar wrinkles and assess the efficacy of the procedure.

METHODS

Patients

Between January 2019 and July 2019 we enrolled 42 patients in this study; all these patients had been evaluated with Doppler ultrasound and then treated with hyaluronic acid filler injection in the Yonsei E1 Plastic Surgery Clinic to correct glabellar wrinkles. Patients with visibly moderate to severe glabellar wrinkle lines who underwent hyaluronic acid filler and botulinum toxin injection and with available follow-up data were included. Patients with a single wrinkle line at the central portion were excluded because this wrinkle has no relation with the supratrochlear artery pathway. Patients with multiple glabellar frown lines were excluded because the focus of the study was on the relation between glabellar lines and the supratrochlear artery. Patients who had a history of trauma or surgery at the glabellar zone were also excluded.

This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Hanyang University Hospital institutional ethics committee (HYUH-2019-12-13). The requirement for informed consent was waived due to the retrospective nature of the study.

Table 1. Rheological Test Results of the Hyaluronic Acid Filler

Filler type	Storage modulus, G' (Pa)	Loss modulus, G'' (Pa)	Tan δ	Phase angle ($^{\circ}$)	Complex viscosity (Pa-s)	Frequency (Hz)
S100 lidocaine	50.7996	21.0613	0.4146	22.5187	87.5232	0.1
S300 lidocaine	130.5210	37.3171	0.2859	15.9556	216.0550	0.1
S500 lidocaine	264.5090	52.8863	0.1999	11.3067	429.3110	0.1

Materials

Rheological characterization of the hyaluronic acid filler products was performed with a controlled-stress rheometer (Discovery HR-2; TA Instruments, New Castle, DE) with a parallel plate diameter of 40 mm and a temperature of 25°C (Table 1). Hyaluronic acid filler (e.p.t.q. S100 lidocaine; Jetema Co, Ltd, Seoul, South Korea) with a relatively low G' was used to correct glabellar wrinkles. Soft tissue filler injection was performed by linear threading with a 30-gauge needle (Figure 2E-F).

Ultrasound-Guided Filler Injection

Patients were maintained in an upright position during ultrasound examination and hyaluronic filler injection. Glabellar wrinkle lines were marked in blue (Figure 2A,B). A 2-dimensional Doppler ultrasound device (E-cube 15ex; Alpinion Co, Anyang, South Korea), offering a real-time color Doppler mode with a high-frequency (8-17 MHz) hockey-stick probe (I08-17; Alpinion), was used to identify the course and location of the supratrochlear arteries. The ultrasound penetration depth was set to 2 cm. The probe was placed horizontally at the eyebrow, including the glabellar line and the medial end of the eyebrow. The supratrochlear artery was detected juxtaposed to the glabellar wrinkle lines (Figure 2C). After detecting the artery, the probe tracked the artery to determine its pathway, which was marked in red to show its position relative to the glabellar wrinkle lines (Figure 2D). The probe was moved up and down only, and the longitudinal axis was excluded. Finally, the hyaluronic acid filler was injected to augment the glabellar wrinkle lines (Figure 2E). Subsequently, botulinum toxin was injected into both glabellar frown lines to reduce the activity of the corrugator supercilii and procerus muscles. The accompanying video (available online at www.aestheticsurgeryjournal.com) further clarifies the identification of the artery by ultrasound.

Primary Safety Measures

The participants' safety profile was described based on the incidence of postprocedure complications. Safety

measures included recording patients' vital signs and adverse events (AEs) as observed by the investigator or reported by the participant throughout the course of the study. AEs were classified according to severity, seriousness, and relation to study treatment.

Secondary Efficacy Outcome Measures

Therapeutic outcomes were described based on comparing preprocedure and postprocedure findings. Serial photographs were taken before, immediately after, and 3 months after the procedure (Figure 2F-G). Wrinkle severity was evaluated based on the 4-grade Facial Wrinkle Scale (FWS) with photonumeric guide (0 = none, 1 = mild, 2 = moderate, 3 = severe).¹⁰ Global Aesthetic Improvement Scale (GAIS)¹¹ scores (5 = exceptionally improved; 4 = very improved; 3 = improved; 2 = no change; 1 = worse) were assessed from the patients' photographs by 2 different physicians immediately and 3 months after the procedure.

Given the importance of determining the subjects' perception and response to aesthetic treatment, this study also assessed the effect of filler treatment based on a 4-point scale of how satisfied patients reported they were with their appearance (Appendix).

Statistical Analysis

All safety parameters of the participants were presented descriptively. The incidence of AEs, serious AEs, and treatment-related AEs was presented and summarized according to the system organ class (SOC) and the preferred term in the Medical Dictionary for Regulatory Activities (version 14.1). Parameters included the overall incidence of AEs (eg, serious, treatment-related, non-treatment-related AEs), incidence by preferred term and within the SOC, incidence by maximum severity within the SOC, and AEs leading to discontinuation within the SOC.

For investigator assessment of FWS-based severity of glabellar wrinkles, the mean scores between treatments were compared by mixed models. Statistical analysis was performed with SAS version 9.4 (SAS Institute, Cary, NC).

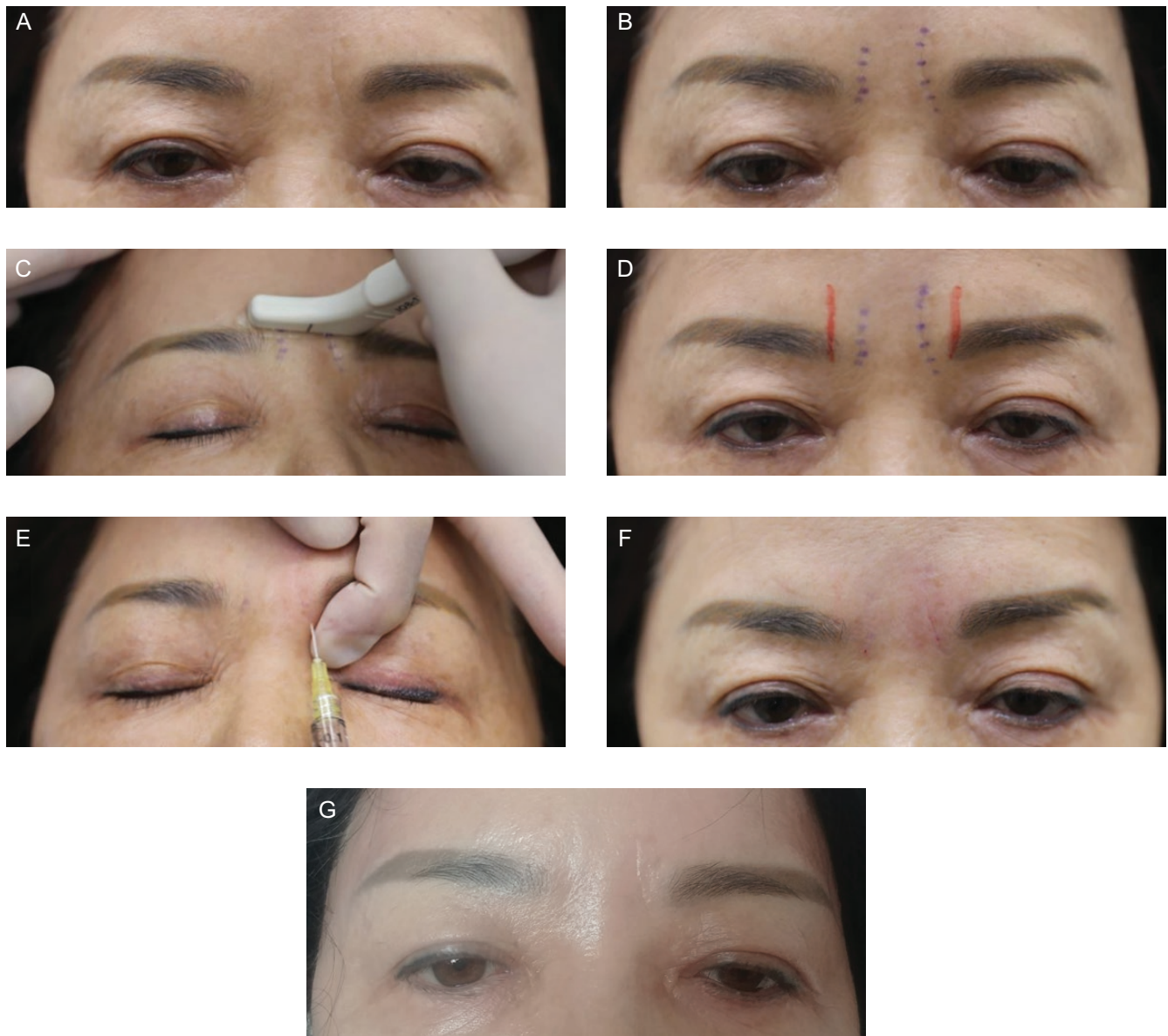


Figure 2. (A) Preprocedure view of a 71-year-old patient. (B) Glabellar wrinkle marked with blue dots. (C) Detection of the supratrochlear artery by Doppler ultrasound probe. (D) The supratrochlear artery was located and marked (red) juxtaposed with the glabellar wrinkle lines (blue dots). (E) The hyaluronic acid filler injected at the glabellar wrinkle lines. (F) Immediately after the procedure. (G) Three months after the procedure.

RESULTS

Subjects

The patients' demographics and baseline characteristics are given in Table 2. Among the 42 patients (4 men and 38 women; mean age, 52.9 years; range, 38–71 years) evaluated in the current study, 32 patients had bilateral wrinkle lines and 10 patients had unilateral wrinkle lines. Among the 10 patients who had unilateral wrinkle lines, 6 and 4 patients had prominent left- and right-sided wrinkle lines, respectively. They did not have prominent wrinkle lines on the

opposite side. The mean time of follow-up was 5 months, and the follow-up period of the study was 3 to 12 months.

Doppler Ultrasound Findings

Among the 74 wrinkle lines, 44 (59%) were located lateral to the glabellar wrinkle lines (Figure 3) and 30 (41%) were located at the glabellar frown lines. In 44 cases, the supratrochlear arteries were located at the deep subcutaneous layer. Among the patients whose supratrochlear artery was located at the glabellar wrinkle lines ($n = 30$), the artery was located at the deep subcutaneous layer in 24.



Video. Doppler ultrasound was used to identify the course and location of the supratrochlear arteries. Watch now at <http://academic.oup.com/asj/article-lookup/doi/10.1093/asj/sjaa197>

Table 2. Demographics and Baseline Characteristics

Patient characteristic (N = 42)	
Sex	
Women	38 (90.5)
Men	4 (9.5)
Mean age [range], years	52.9 [38-71]
No. of wrinkles	74
Bilateral (total)	64 (86.5)
Unilateral	
Left	6 (8.1)
Right	4 (5.4)
Glabella wrinkle severity	
Moderate	46 (62)
Severe	28 (38)
Ultrasound findings	
Location of the supratrochlear artery	
Lateral to glabellar wrinkles	44 (59)
At the glabellar wrinkles	30 (41)
Anatomic layer of the supratrochlear artery at the glabellar wrinkles	
Deep subcutaneous layer	24 (33)
Subdermal layer	6 (8)

Values are presented as n (%). Glabella wrinkle severity is based on the Facial Wrinkle Scale.

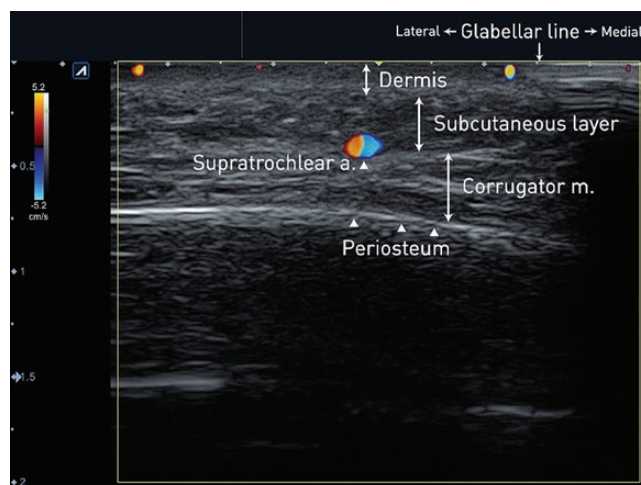


Figure 3. The supratrochlear artery located lateral from the glabellar frown line and located on the subcutaneous layer immediately above the corrugator supercilii muscle.

In 3 patients with bilateral wrinkle lines (ie, 6 cases, 8%), the supratrochlear arteries were detected just beneath the dermal layer, which was the target location for filler injection (Figure 4); hence, we did not perform the injection for safety reasons.

Primary Safety Measures

AEs were generally mild to moderate in severity. After treatment with hyaluronic acid filler under Doppler ultrasound-guided injection, no severe vascular complications occurred. The most frequent treatment-related AE was bruising. There were 3 cases (4%) of mild bruising at one side of the glabellar wrinkle area, but these resolved without any treatment after 2 weeks. There was no lumpiness at the filler injection sites. One participant (1.3%) reported transient eyebrow heaviness (coded as facial paresis), but it resolved without any intervention after 4 weeks. No serious treatment-related AEs were reported, and no discontinuation occurred because of AEs (Table 3).

Efficacy on Glabellar Wrinkle Lines

The mean [standard deviation] baseline FWS was 2.38 [0.49]; the mean FWS score was 0.70 [0.61] immediately after the filler injection and 0.85 [0.74] after 3 months. Compared with baseline, investigator-assessed FWS of glabellar wrinkle remained significantly lower over the 3 months ($P < 0.001$ immediately after the procedure; $P < 0.001$ for 3 months). Responders were defined as those achieving an improvement of at least 1 grade from baseline on the FWS at rest. Significantly greater responder rates

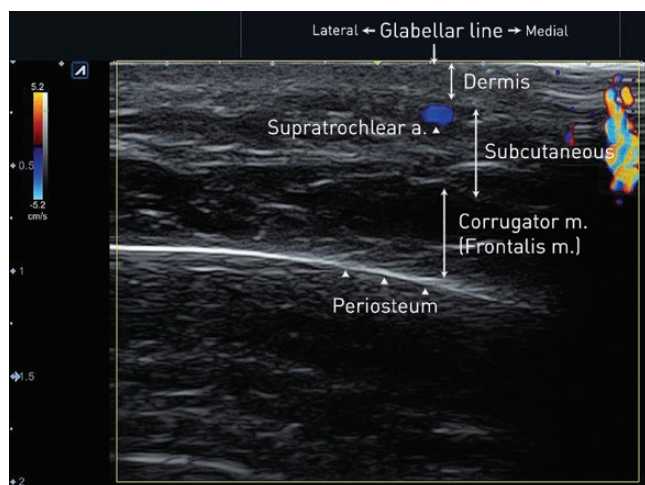


Figure 4. The supratrochlear artery located at the glabellar frown line and in the subdermal layer.

Table 4. Mixed-Model Analysis of the Facial Wrinkle Scale Immediately After the Procedure and 3 Months Postoperatively Relative to Baseline Measurements

Time points	FWS (95% CI)	Mean difference (Δ FWS ^a)	P value
Baseline	2.38 (2.19-2.86)	—	—
Immediately after procedure	0.70 (0.59-0.93)	-1.68	<0.0001
3 months	0.85 (0.67-1.11)	-1.53	<0.0001

CI, confidence interval; FWS, Facial Wrinkle Scale. ^a Δ FWS represents the change in FWS immediately after the procedure and 3 months postoperatively relative to baseline measurements. FWS values were calculated as least-square means and tested by mixed-model analyses for repeated measures.

were achieved immediately after the procedure over the 3 months. Based on achieving grades of none or mild according to investigators' evaluation of severity based on the FWS, the responder rate immediately after the procedure was 92.0%. The responder rate at 3 months was 81.0% (Tables 4 and 5).

Evaluation of the GAIS immediately after the procedure revealed that 52 wrinkles (70.2%; 24 patients with bilateral wrinkles and 4 patients with unilateral wrinkle) were "exceptionally improved," 16 wrinkles (21.6%; 5 patients with bilateral wrinkles and 6 patients with unilateral wrinkle) were "very improved," and 6 wrinkles (8.1%; 3 patients with bilateral wrinkles who received botulinum toxin injection only) had "no change." Evaluation of the GAIS at 3 months after the procedure revealed that 22 wrinkles (29.7%) were "exceptionally improved," 38 wrinkles (51%) were "very improved," 2 wrinkles (2.7%) were "improved," and 12 wrinkles (16.2%; including 6 wrinkles that were not injected with filler)

Table 3. Complications of Study Participants

Complications	
Relative to filler injection	
Bruising	3 (4)
Hematoma	—
Swelling	—
Lump	—
Systemic adverse events	
Transient eyebrow heaviness	1 (1.3)
Vascular compromise	
Skin color change	—
Visual compromise	—

Values are presented as n (%).

Table 5. Mixed-Model Analysis of the Facial Wrinkle Scale at Different Time Points

Time points	FWS (95% CI)	Mean difference (Δ FWS ^a)	P value
Baseline	2.38 (2.19-2.86)	—	—
Immediately after procedure	0.70 (0.59-0.93)	-1.68	<0.0001
3 months	0.85 (0.67-1.11)	-0.15	0.001

CI, confidence interval; FWS, Facial Wrinkle Scale. ^a Δ FWS represents the change in FWS between previous time and each time point. FWS were calculated as least-square means and tested by mixed-model analyses for repeated measures.

showed "no change." None of the patients received additional filler injection.

Immediately after the procedure, 92% of the participants rated their level of satisfaction with their appearances as "satisfied" or "very satisfied." This was maintained throughout the 3 months.

DISCUSSION

In the present study, Doppler ultrasound was used to confirm the location of the supratrochlear artery before soft tissue filler injection. No vascular complications that required intervention occurred. The authors found that, after confirming the artery's location with ultrasound, filler injection into the safely confirmed layer and location to avoid damage to arteries can be achieved as efficiently as with conventional blind filler injection. The use of ultrasound for medical diagnosis has seen continuous development and growth over several decades. The Doppler effect enables detection

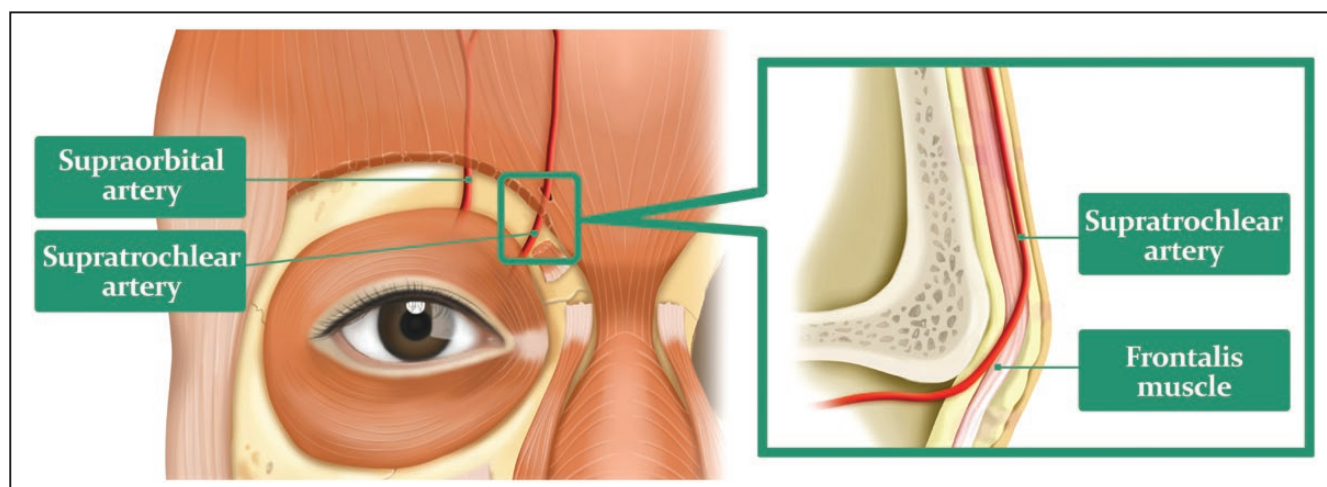


Figure 5. The supratrochlear artery emerges from the superomedial orbit and runs superficially to the corrugator muscle.

of blood flow in vessels and tissues. Because it can detect the facial arteries, Doppler ultrasound can be very useful when performing blind techniques, such as when injecting soft tissue filler, botulinum toxin, and thread lifting. Various literature reports have described preventive guidelines in order to avoid ocular complications.^{5,6} The main approach in preventing complications is to have sufficient anatomic knowledge. However, with Doppler ultrasound, this can be revised to “visualizing the anatomy.”

Anatomy of the Supratrochlear Artery

The supratrochlear artery emerges from the superomedial orbit 17 to 22 mm lateral to the midline, running superficially to the corrugator muscle and deep to the orbicularis oculi and frontalis muscles (Figure 5).¹²⁻¹⁴ It can be concluded that the reference points where the supratrochlear artery comes out are the frontal notch and the medial end of the eyebrow. Then, it runs along the subcutaneous layer 15 to 25 mm above the orbital rim.¹² At the level of the brows, the supratrochlear artery runs vertically in line with the medial canthus (± 3 mm).¹⁵ Another report described the superficial and deep branches of the supratrochlear artery.⁷ The deep branch was absent in approximately 45% of participants in the study, but the superficial branch was always present. Therefore, the authors proposed injecting deeply, thus bypassing the superficial branch of the supratrochlear artery.

Certain Doppler ultrasound machines cannot detect arteries <0.3 mm in diameter.¹⁶ However, previous studies have shown that the diameter of the supratrochlear artery is >0.6 mm and reaches 1.0 mm on average.^{7,17} Additionally, superficial thin veins, which generated the

most frequent complications (ie, bruises) in this study, may have been more difficult to identify with Doppler ultrasound.

Injection Plane of Choice for the Glabella

There are 3 possible layers to inject at the glabella: intradermal, subdermal (subcutaneous), and suprapariosteal. Unlike nasolabial fold correction or nose augmentation by filler injection, glabellar wrinkle lines should be corrected superficially because the procedure is not focused on augmentation but rather on filling the wrinkles. Therefore, the suprapariosteal layer is not appropriate for glabellar wrinkle correction. The subdermal layer, which is considered the upper subcutaneous layer, is useful for glabellar wrinkle correction. We believe that vascular injuries are mainly caused by filler injection into the subdermal layer where the superficial branch of the supratrochlear artery is located. Care should be taken when injecting fillers because the superficial branch of the supratrochlear artery is mostly located in this layer. The intradermal layer is also a useful layer for glabellar wrinkle correction. However, intradermal injection is difficult to perform at the intradermal layer even if the operator intends to inject in this manner. Fillers can be regurgitated at the puncture site and penetrate the subdermal layer where the superficial branch of the supratrochlear artery is located. Furthermore, irregularities after filler injection, such as lumps, can be easily noticed. The dermal thickness is known to be approximately 1.5 mm on average, but when the artery is located at the subdermal layer and the filler is injected beyond the depth, there is a risk of vascular damage. In this study, we did not perform hyaluronic acid filler injection in 3 patients in whom the supratrochlear artery was detected to be superficial and at the exact location of the glabellar wrinkle lines.

The filler was injected in relatively small amounts (0.1–0.3 mL) for glabellar wrinkle correction, and required injection into the intradermal and/or subdermal layers. A 24-MHz ultrasound probe was required to detect these layers specifically. Because this study is based on the relation between the supratrochlear artery in the subcutaneous layer and glabellar wrinkle, we have used an 8- to 17-MHz ultrasound probe to detect the subcutaneous layers. Therefore, it was not possible to detect infiltrated filler material by ultrasound examination after glabellar wrinkle correction.

Vascular Complications of Glabellar Wrinkle Correction

Beleznay et al⁶ reported that visual complications occurred at the glabellar area in 38 cases, of which 20 cases involved autologous fat grafts and 18 cases involved fillers. After 2015, 13 glabellar cases have been additionally reported.¹⁸

A previous Doppler study of 19 volunteers found that in 49% of the cases the location of the supratrochlear artery was at the glabellar frown line.¹⁹ However, the present study used Doppler ultrasound to visualize the layer of the artery in real time in order to detect the type (whether superficial or deep) of the branch of the supratrochlear artery. Filler injection was then performed, taking care to avoid the supratrochlear artery.

Ultrasound-Guided Filler Injection

The depth of the vessels is an important parameter that guides practitioners. However, the depth of the vessel measured by ultrasound can be changed by pressing the skin with the probe. Rather than the depth of the vessel from skin, it is important to identify the anatomic layer of the blood vessels in the glabellar region. The pathway of the supratrochlear artery and its relation with the glabellar wrinkle frown line are very important for glabellar wrinkle correction by soft tissue filler injection. However, the vertical pathway of each artery at the glabellar zone was extremely difficult to detect by Doppler ultrasound. As we aimed to determine the relation between the supratrochlear artery and the glabellar wrinkle lines, after confirming the position of the artery, ultrasound images were obtained by moving the probe up and down. This is a limitation of the study design.

Ultrasound-guided filler injection takes longer than conventional blind filler injection procedures, and physicians need to be accustomed to identifying blood vessels by Doppler ultrasound. Nevertheless, previous studies found that the arteries of the face (particularly

the supratrochlear artery at the glabellar area, the frontal branch of the superficial temporal artery at the temple area, the dorsal nasal artery at the nose, and the facial artery at the nasolabial fold area), which are at high risk during filler treatment, can be detected with ultrasound.^{20–22} However, further studies, such as determining the relation between the artery and the planes of facial soft tissue at various reference points and mapping of the arteries, are still required to reach definite protocols for ultrasound-guided filler injection.

CONCLUSIONS

Doppler ultrasound should be used to determine the location of the supratrochlear artery before correcting glabellar wrinkle lines with filler injections in order to avoid vascular complications. When the supratrochlear artery is detected outside of the glabellar wrinkle lines, injection of hyaluronic acid filler with low storage modulus at the subdermal layer of the glabellar wrinkle is recommended.

Supplementary Material

This article contains supplementary material located online at www.aestheticsurgeryjournal.com.

Acknowledgments

We thank Yun-Jin Kim and Na-Yeon Kim from the Biostatistical Consulting and Research Lab at Hanyang University for their assistance with the statistical analysis.

Disclosures

Dr Lee has been an investigator, speaker, and consultant for Jetema Co, Ltd (Seoul, South Korea), which sponsored the hyaluronic acid fillers, e.p.t.q. s100 lidocaine, s300 lidocaine, and s500 lidocaine. The other authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

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