Experimental Percutaneous Cannulation of the Supraorbital Arteries: Implication for Future Therapy

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PURPOSE. There is some evidence to suggest that thrombolysis has a beneficial effect in retinal vessel occlusion. However, there is concern that this therapeutic approach carries the risk of hemorrhage. Retrograde cannulation of the supraorbital arteries followed by irrigation with fibrinolytic agents may have the potential to minimize the risk of major complications. The study was conducted to investigate the anatomic and sonographic features of the supraorbital arteries.

METHODS. This cadaver dissection study was performed on the orbits of 12 cadaveric specimens. In each orbit, the supraorbital region was dissected, followed by cannulation of the supraorbital vessels and injection of ink. In six orbits, the orbital vessels and the distribution of the injected ink were investigated. Continuous-wave Doppler sonographic analysis of the supratrochlear and the supraorbital artery was performed in 40 orbits of 20 volunteers to measure the distance between the arteries and the midline.

RESULTS. Cannulation with retrograde injection of ink was successfully performed in both the supratrochlear and the supraorbital arteries. The supratrochlear artery exhibited a more superficial course and a larger diameter than the supraorbital artery (1.08 ± 0.19 mm vs. 0.86 ± 0.19 mm [SD]). Dissection to the orbital apex revealed a spread of ink into the ophthalmic and the central retinal arteries. The average distance between the exit of the supratrochlear artery and the midline was found to be 16.4 ± 1.7 mm (range, 13–20). The average distance between the exit of the supraorbital artery and the midline measured 26.5 ± 2.6 mm (range, 23–35).

CONCLUSIONS. The findings of this anatomic and sonographic study support the concept of percutaneous supraorbital vessel cannulation as a potential approach to thrombolysis in retinal vessel occlusion. The supratrochlear artery appears to provide the most reliable access route. (Invest Ophthalmol Vis Sci. 2005;46:1557–1560) DOI:10.1167/iovs.04-1129

Severe retinal vascular occlusive disease, such as central retinal artery (CRAO) or central retinal vein occlusion (CRVO) is associated with a poor visual and ocular prognosis.1,2 Left untreated, 93% of ischemic CRVO may culminate in a final visual acuity of ≤20/200.3 Nonischemic CRVO has better functional results (50% ≤20/200,3 85% ≥20/2004). In addition, neovascular glaucoma develops in 8% of eyes with CRVO overall and in as much as 82% of those with ischemic disease.3 Accordingly, complete obstruction of the central retinal artery results in permanent visual impairment in the majority of cases.

Several experimental and clinical studies have indicated that thrombolysis aimed at early restoration of blood flow has the potential to improve clinical outcomes in CRAO or CRVO.5–10 The spectrum of indications for thrombolytic drugs, such as streptokinase or recombinant tissue plasminogen activator (rt-PA), comprises myocardial infarction, lung embolism, ischemic cerebral stroke, deep vein thrombosis and acute arterial occlusions of the lower limbs.11–14 Thrombolytic therapy in retinal vessel occlusion is in its infancy and as of yet unproven. The risk of hemorrhage is one major problem with thrombolysis. Hemorrhagic stroke, gastrointestinal bleeding or vitreous hemorrhage are among the side effects that have been associated with the intravenous or intraarterial administration of fibrinolytic drugs.11 Moreover, catheter placement within the internal carotid artery during anterograde selective intraarterial thrombolysis may cause neurologic symptoms in 0.54% to 5.66% of cases.1,2

In light of the fact that the occurrence of hemorrhagic adverse events constitutes a dose-dependent problem, the targeted delivery of fibrinolytic agents at low doses should be the ideal approach to thrombolysis in retinal vessel occlusion. The concept of retrograde injection of drugs into the ophthalmic artery was first described by Varley et al.15 in 1968. In their study, vasospasm of the central retinal artery was successfully treated by injecting 40 mg of papaverine injected via a 0.63-mm catheter placed percutaneously in the supraorbital artery.

To date, however, the encouraging results of retrograde injection of drugs into the ophthalmic artery have not been further substantiated by the findings of other investigators. This may be due to a lack of studies on the anatomic organization of the supraorbital arteries, since variations in the anatomy of these vessels have possible implications on the effectiveness or the risk of complications. Normal and variant venous anatomy in the human orbit was recently described16 and even embolizations of carotid cavernous fistulas via the superior ophthalmic vein were successfully performed.17,18

The objective of this study was to investigate size and localization of the supraorbital arteries and to develop a safe and reliable technique for the preparation and cannulation of these vessels.

MATERIALS AND METHODS

The study was performed with the agreement of our institutional review boards. The research adhered to the tenets of the Declaration of Helsinki. All participants gave written informed consent, and donor tissue was also obtained in accordance with the Declaration.

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Continuous-Wave Doppler Sonography
Continuous-wave Doppler sonographic analysis (8 MHz; Kranzbühler; Solingen, Germany) of the supratrochlear and the supraorbital artery was performed in 40 orbits of 20 healthy volunteers (age range, 24–42 years; 12 women, 8 men). In each individual, the exit points of the supratrochlear and the supraorbital arteries were detected in both orbits.

Cadaver Dissection Studies
Dissection studies were performed on the orbits of 12 formalin- and alcohol-fixed human cadaveric specimens. In each specimen, the supraorbital region was dissected, followed by cannulation (19-gauge) of the supraorbital vessels and injection of India ink (Pelikan, Hannover, Germany) to demonstrate vascular territories and anastomoses. The distance between the supraorbital arteries and the midline was measured with a caliper. In six cadaveric specimens, dissection was continued to the orbital apex after removal of the superior orbital wall. In these specimens, the topography of the orbital vessels and the distribution of the injected ink were investigated. Furthermore, we determined axial length (l), diameter, and radius (r) of the supraorbital and orbital vessels. Based on these data, intravascular volumes (V) were calculated for the supratrochlear and the supraorbital arteries, the ophthalmic artery, and the lacrimal and the ethmoidal arteries (V = πr²l).

RESULTS

Continuous-Wave Doppler Sonography
The maximum signal of the supratrochlear artery was located at the medial rim of the eyebrow in close proximity to the trochlea. The average exit point of the supratrochlear artery was found to be at 16.4 ± 1.7 mm (range, 13–20 mm) temporal to the midline (Table 1). Typically, the supratrochlear artery was located at the midportion of the supraorbital rim. The strongest signal was measured at an average of 26.5 ± 2.6 mm (range, 23–35 mm) temporal to the midline. In all subjects examined, blood flow from the internal carotid artery was directed to the supraorbital rim.

Cadaver Dissection Studies

Supratrochlear Artery. The supratrochlear artery was detected in all cadaveric specimens examined. We identified a single vessel that bifurcated to create terminal branches in the subcutaneous tissue on the surface of the orbiculare oculi. Typically, the supratrochlear artery exhibited a more superficial course than the supraorbital artery (Fig. 1). The average distance between the midline and the point where the supratrochlear artery crosses the supraorbital rim was 16.4 ± 2.2 mm (range, 14–21). The outer diameter of the supratrochlear artery at the supraorbital rim was found to be 1.08 ± 0.19 mm (range, 0.8–1.5).

Supraorbital Artery. The anatomy of the supraorbital artery was more variable than the course of the supratrochlear artery. In 10 of 12 cadaveric specimens, the supraorbital artery exited the orbit through the supraorbital foramen and in 2 specimens, through a supraorbital notch. In contrast to the course of the supratrochlear artery, the supraorbital artery bifurcated underneath the orbiculare oculi in most cases. Typically, we observed smaller terminal branches that made anastomoses with the vascular system of the superficial temporal artery. The distance between the midline and the supraorbital artery was 27.2 ± 2.8 mm (range, 23–32). The outer diameter (0.86 ± 0.19 mm; range, 0.6–1.2) was found to be smaller than the outer diameter of the supratrochlear artery.

Anastomoses. In all specimens, anastomoses with the angular artery were found next to anastomoses between the supraorbital artery and the superficial temporal artery. Figure 2 shows a typical vascular cast specimen, demonstrating the strong association between the vascular territories of the internal and external carotid artery in the area of the supraorbital rim.

Orbital Vessels. In all cadaveric specimens examined after removal of the superior orbital wall (Fig. 3), the ophthalmic artery arose as the first branch from the internal carotid artery. The anatomy of the ophthalmic artery was variable. In three specimens, the point of entry of the ophthalmic artery into the optic canal was found laterally, underneath the optic nerve. Moreover, we observed a variable branching pattern. In three of six specimens, the branching point where the ophthalmic artery forms the supratrochlear and supraorbital artery was observed superomedial to the optic nerve. In two cases, the branching point was found superior to the nerve and, in one specimen, in a lateral position. Typically, the branching angle between the supratrochlear artery and the ophthalmic artery was smaller than that between the supraorbital artery and the ophthalmic artery. Of six specimens, five exhibited larger branches of the supratrochlear artery. Branches arising from this artery included the anterior ethmoidal artery (n = 3), both, the anterior and posterior ethmoidal artery (n = 1), and the lacrimal artery (n = 1). Larger branches of the supraorbital artery were found in three of six specimens, including the common ethmoidal artery in two, and the lacrimal artery in one.

Cannulation. Cannulation of the supraorbital vessels was successful in all cases. In all cadaveric specimens examined after dissection to the orbital apex, a spread of India ink into the ophthalmic and the central retinal artery was observed.

Intravascular Volumes. Based on an average axial length of 35 mm and a lumen of 1.5 mm in diameter, the calculated intravascular volume of the ophthalmic artery between the internal carotid artery and the point where the ophthalmic artery bifurcates into the supratrochlear and the supraorbital arteries was 60 μL. For the segment of the supraorbital artery between the ophthalmic artery and the supraorbital rim, we calculated an intravascular volume of 10 μL, whereas the volume of the supraorbital artery with a lumen of 0.92 mm in diameter was found to be 20 μL. Intravascular volumes of the lacrimal and the ethmoidal arteries were 18 μL and 8 μL, respectively.

DISCUSSION
Retinal vascular occlusive disease frequently is associated with underlying cardiovascular disorders. Affected patients are
likely to harbor a variety of microvascular lesions, which, when unmasked by thrombolytic therapy, may lead to intracranial hemorrhage.\textsuperscript{11} In light of the fact that the occurrence of hemorrhagic adverse events constitutes a dose-dependent problem, it has been suggested that the targeted delivery of fibrinolytic agents at low doses would be the ideal approach to thrombolysis in retinal vessel occlusion. Another anatomic investigation has provided evidence that percutaneous cannulation of the supraorbital arteries may be used to deliver drugs to the retinal vascular system.\textsuperscript{19} Anatomic records show that both the supratrochlear artery and the supraorbital artery invariably originate from the ophthalmic artery.\textsuperscript{20} Moreover, none of these arteries communicates with intracranial blood vessels.

Our study supports the consideration of retrograde injection of thrombolytic agents into the supraorbital arteries. Smaller anatomic variability and larger diameter of the supratrochlear artery compared with the supraorbital artery provided easier cannulation and a most reliable access route. Besides, the supratrochlear artery exhibited a more superficial course than the supraorbital artery. Moreover, the branching pattern of the supratrochlear artery and the vessel’s relationship to bony and soft tissue landmarks were remarkably consistent. We identified a single supratrochlear artery that bifurcated to create terminal branches in the subcutaneous tissue, whereas the supraorbital artery typically exhibited smaller terminal branches that made anastomoses with the vascular system of the superficial temporal artery.

Overall, the present results are largely consistent with earlier reports on the anatomy of the supraorbital arteries.\textsuperscript{19,21} However, in our study, the exit points of the supratrochlear artery were found to be much closer to the midline. Both, cadaver dissection studies and continuous-wave Doppler sonographic analysis revealed an average distance of 16.4 mm between the midline and the point where the supratrochlear artery crosses the supraorbital rim. Measurements for the distance between the supraorbital artery and the midline, however, compared favorably to the results of previous studies, ranging from 27.2 to 28.9 mm.

Another interesting finding of our study is the observation that injection of India ink within the supraorbital or the supratrochlear artery resulted in a spread into the ophthalmic and central retinal arteries. Previous studies on the cannulation of supraorbital vessels have not attempted to provide firm experimental evidence for the successful delivery of drugs to the retinal vascular system.\textsuperscript{15,19} The current data are supported by the clinical observation that rapidly changing intravascular pressure such as occurs with sudden occlusion of the carotid artery, may result in reversal of blood flow direction within the supraorbital arteries. Given a sufficient pressure of injection, it seems plausible that these vessels have the potential to provide a reliable route for the retrograde intraarterial instillation of drugs in vivo. In light of the finding that supraorbital artery...
mean peak systolic and end-diastolic blood flow velocities were markedly different, it may be hypothesized that ECG-controlled rapid injections would be optimal.

According to our data, intravascular volumes of the ophthalmic and the supratrochlear arteries were 60 and 10 μL, respectively, indicating that the intraarterial administration of drugs via the supraorbital arteries would require relatively small injection volumes. The current measurements for the length and the diameter of these arteries were consistent with the results of previous investigations. According to Schmidt and Adelmann,19 the average length of the supratrochlear artery is 39.4 mm, with a diameter of 0.96 mm at the proximal and 0.72 mm at the distal ends. However, available data suggest that orbital vessels may exhibit a variant anatomy including numerous anastomoses.20 These variations may become clinically relevant, since regional abnormalities in distribution have the potential to affect the concentration of injected drugs within the central retinal artery. Early reports on the anatomic organization of the orbital vasculature demonstrate that the ophthalmic artery arises from the meningeal artery in 1% and vice versa in 3%.20 In up to 2% of all cases, the ophthalmic artery runs separately along the optic sheath within an anatomic structure termed the canalis ophtalmicus.20

There is a reasonable likelihood that, in a pathologic situation such as retinal artery occlusion, blood flow within the retinal vascular system or the ophthalmic artery is significantly decreased, thereby affecting injection pressures or the dosage of drugs required for the targeted delivery of thrombolytic agents via the supraorbital arteries. Experiments to determine the change of blood flow in patients with retinal vessel occlusion were beyond the scope of the present study. However, a greater understanding of the detailed anatomy of the supratrochlear and orbital arteries will be an important component of future efforts to establish percutaneous supraorbital vessel cannulation as an alternative to systemic thrombolysis in retinal vein or artery occlusion. However, cadaver injection studies do not provide us with physiological information. Further studies are necessary to prove the effectiveness of this therapeutic approach.

References