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Context: Data on the superior ophthalmic vein (SOV) dilation captivate the attention of neurologists as an early sign of several neurovascular disease manifestations, but measurements vary widely in publications. Aims: This study attempts to shed light on disparate data and develop more stringent criteria for determining the dilation of these veins. Settings and Design: To this end, 44 orbits of 25 formalin-embalmed human cadavers without risk factors for SOV dilation were dissected. Materials and Methods: The SOV branching pattern and length were photographed, and multiple segments were analyzed microscopically, histologically, and statistically. Statistical Analysis Used: Simple descriptive statistics as well as linear regression were used to compare the data. Results: The mean SOV diameter was 2.05 ± 0.7 mm. Other morphometric findings included the presence of valves and an unreported branching pattern of the SOV. Conclusion: Knowledge of the mean diameter serves as a diagnostic reference to help recognize SOV dilation, while the unreported variation of SOV (trifurcation at the exit point) may have implications in neurosurgery when using this vein to approach the cavernous sinus.

Key words: Carotid-cavernous sinus fistula, superior ophthalmic vein, superior ophthalmic vein diameter, superior ophthalmic vein dilation, superior ophthalmic vein tunics

The superior ophthalmic vein (SOV) is the primary route of venous drainage from the orbit directly into the cavernous sinus.[1] This fact, together with the relatively large size of this vein, makes it an important alternative for access during carotid-cavernous fistula (CCF) embolization and cannulation for endovascular treatment of indirect CCF.[2] Furthermore, dilation of this vein often represents an early manifestation of several neurovascular diseases, including orbital or facial arteriovenous malformation, venous thrombosis, and CCF.[3] In addition, a dilated SOV can be seen in inflammatory disorders, traumatic hemorrhage lymphoproliferative, and infectious etiologies.[4] It is also described as one of the signs of increased intracranial pressure that physicians need to be alert to and as a finding that may result from increased cerebral swelling due to a variety of causes.[5] Based on the above associations, recognizing dilation of the SOV is important clinically as it raises the possibility of significant underlying pathology.

To date, there have been several detailed studies on the course and diameter of the SOV.[6] Hayreh presented a concise overview of the orbital vasculature anatomy, which described both the superior and inferior ophthalmic veins as constant and the middle and medial ophthalmic veins as inconsistent.[6] At the same time, certain morphometric findings of the orbital venous system are conflicting. For example, Hayreh, Tsutsumi et al., and Brzozowski et al. noted a nonsymmetrical diameter pattern between the right and left SOVs, whereas Lirng et al. observed the SOV showed no side-to-side differences in the majority (68%) of samples examined.[7]

Variability in the SOV diameter is also observed between patients, with the reported values extending from 0.3 to 5.0 mm. Brightbill et al. analyzed computed tomography (CT) scans of 88 patients with sinusitis and normal intracranial pressure and the SOV diameter ranged from 1.4 to 3.6 mm (x̄ = 2.2 mm).[8] Reis et al. found a similar result in cadavers, with a mean diameter of 2.2 mm ± 1.2 mm.[9] From magnetic resonance imaging (MRIs), Tsutsumi et al. reported a mean SOV diameter of 1.7 mm, smaller but still within the range listed above.[10] Using MRI imaging as well, Ozgen and Aydingöz determined a relatively wide range of normal diameters, ranging from 0.3 to 4.6 mm.[11] Similarly, in a study of 69 patients with and without elevated intracranial pressure, Lirng et al. found SOV diameters ranging from 0.5 to 5.0 mm.[12] However, when excluding those with abnormal intracranial pressure (n = 21), the mean SOV diameter was 1.6 ± 1.0 mm, far more consistent with previously published studies [Table 1]. For the 30 mm length vein, the normal diameter of SOV has a broad range in the literature, making it difficult to identify a threshold for

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dilation. Consequently, some investigators have considered the SOV to be dilated if the diameter is >2.5 mm, while others used 3.0 mm as the threshold for dilation.\cite{8,18}

The wide range of the SOV diameter is likely due to several causes. First, ophthalmic veins, including the SOV, have been shown to possess a high degree of variability.\cite{6,14,19} The divergence of data could also result from the investigations being performed on patients who were referred to sonography or MRI for various diseases or issues. Therefore, patients with preexisting conditions for SOV dilation were not excluded from the studies. Diameters have also been measured in vivo, historically using orbital phlebography.\cite{14} More recently, researchers have utilized advanced diagnostic procedures, including orbital ultrasonography,\cite{9,20} high-resolution head CT,\cite{8,10,18,21,22} MRI,\cite{9,10,15,21} digital subtraction angiography,\cite{6} and CT angiography.\cite{22} While these methods allow for a larger sample size, the measurements were done on only one segment of SOV, the part visible on the employed imaging modalities. Some measurements were performed only in the axial plane due to examining the SOV on CT scans of the paranasal sinuses of patients with uncomplicated sinusitis.\cite{10} Moreover, some data were based on the segments near “the rear of the globe,” for patients who had undergone an MRI before the brain due to intracranial pressure elevation.\cite{9,18} Thus, the SOV measurement was not an initial goal of the MRI, and the visibility of the vein was limited in these cases.

An additional motivation for studying the SOV stems from the fact that despite a considerable amount of information on the microstructure of veins in general, data on the SOV tunics (tunica externa, media, and intima) have not been reported. Rather, previous studies measured the external diameter of the SOV without examining the relative thickness of the tunics, the lumen, or the ratio of these to each other. Filling such a gap is important to provide a more complete picture of the SOV.

In an attempt to advance the SOV exploration and provide a more accurate observation of the normal diameter of nondilated ophthalmic veins, we selected cadavers without risk factors for SOV dilation. We documented the vein course and measured the diameter at multiple points through the length of the SOV grossly and histologically. Finally, we calculated the thickness of the tunica externa and tunica media of the SOV and their relationship to the total thickness and the external and luminal diameter of the SOV.

Materials and Methods

Forty-four orbits of 25 formalin-preserved human cadavers were dissected to expose the SOV. Cases included fourteen males (56%) and eleven females (44%), with a mean age of 78.3 ± 13.8 years. Cadavers were selected based on the absence of the risk factors for SOV dilation. For this determination, we examined the gross anatomy of the vessels of the face and the brain for the presence of facial arteriovenous malformation, venous thrombosis, and CCF [Figures 1 and 2]. To exclude one of the concomitant signs of thyroid-associated ophthalmopathy, namely goiter, the thyroid gland was measured [Figure 3]. The present study did not consider bilateral structures as independent measures to eliminate pseudoreplication and obtain the most accurate results. For statistical analysis, PAST 4.13 (PAlentological Statistics, Oyvind Hammer, Norway) was utilized.

For the orbit dissection, a superior approach was used. We started dissection by exposing the anteromedial segment of the SOV. In some cases, the posterior part of the SOV, next to the annulus of Zinn, was identified first. The SOVs were photographed after the dissection was completed [Figure 4].

The preliminary length of the SOV was measured, and the location of the SOV segment above the optic nerve was identified. This identification was done to compare the diameter of the SOV above the optic nerve with other SOV segments. A sketch of the orbital structures was created for later reference. The SOVs were removed starting from the junction of the angular and supraorbital veins and ending at the annulus of Zinn. The branching pattern was analyzed under a dissection microscope. The length of the main trunk was remeasured from where the anterior tributaries of the SOV merged to the posterior end (exit point from the orbit) [Figure 5].

The main trunks of the veins were subsequently cut into 1–2 anterior, 2–5 middle (above the optic nerve), and 2 posterior (next to the annulus of Zinn) segments [Figure 6a]. Cross-sections of the veins’ pieces were photographed under a LEICA EZ4 HD stereo microscope using LAS EZ Ink software. Perimeters of each piece were then measured with ImageJ (National Institutes of Health, Bethesda, Maryland,

<table>
<thead>
<tr>
<th>Publication author/Year</th>
<th>Method</th>
<th>Range (mm)</th>
<th>Mean±SD (mm)</th>
<th>Publication author/Year</th>
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</thead>
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<tr>
<td>Brightbill et al., 2001</td>
<td>In vivo, CT</td>
<td>1.4–3.6</td>
<td>2.2±no data</td>
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<tr>
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<td>-</td>
<td>2.2±1.2</td>
<td>Reis et al., 2009</td>
</tr>
<tr>
<td>Tsutsumi et al., 2015</td>
<td>In vivo, MRI</td>
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<td>1.7±no data</td>
<td>Tsutsumi et al., 2015</td>
</tr>
<tr>
<td>Ozgen and Aydingöz, 2000</td>
<td>In vivo, MRI</td>
<td>0.3–4.6</td>
<td>-</td>
<td>Ozgen and Aydingöz, 2000</td>
</tr>
<tr>
<td>Lirng et al., 2003</td>
<td>No data</td>
<td>1.0–2.9</td>
<td>1.9±no data</td>
<td>Lirng et al., 2003</td>
</tr>
<tr>
<td>Lirng et al., 2003</td>
<td>No data</td>
<td>0.3–4.6</td>
<td>-</td>
<td>Lirng et al., 2003</td>
</tr>
</tbody>
</table>

*Patients with abnormal intracranial pressure removed (n=21). SD: Standard deviation, CT: Computed tomography, MRI: Magnetic resonance imaging.
Figure 1: Arteries of the brain (inferior aspect, frontal pole above). The white arrows point at the intact arteries of the brain (ICA refers to the internal carotid artery). The basilar artery is picked up by the forceps. ICA: Internal carotid artery

Figure 2: The anterior portion of the skull (internal aspect). The roofs of the orbits have been removed. The dura mater is reflected. Cavernous segments of the ICAs (in yellow) have a regular shape and size and there is no abnormal communication with the cavernous sinus. ICA: Internal carotid artery

Figure 3: Neck (anterior aspect). The thyroid gland is of normal shape and size (transverse size of 16 mm and longitudinal 40 mm for each lobe). The numbers on the bottom represent the cadaver’s number and measurement’s date

Figure 4: Left orbit (superior aspect). The roof of the orbit has been removed. SR and levator palpebrae superioris were cut and reflected (posteromedially). The medial rectus muscle and frontal nerve are present. The SOV (in yellow) with its lacrimal branch is picked up by the probe. SR: Superior rectus, MR: Rectus muscle, SOV: Superior ophthalmic vein

United States) or Swift Imaging 3.0 software (Swift Optical Instruments, Inc., Schertz, Texas, United States) and converted into the vessel’s diameter [Figure 6b].

Three representative segments of each SOV main trunk were sent to the Mizzou OneHealth Biorepository in Columbia, MO, for H and E, CD31, and Verhoeff’s staining.

From the histological specimen, external and internal diameters of the SOVs were measured using ImageJ or Swift Imaging 3.0 software and compared with the value in the gross images [Figure 7].

The measurement of the total thickness of vessel walls, tunica externa, and tunica media was performed as the next step [Figure 8]. We examined a subset sample to determine the relative thicknesses of the tunica media and the tunica externa (n = 7) in comparison to the overall SOV diameter.

The ratio between the tunica media and tunica externa was calculated.

Results

In one specimen, the left medial ophthalmic vein (MOV) was observed [Figure 9]. In another orbit, the variation of the SOV trifurcating at the exit point was discovered. In the trifurcated SOV, the two medial branches entered the superior orbital fissure and a lateral branch ran through the inferior orbital fissure separately [Figure 10].

The mean external SOV diameter obtained from gross images taken with the stereo microscope was 2.05 mm ± 0.7. Similar to published data obtained by MRI and phase-contrast
MR angiography, where the diameter of the SOV at the optic nerve crossing point showed “prominent diversity,” we observed wider diversity in the middle segment of the SOV ($\bar{x} = 2.07 \text{ mm} \pm 0.78$) [Table 2].

The mean internal SOV diameter obtained from gross images was $1.67 \text{ mm} \pm 0.74$ [Figure 11]. A linear regression [Figure 12] was performed between the average diameter from images taken with the microscope and histological slides. The $R^2 = 0.78 \ (P < 0.0001, n = 29, \alpha = 0.05)$ indicates a relationship between the measurements.

We investigated the correlation between the right and left SOV length and diameter to adjust the normal mean of SOV diameter to different age groups. No significant relationship between age and diameter was found. The percentage of the right and left SOVs tunica media is very similar and provides 29% of the total thickness of the SOV. The tunica externa constitutes 66% of the total thickness of the SOV.

Discussion

Observation of the MOV in one of the cadavers is not novel [Figure 9]. However, there is still disagreement about its presence, with some researchers stating this is an additional inferior ophthalmic vein. Our results indicate its existence.

In contrast to a single previous finding of the SOV dividing into two or three branches that rejoined posteriorly, we found an unreported variation of the SOV branches at the exit point of the orbit [Figure 10]. The two medial branches entered the superior orbital fissure and a lateral branch ran through the inferior orbital fissure. Even though preoperative internal carotid angiograms are usually obtained, this variation may have implications in neurosurgery of the orbit, especially if SOV cannulation is used to access a CCF.

The histologic examinations indicated the presence of a valve in one of the SOVs [Figure 11], contributing to the debate regarding whether the SOV can possess a valve. This finding complements previous literature where only gross images were examined. We did observe structures resembling valves in two other SOVs; however, only one vein presented with intact endothelium along the entire lumen. This finding excludes the possibility of the separated endothelial layer mimicking a valve.
Even though the cadavers utilized in this study had a relatively narrow age range (x̄ age = 78.3 ± 13.8 years), there was no correlation between age and SOV diameter. This finding corresponds with Lirng et al., who found no correlation through MRI assessment of the SOV. Thus, the limitation of a narrow age range is of lesser importance regarding the analysis of SOV dilation.

The mean external SOV diameter obtained from gross images, 2.05 mm ± 0.7, could serve as a diagnostic criterion to determine whether the SOV is dilated. The SOV diameter measurement could help with the differential diagnosis in patients with unusual “pink eye” where pericorneal or conjunctival injection is of unknown etiology. This finding could point to an underlying significant neurovascular disease. Although SOV dilation does raise some concerns about underlying disease, the high variability of the orbital veins has to be taken into consideration. Furthermore, understanding the diameter of various segments of the SOV is beneficial for different types of diagnostic imaging where only a particular segment of the SOV is observed.

The linear regression found [Figure 9] could be used to determine morphometrical parameters based on histological data. It is relevant to mention that there was some expected difference in the diameter of the actual veins and histological slides due to histological tissue preparation. The tissue gets dehydrated by alcohol and compacted in paraffin, leading to size reduction.

Data on the SOV tunics thickness ratio in a healthy population provides a benchmark upon which future studies can be built. For example, in studying abnormal dilated SOVs and their underlying pathogenesis, a normal reference range is necessary. Therefore, future studies can be developed based on our initial findings.

**Conclusion**

Knowledge of the mean diameter and other measurement findings serves as a diagnostic reference to help physicians recognize SOV dilation. Such recognition is important as it may catch underlying clinically important pathologic conditions that warrant further assessment. Finally, the unreported variation of SOV (trifurcation at the exit point) may have implications in neurosurgery when using this vein to approach the cavernous sinus.

**Acknowledgments**

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Table 2: Mean external diameter from gross images of the superior ophthalmic vein segments

<table>
<thead>
<tr>
<th>Side</th>
<th>Anterior (n=24)</th>
<th>Middle (n=21)</th>
<th>Posterior (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>1.90±0.76</td>
<td>2.03±0.91</td>
<td>2.25±0.8</td>
</tr>
<tr>
<td>Left</td>
<td>1.89±0.56</td>
<td>2.12±0.66</td>
<td>2.35±0.64</td>
</tr>
<tr>
<td>Both, right and left</td>
<td>1.89±0.65</td>
<td>2.07±0.78</td>
<td>2.26±0.67</td>
</tr>
</tbody>
</table>

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Nil.

Conflicts of interest
There are no conflicts of interest.

References