Morphometric Characteristics of Central Retinal Artery and Vein Endothelium in the Normal Human Optic Nerve Head


Purpose. This study documents the morphometric features of arterial and venous endothelia in the different laminar regions of the normal human optic nerve head and speculates on the hemodynamic characteristics of the central retinal artery (CRA) and central retinal vein (CRV).

Methods. Twenty normal human eyes were used. Microcannulation techniques were used to label the cytoskeleton and nuclei of endothelial cells in the CRA and CRV, after which images were captured using confocal microscopy. Length, width, length-to-width ratio, and area measurements were obtained from endothelium and its nuclei. Nucleus position with respect to cell apex and direction of blood flow was also quantified. Comparisons were made between prelaminar, anterior lamina cribrosa, posterior lamina cribrosa, and retrolaminar regions. Venous and arterial endothelial cell morphology was also compared.

Results. There was significant variation in venous endothelial morphology across the different laminar regions; however, no differences were found in arterial endothelial characteristics (all \( P > 0.1065 \)). Significant differences were found between arterial and venous endothelium in all laminar regions apart from the posterior lamina cribrosa, where only nuclear area (\( P = 0.0001 \)) and nucleus position (\( P = 0.0088 \)) were found to be different.

Conclusions. Arterial-like appearance of venous endothelium in the posterior lamina cribrosa, where pressure gradient forces are predicted to be greatest and CRV luminal diameter is known to be narrowest, implicates this as a site of altered forces are predicted to be greatest and CRV luminal diameter is narrowest, implicates this as a site of altered hemodynamic stress. Heterogeneity of venous endothelium may have relevance for understanding ocular vascular diseases such as central retinal vein occlusion. (Invest Ophthalmol Vis Sci. 2011;52:1359–1367) DOI:10.1167/iovs.10-6366

The human central retinal artery (CRA) and central retinal vein (CRV) are essential for preserving visual function because they are the only major vascular structures to serve the inner retina. Both the CRA and CRV traverse a unique physiological environment and experience a range of tissue pressures and neuron-glial interactions as they pass through retro-laminar tissue to enter the intraocular milieu of the eye. In vivo optic nerve measurements performed in our laboratory and other centers have demonstrated the presence of a significant pressure gradient at the lamina cribrosa, which is consequent to the decrease in tissue pressures between prelaminar and retrolaminar regions of the optic nerve head. Previous reports, together with histologic studies also performed in our laboratory, have revealed important correlations between the change in translaminar tissue pressure and the distribution of neuronal cytoskeleton proteins, nitric oxide synthase enzymes, and axonal transport processes, suggesting that optic nerve tissue is cyto-architecturally adapted to the laminar environment. It is unknown if anatomical and physiological variations within the human optic nerve head have a similar influence on regional CRA and CRV endothelial characteristics; however, this knowledge would be useful for improving our understanding of pathogenic mechanisms underlying ocular vascular diseases. Additionally, such knowledge may identify anatomic regions within the optic nerve head that are susceptible to vascular injury.

Endothelial cells perform a vital role in modulating the activity of neuron-glial units that maintain normal visual function. Endothelial cells are exceedingly sensitive to changes in the vascular microenvironment and demonstrate distinctive morphometric behavior in response to changes in luminal shear stress and external pressure patterns. Reliably histometric parameters have been used in previous studies to infer knowledge about regional hemodynamic properties of microcirculations that cannot be resolved by state-of-the-art imaging and radiologic technology. Similar investigations have not been performed on central retinal vasculature, and as a consequence it remains unknown if there are regional variations in the magnitude of hemodynamic force experienced by endothelia in the different laminar regions. An in-depth study of endothelial morphology of the optic nerve head may allow hemodynamic inferences to be made.

This study is a detailed documentation of the morphometric characteristics of arterial and venous endothelium in the normal human optic nerve head. We use our previously described micropipette technique to selectively label the central retinal circulation and perform high-resolution, confocal microscopic examination of endothelial cells. Endothelial morphometric measurements are performed using previously defined histologic parameters, and comparisons are made...
between arterial and venous endothelial cells as well as between the different laminar regions of the optic nerve head. The results of this work may improve our understanding of histopathologic mechanisms underlying ocular vascular diseases that are important causes of visual morbidity worldwide.25

METHODS
This study was approved by the human research ethics committee at the University of Western Australia. All human tissue was handled according to the tenets of the Declaration of Helsinki.

Human Donor Eyes
A total of 20 human eyes from 13 donors were used for this study. All eyes were obtained from the Lions Eye Bank of Western Australia (Lions Eye Institute, Western Australia). Donor eyes used for this research had no documented history of eye or systemic disease. The demographic data and cause of death of each optic nerve donor are presented in Table 1.

Perfusion Technique for Optic Nerve Endothelial Labeling
Our previously reported technique of CRA cannulation, microvascular fixation, and targeted endothelial labeling was used for this work.24 Endothelial morphology was studied by labeling the nucleus and F-actin microfilaments. In brief, glass micropipettes with tapered tips of approximately 150 μm diameter were used to cannulate the CRA of enucleated eyes. Oxygenated Ringer’s solution with 1.0% bovine serum albumin was then perfused through the ocular circulation to remove residual blood followed by sequential perfusion with 4% paraformaldehyde, 0.1% Triton-X-100, and dye to achieve endothelial fixation, permeabilization, and labeling, respectively. The dye consisted of a mixture of actin microfilament label (phalloidin conjugated to Alexa fluor 546, 30 U; Invitrogen, Carlsbad, CA) and nucleus label (1.2 μg/mL bisBenzimide H 33258; Sigma-Aldrich, St. Louis, MO). Syringe pumps and pressure transducers were used to control the flow rate of perfusate during all stages of the experiment. After perfusion, the eye was immersion fixed in 4% paraformaldehyde before sectioning.

Tissue Preparation
We performed preliminary work to examine the effects of different tissue preparation techniques on confocal endothelial image quality. Vibratome- and cryostat-prepared specimens of 12, 50, 100, and 200 μm thickness were optically cleared after sectioning, using previously reported techniques, in an attempt to improve the depth of confocal imaging. Specifically, ethanol,26,27 hydrogen peroxide, benzyl alcohol benzyl benzoate,27 dimethylsulfoxide,28,29 methyl salicylate, and glycerol30–32 were used in varying concentrations for variable periods of time to aid optical clearing. We found that greatest endothelial cell image quality was attained from cryo-sectioned tissue of 12 μm thickness, which was not optically cleared because it minimized extravasation of intravascular dye. Therefore, qualitative and quantitative endothelial measurements were performed only on tissue prepared in this manner. Tissue for cryosectioning was mounted on the cryostat during sectioning. Longitudinal sections were cut along the sagittal plane beginning in the superior portion of each optic nerve and proceeding to the inferior part of the nerve. Specimens were numerically labeled as they were sectioned so that we could determine from which region of the optic nerve they were derived.

Fluorescent and Confocal Scanning Laser Microscopy
Images were collected from preliminar, anterior lamina cribrosa, posterior lamina cribrosa, and retrolaminar regions of the optic nerve head. Each optic nerve head was divided into different laminar regions using previously reported histologic criteria.33 Before confocal microscopy, fluorescent overview images of all sections were captured with the aid of ×4 (Plan NA 0.2; Nikon, Tokyo, Japan) and ×10 (Plan NA 0.45) dry lenses using a microscope (Eclipse E800; Nikon). Low-magnification fluorescent images allowed us to correlate direction of blood flow with cell and nuclear morphology. After fluorescent microscopy, confocal images were acquired using a confocal microscope (Nikon C1 with EZ-C1 software, v. 3.20). Visualization of sections was achieved by simultaneous laser excitation with 405 and 532 nm lines. Images were captured using ×40, ×60, and ×100 objective lenses (Nikon Plan Apochromats) oil lenses, NA 1.0, 1.40, and 1.40, respectively). Arterial and venous endothelial cells were imaged separately. Z-stacks of vascular components, extending from intraluminal to extraluminal sites, were captured in each of the laminar regions. Each z-stack consisted of a depth of optical sections collected at 0.3 μm increments along the z-plane. Because of the tortuous course of central retinal vessels within the optic nerve head, we found that the orientation of endothelial cells was not tangential to the longitudinal plane in all laminar regions in all sections. To minimize orientation artifact during image analysis we did not image vascular structures that lay obliquely to the longitudinal plane. Hence it was not always possible to collect endothelial data from all four laminar regions of all sections.

Table 1. Demographic Details of Optic Nerve Donors and Cause of Death

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<th>Patient ID</th>
<th>Sex</th>
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<td>R</td>
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</table>

L, left; R, right.
Morphometric Analysis of Endothelium

Quantification of all images was done using two software packages (Image J, v. 1.38X; developed by Wayne Rasband, National Institutes of Health, Bethesda, MD, http://rsb.info.nih.gov/ij; and Image Pro Plus, v. 5.1, Media Cybernetics, Bethesda, MD). All images for the manuscript were prepared using commercial software packages (Adobe Photoshop, v. 8.0, and Adobe Illustrator CS2, v. 12.0, Adobe Systems, San Jose, CA). Confocal images in this manuscript were false colored (Look Up Tables, Image J).

Quantitative measurements were performed only when both cell and nuclear borders were clearly defined on confocal images. In some sections it was possible to make quantitative measurements from multiple endothelial cells, whereas in other sections the measurements were limited to only one cell. Measurements were performed only on endothelial cells that were orientated tangential to the longitudinal plane. Z-projections of confocal stacks were used for most measurements; however, in some instances it was necessary to scroll through the z-stack to clearly identify endothelial borders before measurements were acquired. This was particularly the case for arterial endothelial cells where overlay of smooth muscle cells on some z-projections limited visualization of cell borders. The following morphometric measurements were recorded from confocal microscope images (Fig. 1):

1. Endothelial cell length: Defined as the length between endothelial apaxes.
2. Endothelial cell width: Defined as the greatest distance between endothelial cell borders along an axis that was perpendicular to cell length.
3. Nucleus length: Defined as the greatest length between nuclear borders.
4. Nucleus width: Defined as the greatest distance between nuclear borders along an axis that was perpendicular to nuclear length.
5. Distance from cell apex to nucleus in the downstream direction of blood flow: Denoted as variable \( e \) in this report.

All measurements were expressed in micromillimeters.

Endothelial and nuclear morphometric parameters that have previously been shown to convey information about cellular behavior in different physiological environments\(^ {18,22,33–36} \) were calculated using the above measurements. The following estimations were performed: endothelial length-to-width ratio\(^ {18,22,55–56} \), nuclear length-to-width ratio\(^ {18,54} \), endothelial cell area: determined using the formula \( (\text{endothelial length} \times \text{endothelial width}) \times \pi/4 \); nuclear cell area: determined using the formula \( (\text{nuclear length} \times \text{nuclear width}) \times \pi/4 \); \( e \): endothelial cell length ratio.\(^ {36} \)

Data Analysis

All statistical testing was performed using commercial software (R; R Foundation for Statistical Computing, Vienna, Austria).\(^ {37} \) Vascular region was the independent factor in the analysis and was defined as vessel type at a particular region (e.g., prelaminar vein). Measurements were compared between all vascular regions. All one-way analysis of variance (ANOVA) testing included “optic nerve donor” as a random effect using linear mixed modeling to test measurement differences between vessel type/region. The assignment of optic nerve donor as a random effect as described above. All measurements were expressed as mean \( \pm SE \).

RESULTS

General

The mean age of donors was 46.8 \( \pm 5.1 \) years (age range, 19–78 years). We examined 9 right eyes and 11 left eyes from a total of 9 male and 4 female donors. The average postmortem time before eyes were enucleated was 10.4 \( \pm 1.6 \) hours.

A total of 249 endothelial cells were analyzed. This included 69 cells from the prelaminar region, 89 cells from the lamina cribrosa region, and 91 cells from the retrolaminar region. All endothelial cell measurements were found to be normally distributed according to the Shapiro-Wilk test. Age was not
found to correlate with any of the measured parameters (all $P > 0.1814$).

Similar to previous reports we observed a constriction in CRV diameter within the optic nerve head. This was observed to be most prominent in the posterior lamina cribrosa adjacent to collagenous laminar plates (Fig. 2). In some sections we also observed a reduction in the luminal diameter of the CRA in the posterior lamina cribrosa (Fig. 2).

### Arterial Endothelial Cells

Morphologic characteristics of arterial endothelial cells in the different laminar regions of the optic nerve head are shown in Figure 3. Endothelial cells in the CRA were relatively homogeneous in appearance with an elongated, spindle-shaped structure. Endothelial cells were orientated such that their longitudinal axis lay parallel to the direction of blood flow. Abundant F-actin stress fibers, distributed parallel to the longitudinal axis of the cell, were also seen within arterial endothelial cytoplasm. The arterial nucleus was also elongated in appearance and displayed a spindle-shaped morphology in all laminar regions. The position of the nucleus in relation to the whole cell was eccentric and was displaced downstream to the direction of blood flow.

Morphometric values of arterial endothelial parameters are provided in Table 2. There was no significant difference between various laminar regions for any of the measured and estimated morphometric parameters (all $P > 0.1065$). Because there was no significant difference between laminar regions, we have provided mean arterial values for the entire lamina cribrosa region (Table 2) instead of giving separate arterial measures for anterior lamina cribrosa and posterior lamina cribrosa regions.

### Venous Endothelial Cells

Morphologic characteristics of venous endothelial cells in the different laminar regions of the optic nerve head are shown in Figure 4. The mean values of venous endothelial measurements are also provided in Table 2. Similar to arterial endothelial cells, venous endothelial cells were orientated such that their longitudinal axis lay parallel to the direction of blood flow. Only a few venous endothelial cells demonstrated evidence of cytoplasmic F-actin stress fibers. Despite similarities in cellular orientation, there was heterogeneity in venous endothelial morphology between the different laminar regions. Venous endothelial cells were polygonal in shape in all laminar regions apart from the posterior lamina cribrosa. At the posterior lamina cribrosa there was an abrupt transition in morphology with endothelial cells displaying a spindle-shaped cell structure (Figs. 4 and 5). After the posterior lamina cribrosa, within the retrolaminar region, there was an abrupt transition back from spindle-shaped morphology to a polygonal structure.

Venous endothelial cells were shortest and widest in the prelaminar region with an average length-to-width ratio of 4.9. The length of venous endothelial cells gradually increased in the direction of blood flow down the CRV and reached a maximum mean value of $102.3 \mu m$ at the posterior lamina cribrosa (Fig. 5). The mean cell width was also lowest at the...
posterior lamina cribrosa with an average value of 7.9 μm. Estimated mean cell area was lowest at the posterior lamina cribrosa with an average value of 715.0 μm².

The nucleus of venous endothelial cells was displaced downstream in the direction of blood flow in all laminar regions (Fig. 4). In all regions of the optic nerve head, apart from the posterior lamina cribrosa, the nucleus was either oval or polygonal in morphology. In the posterior lamina cribrosa the nucleus displayed spindle-shaped morphology. Mean nuclear area in the posterior lamina cribrosa was lowest out of all the laminar regions with an average value of 79.1 μm². The nuclear length-to-width ratio was greatest at the posterior lamina cribrosa with an average value of 3.8.

The parameters e and e-to-endothelial-cell-length ratio did not vary significantly between any of the venous sectors (P = 0.4099 and 0.2025, respectively). No statistically different endothelial parameters were seen between anterior lamina cribrosa and retrolaminar regions (all P > 0.1836). Posterior lamina cribrosa cells were significantly different from retrolaminar cells for all non-e-related venous parameters (all P < 0.008). Posterior lamina cribrosa cells were also significantly different from prelaminar cells for these parameters (all P < 0.0063) except nucleus length (P = 0.0104) and cell area (P = 0.2230). Cell length-to-width ratio, nuclear length, nuclear width, and nuclear length-to-width ratio were significantly different between posterior lamina cribrosa and anterior lamina cribrosa (all P < 0.0072). The posterior lamina cribrosa cells all had significantly greater length-to-width ratios than any of the other venous segments (all P < 0.0002). The cell length-to-width ratio was significantly different between prelaminar and anterior lamina cribrosa regions (P = 0.0001) and prelaminar and retrolaminar regions (P = 0.0001). The nuclear length-to-width ratio was also significantly different between prelaminar and anterior lamina cribrosa regions (P = 0.0005) and prelaminar and retrolaminar regions (P = 0.0034).

Comparisons between Arterial and Venous Endothelial Cells

Because no significant differences were seen between arterial endothelial cells in the different laminar regions, we pooled all arterial data, to increase statistical power, when making comparisons between arterial and venous measurements. There was no difference in e-to-endothelial-cell-length ratio between artery and any venous segment (P = 0.1165). The comparisons between other parameters are described.

No significant differences were seen between arterial and venous endothelial cells at the posterior lamina cribrosa for any of the cellular measurements and estimations (all P > 0.0276), except nuclear area (P = 0.0001) and e (P = 0.0088), which were both smaller in the vein. In the prelaminar region, venous endothelial cells were significantly different from arterial endothelial cells for all parameters (all P < 0.0078) except for cell area and nuclear area (both P > 0.02). In the anterior lamina cribrosa region, venous endothelial cells were significantly different from arterial endothelial cells for all parameters (all P < 0.0017) except for nuclear width, area, and e (all P > 0.0246). In the retrolaminar region, venous endothelial cells were significantly different from arterial endothelial cells for all parameters (all P < 0.0016), except for nuclear width and cell area (all P > 0.0981).

DISCUSSION

The three major findings from this study are the following: First, CRA endothelial cells demonstrate significant morphometric similarity across the different laminar regions of the human optic nerve head. Second, CRV endothelial cells demonstrate significant morphometric variation across the different laminar regions of the human optic nerve head. Third, CRA and CRV endothelial cells are morphologically distinct in all regions of the optic nerve head apart from the posterior lamina cribrosa.

Endothelial cells are situated in a dynamic environment where they are exposed to a range of exogenous forces, including shear stress generated by the rate of blood flow, pressure stress secondary to the pulsatile nature of blood flow, and external stresses from adjacent tissues. Variations in stress patterns profoundly influence the behavior of endothelial cells and, if sustained, may initiate the cascade of cellular events that result in endothelial damage and vessel occlusion. With regard to shear stress, there is increasing evidence that implicates changes to shear stress patterns as an important pathophysiological mechanism in the process of atherosclerosis. Sites of low shear stress and oscillatory stress have recently been demonstrated to be pro-atherogenic, and regions of high shear stress were shown to be protective against the formation of atherosclerotic plaques. Shear stress is largely influenced by blood flow velocity, which in turn is determined by the pressure gradient acting on the vessel sector per unit diameter. An increase in the pressure gradient and a decrease in vessel diameter will act to increase blood flow velocity and hence shear stress. Modern magnetic resonance techniques permits real-time measurement of shear stress patterns in large-diameter vessels, thereby allowing identification of pro-atherogenic
sites; however, our ability to perform similar in vivo determinations in microcirculations remains limited. As a consequence it has been difficult to elucidate the hemodynamic properties of ocular circulations such as the central retinal vasculature. Endothelial cell and nuclear morphology convey important information about the regional hemodynamic properties of ocular circulations such as the central retinal vasculature. Endothelial cell and nuclear morphology convey important information about the regional hemodynamic properties of the microcirculation. An extensive number of experimental studies have shown that measurements of cell shape, size, position, and orientation permit reliable inference to be made about regional endothelial shear stress, pressure gradient, and blood flow characteristics. Vessels subject to high shear stress typically have elongated endothelial cell borders and align their long axes parallel to the direction of blood flow. Endothelia within these microcirculations also display significant plasticity and alter their morphology in a time- and pressure-dependent manner after regional modifications in blood flow characteristics. A change in blood flow direction is associated with a time-dependent realignment of nuclear long axes, and a gradual reduction in hemodynamic force induces a continuum of change until nuclei eventually appear rounded with no preferred direction of orientation. Endothelial cells that experience very low values of shear stress are also known to adopt a polygonal morphology. Alteration of luminal diameter induces blood flow changes, which in turn modifies shear stress patterns. Cardiovascular system studies have shown that such a change is particularly deleterious to endothelial function downstream to a site of stenosis where abnormal shear stress patterns may provoke the formation of atheroma. These previous findings have important relevance to the human optic nerve head, which is located in a nonuniform physiological environment. Central retinal vasculature most likely experiences a change in shear stress and pressure patterns between retrolaminar and laminar regions as a consequence of the change in luminal diameter and tissue pres-

**Figure 4.** Venous endothelial morphology. Confocal microscope images and schematic outlines demonstrate endothelial morphology in the prelaminar (A, B), anterior lamina cribrosa (C, D), posterior lamina cribrosa (E, F), and retrolaminar (G, H) regions. Venous endothelial cells in all laminar regions were orientated in the direction of blood flow. Scale bar, 50 μm.

**Figure 5.** Transition in venous endothelial morphology between posterior lamina cribrosa and adjacent laminar regions. Low-magnification confocal microscope images illustrate the variation in venous endothelial morphology between anterior lamina cribrosa (ALC) and posterior lamina cribrosa (PLC) regions (A) and between PLC and retrolaminar (RL) regions (B). Insets I and II provide high-magnification images, with schematic outlines, of venous endothelial cells in each region. In ALC (AI) and RL (BII) regions venous endothelial cells were polygonal in shape, and in PLC (AII and BI) the cells appeared similar to arterial endothelium displaying spindle-shaped morphology. The changes in venous endothelial morphology between posterior lamina cribrosa and adjacent laminar regions occurred abruptly. Bold fenestrated lines demarcate each of the laminar regions, and single-ended arrows illustrate the direction of blood flow. Scale bar, 50 μm.
m.6 However, these tissue pressures do not reach arterial blood pressures and are unlikely to influence shear stress.5,51 The findings of the present study are consistent with the results of previous modeling experiments that have implicated shear stress as the predominant morphometric determinant in the arterial circulation.47 The presence of numerous F-actin stress fibers within the cytoplasm of arterial cells in all laminar regions provides further evidence of high shear stress in the CRA.52

Unlike the CRA, endothelia in the CRV demonstrate significant heterogeneity between the different laminar regions. The polygonal morphology of venous endothelial cells in prelamellar, anterior lamina cribrosa, and retrolaminar compartments suggests low shear stress in these regions. Micropipette measurements in our laboratory have demonstrated that retinal vein pressure is equivalent to intraocular pressure at the optic disc, which in a normal human eye approximates to 15 mm Hg.51 Histologic studies of venous endothelium in other low-shear-stress systems have also demonstrated a polygonal endothelial morphology, a paucity of cytosolic stress fibers, and a cellular orientation that is parallel to the direction of blood flow.35,54 Morphologic differences between venous and arterial endothelial cells in the central retinal vasculature are most likely the consequence of flow-mediated rearrangement of cytoskeleton proteins. Although we did not investigate molecular mechanisms underlying these morphologic differences, previous studies have revealed that alterations in fluid shear stress can modulate cytosolic microtubule frameworks via calcium- and tyrosine kinase-dependent pathways.55

The posterior lamina cribrosa in the human optic nerve head is characterized by dense, fenestrated collagen plates that form narrow openings for the transmission of retinal ganglion cell axons.3,8 The transmilar pressure gradient occurs largely across this region1,6,4 and probably plays an important role in determining the regional venous intraluminal pressure gradient. Although there is constriction of both the CRA and CRV within the posterior lamina cribrosa, histologic measurements have revealed that the decrease in luminal diameter is significant only in the CRV.59 We were able to demonstrate many morphometric similarities between arterial and venous endothelia in the posterior lamina cribrosa, suggesting that net shear is comparable within this region. We speculate that the sum of luminal diameter and tissue pressure change in the posterior lamina cribrosa generates a venous hydrodynamic environment that is equivalent to what is typically experienced by endothelia in the arterial microcirculation. In vivo experiments have revealed that venous endothelial cells adopt arterial morphology when exposed to arterial hemodynamic forces.56 This transformation has been demonstrated most clearly in studies where veins have been explanted and surgically grafted into arterial systems.56 Based on the assumption that venous endothelial morphology in the CRV is determined mostly by tissue pressure forces, our results implicate the posterior lamina cribrosa as the site of greatest pressure change within the human optic nerve head. Although we were able to ascertain the medical history of all optic nerve donors before inclusion in this study, we acknowledge that at times it can be extremely difficult to assess the full health status of an individual postmortem. Consequently some of the findings observed in this study may have been influenced by numerous factors, including concomitant disease, medication, or smoking habits, of which we were unaware. This remains one of the limitations of postmortem histologic studies.

Strong scientific evidence suggests that the spectrum of vascular disease that results from arterial endothelial dysfunction is significantly different from those disorders attributed to venous endothelial disease.57 Arterial endothelia are primarily involved in flow-mediated mechano-transduction, where they act as a conduit for the transmission of hemodynamic information, generated by blood flow, to the underlying vessel wall.58 Through the release of potent vaso-constricting and vaso-dilating agents, arterial endothelia are able respond to variations in regional hemodynamic properties and thus modulate microcirculation characteristics in accordance with tissue demands.57 In contrast, the venous endothelium is primarily involved in regulating the hemostatic and inflammatory properties of the microcirculation. There is a vast amount of experimental data to suggest that venous endothelial compromise stimulates neutrophil adherence and thrombus formation.59,60 The findings from this study may therefore have significance for understanding pathogenetic mechanisms underlying ocular vascular diseases. The change in venous endothelial morphology between posterior lamina cribrosa and retrolaminar regions most likely reflects local hemodynamic force alteration, which may predispose venous endothelia to injury at this site, particularly during pathologic states in which shear stress and tissue pressures are modified. As a consequence, this region of the optic nerve head may be a site of thrombus formation and important to the etiology of diseases such as CRV occlusion.61 The present study may thus provide the molecular basis for understanding the histopathologic findings of CRV occlusion previously reported by Green.61 The biochemical and molecular pathways underlying platelet adhesion, vascular inflammation, and athrombosis formation in ocular disease remains largely unresolved. Histopathologic studies of eyes with cardiovascular disease or glaucoma may allow further delineation of some of these patho-physiological pathways.

Acknowledgments

The authors thank staff from the Lions Eye Bank of Western Australia, Lions Eye Institute for provision of human donor eyes; staff from DonateLife, the Western Australian agency for organ and tissue donation, who facilitated the recruitment of donors into the study by referral and completion of consent processes; and Martin Hazelton at Massey University, New Zealand, who provided statistical advice.

References


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