

Morphometric Characteristics of Central Retinal Artery and Vein in the Optic Nerve Head of Patients with Diabetes

I read with great interest the excellent study by Kang et al.¹ in the March 2011 issue. In the context of their study, this short communication is intended to address an aspect of the ocular pathology in diabetic retinopathy.

Diabetic retinopathy is among the leading causes of blindness in the working population in developed countries.² However, the exact etiology and the mechanism of disease progression of diabetic retinopathy are still unresolved. Disturbances have been detected in many aspects of ocular circulation in diabetes, but the role of the hemodynamics in diabetic retinopathy has not been clearly defined.

In a prospective follow-up study of patients with diabetes, the initial changes in the retrobulbar circulation during progression of diabetic retinopathy occurred in the central retinal vein.³ The alteration of the blood flow in the central retinal vein consisted of increased maximum and minimum blood flow velocity and increased index of resistivity. Because the blood flow velocity in the central retinal artery did not change in accordance with the changes in the central retinal vein, a local circulatory disturbance in the central retinal vein of patients with progression of diabetic retinopathy was suggested.

The central retinal artery and vein are in close relationship inside the optic nerve, especially at the level of the lamina cribrosa, where the artery retains its round shape, whereas the vein, being pressed by the artery, takes on an oval or crescent shape.⁴ The gradual constriction of the central retinal vein at this level acts as a throttle that maintains the intraretinal capillary and venous pressure. Even a relatively small reduction in radius greatly increases the difference in the blood pressure on either side of the lamina cribrosa and results in altered blood flow in the vessels inside the optic nerve head. Therefore, variations in vascular caliber may be expected in the central retinal artery and vein in the optic nerve head in diabetes, which may be a cause for the alteration of the retrobulbar venous circulation that was detected in the above-mentioned study.³ The morphometric characteristics of the blood vessel endothelium are influenced by the blood flow pattern.⁵ In their study, Kang et al.¹ reported that, in the central retinal vein, they detected an arterial-like appearance of the venous endothelium in the posterior lamina cribrosa, where pressure gradient forces are predicted to be greatest, and the luminal diameter of the central retinal vein is known to be narrowest. They suggested that changes in venous endothelial morphology between the posterior lamina cribrosa and retrolaminar regions most likely reflect local hemodynamic force alteration that may predispose to venous endothelial 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 may be important in the etiology of diseases such as central retinal vein occlusion.

To my knowledge, a detailed morphometric analysis of the central retinal artery and vein inside the optic nerve head has not been undertaken in patients with diabetes. The results of such an investigation may indicate an alteration in blood vessel diameter in the major blood vessels inside the optic nerve. Furthermore, an analysis of the morphometric characteristics of the endothelium of the central retinal artery and vein in diabetic patients suggests the pattern of blood flow in these blood vessels. Since the total retinal blood inflow and outflow occur via the central retinal artery and vein, the results are

invaluable for understanding the overall intraretinal microcirculation in patients with diabetes.

Galina Dimitrova

Neuromedica Polyclinic, Skopje, Macedonia.

E-mail: galina@sonet.com.mk

References

1. Kang MH, Balaratnasingam C, Yu PK, et al. Morphometric characteristics of central retinal artery and vein endothelium in the normal human optic nerve head. *Invest Ophthalmol Vis Sci.* 2011;52:1359-1367.
2. Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. *Bull World Health Org.* 2004;82:844-851.
3. Dimitrova G, Kato S, Yamashita H, et al. Relation between retrobulbar circulation and progression of diabetic retinopathy. *Br J Ophthalmol.* 2003;87:622-625.
4. Taylor AW, Sehu W, Williamson TH, et al. Morphometric assessment of the central retinal artery and vein in the optic nerve head. *Can J Ophthalmol.* 1993;28:320-324.
5. Fisher AB, Chien S, Barakat AI, et al. Endothelial cellular response to altered shear stress. *Am J Physiol Lung Cell Mol Physiol.* 2001;281(3):29-33.

Citation: *Invest Ophthalmol Vis Sci.* 2012;53:1637.

doi:10.1167/iovs.12-9572

Author Response: Morphometric Characteristics of Central Retinal Artery and Vein in the Optic Nerve Head of Patients with Diabetes

We appreciate the interest that Dr. Dimitrova has expressed in our paper,¹ published in the March 2011 issue.² We agree that a detailed morphometric analysis of the central retinal artery and vein inside the optic nerve head has not been undertaken in patients with diabetes. Diabetic retinopathy remains a leading cause of blindness in the working population of developed countries. However, a general view of the pathogenesis of diabetic retinopathy is that it is a disease of multifactorial origin, with a range of microvascular and neuroglial abnormalities. We are still unable to provide sufficient solid evidence to determine the cause-and-consequence relationship and interpret how the pathologies found in experimental and clinical studies relate to one another and how they contribute to disease progression.^{3,4}

There is abundant evidence suggesting early changes in retinal perfusion before the onset of diabetic retinopathy that may be related to inflammatory changes, loss of capillaries, and progressive ischemia and hypoxia. Structural and functional changes in the retinal vasculature are closely related to diabetes and diabetic retinopathy. The pathogenic role of the vascular endothelium in diabetic retinopathy is thought to be critical, as it is a vast and heterogeneous organ faced with diverse challenges. In addition to regulating vascular tone, the endothelial cells carefully balance and dynamically regulate both barrier function and selective permeability to solutes and immune cells. Endothelial cells in specific locations such as the lamina cribrosa may meet different mechanical forces, including fluid shear, hydrostatic pressure, and cyclical stretching. In pathologic conditions such as diabetes, both hemodynamic conditions and endothelial cells could be significantly altered. In previous studies, our group has attempted to quantify the

morphologic,⁵ pharmacologic,⁶ and functional⁷ changes in the ocular vasculature in the early stage in rat models of induced diabetes. We have also examined pharmaceutical interventions for ameliorating the vascular changes in induced diabetes.⁸

There is no doubt that morphologic analysis of endothelial cells from human eyes could provide valuable information toward understanding the possible pathogenic role of endothelial cells in many ocular diseases. Fortunately, the intravascular perfusion fixation and staining technique developed in our laboratory allows us to investigate the intracellular changes in the whole retinal and choroidal microvasculature and their relationship with retinal neurons and glia in normal, aging, and diseased human donor eyes.⁹ We hope to gain new information from human donor eyes that will help us to further bridge the gap between the findings in experimental and clinical studies.

We cannot overemphasize the importance of study of the pathogenesis of diabetic retinopathy, particularly the possible pathogenic roles of the retinal vasculature. Although the roles of the central retinal artery and vein in the pathogenesis of diabetic retinopathy remain unclear and the role of endothelial cell dysfunction is not well understood, in the future, as we continue to expand our collection of human donor eyes, we may well be in a position to contribute to the understanding of endothelial cell changes in diabetic human eyes and to complement the clinical study by Dimitrova et al.¹⁰

Dao-Yi Yu^{1,2}

Min H. Kang^{1,2}

Chandrakumar Balaratnasingam^{1,2}

Paula K. Yu^{1,2}

William H. Morgan¹

Ian L. McAllister¹

Stephen J. Cringle^{1,2}

The ¹Centre for Ophthalmology and Visual Science and the

²The ARC Centre of Excellence in Vision Science, The University of Western Australia, Perth, Western Australia, Australia.

E-mail: dyyu@cyllene.uwa.edu.au

References

1. Dimitrova G. Morphometric characteristics of central retinal artery and vein in the optic nerve head of patients with diabetes (Letter). *Invest Ophthalmol Vis Sci.* 2012;53:1637.
2. Kang MH, Balaratnasingam C, Yu P, et al. Morphometric characteristics of central retinal artery and vein endothelium in the normal human optic nerve head. *Invest Ophthalmol Vis Sci.* 2011; 52:1359-1367.
3. Gariano RF, Gardner TW. Retinal angiogenesis in development and disease. *Nature.* 2005;438:960-966.
4. Curtis TM, Gardiner TA, Stitt AW. Microvascular lesions of diabetic retinopathy: clues towards understanding pathogenesis? *Eye (Lond).* 2009;23:1496-1508.
5. Su EN, Alder VA, Yu DY, Yu PK, Cringle SJ, Yogesana K. Continued progression of retinopathy despite spontaneous recovery to normoglycemia in a long-term study of streptozotocin-induced diabetes in rats. *Graefes Arch Clin Exp Ophthalmol.* 2000;238:163-173.
6. Su EN, Yu DY, Alder VA, Yu PK, Cringle SJ. Altered vasoactivity in the early diabetic eye: measured in the isolated perfused rat eye. *Exp Eye Res.* 1995;61:699-711.
7. Cringle SJ, Yu D-Y, Alder VA, Su EN. Retinal blood flow by hydrogen clearance polarography in the streptozotocin-induced diabetic rat. *Invest Ophthalmol Vis Sci.* 1993;34:1716-1721.
8. Yu PK, Yu DY, Cringle SJ, Su EN. Tetrahydrobiopterin reverses the impairment of acetylcholine-induced vasodilatation in diabetic ocular microvasculature. *J Ocul Pharmacol Ther.* 2001;17:123-129.
9. Yu PK, Balaratnasingam C, Morgan WH, Cringle SJ, McAllister IL, Yu DY. The structural relationship between the microvasculature, neurons, and glia in the human retina. *Invest Ophthalmol Vis Sci.* 2010;51:447-458.
10. Dimitrova G, Kato S, Yamashita H, et al. Relation between retrobulbar circulation and progression of diabetic retinopathy. *Br J Ophthalmol.* 2003;87:622-625.

Citation: *Invest Ophthalmol Vis Sci.* 2012;53:1637-1638.

doi:10.1167/iovs.12-9703