

# News in Review

COMMENTARY AND PERSPECTIVES

## IOP Asymmetry: Risk Factor for Glaucoma?

**A**symmetric intraocular pressure (IOP) readings have long been considered a hallmark of glaucoma. And now a group of Wills Eye Institute researchers led by George L. Spaeth, MD, has

breathed new life into that old theory.

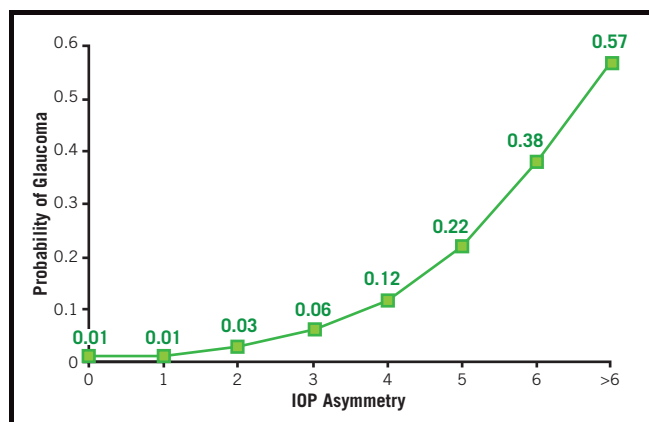
Their investigation of IOP asymmetry in a large group of ethnically diverse primary open-angle glaucoma (POAG) patients has revealed a direct relationship between the amount of IOP asymmetry and the probability of having glaucoma. Specifically, the greater the difference in pressure between fellow eyes, the more likely the patient is to have glaucoma.<sup>1</sup>

“Our data indicate that IOP asymmetry of 6 mmHg or more is strongly indicative, though not absolute proof, of the presence of

glaucoma,” said Alice L. Williams, MD, a resident physician at the Wills Eye Institute.

She noted that researchers had reached a similar conclusion in 1951.<sup>2</sup> “But we believe that its importance has been largely forgotten.”

The collaborative retrospective study involved 326 newly diagnosed glaucoma patients. Diagnosis was based on findings of optic nerve and visual field damage. Patients with any type of prior ocular medical or surgical treatment were excluded. And the controls—326 patients with no apparent glaucoma—were



**CLINICAL TIP.** Take note of patients with asymmetric IOPs, as they may be at greater risk of having glaucoma than patients with symmetric readings.

matched by sex, race, and age (within two years).

The study found that a difference of 3 mmHg is associated with a 6 percent probability of having glaucoma. The risk jumps to a 57 percent probability of having glaucoma when the difference is greater than 6 mmHg. “We were surprised by the strength of the relationship,” Dr. Williams said.

**Further study.** She added that an even stronger study would be prospective and would take several IOP readings instead of just one. “Also, it would be interest-

ing to see if the prevalence of IOP asymmetry depends on the stage of glaucoma.”

Dr. Williams is planning a follow-up study that includes a more balanced representation of the different races because the current data set indicates that importance of IOP asymmetry may differ by race. The distribution of the current study was 28 percent Asian, 21 percent Black, 28 percent European, 14 percent Latino, and 9 percent Middle Eastern/North African.

**Clinical utility.** Still, the current findings have im-

mediate clinical relevance, Dr. Williams said. “When the diagnosis of glaucoma is uncertain, clinicians should monitor patients more closely if the degree

of IOP asymmetry between the two eyes is greater than 4 mmHg,” she said. And when the difference is greater than 6 mmHg, “follow patients extremely closely.”

She stressed that IOP asymmetry alone cannot be used to diagnose glaucoma.

—Miriam Karmel

1 Williams AL et al. *J Glaucoma*.

2013;22(3):215-218.

2 Brav SS, Kirber HP. *JAMA*. 1951;147(12):1127-1128.

*Dr. Williams reports no related financial interests.*

Retina Report

Mild DR: Harbinger of CVD?

The Japan Diabetes Complications Study is a multicenter randomized trial looking at how lifestyle influences complications in people with type 2 diabetes. Recently, an analysis of Japanese patients with type 2 diabetes showed that even those with a mild stage of nonproliferative diabetic retinopathy (DR) have about a 1.7 times higher risk of developing coronary heart disease (CHD) or stroke, after controlling for other known cardiovascular risk factors.<sup>1</sup>

“We previously knew that diabetic retinopathy had a link with cardiovascular disease [CVD],” said lead author Ryo Kawasaki, MD, MPH, PhD, assistant professor of public health, Yamagata University, Yamagata, Japan. “In this study, we clarified it as a biomarker of cardiovascular risk.”

**Study specifics.** The study began with 2,033 Japanese patients, aged 40 to 70, with hemoglobin A<sub>1c</sub> levels of 6.5 percent or more—typical diabetic adults—but who were free of cardiovascular disease. After patients with severe nonproliferative or proliferative disease, potentially confounding ocular diseases, and a history of CVD and familial

hypercholesterolemia were excluded, 1,620 patients remained—many of whom were younger and had fewer risk factors such as high triglyceride levels.

Researchers assessed patients at baseline and each year for eight years for CHD and stroke, adjusting for factors such as age, body mass index, blood pressure, cholesterol levels, and smoking. These same adjustments were made when estimating hazard ratios for severity of DR and the presence of DR lesions such as dot hemorrhages and cotton-wool spots.

About a quarter of participants had mild nonproliferative DR, with a cumulative rate of 8.5 percent for CHD events and 6.6 percent for strokes. About 4 percent had moderate nonproliferative DR, with a cumulative rate of 9.0 percent for CHD events and 6.0 percent for strokes. Adding DR improved the receiver-operating characteristics curve slightly, and the prediction models using DR in addition to conventional cardiovascular risk factors correctly reclassified 9 percent of participants for CHD and 13 percent for stroke.

**Predictive value.** “We used two different methods



**MILD, MODERATE DR.** (1) Dot hemorrhages indicate mild diabetic retinopathy. (2) Retinal hemorrhages and cotton-wool spots are seen in patients with mild to moderate disease.

to statistically evaluate if DR adds capacity to predict CHD and stroke,” said Dr. Kawasaki. “We found this provided significant improvements in reclassification, which may impact clinical usefulness of DR as a biomarker to predict CHD and stroke.”

Dr. Kawasaki said he cannot rule out the possible influence of other unknown risk factors in his study’s findings. Nevertheless, he said, DR appears to be a reliable, independent forecaster. “We may be able to turn the simple fundus photo into a useful screening tool for assessing cardiovascular risk.”

In this study, retinal hemorrhages or microaneurysms were linked with the risk of CHD but not stroke, and cotton-wool spots were linked with incident stroke but not CHD. These results suggest potential pathological pathways for specific retinal signs of CHD and stroke, said Dr. Kawasaki. However, given the small

numbers represented, this needs further validation. Future studies may address other issues as well, such as creating ethnic-specific risk prediction models, he said.

**In the clinic.** “The association between milder DR and CVD also needs to be considered when treating diabetic macular edema (DME) with anti-VEGF agents,” said Dr. Kawasaki. “Given that DME can develop in eyes with relatively mild DR and that patients with mild DR already have an increased risk of cardiovascular disease, we ophthalmologists—along with cardiologists and diabetes experts—may need to monitor patients more closely,” he said, underscoring the importance of establishing early baselines.

—Annie Stuart

1 Kawasaki R et al. *Ophthalmology*. 2013;120(3):574-582.

*Dr. Kawasaki reports no related financial interests.*

## Cornea Update

## Cord Blood Serum May Heal Severe Damage

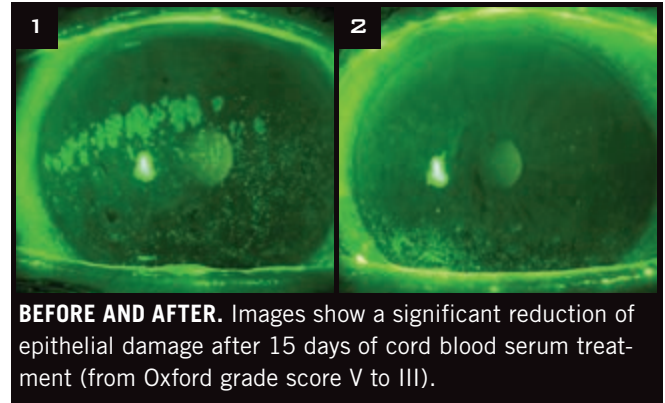
A recent study by Italian researchers indicates that cord blood serum (CBS)—with its higher concentration of growth factors and ready supply of large, quality-controlled samples—may surpass the potential of autologous blood-derived products in treating severe epithelial damage.<sup>1</sup>

For one month, 17 graft-vs.-host disease patients and 13 Sjögren syndrome patients with severe dry eye received a daily dose of 1 mL sterile CBS-based eye-drops such that 0.15 ng of epithelial growth factor was delivered to each eye.

Lengthy conventional

therapy and even autologous serum or platelet-rich plasma had previously fallen short in enhancing healing and reducing pain in some of these patients. But CBS elicited surprising results, said coauthor Emilio C. Campos, MD, professor and chief of ophthalmology at the University of Bologna in Bologna, Italy.

After only a few days of treatment, all patients reported a decrease in pain. At day 15, patients' Ocular Surface Disease Index scores were half those at baseline. At study end, two of the 59 eyes had completely healed, and 23 eyes had only negligible residual dam-



**BEFORE AND AFTER.** Images show a significant reduction of epithelial damage after 15 days of cord blood serum treatment (from Oxford grade score V to III).

age; patients also showed significant reductions in scraping cytology scores and tear osmolarity, as well as significant improvements in corneal esthesiometry.

Eyes with the least amount of initial corneal damage (less than 25 mm<sup>2</sup>) showed the best response. However, duration of epithelial defects did not correlate with response, suggesting that CBS treatment should be initiated in new as well as long-standing disease, said Dr. Campos.

“CBS can be custom-

ized to provide different concentrations and species of growth factors,” said Dr. Campos. To identify rich serum sources of epidermal and other growth factors, Dr. Campos and colleagues are studying the hematological and obstetric characteristics of umbilical cord blood donors.

—Annie Stuart

1 Versura P et al. *Cornea*. 2013; 32(4):412-418.

*Dr. Campos reports no related financial interests.*

### Anticoagulants and PVD

## Keep in Mind Pros, Cons

A retrospective chart review of 336 eyes in patients with acute posterior vitreous detachment (PVD) uncovered a complex relationship between use of oral anticoagulation medication, the presence of vitreous hemorrhage (VH), and the development of retinal tears or detachment.<sup>1</sup>

Specifically, the use of oral anticoagulants increased the likelihood of a VH during an acute PVD event. Forty-three percent

of patients taking aspirin, clopidogrel, or warfarin had a VH, versus 31 percent not taking these medications ( $p = 0.03$ ).

At the same time, the data suggest that anticoagulant use reduces the likelihood of retinal tears or detachment in patients with PVD and VH. Fifty-two percent of these patients not taking aspirin, clopidogrel, or warfarin had retinal tears, compared with 39 percent using these medications. This trend, however,

was not statistically significant.

The study was inspired, in part, by the growing use of anticoagulants among the elderly. Even so, study coauthor Matthew T. Witmer, MD, was impressed by how widespread the use of these drugs was (64 percent) in this cohort drawn from a private retina practice. “The theory was that patients who are taking anticoagulants may be more likely to bleed without developing a retinal break,” said Dr. Witmer, a second-year vitreoretinal fellow at Weill Cornell Medical College, in New York, N.Y.

Since many patients with an acute PVD and VH tak-

ing oral anticoagulation medication still developed a retinal tear or detachment, Dr. Witmer has no plans to alter his clinical routine. “All patients with symptoms consistent with an acute PVD require a detailed retinal examination,” he said. “Just because a patient is taking an oral anticoagulant when they develop an acute PVD and VH doesn't make me less vigilant when searching for a retinal tear or detachment.”

—Miriam Karmel

1 Witmer MT, Cohen SM. *Retina*. 2013;33(3):621-626.

*Dr. Witmer reports no related financial interests.*