

Ophthalmology news - RETINA - Presence of PDR, DME tied to increased risk for cardiovascular disease

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RETINA - Research highlight

Presence of PDR, DME tied to increased risk for cardiovascular disease

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Results demonstrate ophthalmologists' role in helping patients with overall diabetes health

In ophthalmology, it's easy to become myopic—pun intended—in your focus on the eye.

However, a new systematic review and meta-analysis shows that when it comes to patients with diabetes and proliferative diabetic retinopathy (PDR) or diabetic macular edema (DME), it's better to consider the patient's overall health status. That's because the study found a greater risk for cardiovascular disease (CVD), including fatal CVD, in patients with DR or DME.

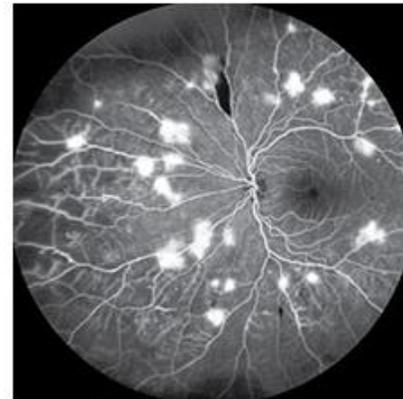
The study, led by Jing Xie, PhD, Singapore Eye Research Institute, Singapore, was published recently in *JAMA Ophthalmology*.

Although previous research has found an association between DR and coronary heart disease, these studies focused on early stages of DR. Also, previous studies have analyzed DR but not necessarily DME, Dr. Xie and co-researchers reported.

In one previous study, The Atherosclerosis Risk in Communities Study, there was a three-fold higher risk of fatal coronary heart disease events among those with DR. However, the Wisconsin Epidemiologic Study on Diabetic Retinopathy found a non-significant increase of heart disease among older patients with mild non-proliferative DR and proliferative DR, according to Dr. Xie and co-researchers. "Evidence from other studies has been inconclusive, possibly because of differences in the exposures compared (e.g., non-proliferative DR versus PDR), methods used (e.g., fundus photography versus clinical ophthalmoscopy), and outcome definitions (e.g., fatal coronary heart disease versus nonfatal stroke)," the researchers wrote.

In the current review, researchers conducted a systematic review of relevant literature and contacted the principal authors of eligible studies for individual participant data regarding CVD, coronary heart disease, stroke, and other specific information. Diabetes was designed as a self-reported physician diagnosis in all included studies. Included studies graded DR with the use of fundus photography findings using the Early Treatment Diabetic Retinopathy Study.

Although 656 studies were identified via database searches, eight ultimately met the meta-analysis criteria and had the additional data required. All eight studies were conducted in the U.S. or Australia. These studies included a total of 7,604 patients with type 2 diabetes. "After a mean follow-up time of 5.9 years (range 3.2 to 10.1 years) across studies, there was a total of 1,203 incident cases of first CVD events (with 286 fatal cases), including 916 coronary heart disease cases (with 242 fatal cases)," the authors reported.



PDR ultra-widefield fluorescein angiography
Source: Royce W.S. Chen, MD

People with DME or proliferative DR were more likely to have incidence CVD (incidence rate ratio, 1.39; 95% confidence interval, 1.16–1.67) and fatal CVD (incidence rate ratio, 2.33; 95% confidence interval, 1.49–3.67) compared with people who did not have DME or proliferative DR. The higher risk for CVD remained after multivariate adjustment for risk factors such as smoking, systolic blood pressure, hypertension medication use, total cholesterol, and body mass index. When researchers adjusted for diabetes duration, diabetes treatment, and glycated hemoglobin A1C level, the association between DR and fatal CVD was still significant.

Researchers think that the presence of microvascular disease in the eye increases the chance of more generalized microangiopathic processes that affect the eye and the myocardium and brain. “Our findings suggest that the presence of DME or proliferative DR may be a marker of generalized microvascular disease, which may contribute to the development of CVD in persons with diabetes,” they wrote. One other issue raised by the authors is the common use of antivascular endothelial growth factor (VEGF) treatments for DME and proliferative DR. Some research has found a potentially increased risk of CVD secondary to long-term systemic suppression of VEGF. The current research provides a baseline risk assessment for the use of anti-VEGF therapy for DME and DR, which could help in future studies, they explained.

One study limitation mentioned by the authors is that DME grading was based only on fundus photography because no data from OCT were available at baseline. Additionally, PDR was graded by fundus photography and not fluorescein angiography. These factors may have underestimated the number of patients with DME or DR.

Take-home messages

Although the findings don’t surprise physicians who reviewed the meta-analysis, they do see it as a stark reminder of the need to help patients with diabetes better monitor their overall health. “The greater than two times incidence rate ratio of fatal strokes/heart attacks for patients with PDR or DME is something significant that I would want to be communicated with fellow physicians and patients,” said Jeffrey Y.H. Chung, MD, board member of the Prevention of Blindness Society of Metropolitan Washington, and in private practice, Laurel, Maryland. “This gives us a powerful incentive and tool to reinforce to patients the importance of diabetic control as well as the relationship between their cardiovascular health and diabetes.”

Dr. Chung, a retinal specialist, characterizes his style with patients as fairly direct, and he even will discuss the risk for death from diabetes complications, particularly in patients who don’t seem as motivated to control their diabetes. This study gives more fuel to support those discussions. “I always discuss with patients the overall health effects as we see patients go to dialysis, lose their legs, and die of strokes/heart attacks and other issues such as infection, which are much more severe in diabetes due to microvascular damage,” he said. “We see this all the time, and it always hits us in a profound way.”

The results do not surprise **cardiologist Adam Splaver, MD, NanoHealth Associates, Hollywood, Florida**. “Poor glycemic control, high sugars, as well as other commonly associated conditions with diabetes such as hyperlipidemia and hypertension are all known inflammatory causes for vascular damage, which leads to diabetic retinopathy and macular edema as well as atherosclerosis and coronary artery disease,” he said. However, he does see the results as a good prompt to refer patients to cardiologists when necessary. “An ophthalmologist who encounters a patient with diabetes and manifestations of end-organ damage such as retinopathy and macular disease should have the patient see a clinical cardiologist and vice versa,” he said.

Although it may not be the ophthalmologist’s role to analyze the overall health of a patient with diabetes, **Alan Mendelsohn, MD, Eye Surgeons & Consultants, Hollywood, Florida**, has found that patients who are followed by an endocrinologist (instead of a primary care doctor) tend to have better ocular health. “Anecdotally, the same diabetics seemingly have been healthier with a decrease in prevalence and severity

of cardiovascular events when followed medically by a cardiologist,” he said. Dr. Mendelsohn has made several recommendations for patients to see endocrinologists as well as cardiologists. He also makes a point to ask for quarterly results from hemoglobin A1C results, which indicate blood sugar control over about a 3-month period. “On each visit, we discuss this lab finding with encouragement for strict diabetic control so as to achieve as low of a hemoglobin A1C level as possible,” he said. He thinks this number can help provide clues for both ocular and CVD health.

Royce W.S. Chen, MD, Helen and Martin Kimmel Assistant Professor of Ophthalmology, Columbia University Medical Center, and attending ophthalmologist, New York-Presbyterian Hospital, New York, observed that the study results are generalizable to white, African American, and Hispanic populations but that Asians are generally underrepresented in these studies. He thinks it would be interesting to see the study results segregated by ethnicities. However, he still sees an important message in the study. “The conclusions are valid and should serve to remind the ophthalmologist that he is a physician and should remember to take care of the whole person in front of him, not just his retinas,” he said.

<https://www.eyeworld.org/presence-pdr-dme-tied-increased-risk-cardiovascular-disease>