

Case Series: Retrospective Review of Incidental Retinal Emboli Found on Diabetic Retinopathy Screening: Is There a Benefit to Referral for Work-Up and Possible Management?

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INTRODUCTION

With the rising utilization of diabetic retinopathy photography screening programs across the country, many clinical and socioeconomic questions remain. For the most part, diabetic retinopathy findings have standard follow-up and referral guidelines.¹ However, management of other pathology, such as retinal arteriolar emboli, in this patient population is less clear.

The association of these lesions with cerebrovascular and cardiovascular morbidity and mortality has been well described in the literature.^{2,3} Retinal emboli are associated with a higher risk of stroke⁴ and, as shown by a pooled analysis of two large, population-based studies, predict a modest increase in all-cause and stroke-related mortality independent of cardiovascular risk factors.⁵

Retinal emboli have been identified in 1.3–1.4%^{6,7} of individuals > 40 years of age. These are plaque-like lesions wedged within retinal arterioles. They are oval- or rhomboid-shaped and have either a reflective or nonreflective appearance.^{8,9} Reflective emboli are composed of cholesterol crystals, whereas nonreflective types consist of fibrin, platelets, and calcium.¹⁰ Cholesterol emboli, also known as Hollenhorst plaques, are the most common, accounting for about

80%.^{7,11} There are various sources for retinal arteriolar emboli. It is thought that cholesterol emboli ulcerate from atheromatous internal or common carotid plaques, platelet-fibrin emboli arise from mural thrombus in the carotid, and calcific emboli originate from cardiac valvular structures.^{12,13}

The relationship between diabetes and retinal emboli is not well characterized. Of the two large studies that have examined retinal emboli—the Beaver Dam Eye Study (BDES)⁶ and the Blue Mountains Eye Study (BMES)⁷—only the BDES found that subjects with retinal emboli had a higher prevalence of diabetes than when compared to those patients without retinal emboli.

Because retinal arteriolar emboli are associated with a higher risk of stroke and cardiovascular disease, patients found to have retinal emboli sometimes undergo cardiovascular assessment.⁵ However, the frequency and variation of cardiovascular assessments and surgical or pharmacological interventions after findings of retinal emboli have not been well described. The purpose of this retrospective case series review was to characterize and assess the management of retinal arteriolar emboli in a population of type 2 diabetic patients.

QUESTIONS

1. What is the relationship among retinal arteriolar emboli and diabetes, vascular disease, and overall mortality?
2. Should patients with asymptomatic retinal arteriolar emboli detected on diabetic retinopathy screening be referred for further cardiovascular evaluation and management?
3. What is the cost-effectiveness of further imaging studies after the incidental detection of retinal arteriolar emboli?

STUDY DESCRIPTION

Research Design and Methods

We conducted a retrospective chart review of all patients presenting to diabetic retinopathy screening clinics at the Nashville and Murfreesboro Tennessee Veterans Administration (VA) Hospitals during the period of 1 May 2003 to 30 September 2006. Screening was performed with high-resolution digital fundus imaging, telemedicine, and centralized image grading. Using a Canon CR6-45NM fundus camera equipped with a Canon EOS D-60 digital camera back, two 45-degree images at 6.3 megapixels resolution were produced of each eye and were transmitted to the Vanderbilt Ophthalmic Imaging Center. At least two trained retinal photography readers, each with > 14,000 cases of grading experience,

analyzed the digital images to identify the presence of lesions associated with diabetic retinopathy and other significant pathology. If intra-arteriolar lesions were found, they were subsequently reviewed and confirmed by a board-certified ophthalmologist. The presumed type of embolus was not characterized. If a retinal embolus was detected, an “urgent alert” was sent to the referring physician per the protocol of the screening program.

Of the 7,819 VA patients who presented to the diabetic retinopathy screening clinics, 149 patients were identified with retinal arteriolar emboli. These patients were referred to their primary care provider for further evaluation and possible treatment. We collected information on cardiovascular disease history, imaging studies, prescribed antiplatelet medications (i.e., aspirin and clopidogrel), and surgical interventions before and after screening.

RESULTS

One hundred fifty-one eyes in 149 male patients (1.9%) in a population of 7,819 diabetic patients were found to have retinal arteriolar emboli. The retinal photography screeners and ophthalmologist agreed on the presence of the embolus in all cases. Of the patients with observed retinal emboli, the average age was 67 years (range of 30–88 years). One hundred and nine of the patients (73%) had previously known cardiovascular disease. Eighty-one patients (54%) were smokers. Only four (2.7%) had documented symptomatic retinal emboli (i.e., amaurosis fugax) based on symptoms described either before

or after screening. Table 1 summarizes the imaging ordered after alerting the primary care physician of the retinal findings.

Of the patients who had a carotid ultrasound, 21 (22%) had significant carotid artery stenosis defined as > 70% stenosis. Five patients (3%), one of whom had amaurosis fugax, underwent carotid endarterectomy in addition to antiplatelet medication. Thirteen patients who underwent echocardiogram were identified to have valvular disease. Of the 106 patients who had a carotid ultrasound or echocardiogram, 34 (32%) had significant abnormalities noted. Table 2 summarizes patients who were prescribed antiplatelet medication before and after screening.

DISCUSSION

Wong and Klein² suggest that the initial approach to patients with retinal emboli should begin with a complete medical assessment for risk stratification focusing on modifiable cardiovascular disease factors, such as hypertension, dyslipidemia, and diabetes. If present, these conditions should be treated, and the aggregate clinical risk profile should be used to guide further assessments. How further imaging studies shape the management of the patient beyond the history and physical exam is not clear. Although a risk-stratification approach may increase clinical confidence in pursuing further assessments, ~ 80% of patients who underwent carotid imaging in our study—all of whom were at higher relative risk because of diabetes—did

not have significant carotid artery stenosis based on vascular studies. This is in agreement with available data suggesting that most people with asymptomatic retinal emboli probably do not have significant carotid stenosis.^{11,14}

Whether echocardiography should be pursued is also uncertain.² In our study, 13 patients had a possible source detected via echocardiography. Although vascular disease was demonstrated in each case, these assessments were not able to positively assign the source of emboli to these lesions.

Patients with both symptomatic and asymptomatic retinal emboli have been shown to be at increased risk of stroke.⁴ Despite the relatively low yield of imaging when the primary care provider did pursue a vascular work-up, the finding of the retinal embolus alone alerted the primary care provider to the increased risk of vascular disease. Forty-two patients (28%) were initiated on antiplatelet therapy only after detection of the emboli; of these, 13 (8.7%) had no previously known cardiovascular disease. Thus, it appears that alerting the patient’s physician when retinal arteriolar emboli are found on routine digital retinopathy screening may aid in identification of patients not currently on antiplatelet therapy but who could benefit from such intervention.

Carotid endarterectomy was performed five times (3.4%) in patients after detection of the retinal emboli. This was performed after carotid ultrasonography demonstrating significant stenosis. This approach is in agreement with a study by Schwarcz et al.,¹⁵ who argued against carotid endarterectomy for patients with retinal emboli in the absence of the traditional indications for endarterectomy (e.g., symptoms, degree of stenosis, age). Additionally, the decision to proceed with carotid

Table 1. Follow-Up Imaging After Retinopathy Screening in 149 Patients

Imaging	n
Carotid ultrasound	96 (64%)
Echocardiogram	60 (40%)
Carotid ultrasound and echocardiogram	50 (34%)
Carotid ultrasound or echocardiogram	106 (71%)

Table 2. Patients on Antiplatelet Medication Before and After Screening

Group	n Using Antiplatelet Before Screening	n Using Antiplatelet After Screening
All patients (n = 149)	87 (58%)	129 (87%)
Carotid stenosis > 70% (n = 21)	9 (43%)	16 (76%)
Valvular disease (n = 13)	8 (62%)	11 (85%)

endarterectomy, given its morbidity and mortality in otherwise asymptomatic patients, is controversial.²

We recognize several limitations of the present study. First, given that this was a retrospective study, there was no standardization in evaluation and management by primary care physicians. Although investigating the primary care physician's management decisions would be useful, the aim of this study was to provide a baseline analysis of the "real-world" management of patients referred for retinal emboli. The clinical decisions of different providers with varying practice methods would paint such a picture. This study was limited to the VA system, which simplifies the analysis because the providers and patients are within a standardized electronic medical records system. Conversely, an analysis of different medical systems and reimbursement schemes would be more complex.

Second, we did not identify the particular type of embolus detected (cholesterol, platelet-thrombin, or calcific). A study by Sharma et al.¹⁶ demonstrated poor intra-observer and inter-observer agreement on classifying retinal emboli. Although clinical manifestations may vary according to type, each can have significant morbidity, and thus it is not clear that subsequent management should markedly differ. Whether the type of embolus would actually make an impact on the evaluation and management of the patient requires further investigation.

Third, we only examined patients with diabetes, a significant pre-

existing risk factor for vascular disease. The management decisions by the Primary Care Provider may have reflected this with more aggressive work-up and intervention. Thus, our results may overestimate rates of follow-up interventions when compared to nondiabetic patients who present with retinal emboli. An analysis of the primary care physicians' decision-making would provide clarification.

Interestingly, we found a greater prevalence of emboli (1.9%) than both the BDES⁶ and BMES⁷ (1.3 and 1.4%, respectively). This is not a surprising finding given that our population was made up entirely of diabetic patients who are, as a whole, at higher risk for vascular disease. In addition, the VA population may have a high prevalence of vascular risk factors other than diabetes, such as smoking, advanced age, and hypertension, compared to the populations in other studies.

We believe it is reasonable to refer patients to their primary care physician on the detection of a retinal embolus found on photography screening for diabetic retinopathy. Although particular strategies to identify those who can benefit from follow-up imaging do not presently exist, initiation of treatment may still be necessary. Further studies are required to examine cost-effectiveness of the cardiovascular assessments after findings of retinal emboli. Clearly, however, this population of type 2 diabetic patients represents a high-risk population for future cardiovascular events

and may warrant more aggressive evaluations.

As we have demonstrated, 28% of patients in our population did require new medical interventions (i.e., antiplatelet therapy) and a few (3%) required aggressive surgical interventions as a result of this referral and work-up. Thus, routine retinal photography screening for diabetic retinopathy gives us a unique opportunity to discover these lesions and thus trigger possible therapeutic interventions before more serious complications ensue.

CLINICAL PEARLS

- Diabetic patients with retinal emboli may have an even higher risk of stroke, cardiovascular disease, and mortality than those with diabetes alone.
- The detection of incidental emboli found when screening for diabetic retinopathy provides an important opportunity to initiate further work-up and management.
- The management of retinal arteriolar emboli includes the identification of risk factors and possible treatment with antiplatelet medication or vascular surgery.

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