

## Case report: The role of hypertension retinopathy graduation in the management of systemic cardiovascular disease

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### ABSTRACT

Moderate to severe hypertensive retinopathies are more likely to correlate with uncontrolled blood pressure in all ages. Mild microvascular changes are expected with natural aging and are therefore more concerning in patients younger than 40. Risk assessment is subsequently determined based on blood pressure measurements and patient symptoms. The goal of this paper is to discuss current opinions regarding the role of grading hypertensive retinopathy in the risk assessment of systemic cardiovascular disease in the context of a clinical case. Management and referral recommendations for clinicians will be summarized. Emergent referral for hospital-based care is indicated in any patient with severe hypertensive retinopathy; pregnant women with moderate hypertensive retinopathy; patients younger than 55 with blood pressure greater than Grade 2; any patient with blood pressure greater than grade Severe; any patient with symptoms of chest pain, headache, dyspnea, or dizziness; and any patient with a symptomatic retinal plaque.

**Keywords:** Cardiovascular disease, hypertension, retinopathy

### Introduction

It is estimated that 50 million people in the United States and up to 1 billion people globally have hypertension.<sup>[1]</sup> Hypertension contributes to and is a modifiable risk factor for cardiovascular disease, which is the leading cause of death in the United States.<sup>[2]</sup> The need for the early detection and proper management of hypertension is important and widespread.

The definition of hypertension has varied. The 2020 Global Hypertension Practice Guidelines, which the International Society

of Hypertension determined and which the American Heart Association endorsed, currently define hypertension as a systolic blood pressure greater than or equal to 140 mmHg and/or a diastolic blood pressure greater than or equal to 90 mmHg [Table 1].<sup>[3]</sup>

### Case Presentation

The patient is a 50-year-old male who presented to the clinic with a chief complaint of a “piece of hair” in the central vision of the left eye for the past year. He denies other changes in vision or ocular pain. He wore single-vision distance glasses. This was his first eye examination at the University of Virginia. The patient’s medical history was significant for malignant hypertension, prior myocardial infarction, and end-stage renal disease. These conditions were managed with oral medication and dialysis. The patient did not smoke.

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**Table 1: Classification of hypertension based on blood pressure measurement from the 2020 Global Hypertension Practice Guidelines<sup>[3]</sup>**

Category	Systolic (mmHg)	Conjunction	Diastolic (mmHg)
Normal Blood Pressure (BP)	<130	And/or	<85
High Normal (BP)	130-139	And/or	85-89
Grade 1 Hypertension	140-159	And/or	90-99
Grade 2 Hypertension	160-169	And/or	100-110
Severe Hypertension	170	And/or	110

The best corrected visual acuity was 20/25 in the right eye and 20/30 in the left eye. The decrease in acuity was because of a high myopic refractive error in both eyes. A dilated fundus examination revealed a posterior vitreous detachment [Figures 1-3] over the left optic nerve, which was the cause of the patient's chief complaint. During the dilated fundus examination, a plaque and a cotton wool spot (CWS) were incidentally found in the right eye. Based on appearance and location, the plaque was thought to be calcific. The patient also had underlying hypertensive retinopathy in both eyes, which was moderate retinopathy in the right eye and mild retinopathy in the left eye using the Mitchell–Wong grading system.

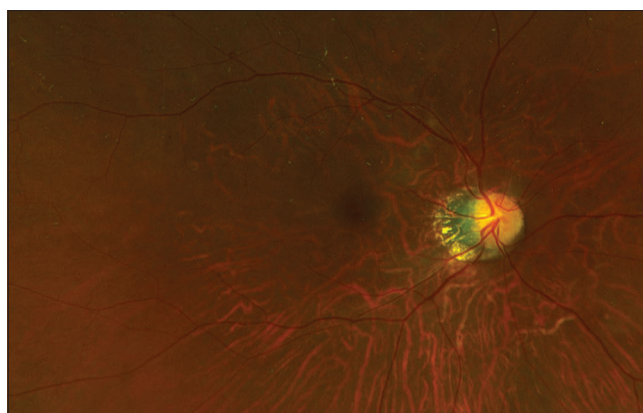
At what level does hypertension begin to manifest in the eye? Do ocular findings correlate with hypertension stratification? What role does hyperlipemia play in this context? Can ocular findings be used to assess cardiovascular risk? The following discussion is aimed at answering these questions.

## Discussion

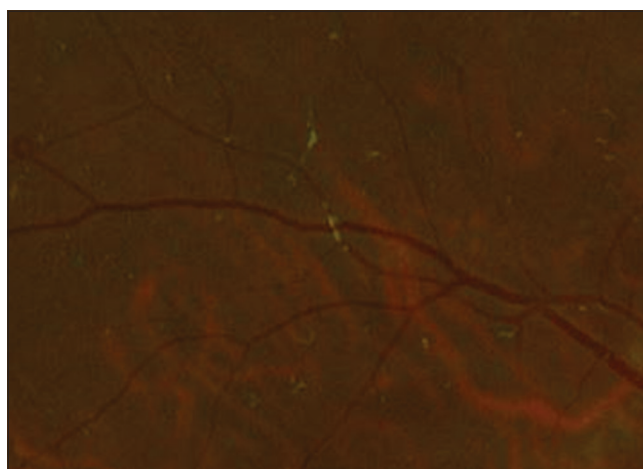
### Hypertension

The human body possesses regulatory mechanisms to overcome transiently elevated blood pressure. Chronically elevated blood pressure leads to prolonged mechanical stress that overwhelms these mechanisms, damaging the lining of arteries and predisposing it to atherosclerotic plaque formation. Increased levels of cholesterol (specifically, low-density lipoproteins) contribute to plaque formation at these damaged sites and promote local inflammation, leading to plaque growth. When such atherosclerotic processes occur in coronary and cerebral arteries, the patient is at risk for myocardial infarction and stroke.<sup>[2]</sup>

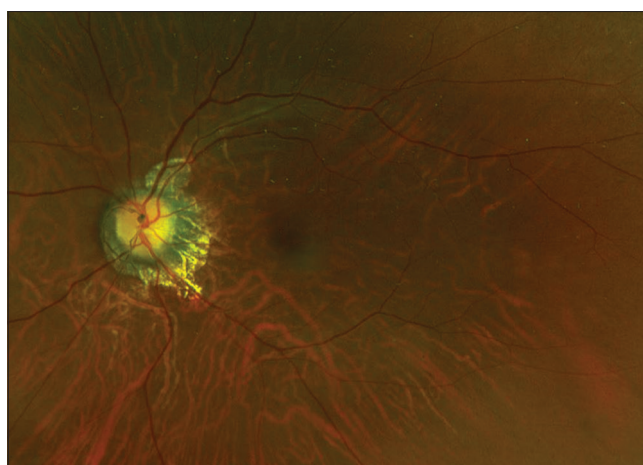
The eye is unique in that blood vessels may be viewed directly using non-invasive techniques.<sup>[4]</sup> During a dilated fundus examination, chronic changes in these blood vessels may include narrowing of the arterioles and an increase in the arteriolar light reflex.<sup>[2]</sup> Arteries typically pass anteriorly over veins, and when they thicken because of atherosclerosis, the compression of veins at these intersections, called “AV nicking,” can be seen.<sup>[4,6]</sup> In severe cases, this compression can lead to a vision-threatening vein occlusion. Once blood pressure is controlled, these vessel changes may not resolve.<sup>[2]</sup>



**Figure 1:** Fundus photo of the patient's right eye depicting the optic nerve surrounded by peripapillary atrophy; a clear macula; and vessels with arteriolar narrowing, arteriovenous (AV) crossing changes, CWS, and calcific plaque in the superior arcade



**Figure 2:** Enlarged area of Figure 1 depicting plaque in the superior arcade, arteriolar narrowing, and an AV crossing change



**Figure 3:** Fundus photo of the patient's left eye depicting the optic nerve surrounded by peripapillary atrophy with an overlying posterior vitreous detachment, a clear macula, and vessels with arteriolar narrowing and AV crossing changes

The blood retinal barrier, which is formed by zonula occludens or tight junctions between retinal pigment epithelial cells and retinal

capillary endothelial cells, is important because it prevents blood from interfering with the visual pathway.<sup>[4]</sup> During episodes of acutely elevated blood pressure, this barrier can be disrupted with resultant hard exudates, macular edema, and flame-shaped or dot and blot hemorrhages. If severe enough to disrupt perfusion, ischemic areas may be seen as cotton wool spots and the optic nerve may be involved, with a typically bilateral disc edema appearing in the area.<sup>[2]</sup> Subconjunctival hemorrhage associated with elevated blood pressure has also been reported.<sup>[5]</sup>

### Grading scales

Multiple scales have been proposed to quantify the level of hypertensive retinopathy in a patient. The first and most widely used is the Keith–Wagener–Barker (KWB) grading system. More recently, Mitchell–Wong published a simplified version which combines KWB Grades 1 and 2, and it favored for its simplicity. We find the Mitchell–Wong grading system to be sufficient for clinical use as KWB stratification of mild retinopathy was shown to have little difference in systemic implications [Table 2].<sup>[7]</sup>

### Hypertension

The association between hypertensive retinopathy and systemic cardiovascular disease has been explored for decades. Foundational work by Gunn, Keith, Wagener, and Barker established a connection between systemic hypertension and the ocular signs summarized above. Until more recently, the usefulness of ocular examination as a prognostic indicator was unknown.<sup>[8]</sup>

The 1990s began an era of population-based studies that utilized more modern fundus photography techniques. The researchers who performed these studies largely agreed that it is not uncommon to have mild signs of hypertensive retinopathy in patients above the age of 40, regardless of whether they have hypertension.<sup>[8,9]</sup> Although a connection between hypertensive retinopathy and 10-year cardiovascular mortality has been well established,<sup>[10]</sup> it has been difficult to correlate hypertensive retinopathy to specific adverse cardiovascular outcomes, such as stroke, target organ damage, and coronary artery disease.<sup>[8]</sup> In 2001, the Atherosclerosis Risk in Communities Study (ARIC) reported that hypertensive retinopathy was an independent risk factor for stroke. It showed that patients with both hypertensive retinopathy and white matter lesions on magnetic resonance imaging had a 5-year relative risk of 18,<sup>[11]</sup> whereas patients with only white matter lesions had a 5-year relative risk of 3.4.<sup>[11]</sup> It was hypothesized that the vascular changes which are visible in the eye occur in tandem in the vasculature of the brain.<sup>[11]</sup>

A 2015 study found that aortic stiffness and carotid hypertrophy (measures of target organ damage) were associated with KWB Grade 1 hypertensive retinopathy (mild on the Mitchell–Wong scale), but only when patients were younger than age 55.7. This study found no difference between KWB Grades 1 and 2, so the Mitchell–Wong grading system was comparable to that of KWB.<sup>[7]</sup>

Hypertensive retinopathy was also reported to be an independent risk factor for carotid artery disease (CAD) in a 2008 study, but this work was based on population data collected in the 1970s.<sup>[13]</sup> Although great progress has been made in this field, patients with co-morbidities, such as diabetes, are frequently excluded from these studies, and although this preserves the integrity of the research, it confounds clinical decision-making, which is rarely so insular.<sup>[11]</sup>

The evidence to suggest that the grade of hypertensive retinopathy should be used to stratify cardiovascular risk is weak.<sup>[8]</sup> Direct blood pressure measurements remain the foremost method of risk stratification. Eye care clinicians may play a role in mitigating adverse cardiovascular outcomes by checking blood pressure in office when ocular risk factors are identified during routine surveillance and making a timely referral. Blood pressure should be checked on patients younger than 55 with mild hypertensive retinopathy and on patients of any age with moderate to severe hypertensive retinopathy. Emergent, hospital-based care is recommended if blood pressure is greater than Grade 2 (systolic greater than or equal to 160 mmHg and/or diastolic blood pressure greater than or equal to 100 mmHg) in a patient younger than 55, if blood pressure is greater than Severe (systolic greater than 170 mmHg and/or diastolic blood pressure greater than 110 mmHg) in a patient of any age, in any patient with bilateral disc edema, in pregnant women, or in patients with symptoms such as chest pain, headache, dyspnea, or dizziness [Table 3].<sup>[14]</sup>

### Hyperlipidemia

In the above cited 2015 study, the presence of plaques was not related to either hypertensive retinopathy scale.<sup>[7]</sup> Hollenhorst plaques were first described in 1958. Carotid artery imaging

**Table 2: Description of Mitchell–Wong grading system<sup>[8]</sup>**

Grade	Signs
None	No datable signs
Mild	Generalized or focal arteriolar narrowing, AV nicking, Cooper wiring
Moderate	Presence of blot or flame hemorrhages, micro-aneurysm, cotton wool spots, exudates
Severe	Presence of moderate retinopathy with optic disc swelling

**Table 3: Proposed guideline for referral based on the Mitchell–Wong level of hypertensive retinopathy<sup>[14]</sup>**

Age	Hypertension Retinopathy		
	Mild	Moderate	Severe
<55	Refer for work-up secondary hypertension. Emergent if in-office is greater than Grade 2	Communicate findings to the primary care physician. Refer for emergent hospital-based care: If in office BP > Severe or if the patient is symptomatic with chest pain, headaches, dyspnea, dizziness, or pregnancy	Refer for emergent hospital-based care
>55	Monitor annually		

techniques decades later determined that a fourth of patients with Hollenhorst plaques have carotid artery stenosis of at least 40%. In addition, population-based studies from the 1990s found a 56% mortality rate because of stroke in patients with retinal plaques.<sup>[15]</sup>

A vascular surgery review from 2007 argues that Hollenhorst plaques are not a strong indicator of impending stroke because they can be present for years with little systemic consequence.<sup>[12]</sup> The review concluded, regardless of type, that incidentally found plaques are less concerning than those found in patients with symptoms, most commonly transient monocular vision loss. The review recommended that intervention be based on the level of carotid artery stenosis rather than on the presence or absence of a plaque.<sup>[15]</sup> It is recommended that patients with retinal plaques who are symptomatic with transient monocular vision loss (TMVL) be referred for emergent, hospital-based care. Cases in which retinal plaques are found incidentally in asymptomatic patients can be managed less emergently.<sup>[16]</sup>

## Conclusion

Signs of moderate to severe hypertensive retinopathy are more likely to correlate with uncontrolled blood pressure in all ages. Mild microvascular changes are expected with natural aging and are therefore more concerning in patients younger than 40. Risk assessment is subsequently determined based on blood pressure measurements and patient symptoms. Retinal plaques have been shown to be a sign of atherosclerosis, but their presence is not currently used in stroke risk stratification. The percentage of carotid artery stenosis is the preferred metric, but plaques may be used as a warning that carotid imaging is indicated.

Both hypertensive retinopathy and retinal plaques are independent indicators of cardiovascular disease, but neither can be used to directly stratify risk. Identification of either hypertensive retinopathy or retinal plaques should prompt the clinician to check blood pressure, question the patient regarding symptoms, and perform a record review in order to make an appropriate referral to mitigate adverse cardiovascular outcomes.

Emergent referral for hospital-based care is indicated in any patient with severe hypertensive retinopathy; pregnant women with moderate hypertensive retinopathy; patients younger than 55 with blood pressure greater than Grade 2; any patient with blood pressure greater than grade Severe; any patient with symptoms of chest pain, headache, dyspnea, or dizziness; and any patient with a symptomatic retinal plaque.

These recommendations have been made based on studies that typically exclude co-morbidities, such as diabetes. The presence of co-morbidities may indicate referral or follow-up sooner than what is reported above.

## Case Conclusion

Although the patient was new to the eye clinic, UVA Cardiology had fortunately already been following the patient. A communication was sent to the patient's cardiologist to coordinate a carotid Doppler if one had not been performed recently. The patient was educated on the exam findings, and baseline fundus photos were taken.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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