



PROGNOSTIC SIGNIFICANCE OF OPTIC DISC HEMORRHAGE

Is ODH a definite indicator of glaucomatous progression?

BY JIN-SOO KIM, MD; YOUNG KOOK KIM, MD; BRIAN A. FRANCIS, MD; AND ALEKSANDR YELENSKIY, MD



A SIGN OF ACTIVE PROGRESSION

BY JIN-SOO KIM, MD; AND YOUNG KOOK KIM, MD

The association of optic disc hemorrhage (ODH) with glaucoma was first recognized more than 100 years ago by Jannik P. Bjerrum, who called it *glaucoma haemorrhagicum*. The phenomenon was subsequently overlooked until the 1970s, when Stephen M. Drance, MD, revisited the issue in his study on splinter hemorrhages in open-angle glaucoma patients.¹ Today, ODH is known to have a strong association with glaucoma development and progression.¹⁻³ However, its low prevalence and transient nature render elucidation of its exact pathogenesis and causal relationship with glaucoma progression difficult.⁴

ODH AND GLAUCOMA PROGRESSION

Previous reports have shown that structural and functional progression is ongoing after the appearance of ODH.^{5,6} Changes to the optic disc and the appearance and enlargement of retinal nerve fiber layer (RNFL) defect can occur subsequent to ODH.^{5,7,8} Researchers have documented the appearance of new glaucomatous visual field (VF) defect² and a faster rate of VF change⁶ after ODH.

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NOT A SIGN BUT A RISK FACTOR

BY BRIAN A. FRANCIS, MD; AND ALEKSANDR YELENSKIY, MD

Since the first report of ODH in glaucoma in 1889, many other studies have emphasized this association. After its rediscovery by Drance and Begg in 1970, numerous investigators have explored ODH as a risk factor for the development and progression of glaucoma. Some recent studies have shown that changes in the optic nerve, RNFL, and VF precede and progress after ODH in glaucoma patients.

However, even with evidence of the association between ODH and glaucoma progression, it should be emphasized that disc hemorrhage is a complex process that cannot be explained by vascular, mechanical, or pressure-related factors alone. Although the occurrence of ODH should be noted as significant, it is not a definite sign of glaucomatous progression, as some have suggested.

ODH can occur in disease states other than glaucoma. Posterior vitreous detachment, elevated resistance of the central retinal vein, diabetic retinopathy or diabetic microvascular disease, leukemia, optic disc drusen, lupus, use of antiplatelet agents, and different types of optic neuropathy

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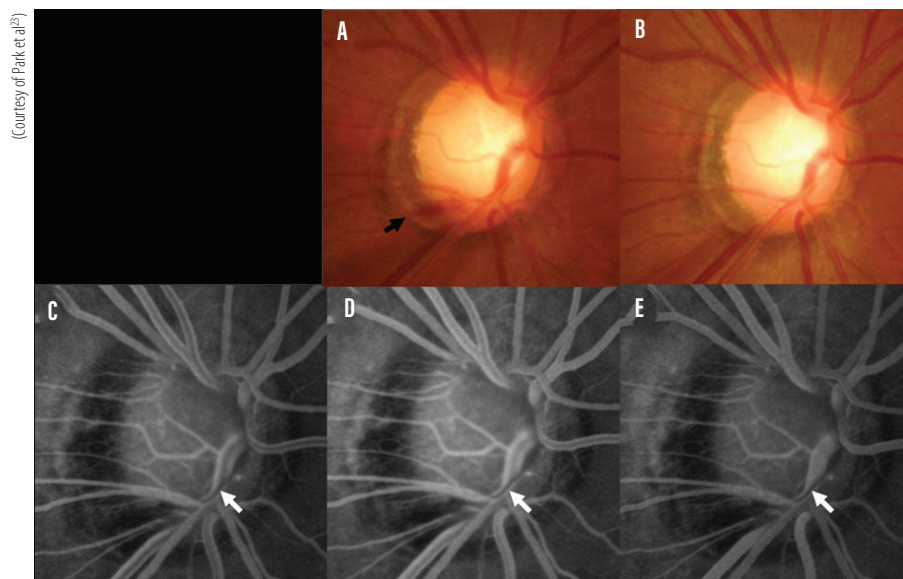


Figure 1. A 47-year-old woman with normal-tension glaucoma. ODH (black arrow) was present at the border of a localized retinal nerve fiber layer defect in her right eye (A). Fluorescein angiography was performed 3 months after disappearance of the ODH in the disc photograph (B). A vessel filling defect (white arrow) was found at the midarteriovenous phase (C), early late phase (D), and late phase of fluorescein angiography (E). The vessel filling defect was proximal to the location of the ODH. This vein is reflected at the cup margin, the proximal location of the ODH.

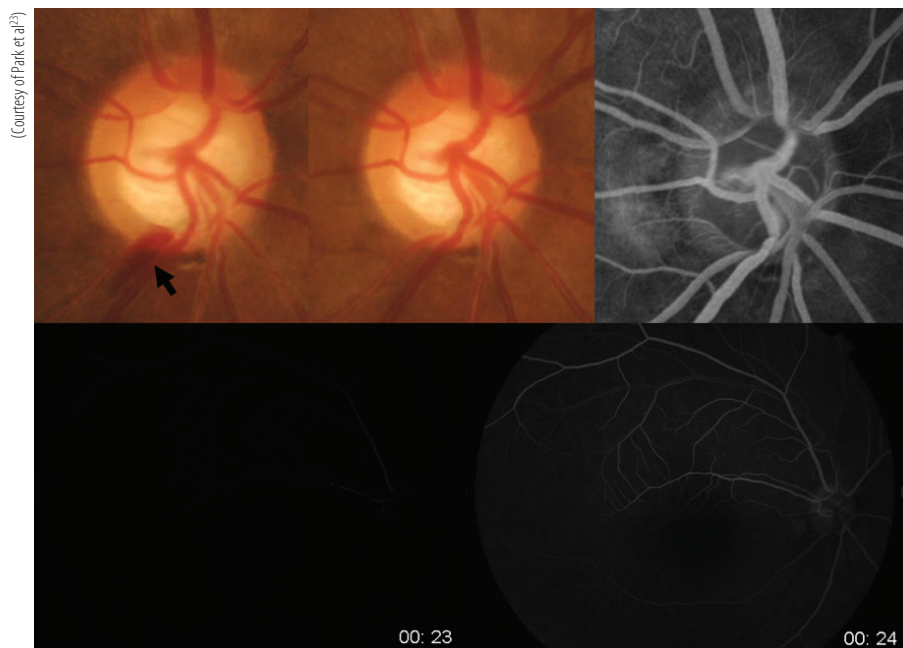


Figure 2. A 54-year-old woman with normal-tension glaucoma. ODH not related to a localized retinal nerve fiber layer defect shows no specific findings suggesting hemodynamic changes, such as vessel filling defect or delayed filling, disc leak, or disc filling defects.

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have been shown to manifest various degrees of disc hemorrhage.¹⁻⁶ Using ODH alone as evidence of glaucoma or glaucomatous progression may be

incorrect without first looking at the full spectrum of causes.

Eyes with ODH do not necessarily always have glaucoma or show faster

rates of progression. Whereas some studies show greater VF progression in eyes with recurrent disc hemorrhage than in those without, other studies show a faster structural progression but similar functional progression.^{7,8} In the Blue Mountains Eye study and the Beaver Dam Study, most ODHs were observed in eyes without glaucoma.^{9,10}

There is strong evidence in the literature to show associations between ODH and glaucomatous progression, including nerve changes, perimetric changes, and ganglion cell loss.¹¹⁻¹⁴ However, there is conflicting evidence whether the clinical significance of solitary, nonrecurrent hemorrhage is of similar to that of recurrent disc hemorrhage. Thus, a solitary finding of ODH may not necessarily indicate the need for more aggressive treatment.

It is important to note that a weakening of the lamina cribrosa (LC) may be implicated in the pathophysiology of disc hemorrhage. There is a strong correlation between laminar disruption and ODH.^{15,16} Thus, ODH may be only a secondary sign of the structural changes implicated in the disease process itself, rather than a prognostic indicator of glaucoma. Certain aspects of disc hemorrhage can be closely related to laminar change in glaucoma patients, but they can also occur independently.¹⁷ This may explain why patients with severe end-stage glaucoma have a relatively lower frequency of ODH.

Many studies have shown that eyes with normal-tension glaucoma (NTG) have a higher incidence of ODH than those with high-tension primary open-angle glaucoma (POAG).¹⁸⁻²² This finding is hard to resolve if one assumes a common disease state in NTG and POAG eyes. Even with adequate IOP-lowering therapy, NTG eyes are more predisposed to hemorrhage. This shows that the prognostic significance of ODH is more nuanced than commonly believed.

ODH suggests vascular damage and an increased likelihood that a significant vascular component is contributing to the disease when ODH occurs. Park et al²³ studied 35 eyes with ODH to analyze the relationship among ODH, vascular abnormalities, and changes in the optic disc and RNFL. They found that approximately half of the eyes with ODH had accompanying localized RNFL defects. Of these eyes, 60% had vascular changes on fluorescein angiography at the site of the ODH (Figure 1). However, almost half of the eyes with ODH did not have an associated RNFL defect, and those eyes did not show vessel filling defects or delayed filling (Figure 2).

CONCLUSION

Although many ophthalmologists have formed opinions about the prognostic significance of ODH in glaucoma, there is still no clear consensus. It is undeniable that there is a strong association between glaucoma and disc hemorrhage. However, we recommend viewing ODH as a risk factor for progression rather than a definitive sign of progression. Clinicians must increase their vigilance and the frequency of monitoring for progression

after ODH, but they should consider other factors before initiating more aggressive treatment, especially surgical intervention.

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"ODH HOLDS CLINICALLY SIGNIFICANT PROGNOSTIC VALUE AS A SIGN OF POTENTIAL GLAUCOMA PROGRESSION AND POSSIBLE NEED FOR TREATMENT INTENSIFICATION."

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"CLINICIANS MUST INCREASE THEIR VIGILANCE AND FREQUENCY OF MONITORING FOR PROGRESSION AFTER ODH, BUT THEY SHOULD CONSIDER OTHER FACTORS BEFORE INITIATING MORE AGGRESSIVE TREATMENT."

**- BRIAN A. FRANCIS, MD;
AND ALEKSANDR YELENSKIY, MD**

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Correspondingly, a study in patients with preperimetric glaucoma showed that ODH was associated with glaucoma progression, specifically with structural change.⁹ These results suggest that glaucoma patients who experience episodes of ODH have a higher likelihood of faster RNFL thinning. It remains unclear, however, whether ODH has a causative role in disease progression. Considering the low frequency of ODH in advanced stages of glaucoma, it is possible that ODH is just one of a number of phenomena detected during the disease course.

LC AND ODH

The pathophysiology of ODH, notwithstanding its strong association with glaucoma progression, has yet to be fully elucidated. Recent advances in spectral-domain OCT with enhanced depth imaging and swept-source OCT with longer wavelengths have made it possible to obtain in vivo images of the LC, which is known to be the initial site of glaucomatous damage.

Many studies have concluded that ODH is the consequence of microvascular disruption resulting from structural alteration of the LC,⁷ whereas others have reported that ODH is associated with compromised blood supply inside the optic nerve head.¹⁰ Indeed, these hypotheses appear to be at least partly related. Strong spatial correlations between ODH and lamellar disruption have been reported,¹¹ and a recent prospective study revealed that lamellar disinsertions were detected more frequently in glaucoma patients with ODH than in those without.

Another recent prospective study showed that glaucomatous eyes with ODH at the site of focal LC defects had frequent and faster VF progression than eyes with ODH unaccompanied by LC alterations or LC alterations unaccompanied by ODH.¹² Considering that the LC is the primary site of glaucomatous damage, ODH can provide secondary clues to the identification of vulnerable LC and thus of patients at high risk of further progression.

TREATMENT INTENSIFICATION AFTER ODH

Even if ODH were an early sign of structural glaucoma progression, it would have less clinical value if the progression could not be altered by more aggressive treatment. The Early Manifest Glaucoma Trial showed that the presence or frequency of ODH was not related to IOP-lowering treatment either before or after controlling for associated factors,¹³ which suggests that ODH might not be a sign of insufficient IOP reduction. Another prospective study in glaucoma patients with ODH, however, showed that greater IOP reduction in combination with more aggressive treatments after ODH contributed to slower rates of progressive VF loss.¹⁴ A recent study showed that glaucoma treatment intensification after ODH may have a beneficial effect in reducing the rate of RNFL thinning.¹⁵

These findings imply that, in glaucomatous eyes with ODH, treatment intensification can slow glaucoma progression. Even if ODH is not the cause of glaucoma progression, it might still be an important sign of the need for treatment intensification.

CONCLUSION

It is hard to deny that ODH is an important sign of active glaucoma progression. Unfortunately, due to current technical limitations in the detection of very early glaucoma progression, clarification of the possible causal relationship between ODH and glaucoma progression will remain difficult into the near future. Although ODH might not be a cause of glaucoma progression, there is sufficient evidence that the two have an association. In any event, ODH holds clinically significant prognostic value as a sign of potential glaucoma progression and possible need for treatment intensification. ■

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