

MACULAR PIGMENT OPTICAL DENSITY AS A STRUCTURAL INDICATOR OF GLAUCOMA



Lower levels of macular pigment may be associated with a thinner macular ganglion cell complex.

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Currently, the only modifiable risk factor for primary open-angle glaucoma is IOP. However, thinning of the inner retinal layers (ie, the ganglion cell complex) in the macula represents an early structural indicator of glaucoma.¹ Interventions or approaches to prevent this thinning may therefore help prevent glaucomatous vision loss.

Low levels of macular pigment, composed of the dietary carotenoids lutein and zeaxanthin in the retina, were associated with a thinner macular ganglion cell complex among women in the Carotenoids in Age-Related Eye Disease Study 2 (CAREDS2).² These findings suggest that dietary supplementation with lutein and zeaxanthin may have beneficial effects for preventing structural changes implicated in early glaucoma.

BACKGROUND

Lutein and zeaxanthin are xanthophyll carotenoids found predominantly in leafy green vegetables. These carotenoids accumulate throughout the retina and central nervous system, with the highest concentration in the macula.³ Notably, higher levels of macular

pigment have been consistently linked to improved BCVA and contrast sensitivity, which may reflect macular pigment's role in filtering short-wavelength blue light.^{4,5} Some studies have also observed a link between low levels of macular pigment and the presence of age-related macular degeneration.^{6,7}

Macular pigment is an attractive target for possible interventions to prevent age-related eye diseases such as glaucoma for several reasons.

Macular pigment levels can be measured simply and noninvasively. Additionally, they can be increased inexpensively (relative to the cost of medical treatment) by consuming carotenoid-rich foods such as leafy green vegetables, broccoli, and eggs or dietary supplements.³ However, the results of prior small case-control studies have been inconsistent with regard to whether low macular pigment is a risk factor for glaucoma.⁸⁻¹¹

AT A GLANCE

- ▶ Macular pigment is composed of the dietary carotenoids lutein and zeaxanthin and has been linked to improvements in vision and a reduced risk of age-related eye diseases.
- ▶ In the Carotenoids in Age-Related Eye Disease Study 2 (CAREDS2), lower levels of macular pigment were associated with thinning of retinal layers that is an early structural indicator of glaucoma.
- ▶ CAREDS2 adds to a growing body of evidence that diets rich in lutein and zeaxanthin may reduce glaucoma risk.
- ▶ Additional research is required to determine whether interventions designed to increase macular pigment levels via dietary carotenoid supplementation can help prevent glaucoma.

“WE OBSERVED THAT LOWER LEVELS OF MACULAR PIGMENT WERE ASSOCIATED WITH A THINNER MACULAR GANGLION CELL COMPLEX, INCLUDING BOTH THE MACULAR GANGLION CELL LAYER AND INNER PLEXIFORM LAYER. THESE ASSOCIATIONS WERE STATISTICALLY SIGNIFICANT ONLY IN THE CENTRAL SUBFIELD OF THE MACULA, THE AREA CORRESPONDING TO THE FOVEA WHERE THE DENSITY OF MACULAR PIGMENT IS HIGHEST.”

SUMMARY OF PRIMARY FINDINGS

CAREDS2 is a longitudinal follow-up study of the original CAREDS cohort, which included 2,005 women recruited from the Women’s Health Initiative observational study.^{12,13} For CAREDS2, we analyzed a sample of 379 women aged 55 to 81 years at CAREDS enrollment who completed baseline macular pigment testing (2001–2004) and underwent OCT imaging approximately 15 years later in CAREDS2 (2016–2019).²

We observed that lower levels of macular pigment were associated with a thinner macular ganglion cell complex, including both the macular ganglion cell layer and inner plexiform layer. These associations were statistically significant only in the central subfield of the macula, the area corresponding to the fovea where the density of macular pigment is highest. Among eyes with manifest primary open-angle glaucoma, lower levels of macular pigment were also associated with thinner retinal nerve fiber layer thickness in the central subfield. Overall, these findings are consistent with earlier studies that also reported an association between low

levels of macular pigment and reduced thickness or volume of the macular ganglion cell complex in healthy and glaucomatous eyes.⁸⁻¹⁰

CONCLUSIONS AND CLINICAL SIGNIFICANCE

The observed association between lower macular pigment and thinner inner retinal layers as an early structural indicator of glaucoma is not well understood. Large-scale prospective studies and randomized controlled trials are required to determine whether interventions to increase macular pigment could decrease the risk of glaucoma development or its progression. The association between macular pigment and inner retinal thickness may reflect the benefits of an overall healthy diet rich in fruits and vegetables that contain protective antioxidants.¹¹ Leafy green vegetables also contain high levels of dietary nitrates, which have been linked to a lower risk of glaucoma in large cohort studies.^{14,15}

The evidence that dietary supplementation with lutein and zeaxanthin may influence glaucoma risk remains in its early stages. That

said, clinicians may consider informing interested patients that an overall healthy diet rich in leafy green vegetables may help lower their risk of ocular disease. ■

1. Hood DC, Raza AS, de Moraes CGV, Liebmann JM, Ritch R. Glaucomatous damage of the macula. *Prog Retin Eye Res*. 2013;32:1-21.
2. Lawler T, Mares JA, Liu Z, et al. Association of macular pigment optical density with retinal layer thicknesses in eyes with and without manifest primary open-angle glaucoma. *BMJ Open Ophthalmol*. 2023;8(0):e001331.
3. Mares J. Lutein and zeaxanthin isomers in eye health and disease. *Annu Rev Nutr*. 2016;36:571-602.
4. Wooten BR, Hammond BR. Macular pigment: influences on visual acuity and visibility. *Prog Retin Eye Res*. 2002;21(2):225-240.
5. Fletcher LM, Engles M, Hammond BR. Visibility through atmospheric haze and its relation to macular pigment. *Optom Vis Sci*. 2014;91(9):1089-1096.
6. Bone RA, Landrum JT, Mayne ST, Gomez CM, Tibor SE, Twaroska EE. Macular pigment in donor eyes with and without AMD: a case-control study. *Invest Ophthalmol Vis Sci*. 2001;42(1):235-240.
7. Bernstein PS, Zhao DY, Sharifzadeh M, Ermakov IV, Gellermann W. Resonance Raman measurement of macular carotenoids in the living human eye. *Arch Biochem Biophys*. 2004;430(2):163-169.
8. Siah WF, Loughman J, O'Brien C. Lower macular pigment optical density in foveal-involved glaucoma. *Ophthalmology*. 2015;122(10):2029-2037.
9. Ji Y, Zuo C, Lin M, et al. Macular pigment optical density in Chinese primary open angle glaucoma using the one-wavelength reflectometry method. *J Ophthalmol*. 2016;2016:2792103.
10. Nagai N, Asato T, Minami S, et al. Correlation between macular pigment optical density and neural thickness and volume of the retina. *Nutrients*. 2020;12(4):E888.
11. Lawler T, Liu Y, Christensen K, Vajaranant TS, Mares J. Dietary antioxidants, macular pigment, and glaucomatous neurodegeneration: a review of the evidence. *Nutrients*. 2019;11(5):1002.
12. Moeller SM, Parekh N, Tinker L, et al. Associations between intermediate age-related macular degeneration and lutein and zeaxanthin in the Carotenoids in Age-Related Eye Disease Study (CAREDS). *Arch Ophthalmol*. 2006;124(8):1151-1162.
13. The Women’s Health Initiative Study Group. Design of the Women’s Health Initiative clinical trial and observational study. *Control Clin Trials*. 1998;19(1):61-109.
14. Kang JH, Willett WC, Rosner BA, Buys E, Wiggs JL, Pasquale LR. Association of dietary nitrate intake with primary open-angle glaucoma: a prospective analysis from the Nurses’ Health Study and Health Professionals Follow-up Study. *JAMA Ophthalmol*. 2016;134(3):294-303.
15. Vergroesen JE, de Crom TOE, Blekkenhorst LC, Klaver CCW, Voortman T, Ramdas WD. Dietary nitrate intake is associated with decreased incidence of open-angle glaucoma: The Rotterdam Study. *Nutrients*. 2022;14(12):2490.

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