

Trends in Hawai'i Ophthalmologists' Recommendations to Patients for Prevention of Age-Related Macular Degeneration

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Abstract

The purpose of this study is to determine the current trends in recommendations made to patients by ophthalmologists in Hawai'i regarding the prevention of age-related macular degeneration (AMD) and to compare these recommendations to preventative therapies described in the literature. A review of the literature was done to determine the preventative interventions that can be made to significantly lower the risk of developing AMD. An anonymous survey was sent to 95 ophthalmologists in clinical practice in Hawai'i in 2020. The survey assessed recommendations for the prevention of age-related macular degeneration. The 4 interventions assessed were avoidance of smoking, utilization of antioxidant vitamins called AREDS2, adherence to a Mediterranean diet, and maintaining a normal body mass index (BMI). Responses were received from 41 ophthalmologists. Overall, 100% of participants responded "yes" to recommending smoking cessation to their patients, 76% of participants recommended AREDS 2, 42% recommended a Mediterranean diet, and 37% of participants recommended maintaining a normal BMI. Smoking cessation or avoidance was universally recommended by the respondents, and 22% recommended all the assessed interventions. The survey results suggest that some interventions, such as maintaining a normal BMI and adopting a Mediterranean diet are not as widely implemented into ophthalmologists' recommendations compared to others, such as AREDS2 formulation vitamins and smoking cessation.

Keywords

Age-related macular degeneration; Patient education; Preventative medicine; Blindness prevention

Abbreviations

*AMD = age-related macular degeneration
aMEDi = alternative Mediterranean Diet Score
Anti-VEGF = anti-vascular endothelial growth factor
AREDS 2 = Age-related Eye Disease Study
BMI = body mass index
CME = continuing medical education*

Introduction

Age-related macular degeneration (AMD) is a leading cause of visual loss in those over 65 years of age in the industrialized world.¹ AMD is characterized by a slow, degenerative process involving the retina. More advanced stages typically progress to neovascular disease (neovascular AMD) or atrophy of retinal tissues and the choriocapillaris (geographic atrophy). Neovascular, or wet, AMD occurs as a result of inappropriate neovascular changes, or growth of abnormal blood vessels, in the choroid of the retina, which is the area between the retina and the sclera. When vasculature grows in a disorganized

fashion and penetrates the innermost membrane, called Bruch's membrane, it can lead to leaking, hemorrhage, and potential scarring.² Dry AMD, or geographic atrophy in its advanced form, occurs as a result of a thickening of the Bruch's membrane. This is usually due to oxidative changes and deposits of lipids or proteins called drusen. This eventually causes atrophic changes to the choriocapillaris, retinal pigmented epithelium, and the photoreceptors.² AMD overwhelmingly affects the aging population, with age being the most significant risk factor for its development. One pooled analysis showed that less than 1.3% of patients with AMD were under 65 years old.³ Other risk factors include smoking, obesity, and race, with AMD most often occurring in White populations. It is expected that this disease will affect higher proportions of people in Hawai'i as the percentage of those over 65 continues to grow. Hawai'i adults over 65 increased by 37.6% between 2010 and 2019, with an annual average increase of 3.5%.⁴

A definitive drug treatment has not been developed for dry macular degeneration. Wet AMD is primarily treated with regular intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) to decrease the rate of neovascularization. This treatment, however, requires persistent and repeated doses and is not curative. One major emphasis in ophthalmologists' practice has been on methods to prevent or mitigate the development of AMD. Several preventative measures to mitigate risk factors have been shown to oppose the development of AMD, including smoking cessation, maintaining a normal body mass index (BMI), Age-related Eye Disease Study (AREDS) 2 vitamin supplementation, and consuming a Mediterranean diet.⁵⁻¹⁴ The established significance of these interventions can be used to help prevent and slow the progression to advanced AMD for patients.

The link between smoking and AMD was established by the Rotterdam Study in 1996.⁵ This cross-sectional study of 6174 patients aged 55 years or older found a significant increased risk of AMD in both current smokers and former smokers compared to non-smokers, particularly of the neovascular form. The relative risk was found to be highest in those with 10 or more pack-years (relative risk, 6.5; 95% confidence interval, 2.9-14.8). Correcting for atherosclerosis status did not impact the analyses, and a significant relative risk was not found when assessing patients 85 years of age or older.

Nutritional supplements (including vitamin C, vitamin E, zinc, copper, and beta carotene) were found to be helpful in prevent-

ing the progression of AMD from moderate to severe disease.^{6,7} Progression prevention was shown in 25% of participants in the first AREDS study in 1993. In the second AREDS study, completed in 2007, the modification of the AREDS formula included the addition of lutein and zeaxanthin. Lutein and zeaxanthin are carotenoids, which have been shown to mitigate oxidative stress in the body and have also been shown to mitigate progression to advanced AMD.^{8,9} Carotenoid antioxidant effects on the retinal pigment epithelium have been reported in studies such as Carotenoids in Age-Related Eye Disease (CAREDS) and the Pathologies Oculaires Liees - a l'Age (POLA) study.^{8,9}

The association between BMI and AMD was established by Seddon et al in 2003 and further strengthened by Clemons et al in 2005.¹⁰⁻¹² Seddon et al performed a cohort study including 261 patients, which identified a statistically significant relationship between increased BMI and risk for progression to advanced AMD (relative risk, 2.35, 95% confidence interval [CI], 1.27-4.34) for BMI 30 or greater, and 2.32 (95% CI, 1.32-4.07) for BMI of 25-29).¹¹ The latter study, performed by Clemons et al, further identified from a cohort of 4757, a statistically significant increased risk for development of central geographic atrophy in obese patients compared to non-obese (odds ratio, 1.93, 95% CI 1.25-2.65).¹²

Merle et al established the association between a Mediterranean diet and reduced incidence of AMD in 2015.¹³ The authors developed the alternative Mediterranean Diet Score (aMeDi), which is scored from 0-9 based on reported data from each patient on how often and in what quantities they consumed certain foods. This study included 2525 patients in the analysis. The assessment measured the intake of vegetables, fruit, legumes, whole grains, nuts, fish, red and processed meats, alcohol, and the ratio of monounsaturated to saturated fats. After adjusting for demographic, behavioral, ocular, and genetic covariates, a high aMeDi score (6-9) was significantly associated with a hazard ratio of 0.74 (95% CI, 0.61-0.91), suggesting that adherence to a Mediterranean diet lowers the risk of progression to advanced AMD.¹³ Furthermore, Chapmen et al performed a systematic literature review, which included 18 randomized control trials and observational studies.¹⁴ The review showed a reduction in progression to advanced stages of AMD via adherence to a Mediterranean diet as a whole, as well as a slowed progression associated with increased intake of select micro and macronutrients. This study included quantitative analysis of nutrients that have been shown to decrease the risk of progression to advanced AMD: fatty acids, carotenoids, beta-carotene, lutein and zeaxanthin, zinc, vitamin D, and vitamin C. The study also reported that increased red meat consumption was associated with an increased risk of progression to advanced AMD. Overall, this review showed that both adherence to a Mediterranean diet as well as increasing intake of some of the individual components of the diet (such as fish oils, carotenoids) and limiting intake of red meat consumption and alcohol consumption can benefit AMD patients through a potential slowing of the progression of their disease.

Although significant associations between AMD and the aforementioned preventative measures have been reported and cited in the literature, it is not known if this information has extended into clinical practice. As of now, there is no protocol for integrating new preventative recommendations into clinical practice and communicating them to patients. There is also no standard of practice involving AMD prevention. This study aims to determine the extent to which of these recommendations is used in clinical practice, using a survey of practicing ophthalmologists in Hawai'i.

Methods

A list of 95 ophthalmologists was provided by the Hawai'i Ophthalmological Society, from the state registration of all ophthalmologists in clinical practice in the state. All 95 ophthalmologists who are currently practicing in Hawai'i were sent an anonymous clinical question through www.surveymonkey.com (SurveyMonkey®, San Mateo, California), a website-based survey tool. Two follow-up emails with links to the survey were sent over the following 6 weeks to those who did not initially respond. When the survey closed, 41 ophthalmologists completed the survey (43% response rate). This study was not advertised as eligible participants were identified prior to recruitment and emailed directly. No reward or incentive was offered for participating.

To assess the types of recommendations made to patients to prevent AMD, ophthalmologists were asked a single question: "When encountering a patient who is interested in preventing AMD or seeking to slow the progression of early AMD, do you...? (select all that apply)". The question answer choices included the 4 interventions shown to aid in preventing AMD: smoking cessation or avoidance, recommendation of taking AREDS 2, adherence to a Mediterranean diet, and maintaining a normal BMI. Delivery of this clinical question and collection of responses from enrolled participants took place over 6 weeks between October and November 2019.

The Mediterranean diet was defined as an increased consumption of vegetables, legumes, fruit, whole grains, and fish; decreased consumption of red meat; and drinking alcohol in moderation (wine limited to 1-2 glasses per day, consumed with meals). The definition of the Mediterranean diet was created based on the components in common between 3 studies which concluded that consuming a Mediterranean diet impacts the reduction in onset of AMD.¹³⁻¹⁵ Although sunlight exposure has been linked to the development of early AMD, the literature suggests that the recommendation of wearing sunglasses has shown marginal preventative effect, so this was not included as an option in the clinical question.¹⁶

The number of responses per category and the different combinations of recommendations reported were collected and analyzed. The data analysis was tabulated using Microsoft® Excel® (Version 16.53, Microsoft Corporation, Redmond,

Washington). This study was reviewed and approved as exempt by the University of Hawai'i Human Studies Program Institutional Review Board (Honolulu, Hawai'i).

Results

Of the 41 participants, 100% reported recommending smoking cessation to their patients. Three-quarters (76%) of participants reported recommending AREDS 2. However, only 42% (n=17) of participants reported recommending a Mediterranean diet, and 37% (n=15) reported recommending maintaining a normal BMI. Of the participants, 22% (n=9) answered recommending all 4 interventions (Table 1), while 24% (n=10) answered recommending 3 of the 4 recommendations, 39% (n=16) answered recommending 2 of the 4 interventions, and 15% (n=6) answered recommending only 1 of the 4 interventions. All participants reported recommending at least one of the 4 interventions.

Discussion

Although significant associations have been made between multiple risk factors and the pathogenesis of AMD, the clinical impact of the data varies. These risk factors and interventions may be disproportionately communicated to patients by ophthalmologists when discussing prevention or mitigation of AMD. The differences in responses could be due to the length of time since the establishment of each risk factor publication. Smoking cessation and the utilization of AREDS 2 are relatively older recommendations, which may be more commonly known and discussed between patient and physician.⁵⁻⁹ The risk factor of increased BMI and the incorporation of a Mediterranean diet to prevent AMD have been reported in more recent studies.¹⁰⁻¹⁵ The lower percentage of ophthalmologists recommending these latter mitigation factors may suggest a delay between information available in the literature and the incorporation of this data into recommendations made to patients. This indicates that preventative action made by the ophthalmologists in Hawai'i has an opportunity for improvement and refinement in the face of an aging population. A standardized method of delivery of preventative information to patients with risk factors could be developed to mitigate the discrepancies in clinical recommendations. Additionally, establishing forms of continuing medical education (CME) for preventative information that enters into the literature could improve the impact on groups of clinicians and subsequently to their patients. Finally, this information may also serve to motivate clinicians and health care professionals outside the field of ophthalmology to arm themselves with potential preventative interventional advice. This would benefit patients with risk factors in cases where they may not have an ophthalmologist and would not otherwise receive this information. It is important to consider that differences in preventative recommendations by specialists, such as those elucidated in this study, may be present within other specialties as well, which may be explored in other studies.

Table 1. AMD Prevention Recommendation Survey Outcomes (N=41)

Recommendation	Participants reporting this recommendation n (%)
Smoking Cessation	41 (100)
Antioxidant AREDS 2	31 (76)
Mediterranean Diet	17 (41)
Maintaining a normal BMI	15 (37)
All of the above	9 (22)

Notably, another potential reason for the observed disproportion in physician-patient recommendations could be the case-by-case differences in relevance of risk factors, as not every patient will be equal regarding smoking status or BMI. Physician recommendations are tailored to each patient based on an array of clinical insights and experiences, and some will be more relevant than others in each case. Broadening the scope of preventative recommendations may prove beneficial as some of the preventative measures such as the Mediterranean diet and AREDS2 have similar preventative effects despite being recommended in unequal proportions (42% vs 76% respectively). Future iterations and follow up of this study could take into consideration the number of years that each clinician who participated in the survey has been in practice. This could highlight any potential differences in rates of recommending interventions that are more recently available in the literature in comparison to number of years in practice.

Limitations

Potential limitations of this study include a limited sample size of practicing ophthalmologists in Hawai'i. Also, not every ophthalmologist who received the invitation for the survey responded, so the sample size was lower than the actual statewide population. The survey relied on self-reporting, therefore, recall bias is a potential variable in the results. Finally, the survey issued to participants did not include an option to list other recommendations than those already listed in the survey. This creates some bias towards the 4 interventions included in the survey and potentially underreports what physicians recommend to patients in practice.

Conclusion

All 4 of the interventions included in this study have shown with statistical significance to aid in preventing or mitigating advancement of AMD. However, only 22% of the ophthalmologists surveyed reported to include all of these interventions when counseling their patients on prevention. Ophthalmologists may be able to help patients secure a better outcome by including all the information of the known risk factors in their recommendations to patients seeking to be proactive about their

ocular health. Therefore, it is important for ophthalmologists as well as other clinicians to practice all preventative measures that have shown to be effective. In doing so, patients would have the best chance at staying up-to-date and informed of the possible ways of improving their own health outcomes.

Moving forward, presentation of these preventative measures and the data that support them may be delivered at ophthalmologic meetings and conferences. This would improve immediate appreciation of new data by clinicians. Thereafter, a standardized protocol for delivering preventative interventional recommendations or establishing CME credits with emphasis on preventative measures in the literature could improve the impact into clinical practice in Hawai'i. Pursuing these avenues and continuing to develop ways to improve and broaden the preventative recommendations given to patients by ophthalmologists in Hawai'i would likely serve to decrease the long-term incidence of this common cause of vision loss in the elderly, especially crucial in the aging population.

Conflict of Interest

None of the authors report any funding or conflicts of interest for related to this manuscript.

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