Dietary Patterns and Their Associations with Age-Related Macular Degeneration

The Melbourne Collaborative Cohort Study

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Objective: To evaluate the association between dietary patterns and age-related macular degeneration (AMD).

Design: Food frequency data were collected from Melbourne Collaborative Cohort Study (MCCS) participants at the baseline study in 1990–1994. During follow-up in 2003–2007, retinal photographs were taken and evaluated for AMD.

Participants: At baseline, 41514 participants aged 40 to 70 years and born in Australia or New Zealand (69%), or who had migrated from the United Kingdom, Italy, Greece, or Malta (31%) were recruited. Of these, 21132 were assessed for AMD prevalence at follow-up.

Methods: Principal component analysis was used to identify dietary patterns (Factors F1-6) among the food items. Logistic regression was used to assess associations of dietary patterns with AMD.

Main Outcome Measures: Odds ratios (ORs) for early stages and advanced AMD in association with dietary patterns.

Results: A total of 2508 participants (12.8%) had early stages of AMD, and 108 participants (0.6%) had advanced AMD. Six factors characterized by predominant intakes of fruits (F1); vegetables (F2); grains, fish, steamed or boiled chicken, vegetables, and nuts (F3); red meat (F4); processed foods comprising cakes, sweet biscuits, and desserts (F5); and salad (F6) were identified. Higher F3 scores were associated with a lower prevalence of advanced AMD (fourth vs. first quartile) (OR, 0.49; 95% confidence interval [CI], 0.28–0.87), whereas F4 scores greater than the median were associated with a higher prevalence of advanced AMD (OR, 1.46; 95% CI, 1.0–2.17).

Conclusions: Rather than specific individual food items, these factors represent a broader picture of food consumption. A dietary pattern high in fruits, vegetables, chicken, and nuts and a pattern low in red meat seems to be associated with a lower prevalence of advanced AMD. No particular food pattern seemed to be associated with the prevalence of the earliest stages of AMD. *Ophthalmology* 2014; $=:1-7 \odot 2014$ by the American Academy of Ophthalmology.



Age-related macular degeneration (AMD) is a complex genetic disease, and the major genetic components are now well understood.¹ However despite this, diet is emerging as a potentially important modifiable risk factor for AMD.^{2–9} To date, results from dietary studies have largely been based on analyses evaluating individual foods or food groups. The results suggest that some aspects of diet could influence the risk of AMD, but the associations found have not been consistent across studies.^{4,10–16} Diets high in trans fat, red meat, and alcohol have been associated with an increased risk of AMD, ^{3–5} whereas higher intakes of fish have been associated with a lower risk of AMD.^{16,17} In general, foods are not consumed in isolation, and intakes of many nutrients are highly correlated to common food sources. Therefore, an integrated approach to the

investigation of dietary impact on chronic disease where dietary patterns are assessed, rather than each individual food or nutrient, may be more informative and predictive of disease risk.^{18–20} Several studies have evaluated dietary combinations and AMD using predefined food groups.^{13,21,22} However, to date, no study has evaluated the associations of dietary patterns derived from principal components analysis (PCA) and AMD. Principal components analysis is a data-driven statistical method used to reduce a large number of intercorrelated variables (e.g., dietary items) into a few distinct factors of intercorrelated variables within each factor that are dissimilar between factors.²³ In this way, foods are grouped according to how they were actually consumed in a cohort, rather than by preconceived ideas of how foods should be consumed.

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These groups of foods are aggregated together into patterns or factors, which are then evaluated for associations with AMD. Associations of dietary patterns with AMD may provide more insight into how diet is associated with the risk of developing AMD than concentrating on individual food items,²⁴ providing information on which health messages can be based. We used PCA to identify dietary patterns among Melbourne Collaborative Cohort Study (MCCS) participants and assessed the associations of these patterns with AMD.

Methods

Study Population

The MCCS recruited 41 514 participants (24 469 women) aged 40 to 69 years at baseline (1990–1994) to examine links between diet and chronic diseases.^{25,26} To broaden the range of dietary intakes, participants born in Greece and Italy were deliberately oversampled to comprise one quarter of the cohort, whereas participants born in Australia, New Zealand, and United Kingdom made up the remainder of the cohort.²⁵

Of the total sample, 27 883 (67%) attended a follow-up examination between 2003 and 2007; 3754 (9%) had died, and 819 (2%) had left Australia or Victoria. The remaining 9058 participants (22%) were lost to follow-up or not interested in participating. Of those who were alive and living in Victoria, the participation rate was 27 883/36 941 (73%), of whom 22 405 (80%) participated in fundus photography. The Human Research Ethics Committees of the Cancer Council Victoria and Royal Victorian Eye and Ear Hospital approved the AMD study protocol. The research adhered to the tenets of the Declaration of Helsinki.

Dietary Assessment

Dietary data were collected at baseline using a self-administered 121-item food frequency questionnaire (FFO) specifically developed for this study.²⁷ Most items were analyzed as daily equivalent frequencies, whereas intakes of olive and vegetable oils were analyzed in milliliters/week. The repeatability of the FFQ after 12 months showed intraclass correlation coefficients >0.50 for most food items.²⁸ Energy intake was calculated using sexspecific standard portions, together with Australian food composition data.²⁹ Participants with estimated energy intakes in the upper and lower 1% of the sex-specific distributions, which suggested that the FFQ had been improperly completed, were excluded. Almost all dietary studies use criteria related to energy intake to exclude people with reported intakes that are unlikely to be real.³⁰ Because we recognize the limitations of FFQs in measuring absolute amounts, people at the extreme 1% of high or low energy intakes were excluded. People with these energy extremes are unlikely to have reported a real usual intake, so including their data might distort the eating patterns identified.

Participants with a history of heart attack, angina, or diabetes at baseline also were excluded from our analysis because these diagnoses had the potential to result in dietary change, and we have evidence from this cohort that this was the case (unpublished data, MCCS internal validation, December 2005).

Age-related Macular Degeneration Detection

At follow-up from 2003 to 2007 (on average, 13 years after the baseline assessment), digital nonstereoscopic 45° macular photographs of both eyes were taken with a Canon CR6-45NM non-mydriatic retinal camera (Canon Inc, Tokyo, Japan). Retinal

photographs were graded for AMD by 2 experienced graders using "OptoLite/OptoMize Pro" software (Digital HealthCare Image Management Systems, Cambridge, UK), according to the International Classification System for grading of AMD.³¹ Quality-control procedures for the photographs in the MCCS have been described.³²

Definitions of Age-related Macular Degeneration

Participants were allocated to a single AMD category according to the more advanced visible changes on the macular images of the worse affected eye. Early stages of AMD were defined as the presence of 1 or more drusen ≥ 125 µm (with or without pigmentary abnormalities) or 1 or more drusen 63 to 124 µm with pigmentary abnormalities in a 6000-µm diameter grading grid centered on the fovea, in the absence of advanced AMD in either eye (geographic atrophy or neovascular AMD).

Covariates

Age, sex, country of origin, smoking status, education level, total energy intake, multivitamin supplement use, body mass index, waist—hip ratio, physical activity, and alcohol consumption were included in logistic regression models and retained if they changed the beta-coefficient for any of the dietary factors by more than 5%.

Statistical Analysis

The PCA²³ of 121 food items plus olive and vegetable oils was performed to extract dietary factors using dietary data collected at baseline. This was followed by orthogonal (varimax) rotation to ensure that the factors were uncorrelated. Factor analysis aims to evaluate which foods are correlated, looking for underlying factors within diets of the population.¹⁹ It is used as a way of reducing many variables to few and has been recently used in dietary epidemiology.²⁴ This means that a factor has a distinct cluster of interrelated items with similarities within, but minimal similarities between the factors. Factors with eigenvalues >2.7were considered to reflect realistic eating patterns and were used in the analysis. Food items with an absolute value of at least 0.2 for the factor loading (the correlation between dietary items and factors) were retained to define the dietary Factors 1 to 6, which is a commonly used cutoff.²⁰ The cutoff used does not affect the calculation of the factor score. For each participant, the factor score is computed as the sum of products of the observed intake frequency values multiplied by their factor loading. Factor scores were then analyzed by quartile and median groupings.

We used binary logistic regression models to estimate the odds ratio (OR) and 95% confidence intervals (CIs) for both early-stage and advanced AMD, adjusting for covariates. In the analyses for advanced AMD, early-stage AMD cases were excluded and vice versa. Factor scores were divided into groups, cut at the median or at quartiles for analysis, with the first quartile as the reference group. Tests for trend across quartiles were then performed using the medians in each group. Interactions among sex, age group, grouped country of birth (participants born in Australia and the United Kingdom compared with Southern European participants), and factor scores were tested before performing the analysis. A subanalysis was performed investigating the associations with country of birth (participants born in Australia and the United Kingdom compared with Southern European participants) and food factors for early-stage and advanced AMD. All analyses were performed using the Statistical Package for the Social Sciences version 19.0.1 (SPSS Inc, Chicago, IL).

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