between aspirin use and AMD was found. As far as I am aware, aspirin was never investigated in this study.

PAULUS T.V.M. DE JONG
Amsterdam, Netherlands

References


Author reply

Dear Editor:

Several questions raised by Dr. De Jong suggest that the description of our methodology to identify cases of age-related macular degeneration (AMD) was unclear. In our large cohorts of men and women, it is not feasible to conduct eye examinations and obtain fundus photographs for all study participants. Instead, medical record data are collected from diagnosing eye doctors to confirm reports of AMD made by study participants on annual questionnaires. Information collected includes date of initial diagnosis of AMD, best-corrected visual acuity, and signs of AMD noted (i.e., drusen, retinal pigment epithelial [RPE] changes, geographic atrophy, RPE detachment, subretinal neovascularization, disciform scar). When other ocular abnormalities are present, we ask the eye doctors to give us their opinion as to whether the AMD by itself is sufficiently severe to explain best-corrected visual acuity loss to 20/30 or worse. Because we don’t conduct eye examinations (and collect fundus photographs) on study participants, but instead rely on participant reports, some under-ascertainment of the AMD endpoint is expected. However, such under-ascertainment is not associated with bias in randomized comparisons. As Dr. De Jong notes, our findings indicate that women assigned to aspirin, compared to those assigned placebo, had a non-statistically significant 18% lower risk of visually significant AMD, findings that are similar to our previously reported findings in men. Thus, the take-home message is that while a large beneficial or harmful effect of aspirin treatment in AMD seems unlikely, our data cannot rule out a possible modest beneficial effect for aspirin in lowering risks of AMD. Finally, the fact that this methodology has identified important risk factors for AMD such as cigarette smoking and body weight, associations also demonstrated in examined populations with fundus photographs, provides reassuring evidence for the construct validity of this methodology.

WILLIAM CHRISTEN, ScD
Boston, Massachusetts

Color Contrast and Drusen Area

Dear Editor:

The Rotterdam group demonstrated that the most important predictor for age-related macular degeneration (AMD) progression was drusen area >10% of the test field. Consistent with this, an estimation of drusen area is part of the Wisconsin, International, Rotterdam, and Age-Related Eye Disease Study (AREDS) AMD grading schemes. However, the categorical grading of drusen area in all 4 schemes makes the results an approximation of the actual area, and thus limits potential inferences.

We performed a cross-sectional study to address the association between drusen area and color contrast sensitivities. We hypothesized that a significant association could allow color contrast sensitivity to be used as a surrogate measure of drusen load, and therefore in itself be predictive of AMD progression risk.

To measure drusen area, we used a software package with a semi-automated algorithm that applies changes in reflectance from images of normal maculas to create a uniform background. The results are expressed as the percentage area of the middle Wisconsin subfield occupied by drusen. Color contrast sensitivity was assessed with a computerized optotype test (ChromaTest, CH Electronics, Bromley, UK) which modulates stimuli along either blue-yellow or red-green color confusion lines. The amplitude of modulation is expressed as a percentage of the displacement along the color confusion line such that the maximum color contrast available is 100%.

Patients were recruited via the Macular Disease clinic at which the diagnosis of AMD was confirmed. Patients with ocular comorbidities or systemic conditions deemed to be significant to visual functioning (e.g., diabetes mellitus) were excluded. Patients performed the ChromaTest for both eyes in turn with the order of color confusion axes and eye side tested first counterbalanced across patients.

Each patient also had mydriatic 30 and 50 degree non-stereoscopic color digital fundus photographs taken (Topcon TRC 50IX retinal camera, Topcon Optical Co., Tokyo, Japan) centered on the fovea. The photographs were anonymized, randomized, and submitted for analysis with 2 independent masked observers using the drusen load software. The correlation between drusen load and color contrast sensitivity was calculated using Spearman’s rank test (SPSS for Windows, version 12, SPSS, Chicago, IL). The study was approved by the Trust research ethics committee and conformed to the 2nd Declaration of Helsinki.

Sixty-seven patients with AMD were recruited. Thirty-two eyes were excluded (from 31 patients) with acuities of worse than 0.3. Fifteen eyes (from 12 patients) were excluded due to photographs of insufficient quality to allow visualization of the macula and 8 images (from 6 patients) excluded due to insufficient space to overlay the Wisconsin middle subfield template. Seventy-nine fundal photographs were therefore suitable, coming from 56 patients (mean age, 73 years; standard deviation [SD], 8 years; male:female ratio, 19:37). Mean red-green color contrast modulation threshold was 24.6% (SD 32.3%), median 9.4% and mean blue-yellow color contrast modulation threshold was 58.7% (SD 30.6%), median 54.4%.

Mean drusen area was 14.5% (SD 15.3%) for observer 1.
and 14.2% (SD 14.1%) for observer 2. For both observers, drusen load was significantly correlated with both red-green and blue-yellow color contrast thresholds ($P<0.005$ for both color confusion axes of both observers). There was no significant correlation between drusen area and visual acuity for either observer. If we take our weakest correlation ($r = 0.32$), then an alpha of 0.05 and a power of 0.8 requires a sample size of 50. Our study is therefore adequately powered for the strength of the association.

This study shows a significant correlation between red-green and blue-yellow color contrast sensitivity and drusen load. The results suggest that the ChromaTest could be used as a surrogate marker of drusen load, and therefore of itself, predictive of AMD progression risk. Extrapolating from this conclusion, the ChromaTest results should be predictive of which patients with AMD Rotterdam stage 3 (soft indistinct drusen with pigmentary abnormalities) are at greatest risk of progressing to AMD Rotterdam stage 4 (or end-stage disease) over 5 years. As an extension of this pilot, we could investigate whether the ChromaTest results predict those patients converting from earlier AMD stages to end-stage disease (a much rarer event). The Rotterdam group found that the overall risk of converting from AMD Rotterdam stage 4 (or end-stage disease) over 5 years. As an extension of this pilot, we could investigate whether the ChromaTest results predict those patients converting from earlier AMD stages to end-stage disease (a much rarer event). The Rotterdam group found that the overall risk of converting from all AMD stages to end-stage AMD was 0.9% over 5 years. Therefore, if we required 10 participants to convert to allow us to assess whether the ChromaTest results were particularly predictive of this event, we would require a sample size of 1000, and so forth. We found no significant association between acuity and drusen load ($r = 0.16$). However, if this is due to our pilot being underpowered, then for an alpha of 0.05 and a power of 0.8, 240 subjects would be required to demonstrate statistical significance with this strength of association.

IZABELA MITRUT, MD
AMIT VERMA, MD
STEPHEN MADILL, FRCPHTh
Edinburgh, Scotland

R. THEODORE SMITH, MD, PhD
New York, New York

N. VICTOR CHONG, FRCPHTh
Oxford, England

References


Functional Visual Loss

Dear Editor:

Managing patients with functional visual loss (FVL) superimposed on organic disease is extremely challenging and frustrating for physicians who care for these patients. For this reason, we commend Ney et al for reviewing the incidence of FVL in their patients with idiopathic intracranial hypertension (IIH). In their retrospective report, 17 of 281 IIH patients manifested FVL (6%). Nine of those 17 patients underwent a surgical procedure related to IIH at some point in their management.

We recently reviewed all IIH patients seen at our institution between 1990 and 2003. Among 353 patients with IIH, we described in detail 20 patients who did not have papilledema at any point in their clinical course (“Idiopathic intracranial hypertension without papilledema”). Out of these 20 patients, 8 patients (20%) manifested FVL at both the initial and final visits. In their review, Ney et al state, “Thirteen of 17 patients had optic nerve-visual field mismatch, with healthy discs, that is, no edema or pallor in the setting of severe visual field loss.” May we conclude that these patients had IIH without papilledema?

At least 20% of patients diagnosed with IIH also have migraine and 68% have other types of headache not necessarily related to their increased intracranial pressure. Managing headache in IIH is crucial and frequently treating both migraine and increased pressure improves outcome. Did any of the subjects reported by Ney et al have migraine or headache in addition to IIH? Did these patients receive any treatment specifically for migraine or other headache syndromes not related to increased intracranial pressure?

None of our 8 patients with FVL and IIH had papilledema, and none of them underwent optic nerve sheath fenestration. However, 4 patients underwent at least 1 lumbar or ventricular shunt procedure due to headaches that were refractory to medical management. Ney et al stated that of the 9 patients with FVL undergoing surgery, 5 underwent optic nerve sheath fenestration at their institutions. Four patients had undergone surgical interventions before presentation at the authors’ institutions, but the nature of the surgical intervention was not stated. How many of these 4 patients underwent shunting procedures as opposed to nerve sheath procedures?

In our experience, IIH patients can almost always be managed medically, and surgical intervention is only rarely required. It is therefore disconcerting that such a high proportion of patients with IIH and FVL find themselves in the operating room. Unfortunately, as stated by Ney et al, aggressive management is indicated in patients with definite organic disease and declining visual function, even if some portion of that decline is deemed to be functional.

References