Macular Function Impairment in Eyes With Early Age-Related Macular Degeneration

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Purpose. To study different aspects of macular function in eyes with early age-related macular degeneration (early AMD: drusen with or without retinal pigment epithelium alterations) and normal visual acuity, to obtain a complete evaluation of macular function impairment in early AMD and to study the relationship between macular function and the ophthalmoscopic signs of early AMD.

Methods. Forty-seven subjects with early AMD and visual acuity better than 20/25 in at least one eye were studied: 34 patients had bilateral early AMD (group 1), 13 had neovascular AMD in the fellow (nonstudy) eye (group 2). Thirty-six age-matched healthy subjects were used as controls. Thirty degree stereoscopic fundus photographs and fluorescein angiography were performed to grade macular lesions. Macular recovery function, central visual field sensitivity, spatiotemporal contrast sensitivity, and the Farnsworth–Munsell 100 hue test were used to study different aspects of macular function.

Results. Except for color vision, all macular function tests were significantly impaired in eyes of patients with early AMD compared to those in control subjects. No functional difference was found between groups 1 and 2. The increase in drusen number negatively influenced macular recovery function. Increasing drusen confluence reduced macular recovery function as well as central visual field sensitivity and some selected spatial frequencies of spatiotemporal contrast sensitivity. Geographic atrophy of the retinal pigment epithelium and focal hyperpigmentation reduced macular recovery function and contrast sensitivity at the highest spatial frequency.

Conclusions. Macular recovery function, central visual field sensitivity, and spatiotemporal contrast sensitivity are adequate and reliable indicators of macular function impairment in early AMD. Macular recovery function is the test that best reflects the ophthalmoscopic characteristics of early AMD because its deterioration parallels the worsening of typical fundus lesions. Function tests are valuable in the evaluation of patients with early AMD, particularly when interventional trials are planned. Invest Ophthalmol Vis Sci. 1997;38:469–477.

Age-related macular degeneration (AMD) is the most important cause of legal blindness among the elderly population in Western countries.[1–5] The neovascular form of this disease, characterized by the presence of serous or hemorrhagic detachment of the RPE (retinal pigment epithelium), choroidal neovascularization, and disciform scarring, is the leading cause of severe visual loss among AMD patients.

Laser photocoagulation has been proven successful in reducing the risk of severe visual loss in selected cases of neovascular AMD.[6–12] To identify the greatest number of treatable cases, it is important to recognize neovascular AMD as early as possible. Neovascular AMD may occur when the patient is still visually asymptomatic; therefore, identification of risk factors for the development of this condition is particularly important. Ophthalmoscopic risk factors, such as the presence of soft, large, confluent drusen and focal

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TABLE 1. Inclusion and Exclusion Criteria of the Study

Inclusion criteria
Age ≥50 years
Visual acuity ≥20/25
Clear ocular media
Good collaboration in performing psychophysical tests
More than 10 drusen localized within 1500 μm of the foveal center in at least one eye (the "study eye")
Exclusion criteria
Age <50 years
Visual acuity <20/25
Ocular hypertension or glaucoma
Ocular or systemic diseases that may affect macular function (e.g., diabetes)
Use of drugs that could affect visual function
Aphakia or pseudophakia
Previous retinal surgery

hyperpigmentation of the RPE, were first identified.[13-19] Many aspects of macular function have also been analyzed to find a more sensitive prognostic indicator.

This work is the baseline report of a long-term prospective study of patients with early AMD (macular drusen with or without retinal pigment epithelium alterations) and normal visual acuity in at least one eye (the study eye). The aim of our prospective study is threefold: to obtain a complete evaluation of the different aspects of macular function in the early asymptomatic stages of AMD; to study the relation between macular function and clinical (ophthalmoscopic) signs of early AMD; and to identify a link between macular function impairment and the evolution of neovascular AMD.

MATERIALS AND METHODS

Population

Patients were selected from the files of the Retinal Vascular Clinic of the Institute of Ophthalmology, University of Padova. Through a preliminary screening examination (including medical history for the specific eye and systemic disorders; visual acuity quantification; and ocular examination for anterior and posterior segment diseases) 47 patients with early AMD in at least one eye were selected from a group of 150 AMD patients, according to the inclusion/exclusion criteria summarized in Table 1. Only one eye of each patient was studied. In cases of bilateral early AMD, we considered the eye with the best corrected visual acuity. If both eyes had equal acuity, one eye was randomly selected.

All subjects were 50 years old or older and had more than 10 drusen, greater than 63 μm, within 1500 μm of the foveal center in the study eye. They had a best corrected Snellen acuity better than 20/25 in the study eye. Subjects who had undergone cataract or retinal surgery and those who were using drugs known to affect macular function (e.g. chloroquine, oxazepam, oral contraceptives) were excluded from the study. All selected subjects had clear ocular media in the study eye (neither corneal and lens opacities nor vitreous thickening along the visual axis) and were free of ocular hypertension, glaucoma, diabetes, and any ocular or systemic disease (other than age-related macular degeneration) that could affect macular function. All selected subjects demonstrated good learning and concentration ability (characteristics which influence psychophysical tests results).

Thirty-six age-matched healthy people were used as controls. They were recruited among patients seen in our outpatient clinic for refractive problems. The same inclusion criteria of the study population were used, except for fundus characteristics (neither macular drusen nor pigment epithelium alterations). All subjects signed informed consent to be involved in this research. The tenets of the Declaration of Helsinki were followed.

Function Tests

All patients underwent the following function tests: visual acuity determination; spatiotemporal contrast sensitivity; macular recovery function (Nictometry); central visual field sensitivity; Farnsworth–Munsell 100 hue test; and the Amsler grid test.

Visual acuity for distance was determined using the Bailey–Lovie Test Chart (ETDRS protocol).[20-21] Visual acuity for near was quantified by means of Jaeger's test. The best correction for any refractive defect was determined.

Contrast sensitivity was determined using a software-controlled electronic system (3.71; Neuroscientific, Farmingdale, NY). Sinusoidal gratings were presented on a black and white monitor (Ikegami PM 580; Ikegami Tsushinki, Utsunomya-City, Japan). Five different spatial frequencies (0.67, 1.67, 4, 10, and 20 cyc/deg) were used. In the first part of the test, sinusoidal gratings were static, whereas in the second part they were temporally modulated at a 16 Hz frequency (static and dynamic contrast sensitivity). A software-controlled staircase method with double-forced choice procedure was used. The mean monitor luminance was 80 cd/m^2; the room background luminance was 10 cd/m^2. The test distance was 191 cm, corresponding to a visual angle of 3°.

Macular recovery function of the study eyes was assessed by means of the Registriert Nyktometer (Carl Zeiss, Germany). Niktometry consists of three steps: a three-minute adaptation to strong light (7000 asb, 2200 cd/m^2); then the light is switched off and dark

adaptation begins: the patient has to read the test chart (10 lines seen through an optical system that projects them to the subject's far point) and the increase in visual acuity as a function of time is recorded for two minutes; the last step is a measure of sensitivity to glare. Minimal intervention by the examiner is required using this technique. Results of nyctometry were quantified by the summation method proposed by Frost-Larsen and Larsen.[22]

Central visual field sensitivity was assessed using the 10-2 visual field program of the Humphrey Field Analyzer, model 630. Standard background luminance of the instrument is 10 cd/m^2; the standard target size is Goldmann III. The 10-2 visual field program measures differential light sensitivity of a circular 20° diameter retinal area centered on the fixation point. The number of fixation losses, false positives, and false negatives is automatically recorded as a measure of the subject's reliability. Central visual field sensitivity was calculated as mean sensitivity of the central 10° (MS).

The Farnsworth–Munsell 100 hue test was performed according to the standard technique.[23] The study eyes were tested monocularly; patients wore correcting lenses for near vision. Interpretation of results was based on total error score and the degree of polarity of error distribution on the diagram.[24] The square root of total error score was also determined to permit a comparison with Verriest's ranges of normality.[25]

An Amsler grid test in the original version (white grid on black background) gave an evaluation of the 10° of visual field surrounding fixation. The test was performed monocularly, while patients wore near correcting lenses, according to the standard technique.[26]

Fundus Photography and Grading

After visual function testing, the subject's pupil was dilated with 1.0% tropicamide. Stereoscopic color fundus photographs of the central 30° of the posterior pole (centered on the fovea) were taken both in the study eye and in the fellow eye. A 30° photograph centered on the optic disc of the study eye was also taken to provide the exact dimensions of the optic disc.

Using a stereo viewer, two of us (MCB, CDA) independently analyzed the photographs of the study eyes according to the grading system (see below). Fundus photographs of the fellow eye were not graded. Any disagreement between the two graders was rectified by an open discussion and review of fundus photographs. If no agreement was achieved, a third observer (EM) was asked to arbitrate.

Fundus photographs of the study eyes were classified according to Bressler's grading system[27] modified for the size of drusen: 63 μm instead of 50 μm was used as the minimum size for AMD drusen.[28,29] A central zone of 3000 μm diameter, centered on the fovea (within a one disc ray diameter of the foveal center) was graded according to the following fundus features: drusen number (<20; ≥ 20), presence or absence of soft drusen, presence or absence of drusen confluence and comparison with the photograph of a standard level ($<$, $\geq$ the standard), presence or absence of focal hyperpigmentation of the RPE, and presence or absence of RPE atrophy.[27,28]

Fluorescein Angiography

Following fundus photography, all patients underwent intravenous retinal fluorescein angiography. According to our standard technique, 5 ml of a 20% solution of sodium fluorescein was rapidly injected into the antecubital vein, then all phases of fluorescein transit in the posterior pole of the study eye were photographically recorded. Some late angiograms of the fellow eye were taken to confirm or exclude exudative AMD.

Statistical Analysis

The statistical analysis of data was performed with the two-sample t-test, using the Statistical Analysis System (SAS System) by SAS Institute (Cary, NC).

RESULTS

Our study population was composed of 47 subjects with early AMD in at least one eye. These subjects were divided in two groups: group 1: 34 patients with bilateral early AMD (13 men and 21 women, aged 51 to 76 years, mean age = 64.76 ± 5.82 years, median = 64 years); group 2: 13 patients with unilateral early AMD and neovascular AMD in the fellow eye (5 men and 8 women, aged 51 to 73 years, mean age = 65.85 ± 6.37 years, median = 67 years). The control group was composed of 36 age-matched healthy subjects with a normal fundus (14 men and 22 women, aged 51 to 75 years, mean age = 64.33 ± 7.03 years, median 67 years). Neither macular drusen nor pigment epithelium alterations were evident in the macular area of these subjects. There was no significant difference in age between AMD patients (group 1 + group 2) and controls ($P = 0.611$) or between group 1 and group 2 ($P = 0.7$).

All AMD subjects had soft (≥ 63 μm) drusen in the study eye, but they showed differences in the number and confluence of these drusen (Table 2) In some study eyes, focal hyperpigmentation and/or atrophy of RPE were also present. The distribution of these fundus characteristics is reported in Table 2.

Fluorescein angiography confirmed the ophthalmoscopic grading, particularly excluding the presence

TABLE 2. Distribution of Fundus Characteristics in Early AMD Eyes*

Factor	*Group 1 (%) (n = 34)*	*Group 2 (%) (n = 13)*
Drusen number		
<20	14.7 (n = 5)	15.4 (n = 2)
≥20	85.3 (n = 29)	84.6 (n = 11)
Drusen confluence		
Absent	2.9 (n = 1)	0.0 (n = 0)
<Standard	35.3 (n = 12)	38.5 (n = 5)
≥Standard	61.8 (n = 21)	61.5 (n = 8)
Focal hyperpigmentation		
Absent	64.7 (n = 22)	69.2 (n = 9)
Present	35.3 (n = 12)	30.8 (n = 4)
Geographic atrophy		
Absent	88.2 (n = 30)	92.3 (n = 12)
Present	11.8 (n = 4)	7.7 (n = 1)

AMD = age-related macular degeneration.
* No statistically significant difference (chi-square test) was found between Group 1 and Group 2 with regard to fundus characteristics of the study eyes. Number of eyes is given in parentheses.

of well-defined or occult choroidal neovascular membranes in the macular region of AMD study eyes.

Spatiotemporal contrast sensitivity was determined in 44 study eyes; two subjects were not able to understand the technique and one was hypoacoustic (unable to hear the tones accompanying gratings presentation). Both static and dynamic contrast sensitivity, at all spatial frequencies, were significantly lower in AMD eyes compared to controls; no significant difference of contrast sensitivity was found between groups 1 and 2 (Table 3). Drusen number did not influence spatiotemporal contrast sensitivity. Eyes with drusen confluence superior to the standard level showed a significant reduction of dynamic contrast sensitivity at 0.67 and 1.67 cyc/deg ($P = 0.029$ and $P = 0.014$, respectively) and reduced static and dynamic contrast sensitivity at 20 cyc/deg (without reaching statistically significant values; $P = 0.061$ and $P = 0.068$, respectively). The presence of geographic atrophy and focal hyperpigmentation were related to a significant reduction of 20 cyc/deg static contrast sensitivity ($P = 0.007$ and $P = 0.043$, respectively). Twenty cyc/deg dynamic contrast sensitivity was also reduced by the presence of geographic atrophy ($P = 0.009$) (Table 4).

Macular recovery function was significantly lower in early AMD eyes compared to normal eyes (88.2 ± 21.3 versus 330.3 ± 34.2; $P < 0.001$), but no difference was found between group 1 and group 2 ($P = 0.117$). Increasing number and confluence of drusen, presence of focal hyperpigmentation, and RPE atrophy were related to a significant decrease of macular recovery function ($P = 0.023$, $P = 0.008$, $P < 0.001$, $P = 0.02$, respectively). (Table 5)

Automated static threshold perimetry was performed in all study eyes; data from three patients were left out of statistical analysis because it was unreliable. MS was significantly lower in study eyes compared to control eyes (29.5 ± 2.7 versus 31.1 ± 0.8 dB; $P < 0.001$); no difference was found between groups 1 and 2 ($P = 0.818$). MS was not significantly influenced by the number of drusen, focal hyperpigmentation, or the presence of RPE atrophy. MS decreased in eyes with drusen confluence superior to the standard level (29.1 ± 3.1 versus 30.4 ± 1.4 dB; $P = 0.061$).

The Farnsworth–Munsell 100 hue test was normal in all AMD patients. The Amsler grid test was normal in all but nine patients. These patients had neither ophthalmoscopic nor angiographic signs of choroidal neovascularization. Two of them had geographic atro-

TABLE 3. Static and Dynamic Contrast Sensitivity (Mean ± SEM) in Early AMD and Control Eyes*

	Spatial Frequency (cyc/deg)	*Controls (n = 36)*	*AMD (n = 44)*	**P** *Value*	*Group 1 (n = 32)*	*Group 2 (n = 12)*	**P** *Value*
Static CS (dB)	0.67	41.1 ± 4.5	24.8 ± 2.4	0.001	23.7 ± 5.2	25.3 ± 2.6	0.772
	1.67	138.3 ± 10.6	77.4 ± 4.7	<0.001	70.1 ± 7.1	80.4 ± 5.9	0.318
	4	209.9 ± 14.7	126.4 ± 6.8	<0.001	111.4 ± 9.2	132.8 ± 8.7	0.192
	10	77.9 ± 8.6	47.6 ± 3.5	0.003	39.1 ± 5.3	51.2 ± 4.3	0.112
	20	14.9 ± 2.0	8.6 ± 1.0	0.002	7.2 ± 1.4	9.2 ± 1.2	0.339
Dynamic CS (dB)	0.67	75.9 ± 5.0	49.8 ± 2.8	<0.001	48.7 ± 5.5	50.3 ± 3.2	0.797
	1.67	83.0 ± 5.1	54.4 ± 2.9	<0.001	51.5 ± 5.2	55.6 ± 3.5	0.520
	4	52.3 ± 3.3	36.9 ± 2.1	<0.001	34.4 ± 3.3	37.9 ± 2.7	0.462
	10	20.9 ± 2.5	13.2 ± 0.9	0.008	12.7 ± 1.4	13.4 ± 1.2	0.727
	20	4.5 ± 0.4	3.0 ± 0.2	0.002	2.9 ± 0.4	3.1 ± 0.3	0.736

AMD = age-related macular degeneration; CS = contrast sensitivity.
* Number of eyes is given in parentheses. Static and dynamic CS values are given in decibels (dB).

TABLE 4. Static and Dynamic Contrast Sensitivity (Mean ± SEM) of 44 AMD Eyes Grouped According to Degree of Drusen Confluence and Presence or Absence of Focal Hyperpigmentation and Geographic Atrophy of Retinal Pigment Epithelium*

		Drusen Confluence		**Focal Hyperpigmentation**		**Geographic Atrophy**	
		<Standard (N = 17)	*>Standard (N = 27)*	*No (N = 30)*	*Yes (N = 14)*	*No (N = 39)*	*Yes (N = 5)*
Static contrast sensitivity (dB)	0.67 cyc/deg	26.0 ± 4.7	24.5 ± 2.8	24.5 ± 3.0	25.4 ± 4.2	24.5 ± 2.4	27.2 ± 9.6
	P	0.765		0.868		0.719	
	1.67 cyc/deg	85.2 ± 9.5	72.2 ± 4.9	77.1 ± 6.2	77.9 ± 7.0	79.6 ± 4.9	60.2 ± 13.8
	P	0.188		0.934		0.190	
	4 cyc/deg	138.6 ± 12.3	120.0 ± 8.0	121.6 ± 8.7	136.2 ± 10.1	126.8 ± 7.6	123.2 ± 8.8
	P	0.192		0.316		0.869	
	10 cyc/deg	54.5 ± 5.9	43.0 ± 4.3	47.3 ± 4.6	48.2 ± 5.4	48.6 ± 3.9	40.2 ± 3.5
	P	0.115		0.907		0.125	
	20 cyc/deg	11.6 ± 2.2	6.9 ± 0.7	9.8 ± 1.4	6.4 ± 0.8	9.0 ± 1.1	5.5 ± 0.6
	P	0.061		0.043†		0.007†	
Dynamic contrast sensitivity (dB)	0.67 cyc/deg	57.9 ± 5.2	45.3 ± 3.0	50.3 ± 3.6	48.8 ± 4.2	50.7 ± 3.1	43.0 ± 3.7
	P	0.029†		0.805		0.381	
	1.67 cyc/deg	63.6 ± 5.1	49.0 ± 3.2	55.2 ± 3.5	52.9 ± 5.1	56.1 ± 3.1	41.2 ± 3.8
	P	0.014†		0.708		0.099	
	4 cyc/deg	41.3 ± 4.1	33.9 ± 2.3	37.4 ± 2.4	35.9 ± 4.3	37.9 ± 2.3	29.1 ± 3.8
	P	0.102		0.735		0.191	
	10 cyc/deg	14.6 ± 1.4	12.4 ± 1.2	14.1 ± 1.3	11.5 ± 1.0	13.6 ± 1.0	9.9 ± 1.3
	P	0.268		0.122		0.211	
	20 cyc/deg	3.6 ± 0.5	2.7 ± 0.3	3.3 ± 0.3	2.5 ± 0.3	3.1 ± 0.3	2.2 ± 0.2
	P	0.068		0.111		0.009†	

* Drusen number did not influence contrast sensitivity.
† Statistically significant difference between groups ($P < 0.05$).

phy and six had RPE focal hyperpigmentation. No relation was found between positivity of Amsler test results and results of the other function tests except for 0.67 cyc/deg static contrast sensitivity, which was significantly lower in eyes with Amsler grid abnormalities ($P = 0.047$).

DISCUSSION

Early AMD is a clinical stage of age-related macular degeneration characterized by the presence of moderate to large macular drusen, with or without retinal pigment epithelium alterations, and normal visual acuity. These patients often complain of a worsened quality of vision. To quantify such subjective and relatively undefined symptoms, we studied macular function in early AMD eyes with a group of function tests more sensitive and specific than Snellen visual acuity. The relationship between macular function impairment and morphologic characteristics of early AMD was also analyzed in detail. The aim of our prospective study was to identify one or more functional risk indi-

TABLE 5. Nyctometry Values (Mean ± SD) in Controls and Early AMD Eyes, Grouped According to Examined Fundus Characteristics (Drusen Number, Drusen Confluence, Focal Hyperpigmentation, and Geographic Atrophy)*

	Early AMD Eyes							
	Drusen Number		*Drusen Confluence*		*FH*		*GA*	
Controls	*<20 (n = 5)*	*≥20 (n = 29)*	*<Standard (n = 12)*	*≥Standard (n = 21)*	*No (n = 22)*	*Yes (n = 12)*	*No (n = 30)*	*Yes (n = 4)*
330.3 ± 34.2	203.29 ± 57.11	68.58 ± 21.75	175.97 ± 46.63	32.50 ± 14.13	125.95 ± 30.61	19.44 ± 9.68	92.90 ± 23.90	26.80 ± 15.90
	$P = 0.023$		$P = 0.008$		$P = 0.002$		$P = 0.029$	

FH = focal hyperpigmentation; GA = geographic atrophy.
* Mean nyctometry value in all early AMD eyes was 88.2 ± 21.3 (controls, 330.3 ± 34.2; $P < 0.001$).

cators for the development of neovascular AMD that are more precocious and sensitive than the well-known funduscopic risk factors. Obviously the baseline results reported here cannot predict follow-up data, but they may contribute to the understanding of morphofunctional interactions in early AMD.

We graded only the central 3000 μm of the macula because previous studies have shown that funduscopic risk indicators from this area were equal or more effective than the corresponding indices from the central 6000 μm.[17]

All study eyes had a minimum of 10 drusen, with or without retinal pigment epithelium alterations, within 1500 μm of the fovea. These fundus characteristics, together with the absence of ophthalmoscopic and angiographic signs of neovascular AMD and with normal visual acuity, correspond well to Collins and Brown's definition of Pre-Age-Related-Maculopathy.[30] We consider this term misleading and prefer to call it early AMD to emphasize that it is a clinical stage of AMD and not a condition of physiologic macular aging. Our data also demonstrate that in early AMD eyes there is a significant impairment of several aspects of macular function when compared to age-matched controls.

Static and dynamic contrast sensitivity, macular recovery function, and mean sensitivity of central 10° are significantly impaired in early AMD subjects compared to age-matched controls. No significant difference was found between subjects with bilateral early AMD (group 1) and subjects with neovascular AMD in the fellow eye (group 2) as far as macular function is concerned. No detectable color vision impairment was found with the Farnsworth–Munsell 100 hue test in early AMD subjects compared to control subjects.

We observed that the increasing number of drusen has no influence on the results of function tests, except for macular recovery function. We also found that drusen confluence superior to the standard level affects macular recovery function, mean sensitivity of the central 10°, and some selected spatial frequencies of contrast sensitivity function (0.67 and 1.67 cyc/deg dynamic contrast sensitivity and 20 cyc/deg static and dynamic contrast sensitivity). When geographic atrophy of RPE is present, macular recovery function and 20 cyc/deg static and dynamic contrast sensitivity are reduced. The appearance of focal hyperpigmentation alters macular recovery function and 20 cyc/deg static contrast sensitivity. Consequently, macular recovery function seems to be the most sensitive test to document the worsening of any examined fundus characteristics.

Other authors have described the impairment of static and dynamic contrast sensitivity at all spatial frequencies in AMD eyes compared to control eyes, but their data cannot be directly compared to ours because of the different methods for contrast sensitivity determination and the different characteristics of the study populations.[30–33] Kleiner et al[33] also found that the impairment of contrast sensitivity function increased with increasing drusen grade, but their concept of drusen grade grouped together drusen number, size, and degree of confluence, so that they could not analyze the influence of the different drusen characteristics on spatiotemporal contrast sensitivity.

Abnormalities of retinal adaptation mechanisms in AMD patients have been reported by other authors. Brown et al,[34] Collins and Brown,[30] and Wu et al[35] found a prolonged recovery time after bleaching in patients with early age-related maculopathy, but they did not accurately assess the clinical characteristics of their patients. A prolonged recovery time after macular bleaching was also demonstrated by Smiddy and Fine in patients with early AMD, but no correlation between severity of drusen and Photostress Test delay was noted.[15] Recently Gaudio and Sandberg reported that dazzle recovery time is commonly slowed in AMD, even when visual acuity is normal, and particularly when RPE atrophy is present.[36]

A correlation between drusen characteristics and macular function was also found by Eisner et al, who conducted many macular function tests on a selected group of patients whose fellow eyes had neovascular AMD (AMD risk eyes).[37,38] Dark adaptation as well as absolute sensitivity, color matching, S-cone sensitivity, and performance on the D-15 color test were significantly impaired in AMD risk eyes compared to control eyes. Our study, where three populations (group 1, group 2, normal subjects) were accurately defined and divided, stresses the importance of precise identification of the study population when reporting function data. We found that all early AMD eyes are functionally superimposable independent of the fellow eye, but the function data from them are completely different from that obtained from control eyes. Recently Steinmetz et al reported that the increased time of return to prebleach sensitivity in patients with macular drusen is related to prolonged regeneration constants of both rods and cones.[39] Our macular recovery function measures cone sensitivity.

Central visual field sensitivity was also significantly impaired in early AMD subjects compared to age-matched control subjects, confirming previous reports.[30,40–43] An increase of central 20° absolute threshold during dark adaptation in AMD subjects was also found by Sunness et al, but they found no significant correlation between the magnitude of sensitivity loss and the severity of drusen (number, size, confluence).[44] This discrepancy between Sunness et al and our results may be the result of different clinical char-

acteristics of the study populations, making a direct comparison difficult. Our population was composed of selected AMD subjects with normal visual acuity, whereas Sunness et al studied subjects with different degrees of visual loss (but visual acuity no lower than 20/60). They also demonstrated that diminished dark-adapted absolute sensitivity may predict the development of advanced AMD and that the status of the fellow eye is not useful in differentiating which patients proceed to advanced AMD in the study eye.[45] This observation is confirmed by our data, which demonstrate the absence of any significant functional difference between group 1 and group 2 study eyes. Some interesting observations helpful to understanding the pathogenetic mechanisms of central visual field impairment in AMD eyes were reported by Sunness et al[46] and Chen et al.[42] Sunness et al demonstrated that sensitivity over drusen and nondrusen areas is not significantly different, so that drusen could be merely an incidental marker of more diffuse retinal pigment epithelium damage.[46] There seems to be a good correspondence, however, between areas of depressed sensitivity and regions with prolonged choroidal filling on fluorescein angiography, with a quantitative correlation between the intensity of fluorescence during transit and retinal threshold.[42] Choroidal perfusion abnormalities may be a hallmark of the diffuse chorioretinal damage hypothesized by Sunness et al.[46]

None of our patients with early AMD showed detectable impairment of color vision, as measured with the Farnsworth–Munsell 100 hue test. This contradicts some earlier reports, which dealt with small numbers of patients,[47,48] but confirms the data reported by Sunness et al.[49] The absence of any detectable impairment of color vision with the Farnsworth–Munsell 100 hue test does not necessarily imply that color vision mechanisms are not altered in the first stages of AMD. This could simply mean that color vision alterations in early AMD are so subtle that any commercially available color vision test is inadequate to detect them.

Our data allow us to definitively confirm that patients with early AMD (macular drusen with or without RPE alterations) and normal visual acuity have a subtle but actual impairment of several macular functions. Macular recovery function, central 10° visual field sensitivity, and spatiotemporal contrast sensitivity all show a significant decrease in early AMD subjects compared to age-matched control subjects. We have also shown that the degree of functional impairment in early AMD eyes is independent of the condition of the fellow eye.

Macular recovery function was found to be the most sensitive indicator of fundus damage. This may be easily explained because adaptation mechanisms originate in the retinal pigment epithelium-photoreceptors complex, so that any damage to these anatomic structures is likely to influence macular recovery function. The decrease of central 10° mean sensitivity seems not to be correlated with fundus grade, except for a trend to worsen with increasing drusen confluence. Progressive impairment of spatiotemporal contrast sensitivity at the higher spatial frequencies (20 cyc/deg), paralleling the worsening condition of the fundus (drusen confluence, presence of geographic atrophy, and focal hyperpigmentation of RPE) is consistent with previous reports that the high frequency visual channels are highly and selectively susceptible to damage.[33] The selective impairment of 0.67 and 1.67 cyc/deg dynamic contrast sensitivity and the saving of 20 cyc/deg dynamic contrast sensitivity with some specific fundus deterioration (drusen confluence and focal hyperpigmentation, respectively), is difficult to explain. This may be due to a selective involvement of different retinal cell populations and neural channels: disjunctive physiologic aging of sustained and transient visual channels has already been hypothesized on the basis of electrophysiologic and psychophysical evidence, but the research in this field is just beginning.[50,51]

Baseline data from this prospective study allowed us to confirm that macular recovery function, central visual field sensitivity, and spatiotemporal contrast sensitivity are adequate and reliable indicators of macular functional impairment in the early stages of AMD. Moreover, these quick and reproducible function tests are useful parameters in the evaluation of patients with early AMD, particularly when interventional trials are planned. Their value as prognostic parameters of neovascular AMD will be determined by the prospective data.

Key Words

age-related macular degeneration, automated perimetry, color vision, contrast sensitivity, dark adaptation

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