• Clinical Research •

Visual functioning in patients with macular degeneration compared to patients with cataracts

Reilley M. Knott[1], *Nathan Grove*[2], *Jennifer L. Patnaik*[2], *Niranjan Manoharan*[2], *Anne M. Lynch*[2], *Karen L. Christopher*[2]

[1]University of Colorado School of Medicine, Aurora 80045-2581, CO, United States
[2]Department of Ophthalmology, University of Colorado School of Medicine, Aurora 80045-2581, CO, United States
Correspondence to: Reilley M. Knott. University of Colorado School of Medicine, 1675 Aurora Ct MS 731, Aurora, CO 80045, United States. Reilley.Knott@cuanschutz.edu
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Abstract

● **AIM:** To compare Visual Functioning Questionnaire-25 (VFQ) response data in patients with age-related macular degeneration (AMD) to patients with cataracts.

● **METHODS:** In total 415 individuals with early or intermediate AMD and 236 patients with visually significant cataracts who completed the VFQ-25 from a single academic eye center registry between July 2014 and May 2022 were identified. The effect of disease (AMD versus cataract) on VFQ composite score was analyzed using univariate and multivariable linear regression, controlling for age, race/ethnicity, history of transient ischemic attack (TIA)/stroke, and visual acuity.

● **RESULTS:** AMD patients were older than the cataract group (76.0±7.4y *vs* 73.2±5.9y, *P*<0.001). There was no difference in sex between groups with both being predominantly female (63% for AMD *vs* 61% for cataracts, *P*=0.801). The VFQ composite score was higher in the AMD group (88.8±10.7 *vs* 82.8±14.5, *P*<0.001). All vision-related and socio-emotional subscales had significantly higher scores among AMD compared to cataract patients. When adjusted for age, race/ethnicity, history of TIA/stroke, better-eye visual acuity, and worse-eye visual acuity, patients with cataracts had a 3.3-point lower VFQ composite score (95%CI: -5.3 to -1.4, *P*<0.001) compared to patients with AMD.

● **CONCLUSION:** Patients with early or intermediate AMD report higher visual functioning compared to patients with cataracts in composite score and all VFQ subscale categories in both unadjusted and adjusted analyses.

● **KEYWORDS:** Visual Functioning Questionnaire; age-related macular degeneration; visual acuity; cataract surgery

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INTRODUCTION

Age-related macular degeneration (AMD) is a leading cause of blindness globally and is the leading cause of visual disability in Americans aged 50 and older[1-2]. AMD affects cells of the central retina (macula) that are responsible for the detailed central vision that is critical for driving, facial recognition, and other psychosocial events of daily life[3-5]. The disease is classified based on the clinical assessment of fundus lesions as either early, intermediate, or late-stage disease[6]. The pathogenesis of this disease is not fully understood but is known to be linked to genetic, age-related, and behavioral factors. Management of early and intermediate stage disease is currently limited to changes in diet, dietary supplementation, and reducing modifiable risk factors such as smoking[7].

Age-related cataract is an opacification of the crystalline lens in the eye that causes a dimming and blurring of vision, affecting millions of people globally[8-9]. Though no treatment has consistently proven successful to delay the progression of cataracts, cataract extraction with intraocular lens implantation has become one of the most successful treatments in all of medicine[10-11]. Though now a curable disease for those with access to care, patients affected by cataracts experience a significant impact on quality of life prior to surgical removal[8,12].

The Visual Functioning Questionnaire-25 (VFQ-25) is a 25-item questionnaire developed by the National Eye Institute (NEI) in 2001 that is a simplified version of the pre-existing 51-item NEI Visual Functioning Questionnaire (NEI VFQ)[13]. This questionnaire is given to patients with low vision or ocular pathology to assess the impact of decreased vision on activities of daily life[14]. The VFQ-25 assesses general health, difficulty with activities such as driving and reading, and social and emotional responses to visual problems. Patient answers to these questions can then be quantified into a composite score and a general health score, as well as subscale scores of either visual or socio-emotional relevance. This screening tool has been translated into other languages and its results are being used to influence ophthalmologic treatment and further understand the visual impacts of disease pathology[15-21]. Previous studies have used the VFQ-25 in the assessment of vision-related quality of life in patients affected by AMD or age-related cataracts, however, there is little direct comparison of response data between these two patient populations[22-26].

The purpose of this study is to compare VFQ-25 responses of patients affected by early to intermediate-stage AMD with those of patients affected by visually significant cataract. Clinicians may utilize this data to better understand the subjective experiences of their patients and to inform interpretation of VFQ results for these and other ocular conditions.

PARTICIPANTS AND METHODS

Ethical Approval This study was approved by the Colorado Multiple Institutional Review Board and adhered to the tenants of the Declaration of Helsinki (IRB number 14-0740).

Database Individuals with early and intermediate AMD and individuals presenting for cataract surgery with visually significant cataract in at least one eye but without AMD were identified in the University of Colorado AMD registry (previously described elsewhere[22]). These individuals were enrolled between July 2014 to May 2022. AMD status was determined at the time of study enrollment by two retinal specialists using multi-modal imaging and the Beckman criteria, with a third specialist to resolve discrepancies[6,27]. Multi-modal imaging included color fundus photos, optical coherence tomography, and fundus autofluorescence. All subjects completed the VFQ-25 upon enrollment in the study. Variables of interest included in this study were age, sex, race/ethnicity, history of diabetes, cardiac disease, transient ischemic attack (TIA)/stroke, kidney disease, smoking status, habitual visual acuity in both eyes, and lens status for the AMD group.

Inclusion and Exclusion Criteria For the purpose of this study, the AMD group was limited to patients with the early or intermediate phenotype of AMD. Within this group, 60 patients (14.5%) were found to have early AMD, and 355 (85.5%) were classified as intermediate AMD. Patients in the cataract group had a visually significant cataract in at least one eye, indicating that the cataract was the primary pathology causing a decrease in vision. Patients that were pseudophakic in one eye were included as these patients still experienced symptoms of the unilateral cataract and the VFQ does not differentiate between the two eyes. Patients in the cataract group did not have AMD (on multimodal imaging and retina examination). Mature cataracts were excluded from this study as they frequently prohibit examination of the posterior anatomy of the eye. This group completed the VFQ-25 during pre-operative assessment for phacoemulsification surgery. Patients with advanced AMD were excluded from this study.

Visual Acuity All reported visual acuities for patients in this study were acquired in a clinic setting *via* Snellen visual acuity at distance and represent the habitual visual acuity at time of study enrollment. Habitual visual acuity was chosen over best corrected visual acuity as this represented patient experience with daily activities and the vision VFQ responses were based upon. Habitual visual acuities were converted to logMAR values for statistical comparisons. Both eyes for each patient were included in this study: better-seeing eye was defined as the eye with the lower logMAR value for each patient and worse-seeing eye was defined as the eye with the same or higher logMAR value.

NEI VFQ-25 This 25-item questionnaire assesses the impact of vision on quality of life. Responses were then used to calculate an overall composite score as well as 12 subscale scores. All calculated scores exist on a scale of 0 to 100 with 100 being the best possible visual functioning. In this study, composite and all subscale scores were compared between groups. Subscales include general health, vision-related subscales of general vision, ocular pain, near activities, distance activities, color vision, and peripheral vision, and socio-emotional subscales of social functioning, mental health, role limitations, dependency, and driving. With the exception of general health, all subscale scores are combined to calculate the composite score.

Statistical Analysis Means, standard deviations (SD), frequencies, and percentages were used to describe demographic and clinical variables. Differences between groups were assessed using two sample *t*-test for age and Fisher's exact test for categorical variables. VFQ-25 Composite Score and subscale scores were compared between groups using two-sample *t*-tests. Composite scores were assessed for differences between groups when stratified by habitual visual acuity (20/20 or better, 20/25-20/30, 20/40, and 20/50 or worse) using two-sample *t*-tests. To compare the effect of AMD versus visually significant cataracts on the VFQ composite scores, multivariable linear regression was used, controlling for age, race/ethnicity, TIA/stroke, better eye visual acuity, and worse eye visual acuity. Covariates in the multivariable model were chosen based on our analysis of differences in patient characteristics between AMD and cataract groups, as well as clinically relevant variables. To assess the effect of inclusion of AMD subjects with unilateral and bilateral cataract and cataract controls with unilateral cataract, we conducted a sensitivity analysis in which these subjects were removed, *i.e.,* we compared bilateral phakic cataract subjects with bilateral pseudophakic AMD subjects. All statistical analyses were done utilizing R version 4.1.3.

RESULTS

We identified 415 individuals with early and intermediate AMD and 236 patients with visually significant cataract without AMD. Table 1 outlines patient demographics and clinical variables. AMD patients were older than the cataract group (mean 76.0±7.4y *vs* 73.2±5.9y, $P<0.001$). There was no difference in sex between groups with both being predominantly female (63% for AMD *vs* 61% for cataracts, $P=0.801$). Differences in race/ethnicity were found to be significant between the two groups ($P<0.001$) with white race being most common among both groups but Hispanic, African American, and Asian races being more common in the cataract group. AMD patients had a higher prevalence of TIA/stroke (5.8% *vs* 1.3%, $P=0.004$). In the AMD group, 225 (54%) patients had previously undergone cataract surgery, 170 (41%) patients were phakic in both eyes, and 20 (4.8%) of patients were phakic in one eye and pseudophakic in the other. In the cataract group, 204 (86%) patients were phakic in both eyes while 32 (14%) patients were phakic in one eye and pseudophakic in the other. No other significant differences in patient characteristics were found between the two groups.

Distributions of VFQ subscale scores by group are displayed in Figures 1 and 2. The mean VFQ composite score was higher in the AMD group compared to the cataract group, 88.8 (SD=10.7) *vs* 82.8 (SD=14.5), $P<0.001$. There was no significant difference in the General Health subscale score between groups ($P=0.327$), but all other vision-related and socio-emotional subscale scores were found to be significantly different between the two groups with the AMD group reporting higher subscale scores in all categories (Table 2). The largest differences were seen in the subscales of near activities (difference in means of 10.2), role limitations (difference in means of 9.4), and general vision (difference in means of 9.1).

In Table 3, composite scores are presented with stratification by habitual visual acuity in the better- and worse-seeing eye. The AMD group demonstrated higher composite scores for all but one level of vision when comparing better-seeing eye and worse-seeing eye measurements. This difference between groups reached statistical significance for the largest visual acuity groups of 20/25–20/30 ($P<0.001$) for both better- and worse-seeing eyes. In univariate analysis, patients with cataracts reported 6.0 point [95% confidence interval (CI): -7.9 to -4.0, $P<0.001$] lower composite scores than patients with AMD. When adjusted for age, race/ethnicity, history of TIA/stroke, better-eye visual acuity, and worse-eye visual acuity, patients with cataracts had a 3.3-point lower VFQ composite score (95%CI: -5.3 to -1.4, $P<0.001$) compared to patients with AMD (Table 4).

Table 1 Patient characteristics for AMD and cataract cases

Variables	AMD cases, *n*=415	Cataract cases, *n*=236	P^a
Age, mean±SD, y	76.0±7.4	73.2±5.9	<0.001
Sex, *n* (%)			0.801
Male	155 (37)	91 (39)	
Female	260 (63)	145 (61)	
Race/ethnicity, *n* (%)			<0.001
White	394 (95)	203 (86)	
Hispanic	7 (1.7)	11 (4.7)	
African American	6 (1.4)	14 (5.9)	
Asian	3 (0.7)	3 (1.3)	
Other/uncertain	5 (1.2)	5 (2.1)	
Type 1 diabetes, *n* (%)	2 (0.5)	0	0.537
Type 2 diabetes, *n* (%)	58 (14)	28 (12)	0.472
History of cardiac disease, *n* (%)	136 (33)	64 (27)	0.157
History of TIA/stroke, *n* (%)	24 (5.8)	3 (1.3)	0.004
Missing	2	0	
History of kidney disease, *n* (%)	38 (9.3)	26 (11)	0.496
Missing	5	0	
Smoking status, *n* (%)			0.916
Never	216 (52)	123 (52)	
Current	10 (2.4)	7 (3.0)	
Former	189 (46)	106 (45)	
Lens status, *n* (%)			<0.001
Phakic both eyes	170 (41)	204 (86)	
Phakic one eyes	20 (4.8)	32 (14)	
Pseudophakic	225 (54)	0	

[a]Welch two sample *t*-test; Fisher's exact test; Fisher's exact test for count data with simulated *P*-value (based on 2000 replicates). AMD: Age-related macular degeneration; SD: Standard deviation; TIA: Transient ischemic attack.

Table 2 Composite and subscale scores for AMD and cataract cases

mean±SD

Variables	AMD cases, *n*=415	Cataract cases, *n*=236	P^a
Composite score	88.8±10.7	82.8±14.5	<0.001
General health	67.9±23.1	69.7±22.4	0.327
Visual subscale scores			
General vision	75.6±13.8	66.5±17.5	<0.001
Ocular pain	90.5±14.8	86.7±19.0	0.008
Near activities	87.2±17.8	77.0±21.7	<0.001
Distance activities	87.8±16.0	76.8±20.9	<0.001
Color vision	98.0±8.6	96.0±11.0	0.015
Peripheral vision	92.6±16.1	87.6±20.6	0.001
Socio-emotional subscale scores			
Social functioning	96.9±9.5	94.2±13.1	0.005
Mental health	84.0±18.3	80.5±20.5	0.032
Role limitations	87.9±20.3	78.5±25.4	<0.001
Dependency	94.9±13.7	91.9±17.3	0.024
Driving[b]	80.8±21.8	74.6±23.0	0.001

[a]Welch two sample *t*-test; [b]56 missing values. AMD: Age-related macular degeneration; SD: Standard deviation.

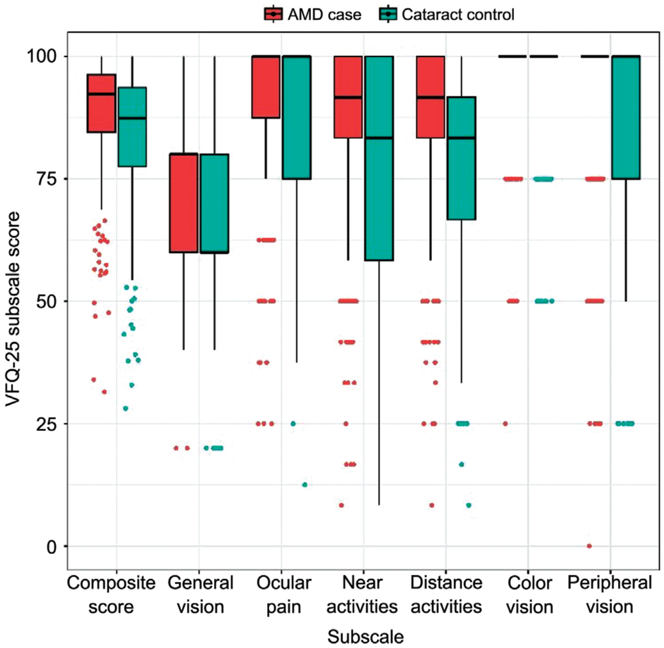

Figure 1 Distributions of visual subscale scores by group VFQ-25: Visual Functioning Questionnaire-25; AMD: Age-related macular degeneration.

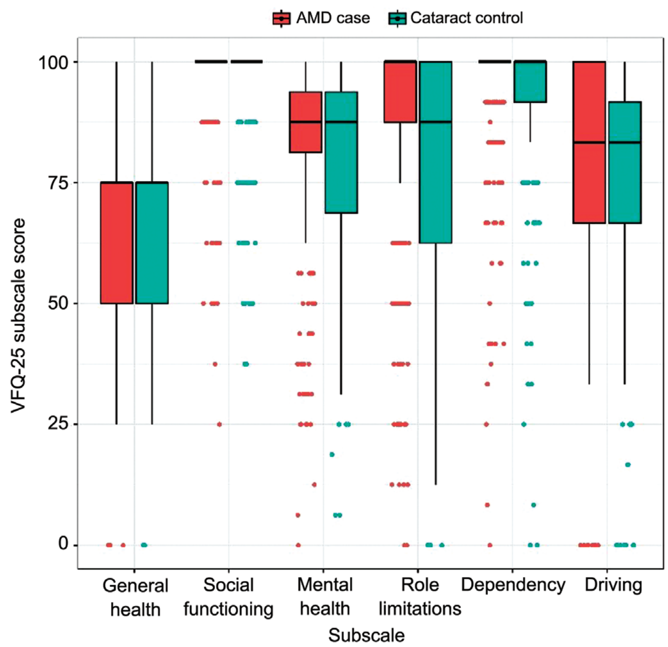

Figure 2 Distributions of socio-emotional subscale scores by group VFQ-25: Visual Functioning Questionnaire-25; AMD: Age-related macular degeneration.

Table 3 Composite visual function score stratified by visual acuity

Habitual visual acuity	AMD cases, *n*	Cataract cases, *n*	Composite visual function score (mean±SD)		P^a
			AMD cases	Cataract cases	
Better-seeing eye					
20/20 or better	175	35	91.6±7.8	90.5±7.2	0.430
20/25–20/30	182	152	88.3±10.8	81.3±15.3	<0.001
20/40	40	35	83.4±12.1	85.1±9.2	0.480
20/50 or worse	16	14	75.7±17.8	73.7±20.8	0.784
Worse-seeing eye					
20/20 or better	58	2	93.2±6.2	79.0±6.6	0.194
20/25–20/30	171	96	90.3±9.9	83.3±13.7	<0.001
20/40	92	58	88.5±8.5	86.0±11.7	0.155
20/50 or worse	93	80	83.4±13.9	79.9±16.8	0.141

[a]Welch two sample *t*-test. AMD: Age-related macular degeneration; SD: Standard deviation.

Table 4 Effect of cataract case status on VFQ composite score

Variable	*n*	Parameter estimate (95%CI)	*P*
Univariate analysis			
Visually significant cataract status	651	-6.0 (-7.9 to -4.0)	<0.001
Stratified by better-seeing eye visual acuity			
20/20 or better	210	-1.1 (-3.9 to 1.7)	0.45
20/25–20/30	334	-7.0 (-9.8 to -4.2)	<0.001
20/40	75	1.8 (-3.3 to 6.8)	0.49
20/50 or worse	30	-2.0 (-16 to 12)	0.78
Multivariable analysis[a]			
Visually significant cataract status	647	-3.3 (-5.3 to -1.4)	<0.001

[a]Adjusted for better eye visual acuity, worse eye visual acuity, age, race/ethnicity, and TIA/stroke. CI: Confidence interval; VFQ: Visual Functioning Questionnaire; TIA: Transient ischemic attack.

When excluding AMD subjects with cataract and unilateral phakic cataract controls in a sensitivity analysis, we found similar results to our primary analysis.

DISCUSSION

In this study, individuals with early and intermediate AMD had higher VFQ-25 composite scores than individuals affected by visually significant cataract in the absence of AMD. This difference persisted across all vision-related and socio-emotional subscale scores but did not significantly differ for the general health subscale. VFQ composite score remained 3.3 points lower for patients with cataracts even after adjusting for age, race/ethnicity, TIA/stroke, and habitual visual acuity of both better- and worse-seeing eyes.

Increasing lens opacification that occurs with cataract is known to have a significant negative impact on vision[28]. Patients with cataracts often describe significant impairment from glare when exposed to bright headlights or sunlight[29]. While visual acuity does worsen with increased cataract severity it does not adequately represent the full negative effect of lens opacification on visual functioning. It has been shown that decreasing contrast sensitivity (CS) is associated with worsening cataracts and is thought to provide more information regarding cataract progression[29]. Previous studies have been performed that utilize the VFQ-25 as a way to better understand how vision affects quality of life in patients affected by cataracts. Wan *et al*[26] used the VFQ-25 and Visual Function Index-14 (VF-14) to evaluate 1052 patients in China diagnosed with bilateral age-related cataracts in an effort to compare the psychometric properties of both tools. The reported VFQ-25 subscale scores in this study were lower than those reported in our present study for the composite score and most subscale scores. However, our studies were similar in that both reported general vision being the lowest vision-related subscale score while role limitations and driving were the lowest socio-emotive subscale scores. Miraftab and Naseripour[8] also found notably lower VFQ-25 scores in cataract patients versus healthy controls in an Iranian cohort, suggesting that reduced visual function associated with cataracts may be widespread across diverse global geographic and cultural settings.

The loss of central vision in AMD can impact visual acuity, allowing it to be a metric for understanding disease progression, but visual acuity does not directly measure the area of vision loss. Physiologically, it is possible that the preserved paracentral or peripheral vision in patients with AMD is able to compensate for central vision loss in many situations but that it continues to cause intermittent difficulties in performing familiar activities. Lindblad and Clemons[23] collected VFQ-25 data for patients diagnosed at the time of initial AMD diagnosis and again at a later time point, separating participants into subgroups by whether they had progression of the disease to advanced-AMD, vision loss, or lens opacification. Looking at the initial VFQ scores reported for the group who had early/intermediate AMD and progressed to advanced, it is worth noting that general vision and driving were the two lowest subscale scores in the vision and socio-emotive categories[30]. These results were in keeping with the findings from our study although scores were generally higher in our study group.

These previous studies have examined how VFQ responses change due to patients being affected by cataracts or AMD, but direct comparison of response data between these two patient populations is not currently present in the literature. We found lower VFQ composite scores among our cataract patients compared to patients with early/intermediate AMD. The knowledge that a curative surgical intervention exists for cataracts may lead patients to be more attentive to their deficits and experience greater frustration with their vision as they await surgery. It has previously been shown that patients who receive cataract surgery are less likely to develop depression[31]. Conversely, patients affected by AMD may be aware that the changes to their vision are irreversible and thus adapt to their visual ability to maintain good functioning[3]. How to better support patients living with AMD as it progresses is an ongoing area of study in ophthalmology and frameworks to support clinicians are being constructed[32].

One notable limitation of this study is that AMD and cataracts are not mutually exclusive processes. Some patients in the AMD group likely had varying degrees of cataracts. However, even allowing for the presence of cataracts, VFQ scores were higher in the AMD compared with the cataract group. Indeed, in sensitivity analysis in which we excluded AMD subjects with cataract and unilateral phakic cataract controls, we found similar results across all analysis. Another limitation is that cataract patients in the registry were enrolled at their preoperative cataract evaluation visits. This may have had some impact on VFQ results in this group, and may have influenced patients to overstate the impact of their visual deficits as they likely understood that corrective cataract surgery was imminent. Finally, habitual visual acuity alone provides a limited view of disease severity. Large levels of corrected refractive error may have some influence in VFQ-25 responses, which was unable to be adjusted for in this study. Future studies could consider incorporating the differences in contrast sensitivity, refractive error, and visual field into the comparison of AMD and cataract to understand impact that this has on vision-related quality of life[33].

This data may be of use to clinicians when evaluating patients with AMD and/or cataracts and assessing their functional status. Though patients affected by AMD and cataracts may have a similar visual acuity, those affected by visually significant cataracts are more likely to experience negative impacts to their quality of life due to their vision[8].

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