

Clinical Characteristics and Impact of Neovascular Age-Related Macular Degeneration on Medical Status, Daily Living, Functioning, and Health Resource Utilization: A Survey of Five Countries

#2208

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INTRODUCTION

- Among the elderly in industrialized nations, age-related macular degeneration (AMD) is highly prevalent and is the leading cause of irreversible blindness¹⁻³:
 - AMD prevalence is 18% among those 70 to 74 years of age and 47% among 85 years and older.
 - AMD accounted for almost 50% of those registered as blind or partially blind.
 - AMD risk factors include age (>50 years), smoking, light-colored eyes, Caucasian ethnicity, hypertension, infections, hardening of the arteries, diabetes, and genetic or familial factors.
- Neovascular (exudative, wet) AMD represents 10% to 15% of all cases of AMD but accounts for 90% of AMD-related severe vision loss and blindness:
 - The development of choroidal neovascularization (CNV) and its sequelae are the hallmark of neovascular AMD.^{1,4}
 - Neovascular AMD often is characterized by rapid disease progression, and many patients with neovascular AMD become blind in the affected eye within 2 years of diagnosis.⁵
- Limited previous research has indicated that AMD is associated with poor patient functioning and well-being:
 - Frequently reported comorbidities among AMD patients include cardiovascular disease, cataract, depression, hearing loss, and systemic hypertension.⁶
 - Impaired vision due to AMD is associated with increased risk of falls and fractures, depression, and the need for daily support services or nursing home care.⁷⁻⁹
 - There is a need for broader burden of illness studies that include comprehensive quality of life assessments and that address the health economic impact of AMD.
- Early intervention is critical in preventing and stabilizing neovascular AMD progression:
 - Existing therapies for the management of neovascular AMD leave substantial unmet medical needs.
 - To date, treatment has excluded many patients with neovascular AMD, the most serious and rapidly progressing form of the disease.¹⁰
 - Therapies for the management of neovascular AMD are in development. As new treatment options become available, key decision makers need to have a better understanding of the impact of the disease on the patients, the physicians, the caregivers, and society at large.
 - Payers are skeptical about the consequences of central vision loss.
 - Patient advocates are seeking more information to illustrate the needs of AMD patients.
 - Physicians can foresee the consequences of disease progression and appreciate the need for early diagnosis and treatment.

OBJECTIVES

To characterize and quantify the humanistic and economic burden of illness in neovascular AMD compared to elderly control subjects in a primary care setting

References

- Ambati J, et al. *Surv Ophthalmol* 2003;48:257-93.
- Gottlieb MD, Justin L. *JAMA* 2002; 288:2233-6.
- Klein R, et al. *Ophthalmology* 1992;99:933-43.
- Lim JI. *Age-Related Macular Degeneration*. New York: Marcel Dekker; 2002.
- Bressler SB, et al. *Am J Ophthalmol* 1982;93:157-63.
- Brody BL, et al. *Ophthalmology* 2001;108:1893-1900.
- Dargent-Molina P, et al. *Lancet* 1996;348:145-9.
- Lee HK, Scudis RJ. *Age Ageing* 2003;32:643-649.
- Ivers RQ, et al. *J Am Geriatr Soc* 1998;46:58-64.
- Moshfeghi DM, Lewis H. *Cleve Clin J Med*. 2003;70:1017-37.

METHODS

Study Design

- A cross-sectional, observational, case-control study was conducted in Canada, France, Germany, Spain, and the United Kingdom. A total of 401 eligible bilateral, subfoveal, neovascular AMD subjects were recruited from retina specialists' offices/clinics and 471 eligible control subjects were recruited from general practitioners' offices/clinics.

Eligibility Criteria

- All should be ≥50 years of age.
- AMD patients should have neovascular AMD in both eyes.
- Control subjects should have best-corrected visual acuity of 20/40 or better.
- Control subjects should be free from any ocular pathology that may impair visual acuity, including diagnosed diabetic retinopathy, glaucoma, or cataract surgery within 6 months prior to assessment.

Study Measures

- Effect of neovascular AMD on the clinical state of patients:
 - Neovascular AMD diagnosis, progression, and treatment
 - Comorbidities
 - Treatment of psychiatric illness
 - Low-vision services and equipment

Effect of neovascular AMD on patient's functioning:

- Physical functioning
- Assisted living services
- Vision-related falls and injuries

Analysis Methods

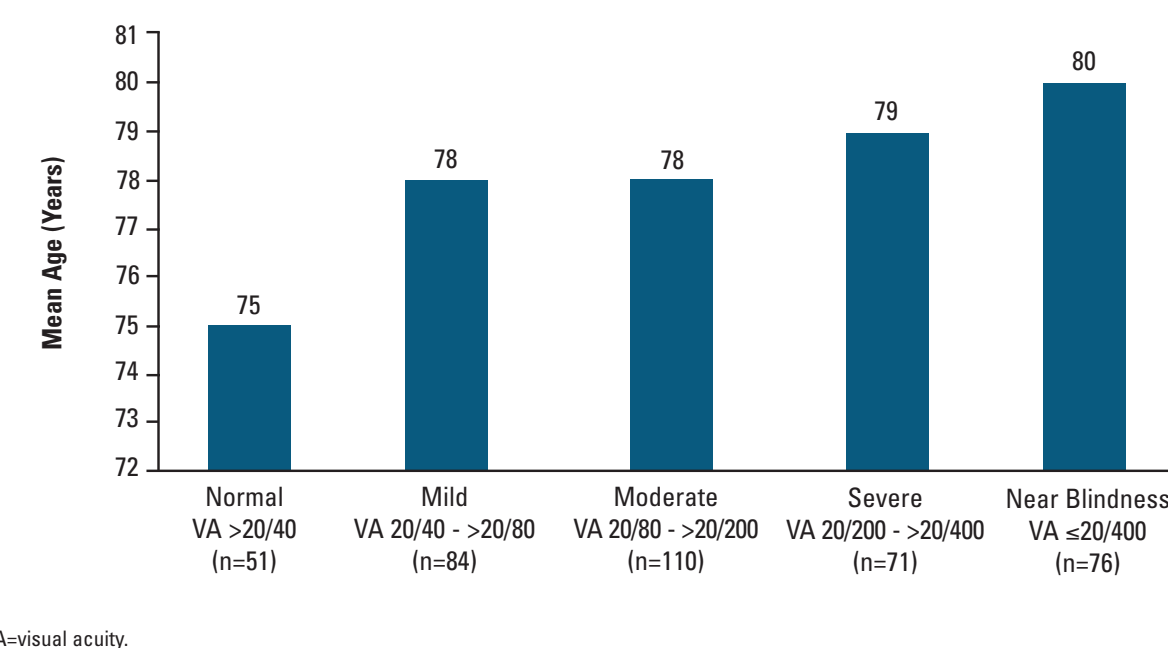
- Summary statistics were reported for all variables.
- Study outcomes were compared between neovascular AMD patients and the control subjects using standard bivariate methods (i.e., chi-square tests and 1-way analysis of variance models) and multivariate methods.
- Demographic data and comorbid disease of the neovascular AMD and control patients were compared. Adjustments for age, gender, race, comorbidities, and country were made in the multivariate analyses.
- The analyses were conducted in the overall study sample. Statistical significance was evaluated at the 0.05 level, with no adjustments for multiple comparisons.

RESULTS

Effect of Neovascular AMD on the Clinical State of Patients

- Overall, the average age of neovascular AMD patients was 78 years. Consistent with the literature, neovascular AMD patients' age was positively associated with severity of the disease ($P=0.0009$) given that higher prevalence of neovascular AMD has been observed in older populations (Figure 1).

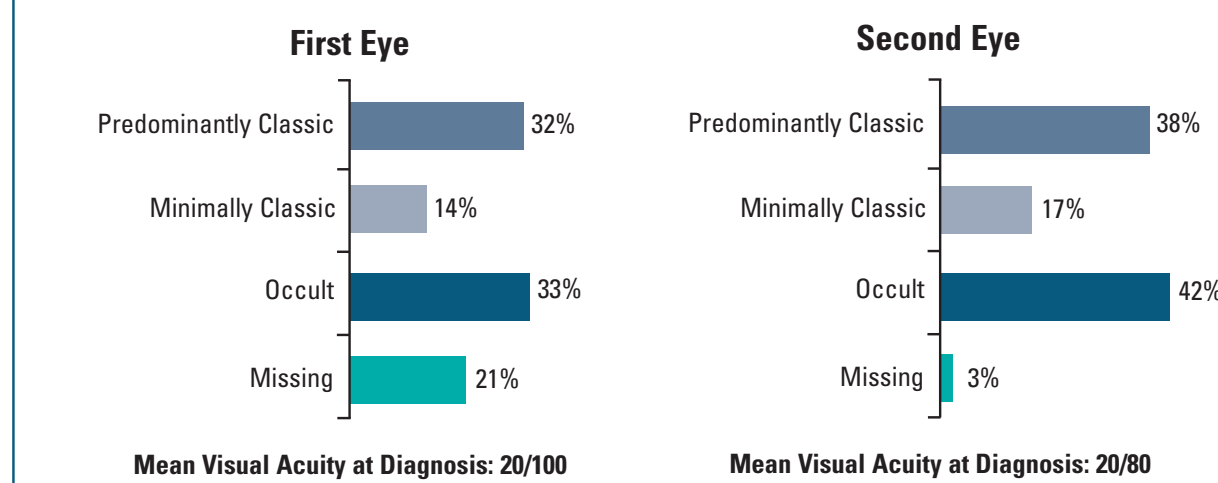
Figure 1. Age Distribution by Better-Eye Visual Acuity in AMD Patients



Results - Continued

- When neovascular AMD patients were diagnosed, their disease was relatively advanced with a mean visual acuity of 20/100 in the first eye and 20/80 in the second eye and with the highest proportion of patients having the occult lesion subtype (Figure 2).
 - Median time from diagnosis of AMD was 2.5 years in the first eye and 1 year in the second eye.

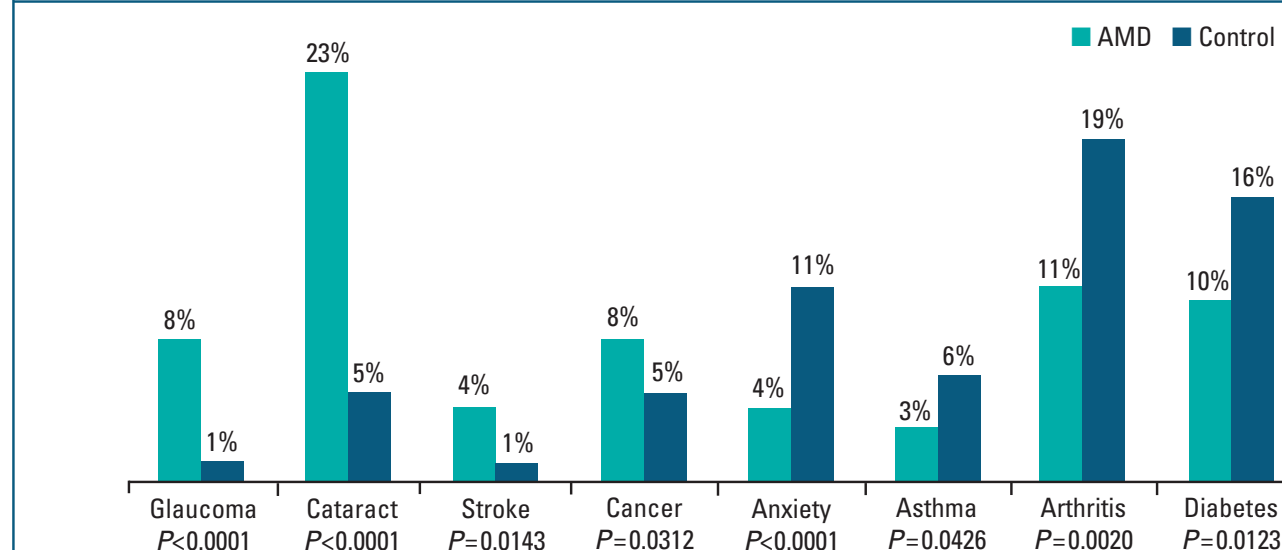
Figure 2. Neovascular AMD Lesion Subtype at Diagnosis



Neovascular AMD disease progressed rapidly.

- Median length of time for the visual acuity to progress from diagnosis to worse than 20/200 was 5 months in the first eye and 8 months in the second eye among those with current visual acuity worse than 20/200.
- Physicians reported that neovascular AMD patients had significantly more comorbid medical conditions than control subjects (mean [95% CI]: 2.5 [2.3, 2.6], 2.2 [2.0, 2.3]; $P=0.0111$), with higher proportions having ocular diseases, stroke, and cancer (Figure 3).

Figure 3. Frequency of Comorbid Diseases



- Even though similar percentages (16%) of neovascular AMD patients and control subjects received prescription anxiety/depression treatment in the past 12 months, neovascular AMD patients were on treatment for an average of 2 months longer (9.5 vs. 7.8 months; $P=0.0297$).

- Almost all the neovascular AMD patients had a slit-lamp exam/ophthalmoscopy in the past 12 months while only half of the patients had the exam in the past 13 to 24 months (Table 1). Other diagnostic tests were done less frequently.

Table 1. Previous Diagnostic Tests Performed

Diagnostic Test	Past 12 Months		Past 13 to 24 Months	
	Performed, %	Mean No. of Tests	Performed, %	Mean No. of Tests
Slit-lamp exam/Ophthalmoscopy	99%	4.1	56%	4.3
Fundus photography	82%	2.9	44%	3.0
Fluorescein angiography	88%	2.7	49%	2.9
Optical coherence tomography	48%	2.4	16%	2.5
Indocyanine green angiography	17%	2.0	12%	2.2
Other*	4%	2.2	3%	2.9

*Includes echography, laser ophthalmoscope funduscopy, etc.

Results - Continued

- Limited numbers of neovascular AMD patients were treated with photodynamic therapy with verteporfin (PDT) or intravitreal corticosteroids (triamcinolone acetonide), the commonly used treatment options for subfoveal neovascular AMD (Table 2). As indicated in the literature, there has been a lack of treatment options available for patients with neovascular AMD.

Table 2. Previous Treatment of AMD

Treatment	Better Eye		Worse Eye	
	Past 12 Mo	Past 13 to 24 Mo	Past 12 Mo	Past 13 to 24 Mo
PDT				
Performed, %	36%	15%	22%	15%
Mean (median) no. of treatments	2.0 (1.0)	1.6 (1.0)	1.8 (1.0)	1.7 (1.0)
IVT Corticosteroids				
Performed, %	8%	0.5%	4%	0.2%
Mean (median) no. of treatments	1.3 (1.0)	1.0 (1.0)	1.4 (1.0)	2.0 (2.0)
PDT with IVT Corticosteroids				
Performed, %	8%	1%	4%	2%
Mean (median) no. of treatments	1.2 (1.0)	1.0 (1.0)	1.2 (1.0)	1.1 (1.0)

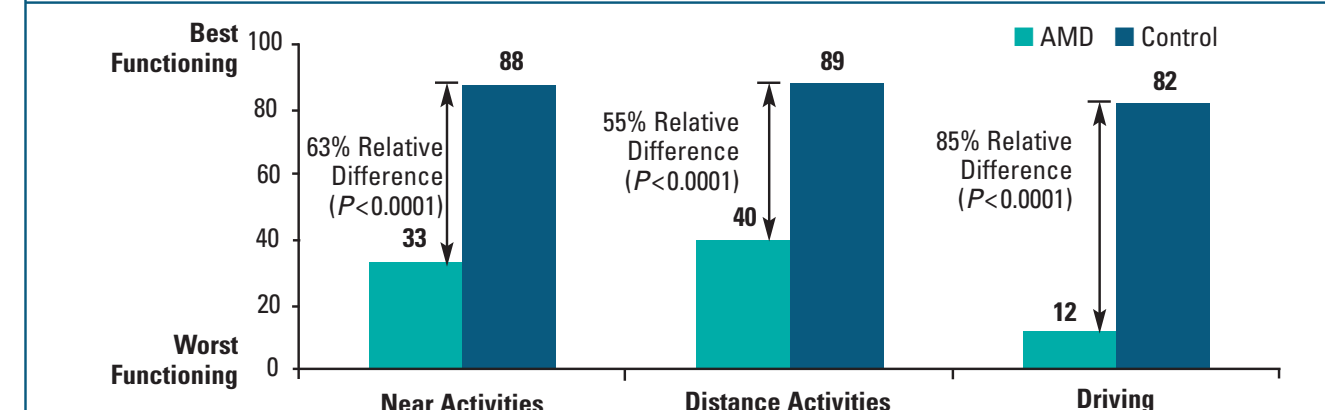
Mo=months.

- On average, neovascular AMD patients visited ophthalmologists/optometrists 3 times for visual impairment management and were prescribed 2 devices for vision enhancement in the past 12 months. Close to half of the patients (45%) were referred for low-vision rehabilitation.

Effect of AMD on Patient's Functioning

- Neovascular AMD patients were significantly debilitated in performing daily activities, which most people take for granted, as measured by the National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) physical functioning scales (Figure 4). They had 63% relative lower ability for near activities (e.g., reading, cooking), 55% relative lower ability for distance activities (e.g., watching TV), and 85% relative lower ability for driving.

Figure 4. Adjusted* Difference in NEI VFQ Physical Functioning Scores Between AMD and Control Patients



*Adjusted for age, gender, race, comorbidities, and country.

- Thus, neovascular AMD patients required significantly more assistance than the control patients. Overall, the proportion of AMD patients receiving assistance with daily activities was 4 times higher than the control patients (29% vs. 7%, $P<0.0001$). Neovascular AMD patients particularly needed assistance with home care (23% vs. 5%), transportation for healthcare (14% vs. 3%), other transportation (11% vs. 2%), and administrative tasks (11% vs. 0.4%; all P values <0.0001).

- Poor visual acuity doubled the risk of a fall for the neovascular AMD patients compared to those without visual impairment (16% vs. 8%, $P<0.0001$). Among those who fell, the mean number of fall-related hospital emergency room visits was 1.3 for neovascular AMD patients and 1.1 for control patients, and of specialist visits was 4.3 and 2.4, respectively.

CONCLUSIONS

- Neovascular AMD is a chronic and progressive disease that can rapidly lead to impaired visual acuity and visual functioning.
- Neovascular AMD patients were observed to have a significantly higher number of comorbid medical conditions compared to a control group of elderly subjects without neovascular AMD.
- Bilateral neovascular AMD requires substantial health resource utilization and assistance with activities of daily living.
- Preserving the vision of patients with neovascular AMD may help preserve independence and functioning. Earlier intervention would provide substantial clinical, economic, and societal benefits.
- AMD patients who did not have treatment options before can now benefit from new and emerging therapies leading to preservation of their visual acuity and functional status.