

Quality of Life With Visual Acuity Loss From Diabetic Retinopathy and Age-Related Macular Degeneration

Melissa M. Brown, MD, MN, MBA; Gary C. Brown, MD, MBA;
Sanjay Sharma, MD, MSc, MBA; Jennifer Landy, MD; Jeff Bakal, MSc

Objective: To compare the quality of life in patients with visual acuity loss occurring secondary to diabetic retinopathy with visual acuity loss occurring secondary to age-related macular degeneration (ARMD).

Methods: Consecutive patients with diabetic retinopathy and ARMD were evaluated using the time trade-off method of utility value analysis. Both groups were stratified according to the degree of visual acuity loss in the better-seeing eye (group 1: 20/20-20/25, group 2: 20/30-20/40, group 3: 20/50-20/100, group 4: \leq 20/200). Utility values obtained from the patients, once stratified for visual acuity group, were compared with use of the *t* test and the Mann-Whitney *U* test. In addition, a 2-way analysis of variance was performed to control for potential confounding variables.

Results: No difference was found between the utility value means of the diabetic retinopathy ($n=333$) and ARMD ($n=246$) subgroups stratified according to visual acuity levels: group 1, $P=.54$; group 2, $P=.96$; group 3, $P=.09$; and group 4, $P=.32$. A 2-way analysis of variance demonstrated that, among the variables of ocular disease, sex, age, and visual acuity in the better-seeing eye, only visual acuity was significantly associated with utility values ($P=.003$).

Conclusions: At similar levels of visual acuity loss, that associated with diabetic retinopathy causes a similar reduction in quality of life to that associated with ARMD. This information has important implications for use in cost-utility analyses of ophthalmic interventions.

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UTILITY ANALYSIS allows quantification of the quality of life associated with a health state.¹⁻⁵ By convention, a utility value of 1.0 is associated with perfect health, while a utility value of 0.0 is associated with death. The closer the utility value is to 1.0, the better the quality of life associated with a health state and the closer the value is to 0.0, the poorer the quality of life associated with a health state.

Utility values associated with ocular diseases have been shown to correlate best with the visual acuity in the better-seeing eye.⁶⁻¹¹ As the visual acuity in the better-seeing eye decreases, the visual utility decreases concomitantly. It has been suggested that utility values are related more to the level of visual acuity loss than to the underlying cause of visual acuity loss.⁶ Nevertheless, the largest study that undertook this analysis was relatively underpowered, with slightly more than 100 subjects in each of the diabetic retinopathy and age-related macular degeneration (ARMD) groups.⁶ For this reason, we undertook a study to evaluate whether the visual acuity loss occurring secondary to diabetic retinopathy had the same ad-

verse effect on quality of life as the visual acuity loss associated with ARMD.

RESULTS

STUDY GROUPS

Study questions were administered to a total of 617 patients: 354 with diabetic retinopathy and 263 with ARMD. Five hundred ninety (95%) came from the vitreoretinal practice and 27 (5%) from the comprehensive ophthalmology practice. Among the 617 total patients, 38 (6.1%) were unable or unwilling to completely answer the study questions. Twenty-one (5.9%) of the 354 patients with diabetes were therefore excluded and 17 (6.4%) of the 263 with patients ARMD were excluded. The remaining 579 patients included 333 (57%) with diabetic retinopathy and 246 (43%) with ARMD.

The clinical parameters of each group are presented in **Table 1**. In the diabetic retinopathy group there were 187 women and 146 men and in the ARMD group there were 163 women and 83 men ($P=.02$). Three hundred two white and 31 non-white patients composed the diabetic retinopathy group, and 245 white and 1 non-white patients comprised the ARMD group

From the Center for Evidence-Based Health Care Economics, Flourtown, Pa (Drs M. M. Brown, G. C. Brown, Sharma, and Landy); the Cataract and Primary Eye Care Service (Dr M. M. Brown) and the Retina Vascular Unit (Dr G. C. Brown), Wills Eye Hospital, Jefferson Medical College, Philadelphia, Pa; and the Cost-Effective Ocular Health Policy Unit, Queens University, Kingston, Ontario (Dr Sharma and Mr Bakal).

PATIENTS AND METHODS

PATIENTS

Included in the study were consecutive patients recruited from 2 ophthalmic practices, one predominantly vitreoretinal, and the second a comprehensive ophthalmologic practice. Patients were considered eligible for the study if they had a diagnosis of diabetic retinopathy or ARMD. The minimum criterion for entrance in the diabetic retinopathy group was a history of diabetes mellitus associated with retinal hemorrhages and/or microaneurysms. The lower threshold criteria for the presence of ARMD included macular drusen in association with a central macular retinal pigment epithelial disturbance. Both dry and exudative forms of ARMD were included. Only patients who had visual acuity loss occurring primarily secondary to diabetic retinopathy or ARMD were included. The exact criteria for the cause of primary visual acuity loss have been previously reported.^{9,10}

Exclusion criteria included the presence of Alzheimer disease or other forms of dementia that were judged to negate the possibility of giving rational answers, visual acuity loss occurring secondary to multiple causes (for example, diabetic retinopathy and cataract), and the inability or unwillingness to answer study questions once they were posed.

All patients underwent a complete ophthalmologic examination, including measurement of best-corrected visual acuity in both eyes, anterior segment examination, and dilated funduscopy. If the visual acuity could be further improved with a pinhole, the pinhole vision was chosen as the best-corrected visual acuity. The pinhole visual acuity was believed to represent the vision that could be obtained by squinting, thus simulating the visual potential in a real-life setting.⁶⁻¹¹

Following the clinical examination and agreement to participate in the study, each patient was asked a series of time tradeoff utility analysis questions that have been previously reported.⁶⁻¹¹ The study questions were administered by one of two of us (either M.M.B. or G.C.B.) using the same written protocol.

Initially, each person was asked how long he or she expected to live. In patients with abnormal visual acuity ($\leq 20/30$ in at least 1 eye), each was asked how much of the remaining time of life he or she would be willing to trade

in return for a treatment that would return permanent good vision to each eye. In patients with good bilateral visual acuity (20/20-20/25), the question was slightly modified to ask how much of the remaining time of life he or she would trade in return for a guarantee of retaining good vision in each eye for the remaining years. The time trade-off utility value was calculated by the following formula: $1.0 - (\text{number of years traded for good vision}) / (\text{number of years of expected remaining life})$. For example, if a person expected to live 10 additional years and would trade 3 of them in return for good vision, the resultant utility value would be 0.7 ($1.0 - [3/10]$).

The subgroups in each of the diabetic retinopathy and ARMD groups were subdivided into 4 visual stratifications based on the visual acuity in the better-seeing eye. The visual acuity strata were defined as follows: group 1: 20/20-20/25 (good reading vision), group 2: 20/30 to 20/40 (legal driving vision), group 3: 20/50 to 20/100 (moderate visual acuity loss), and group 4: less than or equal to 20/200 (legal blindness). The study was approved by the institutional review board of Wills Eye Hospital (Philadelphia, Pa).

STATISTICAL ANALYSES

Statistical analyses were performed using SPSS 10.1 (SPSS Corporation, Chicago, Ill). An analysis of whether the parameters studied were parametric or nonparametric was performed using the 2-sample Kolmogorov-Smirnov test. A comparison of the means of the stratified visual acuity groups was performed using the *t* test for independent samples and the Mann-Whitney *U* test, the analog of the *t* test for independent samples that are nonparametric in distribution. In addition, a 2-way analysis of variance (ANOVA) was performed to control for the variables of sex and age. Categorical variables were studied using a χ^2 analysis. Statistical significance was presumed to occur at the $P = .05$ level.

A sample size power calculation was performed before the study was undertaken, employing values from previous studies^{9,10} with SPSS Sample Power 2 (SPSS Corporation). With a 2-sided α of .05 and a power of 80%, a total of 60 patients per visually stratified subgroup was necessary to demonstrate a 10% difference in mean utility values and a total of 30 patients per subgroup was necessary to demonstrate a 15% difference. Data are given as mean \pm SD unless otherwise indicated.

($P < .001$). The average age of those with diabetic retinopathy was 62.2 ± 11.8 years and of those with ARMD was 73.2 ± 9.8 years. The median age in the diabetic retinopathy group was 65 years and in the ARMD group was 74 years ($P < .001$). The mean number of years of formal education after kindergarten in the diabetic retinopathy group was 13.1 ± 2.7 and in the ARMD group was 12.9 ± 2.7 ($P = .43$). The median number of years of education in each group was 12. The mean time of visual acuity loss to the level of visual acuity at the time of examination was 2.5 ± 4.0 years in the diabetic retinopathy group and 2.1 ± 2.2 years in the ARMD group ($P = .13$).

There were 10 people in the diabetic retinopathy group and 7 in the ARMD group who had visual acuities between 20/20 and 20/25 OU. Excluding these cases, the mean number of years of visual acuity loss to the visual acuity level at the time of entrance into the study was

2.5 ± 4.1 years in the diabetic retinopathy group and 2.1 ± 2.2 years in the ARMD group. The difference between these means was not significant ($P = .13$).

UTILITY VALUES

The mean visual acuity in the better-seeing eye of patients in the diabetic retinopathy group was approximately 20/40. The overall mean visual utility value for the diabetic retinopathy group was 0.79 ± 0.20 (95% confidence interval [CI], 0.77-0.81). The mean visual acuity in the better-seeing eye of the ARMD group was approximately 20/45. The overall mean visual utility value for the ARMD group was 0.74 ± 0.23 (95% CI, 0.71-0.77). The Kolmogorov-Smirnov test for normality revealed that the distribution of the overall utility values of both groups was nonparametric ($P < .001$); thus, the Mann-Whitney

rank sum *U* test was employed to compare the 2 groups. There was a significant difference between the mean utility values of the groups ($P = .02$).

When the utility values of the diabetic retinopathy and ARMD subgroups were stratified according to the visual acuity in the better-seeing eye, however, the Kolmogorov-Smirnov test revealed a more normal distribution for each of the subgroups (group 1, $P = .37$; group 2, $P = .35$, group 3, $P = .20$, group 4, $P = .96$). Since the distribution of utility values among the subgroups seemed to be parametric while the overall utility values were nonparametric, both the *t* test and Mann-Whitney rank sum *U* test were used to analyze the subgroups. The utility values for each of the subgroups stratified according to visual acuity level in the better-seeing eye are presented in **Table 2**. No significant difference was noted between the mean utility values in any of the visual acuity stratified subgroups using either the *t* test for independent samples or the Mann-Whitney rank sum *U* test.

A 2-way ANOVA incorporating the strata based on the visual acuity in the better-seeing eye was also performed to examine the effects of sex, age, and disease type (diabetic retinopathy or ARMD). The results of the ANOVA are presented here and in **Table 3**. Our model was associated with an *F* score of 19.27 ($P < .001$). In this model, disease type ($P = .21$), age ($P = .71$), and sex ($P = .06$) make nonsignificant contributions, while the contribution of visual acuity to utility values is significant ($P = .003$).

Table 1. Clinical Parameters of Patients With Diabetic Retinopathy and Age-Related Macular Degeneration*

Parameter	Diabetic Retinopathy (n = 333)	ARMD (n = 246)	P Value
Mean age, y	62.2	73.2	<.001
Mean years of education	13.1	12.9	.43
Sex			
Men	146	83	.02
Women	188	163	
Race			
White	302	245	<.001
Nonwhite	32	1	
Time of visual loss to present level, y	2.5	2.1	.13

*ARMD indicates age-related macular degeneration.

The study herein demonstrates that when patients are stratified according to visual acuity in the better-seeing eye, the quality of life associated with visual acuity loss from diabetic retinopathy is similar to that associated with visual acuity loss occurring secondary to ARMD. In this situation, it seems to be the degree of visual acuity loss rather than the underlying disease causing the visual acuity loss that is primarily responsible for the reduction in quality of life. This has been suggested previously,⁶ although the prior study undertaken did not have the power of our study. Conclusive data concerning utility values for other ocular diseases, such as cataract, are pending.

Ocular utility values have been demonstrated previously to correlate most closely with visual acuity in the better-seeing eye.¹² We therefore used the same criterion of visual acuity in the better-seeing eye for analysis in this study. Visual acuity in the poorer-seeing eye correlates with ocular utility values as well but not nearly to the extent of visual acuity in the better-seeing eye.¹² When the results of averaging the visual acuities in each eye are correlated with ocular utility values, the results seem to be the same as when the visual acuity in the better-seeing eye is used (M.M.B and G.C.B., unpublished data, 2002).

Our diabetic retinopathy and ARMD groups were similar according to time of visual acuity loss and level of education. The composition of age, sex, and race, however, differed among the groups. While the dissimilarity of these latter parameters is a potential weakness of the study, it has been previously shown that utility values are independent of age and sex.^{5,6,9,10,12} In addition, once these variables were controlled for in the ANOVA, only visual acuity was significantly associated with utility. The effect of race on utility values is uncertain and was not incorporated into the ANOVA owing to low numbers of patients in some of the cells. The differences in age, sex, and race in our diabetic retinopathy and ARMD cohorts most likely reflect the older age of those with ARMD compared with those with diabetic retinopathy,^{13,14} the longer life expectancy of women in the United States compared with that of men,¹⁵ and the greater proportion of whites affected by ARMD compared with African Americans.¹⁶

The similarity of visual utility values in patients with diabetic retinopathy and ARMD facilitates their use in cost-utility analyses.^{17,18} With cost-utility analysis, the improvement in quality of life and/or length of life conferred by an

Table 2. Comparison of Means of Visual Utility Values in Patients With Diabetic Retinopathy and Age-Related Macular Degeneration*

Group	Diabetic Retinopathy	ARMD	P Value	
			t Test	MW
Overall	0.79 ± 0.20 (0.77-0.81) (n = 333)	0.74 ± 0.23 (0.71-0.77) (n = 246)02
1	0.86 ± 0.17 (0.82-0.90) (n = 72)	0.84 ± 0.21 (0.82-0.86) (n = 60)	.54	.83
2	0.80 ± 0.19 (0.77-0.83) (n = 130)	0.80 ± 0.19 (0.75-0.85) (n = 65)	.96	.89
3	0.77 ± 0.18 (0.73-0.81) (n = 95)	0.71 ± 0.22 (0.65-0.77) (n = 57)	.09	.12
4	0.60 ± 0.19 (0.54-0.66) (n = 36)	0.59 ± 0.22 (0.53-0.65) (n = 65)	.83	.69

*Visual acuity in better seeing eye: group 1 = 20/20-25/25; group 2 = 20/30-20/40; group 3 = 20/50-20/100; and group 4 ≤20/200. Data are given as mean ± SD (95% confidence interval) unless otherwise indicated. ARMD indicates age-related macular degeneration; MW, Mann-Whitney rank sum *U* test; and ellipses, not applicable.

Table 3. Two-Way Analysis of Variance Incorporating Disease Type, Visual Acuity, Sex, and Age*

Source	Type III	Mean Square	F	P Value
Model	5.69	0.65	F ₈ = 16.9	...
Disease	0.07	0.07	F ₁ = 0.28	.2
Visual acuity	4.09	1.37	F ₃ = 35.5	.003
Sex	0.17	0.17	F ₁ = 3.82	.06
Age	0.004	0.004	F ₁ = 0.12	.72

*R² = 0.21. Ellipses indicate not applicable.

intervention can be amalgamated with the costs of the intervention to arrive at the dollars expended for the patient-perceived value gained. It should be noted that the utility values presented herein were all derived from patient interviews. Although utility values can be obtained from surrogate responders, they are often quite different from those obtained from patients who actually have the disease.⁷

Ocular utility values seem to have good reproducibility on both a short- and long-term basis.^{19,20} Utility values differ from many other quality-of-life instruments²¹⁻²⁶ in that they are a measure of patient preferences for a health state. Most other quality-of-life instruments measure the function associated with a health state rather than the preference or desirability of it. Both types of instruments have valuable applications and are likely to be complementary.

The generic systemic quality-of-life instruments, such as the Short-Form 36 and the Sickness Impact Profile, have not been found to correlate as well with visual function as ophthalmic measures, such as the Visual Function 14.²¹⁻²⁴ The Visual Functioning 14²⁵ and the newer Visual Function Questionnaire 25²⁶ are designed to apply to ophthalmic conditions and therefore are not generally applicable to nonophthalmic conditions. While they can be applied very effectively to ophthalmic interventions, ophthalmic interventions represent only a very small percentage of the total spectrum of health care interventions.²⁷ Additionally, the above-mentioned measures have not been applied in cost-effectiveness analysis. Utility value analysis allows measurements across all specialties in health care, but, more importantly, can be used for cost-effectiveness analysis. This is deemed to be a critical factor in improving quality²⁸ in an era in which the United States has been ranked by the World Health Organization²⁹ as No. 37 in the world in its use of a method that measures the efficacy of health care resource expenditure.

In summary, we found that ocular utility values obtained from patients with diabetic retinopathy and ARMD, when stratified for level of visual acuity loss, seem to be similar. This finding strongly suggests that for these 2 diseases, the decrease in quality of life induced by visual acuity loss is related more to the degree of central acuity loss than to the underlying cause of visual acuity loss.

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Corresponding author and reprints: Melissa M. Brown, MD, MN, MBA, Center for Evidence-Based Health Care Economics, Suite 210, 1107 Bethlehem Pike, Flourtown, PA 19031 (e-mail: lissa1011@aol.com).

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