

VALUE BASED OPHTHALMOLOGY

Quality of life and systemic comorbidities in patients with ophthalmic disease

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Aim: To ascertain the effect of serious systemic comorbidities upon the quality of life of patients with ophthalmic diseases.

Methods: Time tradeoff utility values were obtained in consecutive ophthalmic patients who presented with ocular disease. Multivariate analysis was undertaken to evaluate whether the systemic comorbidities of diabetes mellitus, heart disease, cancer, cerebrovascular accident, and/or renal failure requiring dialysis influenced ocular utility values.

Results: Among the 390 patients with ocular diseases studied, 250 had the systemic comorbidities of diabetes mellitus, heart disease, cancer, stroke, and/or renal failure requiring dialysis, while 140 lacked these comorbidities. There was no statistically significant difference ($p = 0.091$) between the comorbidity and no comorbidity groups in self assessed quality of life as measured by ocular utility values after taking into account potentially confounding variables.

Conclusions: In patients with ocular disease, ocular utility values related to the visual loss do not appear to be affected by the presence of select, concomitant, serious systemic diseases. Thus, visual loss seems to cause a similar diminution in self assessed quality of life in those who do and do not have serious associated systemic comorbidities. This information has important implications for the calculation of cost effective analyses.

Utility values reflect the quality of life associated with a health state.¹ By convention, utility values range from 1.0 (perfect health) to 0.0 (death). The higher the utility value, the better the quality of life associated with a health state and the lower the value, the poorer the quality of life. Utility values can be obtained from patients or from surrogate respondents such as physicians, administrators, and the general public, although those obtained from patients who actually have a given health state are believed to be the most relevant.²

In the realm of ophthalmology, both time tradeoff and standard gamble utility values in patients with ocular disease appear to be most dependent upon the visual acuity in the better seeing eye.^{3–5} Time tradeoff utility values are calculated by subtracting the proportion of theoretical remaining years of life a person is willing to trade in return for a perfect health state from 1.0, while standard gamble utility values are calculated by subtracting from 1.0 the percentage risk of immediate death a person is willing to assume if the alternative scenario is a perfect health state. Time tradeoff utility values have been shown to more closely correlate with visual acuity than have standard gamble utility values.⁴

Utility values appear to be most dependent upon the visual acuity in the better seeing eye. As the visual acuity in the better seeing eye decreases, so do the corresponding utility values. Age, sex, level of education, and the underlying cause of visual loss have been shown not to be confounding factors with regard to utility determination in patients with ocular disease,^{3–5} but the effect of systemic comorbidities upon utility values in patients with visual loss has not been well studied.

Because of the relative lack of information concerning the effect of comorbid systemic diseases upon utility values in patients with visual loss, the authors undertook a study to ascertain whether patients with visual loss and serious systemic comorbidities had visual utility values different from those with similar levels of visual loss and absence of the same comorbidities. In essence, the purpose of the study was to ascertain whether the quality of life associated with visual loss

is affected to the same degree in patients with and without serious systemic comorbidities.

PARTICIPANTS AND METHODS

Participants were drawn from a group of consecutive, ambulatory adult patients with ocular diseases seen in the ophthalmology practices of two of the authors (GCB and MMB). The first practice was primarily a vitreoretinal practice and the second a comprehensive ophthalmology practice. The interviews were conducted by MMB and GCB using a standardised questionnaire previously described.^{3–5} The study was approved by the Wills Eye Hospital institutional review board.

Inclusion criteria required a willingness to answer the time tradeoff utility questions described below. Additionally, it was required that the cause of visual loss be the same in each eye when bilateral ocular disease affecting vision was present. Exclusion criteria included the presence of Alzheimer's disease or another form of dementia which precluded the ability to answer the study questions. Those who were unable or unwilling to answer the study questions once they were posed were also excluded.

Each patient underwent a history that included questions concerning the presence or history of (1) cardiac disease, (2) diabetes mellitus, (3) cancer, (4) cerebrovascular accident, and/or (5) renal disease. These diseases were selected because they collectively account for the majority of annual deaths⁶ and a large portion of healthcare expenditures in the United States.⁷ If a patient had at least one or more of these five systemic diseases, he or she was classified in the comorbidity group. Patients in the no comorbidity group had none of the five diseases listed above. Patients were also asked about their highest level of formal education.

The patients were considered to have cardiac disease if they had a history of myocardial infarction, known atherosclerotic coronary artery disease, or congestive heart failure. With regard to diabetes mellitus, both type 1 and 2 diabetics were

included. The presence of cerebrovascular accident was ascertained by history; patients who did and did not have a full recovery were included. Since the study was office based, only patients who were ambulatory or could sit in a wheelchair were included in the cerebrovascular accident group. A patient was considered to be in the cancer group if he or she had a previous history of cancer (other than skin cancer), regardless of the stage or current therapeutic regimen. Only patients who were on dialysis were considered to be in the renal failure group.

All patients underwent a complete ophthalmological examination, including best corrected Snellen visual acuity measurement in each eye, slit lamp examination and dilated funduscopy. In those instances in which the visual acuity was further improved with a pinhole, the pinhole vision was selected as the best visual acuity in the eye under consideration. Snellen visual acuity measurement was selected since it is the most common visual measurement tool in clinical practice, and the pinhole visual acuity was selected because it was believed to represent the vision that could be further obtained by squinting, thus simulating the visual potential in a real world setting.³⁻⁵

After the clinical examination, each patient was asked a series of time tradeoff utility analysis questions that have been previously reported.³⁻⁵ In essence, each person was asked how long he or she expected to live. In patients with abnormal vision (20/30 or less in at least one eye), each was asked how many of those remaining years 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 vision (20/20–20/25) in both eyes, the question was modified slightly to ask how many remaining years 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 tradeoff utility value was then calculated by dividing the number of years traded by the number of expected remaining years of life and subtracting this proportion from 1.0.

Statistical analyses

All analyses were performed using SPSS 10.0 for Windows. Demographic variables were described within both the comorbid and non-comorbid groups, and compared using χ^2 tests for categorical variables and the two tailed Student's *t* test for continuous variables. Initially, in order to determine if there was a difference in overall mean ocular utility between the two groups, a Student's *t* test was performed. Next, a multiple linear regression was performed in order to account for other potential confounding variables, in particular visual acuity, which is known to highly affect visual utility scores. In our model, visual utility was the main outcome variable, while the presence or absence of comorbid diseases was the main independent variable of interest. The analysis controlled for age, sex, race, years of education, and vision in the better seeing eye.

In order to determine if any particular comorbid disease was associated with different utility values, a second multiple linear regression was performed. However, instead of using presence or absence of a comorbid disease as the main independent variable, we used five separate independent variables (presence or absence of diabetes, heart disease, cerebrovascular accident, cancer, and renal disease requiring dialysis). In this way we were able to determine if any one of the comorbid diseases was associated with significantly different visual utility values. Statistical significance was presumed to occur at the $p = 0.05$ level.

RESULTS

In all, 417 patients were interviewed over an 8 month period. Among these, 27 (6.5%) were excluded because they were unable or unwilling to answer the questions posed. Eighteen patients, 6.7% of the comorbidity group, were excluded, while nine patients, 6.0% of the no comorbidity group, were excluded. Thus, a total of 390 patients were entered into the study. Included were 147 men and 243 women. The mean age was 66 years (standard deviation 12.4; 95% confidence interval, 64.8–67.2), with a range of 27–89 years. There were 370 white and 20 black people, and the mean level of education was 13.4 years (SD 3.1; 95% CI, 13.1–13.7).

Overall, 250 patients had one or more serious, systemic comorbidities and 140 had none. Diabetes mellitus was present in 173 of the 250 (69%) patients in the group with comorbidities, cardiac disease in 101/250 (40%), cancer in 52/250 (21%), previous cerebrovascular accident in 42/250 (17%), and renal disease requiring dialysis in 13/250 (5%).

The clinical characteristics of the two groups are shown in Table 1. Women comprised 62% of the comorbidity group and 64% of the no comorbidity group, while white people comprised 94% of the comorbidity group and 96% of the no comorbidity group. The mean age was 66.4 years in the comorbidity group and 65.5 in the no comorbidity group, and the number of years of formal education after kindergarten was 13.2 in the comorbidity group and 13.7 in the no comorbidity group. There was no significant difference in any of these parameters between the groups with and without comorbidities.

The mean utility value for the comorbidity group was 0.77 (SD 0.23; 95% CI, 0.74–0.80) and for the no comorbidity group was 0.87 (SD 0.19; 95% CI, 0.84–0.90). The difference between the means of these groups was significant ($p = 0.000003$), but the overall values did not take into account the variations in visual acuity levels in the better eye within the groups. Our multivariate analysis showed there was no statistically significant difference between the comorbidity group and no comorbidity group after taking into account the visual acuity in the better seeing eye and other potentially confounding variables ($p = 0.091$) (Table 2). When looking at the effect of the different disease entities, while controlling for visual acuity and

Table 1 Clinical features of the groups with and without systemic comorbidities

Feature	Comorbidities (n=250)	No comorbidities (n=140)	p Value
Sex	96 (38%) men 154 (62%) women	51 (36%) men 89 (64%) women	0.66
Race	235 (94%) white people 15 (6%) black people	135 (96%) white people 5 (4%) black people	0.32
Age (mean)	66.4 years (SD = 12) (95% CI, 64.9–67.9)	65.5 years (SD = 14) (95% CI, 63.2–67.8)	0.52
Education	13.2 years (SD = 3.1) (95% CI, 12.8–13.6)	13.7 years (SD = 3.1) (95% CI, 13.2–14.2)	0.11

SD = standard deviation, CI = confidence interval.

Table 2 Association between the presence of comorbid diseases and visual utility values, using multiple linear regression

Predictor variable	β Coefficient	p Value
Constant	0.612	<0.0005
Age (continuous)	-0.000257	0.749
Sex (referent to male)	0.00277	0.889
Race (referent to white people)	0.0202	0.350
Years of education (continuous)	0.00194	0.749
Vision in better seeing eye (logMAR scale between 0 and 1)	0.359	<0.0005
Comorbid diseases (referent to none)	-0.0349	0.091

Table 3 Association between particular comorbid diseases and visual utility values, using multiple linear regression

Predictor variable	β Coefficient	p Value
Constant	0.522	<0.0005
Age (continuous)	0.000232	0.782
Sex (referent to male)	0.00386	0.848
Race (referent to white people)	0.0311	0.475
Years of education (continuous)	0.00220	0.494
Vision in better seeing eye (logMAR scale between 0 and 1)	0.327	<0.0005
Presence of diabetes mellitus	0.0100	0.628
Presence of heart disease	-0.0108	0.632
Presence of cerebrovascular accident	-0.0660	0.034
Presence of cancer	-0.0255	0.308
Presence of renal failure requiring dialysis	-0.0488	0.191

other demographic characteristics, we found that only a cerebrovascular accident was significantly associated with different visual utility scores ($p = 0.034$) (Table 3). The presence of diabetes, ($p = 0.628$), heart disease ($p = 0.632$), cancer ($p = 0.308$), and renal failure ($p = 0.191$) was not associated with different visual utility scores. With regard to stroke, a person who had a cerebrovascular accident tended to have a visual utility score of 0.066 less than a person who did not have a cerebrovascular accident.

In order to determine if we had adequate power to detect a difference in utility values between the two groups, a post hoc power calculation was performed. Assuming an alpha level of 5%, and 80% power, this study had the sample size to detect a difference in utility values of 0.065 between the comorbidity and no comorbidity groups.

DISCUSSION

This study failed to demonstrate a significant difference in ophthalmic utility values between the comorbidity and no comorbidity groups after taking into account the visual acuity in the better seeing eye and other potentially confounding variables such as age, sex, race, and level of education. When the comorbidity and no comorbidity group mean ocular utility values as a whole were compared, however, there was a significant difference in utility values between the groups. This occurred because the group with systemic diseases had a greater proportion of patients with more severe visual loss. Nevertheless, the overall ocular utility values of the groups are not relevant for our analysis. Since ophthalmic utility values have been shown to correlate most directly with the visual acuity in the better seeing eye,³⁻⁵ a valid comparison requires the visual stratification employed here.

Utility values reflect the quality of life associated with a given health state.^{1-5, 8} Thus, it appears that visual loss to a given level causes the same decrease in quality of life whether a patient has or does not have one of the serious systemic diseases we studied. The corollary follows that the benefit from an ocular intervention which improves visual loss to a given level is likely to yield the same improvement in quality of life irrespective of whether these serious systemic comorbidities are absent or present. Thus, a person with diabetes mellitus or cancer and bilateral cataracts decreasing vision to the 20/200 level should theoretically derive the same benefit from cataract surgery as a person with similar preoperative vision who has no systemic comorbidities.

In patients with multiple health state abnormalities, it has been suggested that multiplying the respective health state utility values obtained for each condition allows a final representative utility value of an individual.^{8, 9} This methodology has been referred to as the "decomposed" method of assessing the utility value.^{8, 9} With the decomposed method, for example, the utility values for a patient with diabetes mellitus (utility value of 0.88¹⁰) and eye disease (utility value of 0.67 for 20/100 vision in the better seeing eye⁴) are multiplied ($0.88 \times 0.67 = 0.59$) to yield a final utility value for the combined health state. In this diabetic patient, the improvement of vision to 20/25 (utility value of 0.87⁴) after cataract surgery would be expected to yield a final utility value of 0.77 (0.88×0.87). Thus, the improvement in overall utility value after cataract surgery in such a diabetic patient would be 0.18 ($0.77-0.59$). For a patient with otherwise normal health, improvement of the vision in the better seeing eye from 20/200 (utility value of 0.67) to 20/25 (utility value of 0.87) would yield a utility gain of 0.20 ($0.87-0.67$). The otherwise healthy patient would therefore have a greater utility value gain from cataract surgery than the comparable diabetic patient if one adheres to the decomposed methodology. Our data suggest otherwise—that visual utility values are unaffected by accompanying systemic comorbidities. At least with regard to vision, patients with comorbid diseases should experience the same improvement in quality of life from an ophthalmic intervention as those with good systemic health.

When we analysed the comorbidities individually, cerebrovascular accident was an exception in that patients with a previous cerebrovascular accident tended to have lower ocular utility values for the same degree of visual loss when compared with the other individual comorbidity groups. We are uncertain of the meaning of this finding, although it suggests that visual loss in patients with stroke may cause an even more profound diminution in quality of life than in healthy patients or those with other systemic comorbidities. This runs counter to the decomposed methodology line of thought in that one would expect stroke patients to have a higher ocular utility value than a systemically healthy patient for the same degree of visual loss.

Judging from the information presented here, it appears that employing a decomposed methodology is unnecessary in a decision analysis tree when evaluating the cost effectiveness of interventions for ocular diseases. The decomposed methodology may not be applicable since the ocular utility values in patients with visual loss did not appear to be substantially affected by the presence of concomitant systemic diseases. Multiplying the various utility values of coexistent health states in ophthalmic patients when evaluating the incremental cost effectiveness of an ophthalmic intervention would be expected to substantially affect the outcome, compared with using ophthalmic utilities alone.^{1, 8, 9, 11} The fact that ophthalmic utilities are not affected by associated comorbidities should theoretically lead to more accurate cost effective analyses.¹²⁻¹⁵

Although the present study suggests the serious systemic diseases evaluated here do not affect the utility values obtained in patients seen primarily for ocular diseases, it cannot be ascertained from the present data whether utility

values for non-ophthalmic health states are affected by the coexistence of serious systemic diseases. Additionally, the present study did not evaluate the severity of systemic diseases. Further analyses outside the realm of this paper are certainly required.

As with any study, the present analysis has potential weaknesses. The groups studied here were well matched with regard to sex, race, age, and level of education but the underlying ophthalmic diseases themselves were not matched in the comorbidity and no comorbidity groups. The inclusion of diabetes mellitus as a serious systemic disease precluded this possibility, since many of the ocular patients had diabetic retinopathy as the primary cause of ocular disease. This limitation notwithstanding, we have previously shown that the degree of visual loss in the better seeing eye, rather than the underlying disease process causing the visual loss, correlates most directly with ocular utility values.⁴ The length of time of visual loss was not factored into the analysis, but it has been shown that utility values in ocular patients often do not appear to differ in groups that have a mean visual loss of less than one year versus many years.^{3,4}

Lack of masking of the interviewers is also a potential weakness, but it is uncertain how this would affect the data. None the less, reproducibility of utility data using the authors' methodology has been demonstrated when masking of the original values was employed.¹⁰

In addition, while the diseases that most commonly cause death and serious morbidity in the United States were selected for analysis in the current study, the effects of other systemic diseases, such as pulmonary disease and depression, that could theoretically influence ophthalmic utility values were not evaluated. The presence of depression in patients with diabetes mellitus has been shown to have an effect upon diabetic utility values.¹⁰

In summary, when adjustments were made for visual acuity and other possible confounding variables, we were unable to demonstrate a significant ocular utility value difference between a group of ophthalmic patients who had serious systemic comorbidities and one that did not. This information is important because the inclusion of a conversion factor for systemic comorbidities can substantially affect the results obtained with decision analysis used in cost effective analysis. Nevertheless, we believe the effect of comorbidities upon utility values deserves further evaluation.

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