# Visual Functioning and General Health Status in Patients With Uveitis

*Rhett M. Schiffman, MD, MS, MHSA; Gordon Jacobsen, MS; Scott M. Whitcup, MD*

**Objective:** To measure the visual functioning and quality of life in patients with uveitis.

**Methods:** Consecutive adult patients with noninfectious uveitis were enrolled. The Medical Outcomes Study 36-Item Short Form (SF-36) and the National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) were administered by a trained interviewer. Sociodemographic and clinical data were also collected.

**Results:** Seventy-six patients were enrolled. The overall NEI VFQ-25 score was significantly lower among patients with uveitis than in a normal reference group ($P<.001$). The SF-36 physical (PCS) and mental (MCS) component summary scores were also significantly lower among patients with uveitis than in the general US population ($P<.007$). Among patients with uveitis, visual acuity, binocular involvement, intensity of therapy, employment status, and PCS and MCS scores were all significantly associated with overall NEI VFQ-25 scores in multivariable analysis. Medical comorbidity, ocular comorbidity, and NEI VFQ-25 scores were significantly associated with PCS scores. Medical comorbidity and NEI VFQ-25 scores were significantly associated with MCS scores. Regression models including NEI VFQ-25 scores explained an additional 7% of the variance in PCS scores and 16% of MCS scores. Models including both PCS and MCS scores explained an additional 12% of the variance in NEI VFQ-25 scores.

**Conclusions:** Patients with uveitis reported markedly poorer visual functioning and general health status than normal subjects. Patients with more severe uveitis have poorer visual functioning and general health status than patients with milder disease. Visual functioning and general health status measurement contribute complementary information and should both be performed in patients with uveitis to measure the effect of disease and its therapy on their quality of life.

*Arch Ophthalmol. 2001;119:841-849*

*From the Departments of Eye Care Services (Dr Schiffman) and Biostatistics and Research Epidemiology (Mr Jacobsen), Henry Ford Health System, Detroit, Mich, and the Clinical Branch, National Eye Institute, Bethesda, Md (Dr Whitcup).*

UVEITIS is a leading cause of ocular morbidity in the United States, although population-based estimates of its true incidence and prevalence are not available. In its more severe forms, uveitis is responsible for 10% of the cases of severe visual handicap in the United States[1] and is associated with systemic illness in 21% to 32% of cases.[2,3] Severe uveitis often requires systemic treatment with corticosteroids or other anti-inflammatory agents, and these treatments may lead to a wide array of adverse advents and reductions in health-related quality of life (HR-QOL). To date, these disease- and treatment-related reductions in HR-QOL have not been measured in a comprehensive manner.

A number of questionnaires have been developed to measure HR-QOL, but perhaps the best known and most widely validated is the Medical Outcomes Study 36-Item Short Form (SF-36) questionnaire.[4] The SF-36 was used in the Medical Outcomes Study[5] and subsequently as part of numerous outcomes studies of medical diseases (eg, diabetes and hypertension) and ophthalmic conditions (including cataract, glaucoma, age-related macular degeneration, diabetic retinopathy, corneal transplantation, and ocular melanoma).[6-11] The SF-36 measures health status in 8 dimensions, including physical functioning, role limitation caused by physical disability (role-physical), bodily pain, general health, vitality, social functioning, role limitation caused by emotional disability (role-emotional), and mental health. Two summary scores have been developed: the physical component summary (PCS) score and the mental component summary (MCS) score.[12] Extensive normative and disease-specific data have been published for the SF-36.[12]

It has become clear, however, that generic outcomes questionnaires such as the SF-36 do not have sufficient content

## PATIENTS AND METHODS

### PATIENT SELECTION

This study was conducted at the uveitis clinic of the Warren G. Magnuson Clinical Center at the National Institutes of Health, Bethesda, Md. The clinic serves a referral population primarily from the mid-Atlantic states.

Consecutive patients seen with a diagnosis of noninfectious uveitis, 18 years or older and English speaking, were enrolled in the study. Patients with severe systemic disease not related to uveitis or its treatment and patients unwilling to provide written informed consent were excluded. Patients were enrolled from November 26, 1996, to January 20, 1998. The study was approved by the National Eye Institute Institutional Review Board.

### DATA COLLECTION

Data collected included age, race, sex, and socioeconomic status (including annual household income, highest educational level achieved, and employment status).

The SF-36 and NEI VFQ-25 were administered by a trained and certified interviewer. The questionnaires were completed before the ophthalmic examination to reduce the influence of the clinical encounter on patient responses.

The clinical data collected included diagnosis; monocular and binocular "walking-around" Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity; predominant location of inflammation (anterior, intermediate, posterior, or panuveitis); laterality (unilateral or bilateral involvement); disease activity (defined as the presence of active intraocular inflammation based on slitlamp examination); and chronicity (acute, $<$6 weeks; or chronic, $\geq$6 weeks). The type of immunosuppressive treatment prescribed was recorded as follows: (1) topical or periocular therapy, (2) systemic corticosteroids, or (3) other systemic immunosuppressive therapy (such as cyclosporine). The presence or absence of systemic involvement either from the primary disease (such as pulmonary or cardiac involvement with sarcoidosis) or as a consequence of treatment (such as hypertension, diabetes, or renal failure) was recorded. We also recorded the presence of medical comorbidities (using a 16-item medical comorbidity checklist taken from the Medical Outcomes Study[5]) and ocular comorbidities (including optic nerve disease, glaucoma, cystoid macular edema, and previous ocular surgery). Walking-around visual acuity was measured with the use of the patient's usual correction and standard ETDRS charts under controlled conditions.[17]

### STATISTICAL METHODS

#### Univariate Analyses

The SF-36 summary and subscale scores were computed according to published algorithms[4,12] and compared with mean scores of the general US population within the same age strata as our population (mean age, 42 years). The NEI VFQ-25 item composite and subscale scores were also computed with published algorithms and compared with the reference group of 122 normal subjects derived from the field test of the NEI VFQ-25.[16] This data set was kindly provided by the NEI VFQ-25 Analytical Core Laboratory at University of California–Los Angeles.

Analysis of variance was used to test for differences in SF-36 and NEI VFQ-25 scores between subgroups of interest. In the case of multiple-subgroup comparison, such as by intensity of treatment, Tukey studentized ranged test was used to maintain an experiment-wise rejection level of less than .05.

#### Multivariable Regression Analysis

As functional status measurements may be significantly influenced by sociodemographics and comorbidity, we used ordinary least-squares regression with a backward stepwise technique to adjust for demographics (age, race, sex), socioeconomic status (education, income, and employment status), medical and ocular comorbidity (as the unweighted sum of each), and clinical variables (including disease location, bilaterality, systemic involvement, active disease status, treatment intensity, and binocular walking-around visual acuity analyzed as logMAR acuity).[17] $P \leq .05$ for model inclusion was used in the stepwise regression. To determine the proportion of variance in VR-QOL explained by HR-QOL, we included the PCS and MCS scores in the stepwise regression on NEI VFQ-25 scores. Similarly, to determine the proportion of variance in HR-QOL explained by VR-QOL, we allowed the NEI VFQ-25 scores to be included in the PCS and MCS regression models. To minimize the effect of multiple comparisons, regression analysis was restricted to the overall NEI VFQ-25 scores and the PCS and MCS scores. We did not perform regressions on subscale scores. Despite the relatively large number of variables considered given the sample size, the final models always contained many fewer variables, minimizing the likelihood of overparameterization. Model stability was also assessed by evaluating the residual diagnostics; all resulting models were stable.

to describe important elements of functioning for patients with ocular diseases. Consequently, vision-specific questionnaires, such as the Activities of Daily Vision Scale[13] and the Visual Function Index (VF-14).[14] have been developed to meet this need. In general, these questionnaires demonstrate a mild to moderate correlation with visual acuity[13-15] and general health status,[6,13-15] suggesting that they capture aspects of visual functioning that are not reflected in visual acuity and general health status measures.[13,14] However, these questionnaires were originally designed to assess the outcomes of cataract surgery and were targeted to visual functioning. Consequently, they were not believed to capture the full range of vision-related disability that patients with diverse ophthalmologic conditions found relevant. Moreover, these questionnaires had not been validated across multiple ophthalmologic conditions. Consequently, the National Eye Institute sponsored the development of a vision-related QOL (VR-QOL) questionnaire, the National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25), that could be used for persons with diverse eye diseases.[8,16] The 25-item NEI VFQ-25 is both reliable (Cronbach $\alpha$, 0.41-0.86) and valid, containing 12 scales: General Health, General Vision, Near Vision, Distance Vision, Driving, Peripheral Vision, Color Vision, Ocular Pain, and Vision-Specific

**Table 1. Demographic Information**

| | No. (%) of Patients* |
|---|---|
| Age, y | |
| Mean | 42.3 |
| Range | 19-69 |
| Sex | |
| M | 29 (38) |
| F | 47 (62) |
| Race | |
| White | 35 (46) |
| African American | 25 (33) |
| Hispanic | 5 (7) |
| Asian | 4 (5) |
| Native American | 1 (1) |
| Other | 3 (4) |
| Mixed | 3 (4) |
| Education | |
| Some high school | 6 (8) |
| Completed high school | 13 (17) |
| Vocational school | 3 (4) |
| Some college | 19 (25) |
| Completed college | 13 (17) |
| Some graduate school | 5 (7) |
| Completed graduate school | 17 (22) |
| Employment status | |
| Employed | 53 (70) |
| Unemployed | 6 (8) |
| Vision disabled | 10 (13) |
| Non–vision disabled | 3 (4) |
| Working retired | 2 (3) |
| Nonworking retired | 2 (3) |
| Annual household income, $ | |
| <10 000 | 5 (7) |
| 10 000-19 999 | 10 (13) |
| 20 000-29 999 | 11 (14) |
| 30 000-39 999 | 9 (12) |
| 40 000-49 999 | 6 (8) |
| 50 000-59 999 | 9 (12) |
| 60 000-69 999 | 3 (4) |
| 70 000-79 999 | 1 (1) |
| ≥80 000 | 18 (24) |
| Prefer not to answer | 4 (5) |

*Because of rounding, percentages may not all total 100.

**Table 2. Disease Characteristics**

| | No. (%)* |
|---|---|
| Location | |
| Anterior | 13 (17) |
| Intermediate | 17 (22) |
| Posterior | 26 (34) |
| Panuveitis | 20 (26) |
| Disease | |
| Idiopathic | 20 (26) |
| Sarcoidosis | 13 (17) |
| Vogt-Koyanagi-Harada | 7 (9) |
| Behçet | 5 (7) |
| Multifocal choroiditis | 4 (5) |
| Pars planitis | 4 (5) |
| Birdshot | 3 (4) |
| HLA-B27 | 3 (4) |
| Multiple sclerosis | 2 (3) |
| Reiter syndrome | 2 (3) |
| Ankylosing spondylitis | 1 (1) |
| Acute zonal occult outer retinopathy | 1 (1) |
| Juvenile rheumatoid arthritis | 1 (1) |
| Serpiginous choroidopathy | 1 (1) |
| Sympathetic ophthalmia | 1 (1) |
| Other | 8 (10) |
| Laterality | |
| Bilateral | 70 (92) |
| Unilateral | 6 (8) |
| Additional characteristics | |
| Disease active | 23 (30) |
| Systemic involvement | 22 (29) |
| Ocular comorbidity | 51 (64) |
| Mean ± SD comorbidities per subject | 1.1 ± 1.1 |
| Optic nerve involvement | 15 (20) |
| Glaucoma | 18 (24) |
| Cystoid macular edema | 17 (22) |
| Medical comorbidity | 63 (83) |
| Mean ± SD comorbidities per subject | 1.9 ± 1.4 |
| Treatment intensity | |
| No treatment | 5 (7) |
| Corticosteroids | 65 (86) |
| Topical or periocular (alone) | 14 (18) |
| Systemic (alone or in combination) | 51 (67) |
| Cytotoxic or other immunosuppression | 13 (17) |
| Binocular visual acuity | |
| Mean | 20/28 |
| Range | 20/20-HM† |

*Because of rounding, percentages may not all total 100.
†HM indicates hand motions.

Role Limitations, Dependency, Social Functioning, and Mental Health.[16] An overall score can also be computed from each of the vision-related scales (ie, the General Health scale is excluded from the scoring of the overall score).

In this study, we used the NEI VFQ-25 and the SF-36 to measure visual functioning and general health status in a population of patients with uveitis seen at the National Eye Institute. This study examined whether patients with uveitis have lower general health status scores and visual functioning scores than normal subjects. This study also investigated the association between the severity of uveitis (based on characteristics such as location, laterality, and intensity of immunosuppressive therapy) and visual functioning and general health status.

## RESULTS

Seventy-six patients were enrolled in this study. No eligible patients refused to participate. The demographic characteristics of these patients are described in **Table 1**. The mean age was 42.3 years (range, 19-69 years), and 62% of the patients were female. Forty-six percent were white and 33% African American. Seventy-one percent had received at least some college education. Seventy percent were employed; however, 13.2% were disabled because of their vision. Sixty-one percent earned $30 000 or more in annual household income.

The clinical characteristics of this population are described in **Table 2**. Seventeen percent of the patients had anterior uveitis, 22% had intermediate uveitis, 34% had posterior uveitis, and 26% had panuveitis. Disease

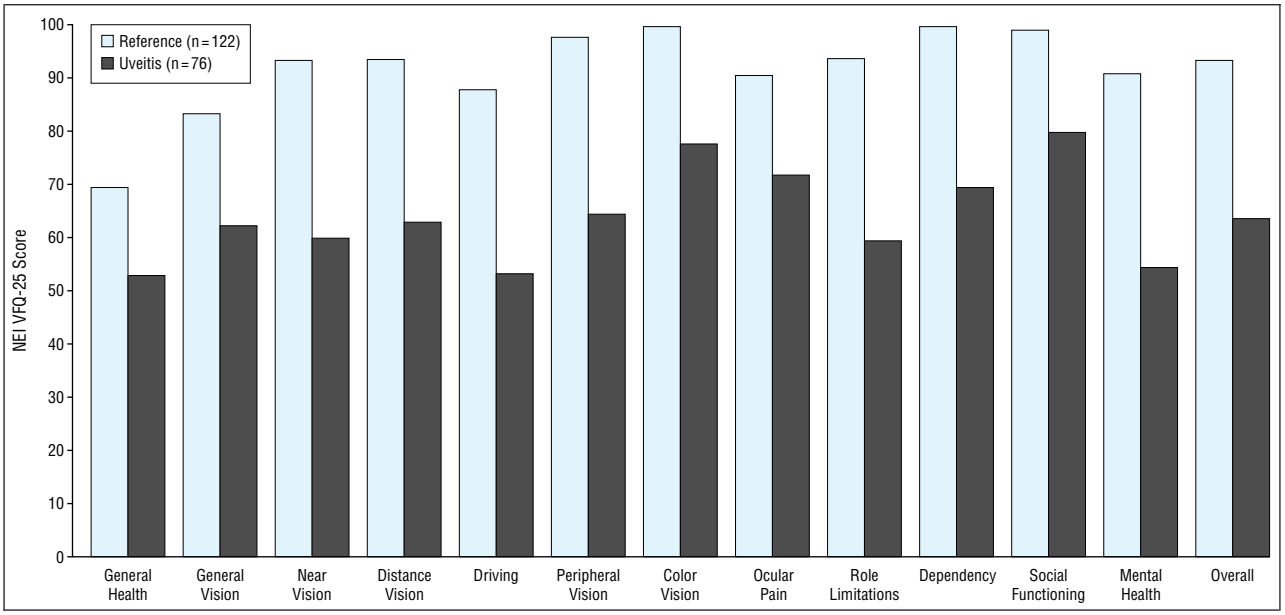


**Figure 1.** *National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) scores for patients with uveitis vs reference group, adjusted for age (all* P*<.001).*

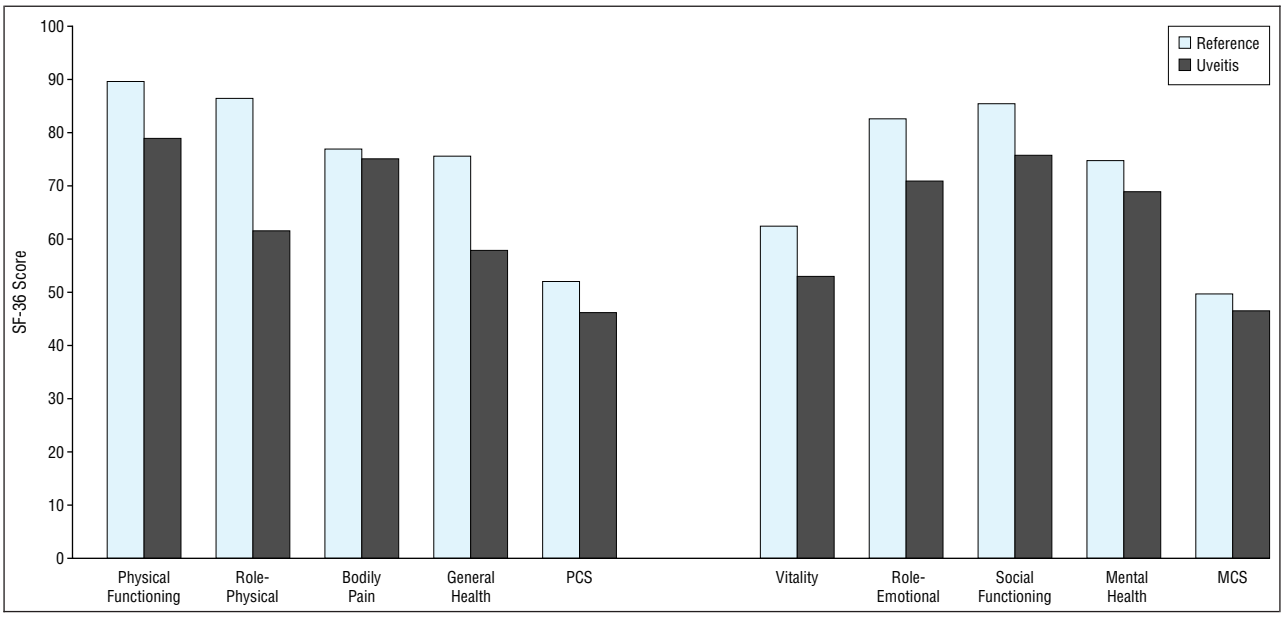


**Figure 2.** *Medical Outcomes Study 36-Item Short Form (SF-36) scores for patients with uveitis vs reference group (all* P*<.01 except bodily pain [*P*=.50]). PCS indicates physical component summary score; MCS, mental component summary score.*

was idiopathic in 26%; 17% had sarcoidosis, 9% had Vogt-Koyanagi-Harada disease, 7% had Behçet syndrome, and 8% had HLA-B27–associated disease (including Reiter disease and ankylosing spondylitis). Nearly all patients (99%) had chronic disease, and 92% had bilateral involvement. Thirty percent of patients were diagnosed as having active inflammation on their current examination. Twenty-nine percent had a systemic manifestation of their disease. Sixty-four percent had a notable ocular comorbidity, and 83% had a medical comorbidity. Seven percent were receiving no therapy for their uveitis; 86% received corticosteroid therapy (18% received topical corticosteroids alone) and 17% received cytotoxic agents or cyclosporine. The mean binocular walking-around visual acuity was 20/28 (range, hand motions to 20/20).

## GENERAL HEALTH STATUS AND VISUAL FUNCTIONING OF PATIENTS WITH UVEITIS COMPARED WITH NORMAL SUBJECTS

Visual functioning as measured by the NEI VFQ-25 overall score was markedly lower for patients with uveitis than for the reference group from the NEI VFQ-25 field test before and after adjusting for differences in age (**Figure 1**). This was also true for each of the subscale scores. All differences were highly statistically significant ($P<.001$).

General health status as measured by the SF-36 PCS (46.4 vs 52.2; $P<.001$) and MCS (46.6 vs 49.9; $P=.007$) scores was lower for patients with uveitis than for the age-matched US population norms (**Figure 2**). This was also true for each of the subscales with the exception of bodily

**Table 3. NEI VFQ-25 Scores***

| | General Health | General Vision | Near Vision | Distance Vision | Driving | Peripheral Vision | Color Vision | Ocular Pain | Role Limitations | Dependency | Social Functioning | Mental Health | Overall Composite Score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Laterality | | | | | | | | | | | | | |
| Bilateral (n = 70) | 52.5 | 62.3 | 60.5 | 62.1 | 52.9† | 65.9 | 79.6 | 72.0 | 58.4‡ | 69.6 | 78.3 | 51.7 | 63.3 |
| Unilateral (n = 6) | 66.7 | 76.7 | 75.0 | 76.4 | 82.5 | 62.5 | 79.2 | 70.8 | 83.3 | 80.6 | 91.7 | 68.8 | 76.2 |
| Location | | | | | | | | | | | | | |
| Anterior (n = 13) | 63.5 | 70.8 | 79.5 | 69.2 | 57.3 | 79.2 | 88.5 | 65.4 | 70.2 | 86.5 | 86.5 | 60.1 | 72.2 |
| Posterior/panuveitis (n = 46) | 46.2§ | 60.0 | 54.7† | 59.2 | 50.0 | 58.2§ | 72.8‡ | 73.6 | 55.7‡ | 64.5§ | 73.9 | 51.1 | 59.6‡ |
| Activity | | | | | | | | | | | | | |
| Active (n = 23) | 56.8 | 53.0† | 50.7§ | 54.0§ | 43.8‡ | 59.8 | 69.6§ | 66.8 | 52.2 | 61.6 | 67.4† | 39.7† | 54.3† |
| Inactive (n = 53) | 52.4 | 67.9 | 66.4 | 67.3 | 59.7 | 68.3 | 84.0 | 74.1 | 63.9 | 74.4 | 84.6 | 58.8 | 68.6 |
| Ocular comorbidity | | | | | | | | | | | | | |
| No (n = 25) | 62.0 | 75.2 | 72.0 | 71.8 | 65.1 | 77.0 | 84.0 | 73.0 | 68.5 | 79.0 | 88.5 | 60.8 | 72.5 |
| Yes (n = 51) | 49.5§ | 57.6† | 56.5§ | 59.1§ | 49.7‡ | 60.0§ | 77.5 | 71.3 | 56.4‡ | 66.3 | 74.8§ | 49.3‡ | 60.2§ |
| Optic nerve involvement | | | | | | | | | | | | | |
| Yes (n = 61) | 51.7 | 53.3§ | 54.4 | 53.1‡ | 37.5§ | 48.3† | 68.3‡ | 72.5 | 50.8 | 60.0 | 65.2§ | 41.3‡ | 54.0§ |
| No (n = 15) | 54.2 | 65.9 | 63.4 | 65.8 | 59.2 | 70.0 | 82.4 | 71.7 | 62.7 | 73.1 | 82.6 | 55.9 | 66.81 |
| Glaucoma | | | | | | | | | | | | | |
| Yes (n = 18) | 48.6 | 56.7 | 60.2 | 56.3 | 51.7 | 47.1† | 75.0 | 60.4§ | 58.3 | 61.6 | 71.5 | 47.2 | 57.8 |
| No (n = 58) | 55.3 | 65.5 | 62.1 | 65.4 | 56.0 | 71.1 | 81.0 | 75.4 | 61.0 | 73.3 | 81.8 | 54.8 | 66.3 |
| CME | | | | | | | | | | | | | |
| Yes (n = 17) | 56.3 | 58.8 | 52.9 | 57.1 | 55.9 | 63.2 | 77.9 | 72.8 | 54.4 | 65.7 | 7.9 | 47.4 | 59.9 |
| No (n = 59) | 53.0 | 64.7 | 64.1 | 65.0 | 54.8 | 66.4 | 80.1 | 71.6 | 62.1 | 71.9 | 79.7 | 54.7 | 65.5 |
| Surgery | | | | | | | | | | | | | |
| Yes (n = 28) | 50.0 | 59.3 | 60.1 | 60.9 | 47.1 | 56.3 | 75.0 | 71.0 | 58.9 | 66.4 | 72.7 | 49.1 | 60.6 |
| No (n = 48) | 55.9 | 65.8 | 62.5 | 64.7 | 59.9 | 71.3 | 82.3 | 72.4 | 61.2 | 72.9 | 83.1 | 55.3 | 66.4 |
| Systemic involvement | | | | | | | | | | | | | |
| Yes (n = 22) | 38.6† | 60.0 | 54.5 | 55.7‡ | 47.2 | 53.6§ | 72.7 | 69.9 | 48.3§ | 61.4 | 66.1§ | 51.1 | 56.9‡ |
| No (n = 54) | 59.9 | 64.8 | 64.5 | 66.4 | 57.8 | 70.4 | 82.4 | 72.7 | 65.3 | 74.2 | 84.5 | 53.8 | 67.3 |
| Treatment intensity | | | | | | | | | | | | | |
| No medications (n = 5) | 70.0 | 72.0 | 86.7 | 80.0 | 75.0 | 85.0 | 80.0 | 85.0 | 87.5 | 90.0 | 95.0 | 91.3 | 85.7 |
| Topical/periocular medications (n = 14) | 66.1 | 60.0 | 70.8 | 67.9 | 62.5 | 67.9 | 87.5 | 75.9 | 70.5 | 85.7 | 80.4 | 60.3 | 71.2 |
| Corticosteroids only (n = 39) | 48.1 | 64.6 | 59.6 | 64.6 | 54.9 | 63.8 | 80.1 | 68.6 | 57.7 | 67.3 | 79.3 | 47.0 | 61.3 |
| Cytotoxic drugs (n = 13) | 48.1 | 54.3 | 43.5§ | 46.1§ | 35.7 | 58.9 | 66.1 | 70.5 | 43.8§ | 49.4§ | 67.0§ | 41.1§ | 78.3§ |
| Medical comorbidity | | | | | | | | | | | | | |
| No (n = 13) | 75.0 | 66.2 | 75.0 | 73.4 | 65.4 | 80.8 | 92.3 | 75.0 | 67.3 | 85.9 | 87.5 | 48.6 | 72.0 |
| Yes (n = 63) | 49.2† | 62.9 | 58.9‡ | 61.2‡ | 52.7 | 62.5§ | 77.0§ | 71.2 | 58.9 | 67.3‡ | 77.6 | 54.0 | 62.7 |

**NEI VFQ-25 indicates National Eye Institute Visual Functioning Questionnaire; CME, cystoid macular edema.*
†P<.01.
‡P<.10.
§P<.05.

pain. All differences (other than bodily pain) were highly statistically significant ($P<.01$).

## GENERAL HEALTH STATUS AND VISUAL FUNCTIONING AMONG PATIENTS WITH UVEITIS

**Table 3** gives the NEI VFQ-25 scores. Patients with bilateral disease had significantly lower Driving scores and borderline significantly lower Role Limitation scores than patients with monocular disease.

Patients with posterior uveitis or panuveitis had significantly lower General Health, Near Vision, Peripheral Vision, and Dependency scores than patients with anterior uveitis. Patients with posterior or panuveitis also had borderline lower Color Vision, Role Limitation, and overall scores.

Patients with active disease had significantly lower General Vision, Near and Distance Vision, Color Vision, Social Functioning, Mental Health, and overall scores than patients with inactive disease. Patients with active disease also had borderline lower Driving scores.

Patients with ocular comorbidity had significantly lower General Health, General Vision, Near and Distance Vision, Peripheral Vision, Social Functioning, and overall scores than patients without ocular comorbidity. They also had borderline lower Driving, Role Limitation, and Mental Health scores. As expected, patients with glaucoma had lower Peripheral Vision scores and lower Pain scores (indicating more pain).

**Table 4. Final Stepwise Models: NEI VFQ-25 Item Composite Score***

| NEI VFQ-25 Variable | Excluding SF-36 Summary Scores | | Including SF-36 Summary Scores | |
|---|---|---|---|---|
| | Parameter | *P* | Parameter | *P* |
| Poorer binocular visual acuity | −17.8 | .002 | −18.7 | <.001 |
| Active disease | −11.6 | .004 | −7.1 | .04 |
| More intensive treatment | −7.2 | .001 | −4.8 | .01 |
| No. of medical comorbidities | −3.6 | .01 | NA | NA |
| Employed | 13.6 | <.001 | 8.8 | .01 |
| PCS score | NA | NA | 0.7 | <.001 |
| MCS score | NA | NA | 0.5 | <.001 |
| $R^2$ | 0.60 | NA | 0.72 | NA |

**NEI VFQ-25 indicates National Eye Institute Visual Functioning Questionnaire; SF-36, Medical Outcomes Study 36-Item Short Form; PCS, physical component summary; MCS, mental component summary; and NA, not applicable. For ordinal or numeric data, a positive parameter indicates that as the value of the independent factor increases, the value of the dependent factor increases by the amount of the parameter. For dichotomous data (eg, present or absent), the value of the dependent value increases by the amount of the parameter if the independent factor is present. A negative parameter indicates the opposite. For visual acuity, the dependent variable changes by the amount of the parameter for each 1-point change in logMAR acuity, which corresponds to a 10-fold change in the visual angle (eg, 20/20 to 20/200). For medical and ocular comorbidity, the dependent variable changes with a change in the number of comorbidities. For PCS, MCS, and NEI VFQ-25 composite scores, the dependent variable changes by the amount of the parameter for each single point change in the dependent variable. The $R^2$ is the proportion of the variation in the dependent factor that is explained by all the independent variables in the model.*

Patients with systemic involvement had significantly lower General Health, Peripheral Vision, Role Limitation, and Social Functioning scores than patients with only ocular involvement. Distance Vision scores and overall scores were also lower in patients with systemic involvement, although the differences did not reach statistical significance.

Visual functioning scores decreased as the intensity of immunosuppressive treatment increased. There were statistically significant differences in Near and Distance Vision, Role Limitation, Dependency, Social Functioning, Mental Health, and overall scores.

Patients with medical comorbidity had significantly lower General Health, Peripheral Vision, and Color Vision scores. There was a trend toward lower Near and Distance Vision and Dependency scores.

In multivariable analysis, lower NEI VFQ-25 item composite scores were associated with poorer binocular visual acuity, disease activity, increasing intensity of treatment, number of medical comorbidities, and employment status (not currently employed). This model accounted for 60% of the variance in the NEI VFQ-25 item composite scores ($R^2$) (**Table 4**). When PCS and MCS scores were added to the model, both were statistically significant, and the $R^2$ increased to 72%. The number of medical comorbidities was no longer significant.

**Table 5** gives the SF-36 scores. There were no significant differences in SF-36 scores between patients with monocular and binocular involvement. Patients with posterior or panuveitis had significantly lower bodily pain (more pain) and general health scores than patients with anterior or intermediate disease. There was also a trend toward lower PCS scores in these patients with more posterior ocular disease.

Patients with active disease had significantly lower role-physical scores. They also had lower well-being and MCS scores. There were borderline lower role-emotional scores among patients with active disease. There were no differences in SF-36 scores between patients with and without ocular comorbidity.

As expected, patients with associated systemic disease had lower HR-QOL measures. Patients with systemic involvement had significantly lower physical functioning, bodily pain, general health, and PCS scores.

There were statistically significant differences in General Health scores with increasing intensity of treatment. Patients with medical comorbidity reported significantly lower General Health and PCS scores.

In multivariable analysis, lower PCS scores were associated with more intensive treatment, greater number of medical comorbidities, and employment status (disabled). Unexpectedly, lower scores were associated with fewer ocular comorbidities. This model explained 50% of the variance in PCS scores (**Table 6**). The NEI VFQ-25 score was a significant predictor when added to the model, and medical and ocular comorbidity remained significant. This model explained 57% of the variance.

Lower MCS scores were associated only with disease activity and explained only 8% of the variance (**Table 7**). The NEI VFQ-25 score was a significant predictor when added to the model. A model that included only medical comorbidity and NEI VFQ-25 scores explained 24% of the variance in MCS scores.

## COMMENT

This study confirms our clinical observations that uveitis has a significant impact on both general health status and visual functioning. Both visual functioning and general health status were markedly lower in patients with uveitis than among reference groups. The overall NEI VFQ-25 scores among patients with uveitis was actually lower than among patients with age-related macular degeneration enrolled in the NEI VFQ-25 Field Test[16] despite the fact that the patients with uveitis were younger and had better mean visual acuity. This finding was the result of lower Peripheral Vision, Color Vision, Ocular Pain, Limitation, Dependency, and Mental Health scores among patients with uveitis, indicating that uveitis has a much more pervasive impact on VR-QOL than does age-related macular degeneration. Among the 6 conditions included in the Field Test (age-related macular degeneration, diabetic retinopathy, glaucoma, cataract, cytomegalovirus infection, and poor vision), only patients with poor vision had lower NEI VFQ-25 scores than did those with uveitis. It should be noted, however, that neither this study nor the NEI VFQ-25 Field Test was population based, and the enrolled patients may not be representative of all patients with these conditions. Therefore, these results may not be directly comparable.

With respect to general health status, all subscale scores, with the exception of that for bodily pain, were lower in patients with uveitis than in an age-matched reference

**Table 5. SF-36 Scores***

| | Physical Functioning | Role-Physical | Bodily Pain | General Health | PCS | Vitality | Role-Emotional | Social Functioning | Mental Health | MCS |
|---|---|---|---|---|---|---|---|---|---|---|
| Laterality | | | | | | | | | | |
| Bilateral (n = 70) | 78.6 | 60.7 | 74.8 | 57.6 | 46.0 | 52.4 | 75.0 | 71.9 | 69.2 | 46.7 |
| Unilateral (n = 6) | 85.8 | 70.8 | 80.5 | 60.0 | 50.6 | 60.0 | 87.7 | 61.2 | 66.0 | 45.5 |
| Location | | | | | | | | | | |
| Anterior (n = 13) | 86.9 | 71.2 | 84.8 | 67.3 | 50.1 | 58.5 | 81.9 | 84.6 | 72.3 | 49.0 |
| Posterior/panuveitis (n = 36) | 76.1 | 57.1 | 71.1† | 50.5‡ | 44.2§ | 51.6 | 76.8 | 64.5 | 69.2 | 46.5 |
| Activity | | | | | | | | | | |
| Active (n = 23) | 76.3 | 45.7‡ | 72.1 | 57.2 | 45.7‡ | 47.0 | 68.7§ | 57.9 | 58.3† | 41.5‡ |
| Inactive (n = 53) | 80.4 | 68.4 | 76.6 | 58.0 | 46.6 | 55.5 | 79.2 | 76.8 | 73.6 | 48.9 |
| Ocular comorbidity | | | | | | | | | | |
| No (n = 25) | 80.2 | 52.0 | 75.6 | 57.5 | 44.7 | 54.2 | 76.7 | 76.0 | 73.8 | 49.0 |
| Yes (n = 51) | 78.6 | 66.2 | 75.1 | 57.9 | 47.2 | 52.4 | 75.6 | 68.6 | 66.6 | 45.4 |
| Optic nerve involvement | | | | | | | | | | |
| Yes (n = 61) | 83.0 | 61.7 | 79.3 | 56.0 | 49.0 | 54.7 | 78.6 | 62.2 | 60.3 | 43.1 |
| No (n = 15) | 78.2 | 61.5 | 74.2 | 58.2 | 45.7 | 52.5 | 75.3 | 73.2 | 21.7 | 47.5 |
| Glaucoma | | | | | | | | | | |
| Yes (n = 18) | 75.6 | 63.9 | 75.3 | 55.8 | 46.8 | 50.6 | 50.6 | 64.8 | 62.9 | 43.6 |
| No (n = 58) | 80.3 | 60.8 | 75.2 | 58.4 | 46.2 | 53.7 | 53.7 | 73.0 | 70.8 | 47.6 |
| CME | | | | | | | | | | |
| Yes (n = 17) | 85.6 | 75.0 | 76.9 | 63.4 | 50.6 | 49.7 | 72.9 | 68.6 | 25.1 | 43.0 |
| No (n = 59) | 77.3 | 57.6 | 74.8 | 56.2 | 45.1 | 53.9 | 76.9 | 71.8 | 70.4 | 47.7 |
| Surgery | | | | | | | | | | |
| Yes (n = 28) | 80.4 | 70.5 | 78.0 | 55.2 | 48.3 | 54.8 | 76.9 | 67.9 | 64.8 | 44.8 |
| No (n = 48) | 78.4 | 56.3 | 73.6 | 59.3 | 45.2 | 51.9 | 75.4 | 72.9 | 71.4 | 47.7 |
| Systemic involvement | | | | | | | | | | |
| Yes (n = 22) | 65.0† | 53.4 | 64.0† | 45.2† | 40.2† | 46.4 | 71.1 | 65.2 | 68.0 | 46.5 |
| No (n = 54) | 84.9 | 64.8 | 79.8 | 62.9 | 48.9 | 55.6 | 78.0 | 73.5 | 69.4 | 46.7 |
| Treatment intensity | | | | | | | | | | |
| No medications (n = 5) | 95.0 | 85.0 | 92.0 | 72.0 | 54.5 | 67.0 | 73.2 | 80.2 | 80.0 | 48.7 |
| Topical/periocular medications (n = 14) | 91.8 | 83.9 | 87.0 | 71.1 | 52.4 | 58.6 | 88.1 | 85.9 | 76.6 | 50.1 |
| Corticosteroids only (n = 39) | 72.7 | 51.3 | 70.6 | 53.2 | 43.6 | 47.6 | 65.8 | 71.3 | 65.4 | 45.0 |
| Cytotoxic drugs (n = 13) | 79.3 | 57.1 | 69.4 | 50.2‡ | 45.2 | 51.4 | 64.3 | 74.3 | 64.3 | 44.5 |
| Medical comorbidity | | | | | | | | | | |
| No (n = 13) | 88.1 | 65.4 | 84.2 | 72.9 | 53.1 | 48.8 | 73.2 | 58.9 | 61.6 | 40.7 |
| Yes (n = 63) | 77.3 | 60.7 | 73.4 | 54.7† | 45.0‡ | 53.8 | 76.6 | 73.6 | 70.5 | 47.8 |

**SF-36 indicates Medical Outcomes Study 36-Item Short Form; PCS, physical component summary; MCS, mental component summary; and CME, cystoid macular edema.*

†P<.01.

‡P<.05.

§P<.10.

**Table 6. Final Stepwise Models: Physical Component Summary Scores***

| | Excluding NEI VFQ-25 Composite Scores | | Including NEI VFQ-25 Composite Scores | |
|---|---|---|---|---|
| PCS Variable | Parameter | *P* | Parameter | *P* |
| More intensive treatment | −3.0 | .02 | NA | NA |
| No. of medical comorbidities | −4.0 | <.001 | −3.1 | <.001 |
| No. of ocular comorbidities | 3.2 | <.001 | 3.5 | <.001 |
| Employed | 5.3 | .02 | NA | NA |
| NEI VFQ-25 | NA | NA | 0.2 | <.001 |
| $R^2$ | 0.50 | NA | 0.57 | NA |

**See the footnote to Table 4 for explanation and abbreviations.*

**Table 7. Final Stepwise Models: Mental Component Summary Scores***

| | Excluding NEI VFQ-25 Composite Scores | | Including NEI VFQ-25 Composite Scores | |
|---|---|---|---|---|
| MCS Variable | Parameter | *P* | Parameter | *P* |
| Active disease | −7.6 | .02 | NA | NA |
| No. of medical comorbidities | NA | NA | 2.4 | .04 |
| NEI VFQ-25 | NA | NA | 0.3 | <.001 |
| $R^2$ | 0.08 | NA | 0.24 | NA |

**See the footnote to Table 4 for explanation and abbreviations.*

group drawn from the general US population. The summary scores are standardized to the US population such that the general population has a mean value of 50 and an SD of 10. On the basis of published normative tables, the reduction in the PCS scores seen in this uveitis population places these patients in the 26th percentile for the gen-

eral US population. For patients with uveitis who have systemic involvement, these scores correspond to only the 17th percentile for the general population. Compared with the general population, this level of functioning is associated with a 32% increase in the probability of dying in the next 5 years.[12] Mental health is also significantly affected, with the MCS scores for this sample corresponding to only the 31st percentile for the general population.[12]

Among patients with uveitis, those with bilateral disease, posterior uveitis or panuveitis, systemic involvement, active disease, and ocular and medical comorbidity all had significant reduction in some aspects of visual functioning. In multivariable regression analysis, poorer visual acuity, binocular involvement, more intensive therapy, being unemployed, and lower physical and mental health status were all associated with lower overall visual functioning scores and explained a striking 74% of the variance in visual functioning scores.

As expected, posterior uveitis or panuveitis, systemic disease, and medical comorbidity were all associated with decreased physical functioning. Interestingly, active disease was associated with decreases in mental rather than physical scores, indicating the impact that active disease and its treatment can have on patients' emotional well-being. In multivariable analysis, more medical comorbidity, less ocular comorbidity, and lower visual functioning scores were all associated with poorer physical health status and explained 57% of the variance in PCS scores. Less medical comorbidity and poorer visual functioning were associated with poorer mental status and explained 24% of the variance.

Thus, while there was an association between visual function and general health status in this population, these 2 measures are complementary, since unexplained variance remained in the full models of both NEI VFQ-25 and SF-36 summary scores indicating that each measure provides distinct information.

This study has limitations in that it was conducted on patients who had been referred to the National Institutes of Health; these patients may not be representative of patients with uveitis elsewhere. In addition to being volunteers in clinical trials, these patients are likely to have more severe or refractory disease, and consequently their disease may have more negatively affected their QOL. Moreover, patients with uveitis enrolled in this study had a higher socioeconomic status than do patients in the general population.

We did not enroll a concurrent control group. This is in part because "normal" subjects are not routinely seen at the National Institutes of Health. Another reason is that well-established normative data have been published for the SF-36 and, to a lesser extent, the NEI VFQ-25 specifically to permit these types of comparisons. Although differences in the way in which "normal control subjects" were selected could have influenced our results, it seems unlikely to have caused the large difference measured in this study.

We performed univariate comparisons for each of the subscales for the SF-36 and NEI VFQ-25 but did not adjust the *P* value for significance. This was because these comparisons were designated a priori. However, in the cases of intensity of treatment where multiple subgroups existed, we did use procedures to maintain the overall rejection level for those multiple comparisons at $P<.05$. Moreover, we limited our regression analyses to the summary scores only.

It should be pointed out that this modest sample size limits the power to detect significant differences when subgroup analyses are performed. This may be particularly relevant with "borderline" *P* values when the magnitude of the difference is large but the sample size is small, as was often the case in these subgroup analyses. It is possible that many of these differences would have achieved greater statistical significance if these subgroups had had larger sample sizes. This sample size could also have led to unstable regression models when many potential predictors were analyzed. However, we did not detect any instability in our modeling.

In summary, these results confirm that uveitis in this population is associated with significant reductions in both vision and HR-QOL compared with controls. Moreover, more severe uveitis is associated with an increasingly negative impact on vision and HR-QOL.

Although visual function and general health status were correlated, the information they provide is complementary and should be assessed independently when a disease such as uveitis, which can have prominent systemic features, is evaluated. These results also suggest that the NEI VFQ-25 is a valid measure of the impact of uveitis on visual functioning.

We believe these results can now be used to assist patients and others to understand the impact of uveitis on QOL. They may also be used to design clinical trials in uveitis that use QOL as a treatment end point.

*Accepted for publication December 1, 2000.*

*Corresponding author and reprints: Rhett M. Schiffman, MD, MS, MHSA, Eye Care Services K-10, Henry Ford Health System, 2799 W Grand Blvd, Detroit, MI 48202 (e-mail: rmschfmn@aol.com).*

## REFERENCES

1. *Interim Report of the National Advisory Eye Council, Support for Vision Research*. Bethesda, Md: US Dept of Health, Education, and Welfare, National Institutes of Health; 1976:20-22.
2. Perkins ES, Folk J. Uveitis in London and Iowa. *Ophthalmologica*. 1984;189:36-40.
3. Henderly DE, Genstler AJ, Smith RE, Rao NA. Changing patterns of uveitis. *Am J Ophthalmol*. 1987;103:131-136.
4. Ware JE Jr, Snow KK, Kosinski M, Gandek B. *SF-36 Health Survey Manual and Interpretation Guide*. Boston, Mass: Health Institute, New England Medical Center; 1993.
5. Stewart AL, Greenfield S, Hays RD, et al. Functional status and well-being of patients with chronic conditions: results from the Medical Outcomes Study. *JAMA*. 1989;262:907-913.
6. Mangione CM, Phillips RS, Lawrence MG, Seddon JM, Orav EJ, Goldman L. Improved visual function and attenuation of declines in health-related quality of life after cataract extraction. *Arch Ophthalmol*. 1994;112:1419-1425.
7. Parrish RK. Visual impairment, visual functioning, and quality of life assessments in patients with glaucoma. *Trans Am Ophthalmol Soc*. 1996;94:919-1028.
8. Mangione CM, Lee PP, Pitts J, Gutierrez P, Berry S, Hays RD. Psychometric properties of the National Eye Institute Visual Function Questionnaire (NEI-VFQ). *Arch Ophthalmol*. 1998;116:1496-1504.
9. Lee PP, Whitcup SM, Hays RD, Spritzer K, Javitt J. The relationship between visual acuity and functioning and well-being among diabetics. *Qual Life Res*. 1995;4:319-323.

10. Musch DC, Farjo AA, Meyer RF, Waldo MN, Janz NK. Assessment of health-related quality of life after corneal transplantation. *Am J Ophthalmol*. 1997;124:1-8.
11. COMS Quality of Life Study Group. Quality of life assessment in the Collaborative Ocular Melanoma Study: design and methods: COMS-QOLS report No. 1. *Ophthalmic Epidemiol*. 1999;6:5-17.
12. Ware JE, Kosinski M, Keller S. *SF-36 Physical and Mental Health Summary Scales: A User Manual*. Boston, Mass: Medical Outcomes Trust; December 1994.
13. Mangione CM, Phillips RS, Seddon JM, et al. Development of the "Activities of Daily Vision Scale." *Med Care*. 1992;30:1111-1126.
14. Steinberg EP, Tielsch JM, Schein OD, et al. The VF-14: an index of functional impairment in patients with cataract. *Arch Ophthalmol*. 1994;112:630-638.
15. Linder M, Chang TS, Scott IU, et al. Validity of the visual function index (VF-14) in patients with retinal disease. *Arch Ophthalmol*. 1999;117:1611-1616.
16. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD, for the National Eye Institute Visual Function Questionnaire Field Test Investigators. Development of the 25-Item National Eye Institute Visual Function Questionnaire. *Arch Ophthalmol*. In press.
17. Ferris FL, Kassoff A, Bresnick GH, et al. New visual acuity charts for clinical research. *Am J Ophthalmol*. 1982;94:91-96.

## *ARCHIVES Web Quiz Winner*

Congratulations to the winner of our February quiz, Mallika Goyal, MD, Retina Service, Apollo Eye Hospital, Hyderabad, India. The correct answer to our February challenge was leukemia. For a complete discussion of this case, see the Clinicopathologic Reports section in the March ARCHIVES (Esmaeli B, Medeiros LJ, Myers J, Champlin R, Singh S, Ginsberg L. Orbital mass secondary to precursor T-cell acute lymphoblastic leukemia: a rare presentation. *Arch Ophthalmol*. 2001;119:443-446).

Be sure to visit the *Archives of Ophthalmology* World Wide Web site (http://www.archophthalmol.com) and try your hand at our Clinical Challenge Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of the book *One Hundred Years of* JAMA *Landmark Articles*.

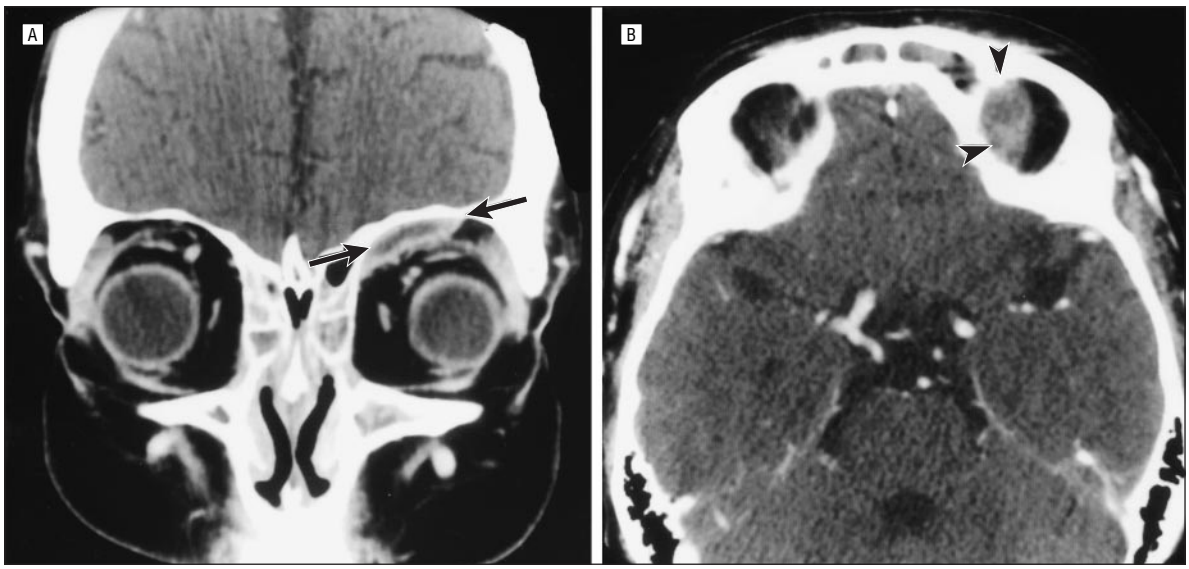


**Figure 1.** *Enhanced computed tomography images reveal the left superior medial orbital mass. A, Coronal computed tomography image shows the left extraconal, marginally enhancing mass (arrows). B, An axial computed tomography image also demonstrates the superior orbital mass (arrowheads).*