that environmental factors such as smoking contribute to risk of vision loss and CNV in AMD.[3] Although there has been progress in understanding risk factors for CNV in AMD, there is a relative paucity of data for CNV owing to other causes such as OHS.

The OHS-CNV patients were more likely to have a history of smoking than the OHS-control subjects. Smoking is a reported risk factor for a number of conditions, including the onset of exudative AMD from nonexudative AMD, and the development of polypoidal choroidal vasculopathy.[3,4] A recent study from the same region as this study also reported the odds for CNV associated with OHS are 3 times higher in smokers.[5] Our data also yielded a significantly higher incidence of cigarette smoking in patients with OHS-CNV versus OHS-control patients. This finding holds clinical value, in that counseling OHS patients without CNV on smoking cessation may decrease their risk of developing CNV.

This study has limitations. First, the number of subjects enrolled in this study is small compared with the larger sample sizes utilized in assessing these genes in AMD.[1,5] However, OHS is less common than AMD and enrolling asymptomatic subjects without other ocular disease to prompt an eye examination is challenging. This introduces sample bias in that the control subjects presented to the retinal service for other concerns (floaters, posterior vitreous detachment, retinal tear/detachment, etc). In addition, there was a significant difference in age between the OHS-CNV and OHS-control groups, with the control group being older. A recent study found an increase risk associated with age and CNV in OHS patients, which was not reflected in this study.[5]

In conclusion, this study did not show a correlation between ARMS2, C3, MT-NDH2, and CFH alleles in the development of CNV associated with OHS. There was a significantly higher incidence of cigarette smoking in patients with OHS-CNV versus OHS-control patients. This study suggests that ARMS2, C3, MT-NDH2, and CFH may not play a role in CNV in OHS. Further studies are needed to investigate factors and the pathogenesis of CNV in OHS.

Martin F. Wilkes, MD[1,2]
Daniel M. Miller, MD, PhD[1,2]
Matthew D. Mitchell[1]
Brent Zanke, MD[3]
Michael R. Petersen, MD, PhD[1]
Robert A. Sisk, MD[1,2]
Christopher D. Riemann, MD[1,2]
Robert E. Foster, MD[1]

[1]*Cincinnati Eye Institute, Cincinnati, Ohio;* [2]*University of Cincinnati Department of Ophthalmology, Cincinnati, Ohio;* [3]*ArcticDx, Bonita Springs, Florida*

Financial Disclosure(s): Supported by a grant from the Cincinnati Eye Institute Foundation, Cincinnati, Ohio. Supported by a grant from Macula Risk. Brent Zanke — Medical Director — Arctic Dx.

References

1. Seddon JM, Reynolds R, Maller J, et al. Prediction model for prevalence and incidence of advanced age-related macular degeneration based on genetic, demographic, and environmental variables. Invest Ophthalmol Vis Sci 2009;50:2044–53.
2. Grossniklaus HE, Green WR. Choroidal neovascularization. Am J Ophthalmol 2004;137:496–503.
3. Dhubhghaill SS, Cahill MT, Campbell M, et al. The pathophysiology of cigarette smoking and age-related macular degeneration. Adv Exp Med Biol 2010;664:437–46.
4. Cackett P, Yeo I, Cheung CM, et al. Relationship of smoking and cardiovascular risk factors with polypoidal choroidal vasculopathy and age-related macular degeneration in Chinese persons. Ophthalmology 2011;118:846–52.
5. Chheda LV, Ferketich AK, Carroll CP, et al. Smoking as a risk factor for choroidal neovascularization secondary to presumed ocular histoplasmosis syndrome. Ophthalmology 2012;119:333–8.

Development and Validation of Quality-of-Life Questionnaires for Birdshot Chorioretinopathy

Birdshot chorioretinopathy (BCR) is a rare form of chronic posterior uveitis, usually requiring long-term, systemic immunosuppression.[1] The severe impact of the disease on acuity, visual field, color discrimination, and electrodiagnostics is well-documented,[1,2] but studies on quality of life (QoL) have been limited. Furthermore, existing QoL tools fail to capture the unique and wide range of symptoms associated with BCR and BCR medications.

Methods

Ethical approval was granted by the Royal Free London Hospital. All procedures, such as prior informed consent, were conducted in accordance with the Declaration of Helsinki.

Item development was via face-to-face meetings of the Item Generation Group (composed of 2 patients with BCR, a consultant ophthalmologist, and a psychologist). From this bank, 3 questionnaires were derived: the Birdshot Disease & Medication Symptoms Questionnaire (BD&MSQ) with 43 items, the QoL impact of BCR (QoL BCR) with 25 items, and the QoL impact of BCR medication (QoL Meds) with 25 items. The content of the 2 QoL questionnaires was similar, except that the QoL BCR focused on the daily impact of experiences attributable to the disease and the QoL Meds focused on the daily impact of experiences attributable to medication. Four-point Likert scales were used, with lower scores indicating worse QoL. The 3 questionnaires were then administered to a second group—8 volunteers with BCR and 1 person with no eyesight problems—as an on-line survey. Participants and Item Generation Group members were selected in accordance with the usual standards for survey methodology.[3]

A factor analysis of the questionnaires was conducted to refine their structure. The thresholds for acceptability were: Kaiser-Meyer-Olkin ≥ 0.6; Cronbach's $\alpha \geq 0.7$, and the factor loading threshold of >0.6.[4] All statistical analyses were done using SPSS 21 (IBM Corp, Armonk, NY).

Members of BCR support groups and a community control group were invited by email to participate in an online questionnaire.

Results

Out of 292 support group members with BCR, 152 responded, a response rate of 52%. Seventy-three percent (111 of 152) were women. The age range was 29 to 76 years old, with a mean (± SD) of 53.12±9.63 SD.

Of the 33 healthy community controls, it was possible to closely match 18 of them with the BCR group for age and sex. The matched controls had healthy eyesight apart from corrected refractive error.

In the development of the BD&MSQ, after incomplete responses were eliminated, there were 141 BCR participants. Factor analysis found 21 items forming 8 factors, 2 factors representing a Birdshot disease symptoms domain, and 6 representing a medication symptoms domain. Together, these accounted for 57.75% of the variance in scoring after extraction.

In the development of the QoL BCR, after incomplete responses were eliminated, there were 150 participants. Factor analysis revealed 20 items forming four factors, accounting for 71.98% of the total variance.

In the development of the QoL Meds, after incomplete responses were eliminated, there were 126 participants. (This number is lower than the other 2 questionnaires because fewer participants reported medication use). Three factors were found, consisting of 12 items, accounting for 70.1% of the total variance.

For all 3 questionnaires, the thresholds for acceptability for Kaiser-Meyer-Olkin, Cronbach's α, and factor loadings were met or exceeded. The subscales for the 3 questionnaires that resulted from the factor analyses are shown in Table 1 (available at www.aaojournal.org).

Construct validity was assessed by comparing the BCR group and control group using Wilcoxon's tests. Table 2 (available at www.aaojournal.org) shows that the BCR group scored significantly lower than controls on the BD&MSQ and QoL BCR scales and subscales, at a minimum $P < 0.01$. The profile of non-BCR medication was similar in both groups. Figure 1 (available at www.aaojournal.org) shows box-and-whisker plots for the total scores for the 2 scales. (Comparison was not possible for the QoL Meds because controls did not take BCR medication).

Construct validity was further assessed by comparing outcomes in BCR patients taking different amounts of prednisolone daily. Using analysis of covariance to control for any effect of the duration of time since diagnosis, patients with BCR taking >10 mg of prednisolone daily had significantly worse BD&MSQ ($P < 0.01$) and QoL BCR ($P < 0.05$), and non-significantly worse QoL Meds scores, compared with patients with BCR taking a lower dose or no dose of prednisolone daily.

Concurrent validity was also assessed. For the BCR participants, there was a strong negative correlation between the Visual Function Questionnaire Utility Index health state classification[5] and each of the new measures at a minimum of $r = -0.546$, $P < 0.000001$, indicating acceptable concurrent validity.

Discussion

In this study, we describe the development of 3 novel patient-reported outcome measures (PROMs) for BCR, directed toward capturing (a) key symptoms of BCR and symptoms of medication for BCR (BD&MSQ), (b) QoL (QoL BCR), and (c) the impact of BCR medication on QoL (QoL Meds), in this rare but debilitating condition. In addition to providing the first disease-specific PROMs for use in BCR, this study provides an example of how PROMs can be developed for even rare conditions.

These new instruments (available from the authors) may be of value in clinical trials for this condition, with a view to assessing change in symptoms and QoL arising from either disease or medication. When using the BD&MSQ, we suggest that the 2 domains—disease symptoms and medication symptoms—be scored separately, because each provide important independent information. The medians shown in Table 2 (available at www.aaojournal.org) for each domain and subscale can act as a guide to the severity of QoL problems at baseline. For example, a BCR patient who scores an average of 2.67 on the Birdshot disease domain of the BD&MSQ can be considered to be experiencing a typical level of QoL difficulty for BCR patients. Validity and reliability measures indicate that these tools have excellent psychometric properties and so can be used with confidence for patient reporting of symptoms and QoL in BCR.

John A. Barry, PhD[1]
Annie Folkard, BA[2]
Alastair K. Denniston, FRCOphth, PhD[3]
Eileen Moran, MSc[4]
William Ayliffe, FRCS, PhD[5]

[1]*University College London, Medical School, Royal Free Hospital, London, UK;* [2]*Birdshot Uveitis Society, Wimbledon, London, UK;* [3]*Queen Elizabeth Hospital Birmingham, Birmingham, UK;* [4]*Department of Neurology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania;* [5]*Gresham College, Barnard's Inn Hall, Holburn, London, UK*

References

1. Rothova A, Berendschot TT, Probst K, et al. Birdshot chorioretinopathy: long-term manifestations and visual prognosis. Ophthalmology 2004;111:954–9.
2. Holland GN, Shah KH, Monnet D, et al. Longitudinal cohort study of patients with birdshot chorioretinopathy II: color vision at baseline. Am J Ophthalmol 2006;142:1013–8.
3. De Vaus DA. Surveys in Social Research. 5th ed. London: Allen & Unwin; 2002:94–119.
4. Tabachnick BG, Fidell LS. Using Multivariate Statistics. Allyn and Bacon; 2001:619–46.
5. Kowalski JW, Rentz AM, Walt JG, et al. Rasch analysis in the development of a simplified version of the national eye institute visual-function questionnaire-25 for utility estimation. Qual Life Res 2012;21:323–34.

Adult Ophthalmology Inpatient Consults at a Tertiary Care Teaching Hospital

Ophthalmology consultation is commonly requested for inpatients in a tertiary hospital,[1–4] and there is often lack of familiarity with ocular pathology among other medical professionals.[3,5] This study was designed to identify the characteristics of inpatient consultations performed at an adult tertiary care hospital and recommend guidelines for developing an ophthalmology consult service and resident consult curriculum.

Table 1. Items for the final versions of the Birdshot Disease & Medication Symptoms Questionnaire (BD&MSQ), QoL impact of BCR (QoL BCR), and QoL impact of BCR medication (QoL Meds).

Subscale	BD&MSQ	Subscale	QoL BCR	Subscale	QoL Meds
Lights	Fluttering lights	Mood and relationships	Anger	Mood and relationships	Unreasonable behavior
	Flashing lights		Depression		Personal relationships
Vision	Simple repeat pattern		Irritability		Being a good family member
	Loss of night vision		Ability to socialize		Anger
	Poor light-dark adapt		Tearfulness		Irritability
	Loss of color		Frustration	Vision	Using a computer
	Lack of contrast		Anxiety		Reading
Skin	Skin lesions		Personal relationships		Driving
	Skin discoloration		Professional and work relationships		Watching TV
	Lumps under skin		Ability to focus	Low mood	Depression
					Anxiety
Body pain	Painful muscles	Daily activities	Watching TV		Tearfulness
	Pain in legs		Using a computer		
	Aching joints		Reading		
			Working		
Breathless &	Shaking				
Shaky	Breathing difficulty	Unhappy Families	Feeling violent		
Mood	Impending doom		Unreasonable behavior		
	Depression		Being a good family member		
Sleep	Disturbed sleep				
	Constantly tired	Feeling unwell	Nausea		
Hair loss	Loss of eyebrows		Headache		
	Loss of hair		Unwell		
			Over-consuming alcohol		

Table 2. Differences between the Groups of 18 Birdshot Chorioretinopathy (BCR) and Healthy Controls Matched for Age and Sex, for Birdshot Disease & Medication Symptoms Questionnaire (BD&MSQ) and QoL Impact of BCR (QoL BCR) Scores

Outcome Measure	Group	Median	Interquartile Range (Range)	Wilcoxon's Z
BD&MSQ vision	BCR	2.67	1.50 (1.1–3.8)	−3.623***
	Control	4.00	0.33 (2.8–4.0)	
BD&MSQ lights	BCR	2.67	1.00 (1.0–3.7)	−3.735***
	Control	4.00	0.00 (3.7–4.0)	
BD&MSQ mood	BCR	3.00	1.50 (1.0–4.0)	−3.091**
	Control	4.00	0.50 (2.5–4.0)	
BD&MSQ body pain	BCR	2.67	1.00 (1.0–4.0)	−2.642**
	Control	4.00	0.67 (2.3–4.0)	
BD&MSQ hair loss	BCR	3.00	1.50 (1.5–4.0)	−3.015**
	Control	4.00	0.00 (2.0–4.0)	
BD&MSQ skin	BCR	3.00	1.33 (2.0–4.0)	−3.226**
	Control	4.00	0.00 (3.3–4.0)	
BD&MSQ sleep	BCR	2.00	1.50 (1.0–4.0)	−2.166*
	Control	3.00	2.00 (1.0–4.0)	
BD&MSQ total score	BCR	2.76	0.56 (1.9–3.9)	−3.363***
	Control	3.76	0.48 (3.29–4.0)	
QoL BCR mood and relationships	BCR	2.40	1.30 (1.7–4.0)	−3.416***
	Control	3.90	0.10 (2.8–4.0)	
QoL BCR daily activities	BCR	2.50	1.75 (1.0–4.0)	−3.250**
	Control	3.75	0.50 (2.5–4.0)	
QoL BCR unhappy families	BCR	3.67	0.67 (2.3–4.0)	−2.966**
	Control	4.00	0.00 (4.0–4.0)	
QoL BCR feeling unwell	BCR	3.25	1.50 (2.0–4.0)	−3.300***
	Control	4.00	0.00 (3.8–4.0)	
QoL BCR total score	BCR	2.93	0.95 (2.2–4.0)	−3.461***
	Control	3.91	0.18 (3.3–4.0)	

*$P < 0.05$;
**$P < 0.01$;
***$P < 0.001$. Significance values are 2-tailed.

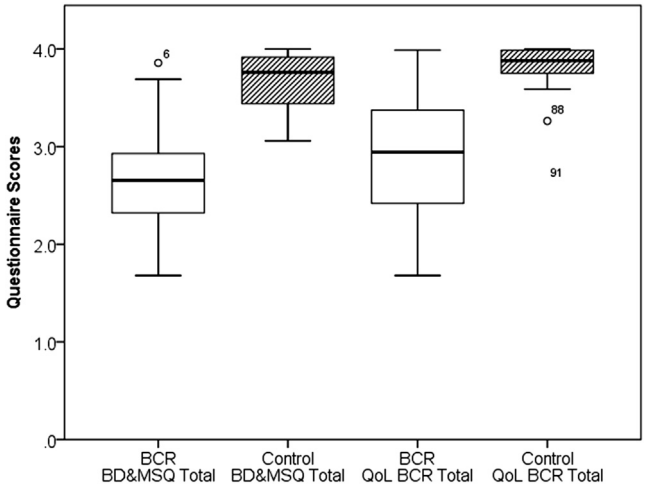

Figure 1. Box and whisker plot showing Birdshot Disease & Medication Symptoms Questionnaire (BD&MSQ) and the quality of life (QoL) impact of BCR (QoL BCR) scores in the Birdshot chorioretinopathy (BCR) group (white boxes) compared with age- and sex-matched controls (shaded boxes).