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The Burden of Retinal Venous Occlusion: An Assessment of Fellow Eyes in 1000 Cases

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Objective: To assess retinal vein occlusion (RVO) clinical features to create a simulation model quantifying the preference-based, patient value gain (benefit) and cost-utility (cost-effectiveness) of RVO therapy.

Design: Retrospective analysis data integrated with patient utilities and an ocular cost-utility model for RVO.

Participants: One thousand consecutive Wills Eye Hospital Retina Service RVO patients seen from January 2010 through April 2011.

Methods: Value-Based Medicine analysis assessing the demographic features and vision in affected eyes and fellow eyes of RVO patients.

Main Outcome Measures: Presenting vision, final vision, conversion incidence of fellow eyes to RVO, and patient value gain in quality-adjusted life-years (QALYs).

Results: Among 1000 patients, 332 (33.2%) presented with central retinal vein occlusion (CRVO), 53 (5.3%) with hemiretinal vein occlusion (HRVO), and 615 (61.5%) with branch retinal vein occlusion (BRVO). Mean follow-up for the entire RVO cohort was 3 years. One hundred and one patients (10.1%) had bilateral baseline RVO and, among the 826 unilateral cases seen more than once, 37 (4.5%) developed a fellow-eye RVO, a unilateral-to-bilateral conversion rate of 1.5%/year. Among the 101 baseline bilateral cases, 66% (66/101) had the same RVO variant bilaterally (CRVO/CRVO, HRVO/HRVO, or BRVO/BRVO). Mean CRVO baseline vision was $20/63^{-2}$ and final vision was $20/63^{-1}$ ($P = 0.16$). Thirty percent of patients had less than or equal to baseline fellow-eye vision. Within combined HRVO/BRVO cohorts, mean baseline vision was $20/50^{-2}$ and final vision was $20/50^{+1}$ ($P = 0.0004$). Thirty percent of patients also had less than or equal to baseline fellow-eye vision. The proportion of RVO patients with fellow-eye vision less than or equal to the RVO primary-eye baseline vision increased to 44% by year 16.

Conclusions: Thirty percent of all RVO patients had less than or equal to baseline vision in the fellow eye. Among unilateral RVO cases, 1.5%/year developed fellow-eye RVO. These findings have implications for cost-utility analysis, because bilateral vision loss yields greater QALY loss and an increased financial burden compared with unilateral loss. Referent to total therapeutic QALY gain (100%), if a treated RVO was always considered the better-seeing eye, the actual clinical scenario demonstrates that the average CRVO patient gains 38% as much value and the average HRVO/BRVO patient gains 37% as much. *Ophthalmology Retina 2017;■:1–9 © 2017 by the American Academy of Ophthalmology*

Retinal vein occlusion (RVO) is frequently encountered by ophthalmologists. Cugati et al,[1] in pooled data from combined population-based cohorts in the Blue Mountains Eye and Beaver Dam Studies, found a prevalence of 1.14% (96/8384) among participants aged 43 to 97 years. Although RVO is typically seen in the same population as age-related macular degeneration (AMD) and diabetic retinopathy, the latter 2 entities have a higher incidence of bilaterality than RVO.[2–4]

Multiple researchers have shown that vision-related quality-of-life is closely associated with vision in the better-seeing eye.[5–17] Thus, a disease associated with bilateral ocular involvement and visual loss generally has a greater adverse impact upon quality of life than one associated with unilateral vision loss. Involvement of the second eye also results in a greater associated financial burden.[2–4,15,18]

When one keeps the paradigm of unilateral/bilateral vision loss and quality of life in mind,[5–17] it becomes apparent that RVO patients' fellow-eye vision is quite relevant to quality of life. Although numerous studies have addressed visual outcomes associated with RVO, few have emphasized vision in the fellow eye, especially in clinical practice.[19,20] We therefore undertook a study of consecutive patients presenting with central retinal vein occlusion (CRVO), hemiretinal vein occlusion (HRVO), and/or branch retinal vein occlusion (BRVO) to ascertain the vision in affected and fellow eyes to facilitate the creation of a robust health care economic model closely simulating the clinical features of RVO.

Methods

The records of 1074 consecutive patients seen on the Retina Service at Wills Eye Institute with a diagnosis of RVO were reviewed. The study was approved by the Wills Eye Hospital Institutional Review Board and adhered to the Health Insurance

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Portability and Accountability Act and the Declaration of Helsinki and its amendments through 2013.

Inclusion Criteria. The cases of consecutive patients with prevalent and/or incident: (1) CRVO, (2) HRVO, and/or (3) BRVO were included. Among the BRVO variants were quadrantic, macular, and single peripheral BRVOs.

Exclusion Criteria. Features that precluded study entrance included the following: (1) the presence of choroidal neovascularization in the presenting RVO eye, (2) diabetic retinopathy mimicking an RVO, (3) the ocular ischemic syndrome mimicking an RVO,[21] and (4) multiple peripheral RVOs secondary to an occlusive and/or inflammatory retinopathy. Macular degeneration and/or diabetic retinopathy in the fellow eye were not exclusion criteria.

Demographic and Clinical Information. Age and gender were recorded, as were ocular examination findings, the latter including best-corrected Snellen visual acuity and anterior and posterior segment examinations. The cases reviewed were seen over an approximately 16-month period from January 2010 through April 2011.

Vision

Best-corrected Snellen vision was measured at the baseline examination and the most recent examination in the presenting RVO eye. Vision was also measured in the fellow eye to ascertain whether it was better than, the same as, or worse than in the presenting RVO eye. Snellen visual acuities were converted to Early Treatment Diabetic Retinopathy Study (ETDRS) format for analyses. When the pinhole vision improved the best-corrected vision, the former was used as the best-corrected vision, because these individuals typically squint, if necessary, to improve their acuity.

This analysis was NOT designed to evaluate which form of therapy, if any, was most efficacious for RVO. The intent was to gather visual acuity data, especially in the fellow eye, to allow the creation of a robust cost-utility model that accurately simulates the clinical scenario.

Value Gain

The most sophisticated form of comparative effectiveness is preference-based, which considers the *patient (human) value gain* (improvement in quality of life and/or length of life), or benefit, gained from an intervention.[8,9] This methodology uses utilities to assess quality of life and quality-adjusted life-years (QALYs) to quantify total patient value gain. Value-Based Medicine[2,3,8,9,15] is a standardized methodology of assessing preference-based patient value gain and cost-utility analysis. Standardization is critical because over 27 million different variables can enter into a cost-utility analysis, with just 1 different variable preventing a valid comparison across studies.[22]

Utilities. Time tradeoff, vision-related utilities were applied to the model. They were derived from numbers previously published by Brown and associates[5–8,14,16,17] and amended with data from a cohort of over 1200 patients with ocular diseases. These utilities are reproducible and validated across age, gender, level of education, ethnicity, income, and the presence of comorbidities. With anchors of 0.0 (death) and 1.0 (20/20 vision in both eyes permanently), vision utilities most closely correlate with visual acuity in the better-seeing eye.[5–8,14,16,17] As vision in the better-seeing eye improves the utility improves, and as vision in the better-seeing eye worsens the associated utility decreases. In this system, no perception of light bilaterally is associated with a utility of 0.26.[16] Utility × time (in years) equals the number of QALYs accrued by a person over time. A comparison of the QALYs accrued with and without treatment allows quantification of the patient value gain conferred by an intervention.

The *first-eye model* assumes that vision in the contralateral eye is normal unless data show otherwise, whereas the *second-eye model* assumes that vision in the fellow eye has previously deteriorated from the disease process under study or some other ocular disease.[2–4,15,18] The *combined-eye model* is composed of the sum of the weighted averages of the first-eye and second-eye models, and thus most closely simulates the actual clinical scenario.[2–4,15,18]

With the first-eye model, therapeutic value gain is typically less than that accrued with the second-eye model. Markov modeling can take into account the annual conversion rate of unilateral RVO to bilaterality.[2–4,15,18] The second-eye model, which is the model most often utilized in the literature,[23–26] typically confers greater therapeutic patient value than the first-eye model because the visual acuity is decreased in both eyes in the second-eye model, vs. in 1 eye in the first-eye model. Use of the second-eye model alone can yield falsely high patient value gains and falsely low cost-utility ratios.

The information presented herein is applicable to cohorts of patients with CRVO, HRVO, and/or BRVO, rather than an individual with an RVO for whom utility change is less complex to calculate. Thus, the information is relevant for application to clinical trials involving RVOs.

Costs

Societal costs include direct ophthalmic medical costs and the costs saved by therapy that accrue against the direct ophthalmic medical costs. Among the latter are direct nonophthalmic medical costs for depression, trauma, and facility admissions[27]; direct nonmedical costs, especially caregiver costs[28]; and indirect medical costs, such as vison-related salary loss.[29] Though the direct ophthalmic medical costs are applicable to all treated patients in a cost-utility analysis, the other costs accruing against the direct medical costs are not. These other costs parallel the proportion of second-eye model QALY gains in the combined-eye model.[2–4,15,18]

Statistics

The unpaired t test was utilized to assess differences between the CRVO and BRVO cohorts for continuous variables such as age and vision. The Pearson chi-square test evaluated categorical variable differences between the 2 cohorts. Statistical significance was presumed to occur at $P < 0.05$.

Results

Using the exclusion criteria, 74 cases were deleted, resulting in 1000 cases included in the final tally. Among the 1000 consecutive cases reviewed, there were a total of 1101 RVOs at baseline ophthalmic examination. Thus, 101 patients (10.1%) also had an RVO in the fellow eye to the one presenting with an RVO. Overall, 33.2% (332/1000) of baseline patients presented with a CRVO, 5.3% (53/1000) with an HRVO, and 61.5% (615/1000) with a BRVO (Table 1).

Follow-up

The mean follow-up for the entire cohort of 1000 patients was 35.9 months (standard deviation [SD] = 41.9, 95% confidence interval [CI] = 33.1–38.7). Among the CRVO patients, 30 of 332 (9.0%) were seen at only 1 visit; among the HRVO/BRVO patients, 52 of