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Impact of Incidence and Progression of Diabetic Retinopathy on Vision-Specific Functioning

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Purpose: To investigate the independent impact of the incidence and progression of diabetic retinopathy (DR) on visual functioning (VF).

Design: Population-based cohort study.

Participants: A total of 518 participants aged 40 to 80 years (baseline visit 2007–2009 and second visit 6 years later, 2013–2015), with diabetes, clinical data, and VF information at both visits.

Main Outcome Measures: VF-7 scores, converted to interval-level person measures (in logits) using Rasch analysis.

Methods: Incident DR was defined using the Modified Airlie House classification as "none or minimal" DR at baseline and at least mild nonproliferative DR at follow-up; incident vision-threatening DR (VTDR; severe non-proliferative DR, proliferative DR, and/or clinically significant macular edema) as no VTDR at baseline, and present at follow-up; and DR progression as at least a 1-step worsening in DR at follow-up from mild or worse status at baseline. The longitudinal associations between incident DR, VTDR, and DR progression, as well as change in composite and individual item scores of VF, were assessed using multivariable linear regression models.

Results: Of the 518 participants (mean age $\pm$ standard deviation [SD] 59.8$\pm$9.0 years; 47.7% female), 42 (9.8%), 14 (2.8%), and 32 (42.7%) had incident DR, incident VTDR, and DR progression, respectively, at follow-up. In models adjusting for traditional confounders, persons with incident DR and VTDR had a 13.7% ($\beta = -0.60$; 95% confidence interval [CI], -0.96 to -0.24; $P = 0.001$) and 23% ($\beta = -1.00$; 95% CI, -1.61 to -0.38; $P = 0.001$) reduction in mean VF scores at follow-up. Furthermore, individuals with incident DR had similar independent reductions in scores for 7 individual items of the VF-7, whereas those with incident VTDR had the largest reductions for activities like cooking (31%; $P = 0.003$), reading the newspaper (29.6%; $P < 0.001$), and seeing street signs (28%, $P = 0.001$) at follow-up. Progression of DR was not independently associated with change in overall VF ($\beta = -0.18$; 95% CI, -1.00, 0.64; $P = 0.660$).

Conclusions: Incident DR, particularly vision-threatening stages, has a substantial negative impact on people's overall vision-dependent functioning and specific activities such as cooking, seeing street signs, and reading the newspaper. Our findings reinforce the need for strategies to prevent or delay the development of DR. *Ophthalmology 2018;■:1–9 © 2018 by the American Academy of Ophthalmology*

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Diabetic retinopathy (DR) is a serious microvascular complication of diabetes.[1] Nearly all patients with type 1 and more than 60% of those with type 2 diabetes will develop some degree of DR after 20 years of having the disease.[2] In the early nonproliferative stages, DR is mostly asymptomatic but may cause significant and disabling vision loss once the disease progresses to vision-threatening DR (VTDR), including severe nonproliferative DR (NPDR), proliferative DR (PDR), and clinically significant macular edema (CSME).

DR and associated visual impairment affect people's ability to perform daily living vision-dependent activities, such as reading, household tasks, and driving, resulting in higher risk of falls and morbidity.[3,4] DR also has a substantial socioemotional impact, being linked with social isolation and higher rates of depression.[5,6] Several population-based studies have shown a consistent cross-sectional association between the presence of DR and poor vision functioning (VF).[7,8] However, the cause–effect nature of this relationship is unclear. To date, only the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) has reported on the longitudinal association between DR progression and VF in individuals with type 1 diabetes, with no significant longitudinal associations found between these 2 parameters.[9] No population-based data exist on the impact of the incidence and progression of DR on VF

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in Asian people with diabetes, who may have different functional needs. Such data are important, as differences in living conditions, lifestyle, and cultural and environmental habits may mean that individuals with DR in Asian populations face different restrictions in activities of daily living as compared with those in Western populations. Addressing this knowledge gap will therefore enable us to clarify the temporal relationship between the development and progression of DR and its impact on VF, which will in turn inform the establishment of effective and timely strategies to alleviate the negative patient-centered impact of DR.

In this study, we examined the impact of the 6-year incidence and progression of DR on change in overall and item-specific VF, assessed using Rasch-scaled data from the modified version of the Visual Function Index (VF-11)[10] in a population-based cohort study of Singaporean Indian adults. Rasch analysis, a form of item response theory, has been shown to increase relative precision of measurement[11,12] and sensitivity to change[13] of patient-reported outcomes compared with traditional psychometric methods. We hypothesize that though both incidence and progression of DR will be associated with reductions in VF, incident (i.e., "new") DR will be associated with significantly greater reduction in VF than progression of DR, as individuals with incident DR have had less time to adapt to vision loss.

Methods

Study Population and Design

The Singapore Indian Eye Study (SINDI-1 and SINDI-2) is a population-based cohort study of Indian adults (aged 40−80 years) living in Singapore, with baseline and follow-up assessments conducted between 2007 and 2009 and between 2013 and 2015, respectively.[14,15] A total of 3400 participants (75.6% response rate) took part in SINDI-1. Of the 3400 participants at the baseline visit, 1320 (38.8%) had diabetes, of which 1288 (97.6%) had gradable fundus photographs. Of these, 743 (57.7%) returned for the 6-year follow-up examination and had gradable fundus photographs. A total of 518 of the 743 participants (69.7%) had complete clinical and VF-11 data at both visits and were included in our analyses, leaving 770 (545 lost to follow-up and 225 with incomplete clinical information) as nonparticipants.

The study was conducted at the Singapore Eye Research Institute. The protocol comprised a comprehensive, standardized examination to collect clinical and questionnaire data.[14,15] All protocols followed the principles of the Declaration of Helsinki and received approval by the Singhealth Institutional Review Board. Written informed consent from participants was obtained prior to participation in the study.

Assessment of Visual Functioning

The VF-11, a modified version of the Visual Function Index VF-14, which has been culturally validated in a Singapore population, was used to assess VF.[10] The questionnaire was translated into Tamil and back-translated into English by 2 interpreters who were fluent in both languages. Participants were given the choice to be interviewed in Tamil or English. Rasch analysis was used to assess the psychometric properties of the VF-11 using the Andrich rating scale model with Winsteps software technology (version 3.92, Chicago, IL).[16,17] To generate valid pre-post person measures, the data were anchored to item measures and structure calibrations at baseline for the subsequent analyses. To establish that differences between the scores were valid indicators of changes over time, differential item functioning (item bias) for time (baseline vs. follow-up) was assessed.[18] Rasch analysis revealed substantial differential item functioning for time for items 1 and 6 ("problems seeing stairs" and "problems playing games," respectively) and item misfit for items 10 and 11 ("problems driving during the day" and "problems driving at night," respectively); and these 4 items were subsequently deleted (Table S1, available at www.aaojournal.org). The remaining 7 items assessed cooking, reading the newspaper, recognizing people, seeing signs, reading small print, filling out lottery forms, and watching television. We generated transformed individual person measures for the composite VF-11 score utilizing the remaining 7 items, as well as for each of the 7 individual items. The raw questionnaire scores have higher values for worse VF, whereas the scores were reversed during Rasch analysis, where a high person measure (in logits) indicates that a person possessed a high level of VF. As our composite VF-11 score is a measure of 7 items only, henceforth we will be using VF-7 instead of VF-11.

The raw score can range from a minimum of 0 (person answers "unable to do" for all 7 items) to a maximum of 28 (person answers "no problem" for all 7 items), and the logit range would correspond to this 0 to 28 range in raw scores. However, because the relationship between raw and Rasch-transformed scores (logits) is ogival rather than linear, a raw score change in the middle of the "impairment" spectrum results in a smaller change in logit scores compared with a raw score change at the extreme ends of the spectrum. For our sample population, in the middle of the "impairment" spectrum, a 1-step increase in raw scores equates to ∼0.33 logit increase in Rasch scores. In contrast, at the extreme top end of the spectrum (i.e., very "able" participants, where most of our sample resides), a 1-unit raw score increase equates to a ∼0.8 logit increase in Rasch scores.

Assessment of Diabetic Retinopathy

Two-field fundus images were taken using a Canon DGI non-mydriatic fundus camera and graded for severity of DR by trained graders at the University of Sydney, Australia, using the modified Airlie House classification system into no or minimal (Early Treatment of Diabetic Retinopathy Study level 10−20), mild NPDR (level 35), moderate NPDR (level 43−47), severe NPDR (level 53), and PDR (level 61−90) using data from the better eye.[19] The better eye was defined as the eye with the less severe DR level or, by convention, the right eye in patients who had the same severity level for both eyes. VTDR was defined as the presence of severe NPDR, PDR, and/or CSME using the Eye Diseases Prevalence Research Group definition.[20]

Assessment of Other Covariates

Questionnaires to collect sociodemographic characteristics (education, income level, occupation), lifestyle factors (smoking, alcohol consumption), self-reported family and medical history (diabetes, hypertension, stroke, cardiovascular disease [CVD]), ocular history (presence of cataract, glaucoma, DR, and age-related macular degeneration [AMD]), current medication, and insulin use were administered by trained interviewers.

Clinical covariates were obtained via a standardized clinical examination. Visual acuity (VA) was measured monocularly using a logarithm of the minimum angle of resolution (logMAR) number chart (Lighthouse International, New York, NY) at a distance of 4 m. Both presenting visual acuity (PVA), ascertained with the participant wearing his or her "walk-in" optical correction (i.e., spectacles or contact lenses), if any, and best-corrected visual