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## An objective structural and functional reference standard for glaucoma that is associated with quality of life

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Glaucoma is the leading cause of irreversible loss of vision. Although blindness is the most feared consequence of glaucoma, there is growing evidence that even mild disease may significantly impact the quality of life (QoL). In the context, glaucomatous visual field loss has been associated with an increased risk of depression, falls, hip fracture, motor vehicle collisions, and increased mortality. The QoL in glaucoma has been studied using patientreported outcomes such as the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25). Previous studies have demonstrated that patients with glaucoma (traditionally defined using subjective clinical assessment of visual fields and optic nerve damage) have lower NEI VFQ-25 scores than healthy patients. Therefore, the study by Naithani et al. aimed to compare self-reported QoL outcomes between glaucoma suspects, glaucoma patients and controls, on the basis of an objective reference standard for glaucomatous optic neuropathy (GON).

This cross-sectional study included 1884 eyes of 1019 patients. To assess patients' QoL, the NEI VFQ-25 was administered. All eyes were classified according to the presence and topographic correspondence of functional and structural damage, as assessed by standard automated perimetry (SAP) and spectral-domain optical coherence tomography (SD-OCT). To be diagnosed with glaucoma, patients had to meet the criteria for global or localized loss in at least one eye. An eye was consi-

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Naithani R, Jammal AA., Estrela T, Onyekaba NE, Medeiros FA. Association of an Objective Structural and Functional Reference Standard for Glaucoma with Quality of Life Outcomes. Ophthalmol Glaucoma. 2023;6(2):160-168. dered to have GON if any of the following was present: 1) global retinal nerve fiber layer (RNFL) thickness outside normal limits and abnormal SAP results (Glaucoma Hemifield Test results outside normal limits or pattern standard deviation with p < 5%); 2) at least one superior sector (temporal superior or nasal-superior) with an RNFL thickness outside normal limits and an abnormal SAP result in the inferior hemifield (inferior hemifield mean deviation [MD] with p < 5%; 3) at least one inferior sector (temporal inferior or nasal-inferior) with an RNFL thickness outside normal limits and an abnormal SAP result in the superior hemifield (superior hemifield MD with p < 5%). The superior and inferior SAP hemifield MD were calculated as the average of the total deviation values in each hemifield. For a patient to be considered normal, both the SD-OCT and SAP results had to be normal in both eyes. Finally, patients who did not meet the criteria for normal or glaucoma were classified as glaucoma suspects.

The association between NEI VFQ-25 Rasch-calibrated scores and diagnostic groups was assessed by multivariate regression analysis, controlling for confounding demographic and socioeconomic variables such as age, sex, race, income, marriage status, insurance status, and highest education level.

Overall, eyes classified as normal, glaucoma suspect, and glaucoma had decreasing mean scores in the SAP MD ( $0.2 \pm 1.0 \text{ dB}$ ,  $-0.9 \pm 2.4 \text{ dB}$ ,  $-6.2 \pm 7.0 \text{ dB}$ , respectively; p<0.001) and the RNFL thickness (97.8 ± 9.5 µm, 89.0 ± 13.1 µm, 64.5 ± 12.8 µm, respectively; p<0.001) on SD-OCT. The mean Rasch-calibrated NEI VFQ-25 score was significantly different among normal, suspect, and glaucoma groups (p<0.001). When

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adjusted for confounding socioeconomic variables, patients with glaucoma had significantly worse QoL than normal patients (p < 0.001).

The study results demonstrate that a diagnostic classification based on objective structural and functional metrics was significantly associated with glaucoma patients' QoL. Subjects with glaucoma, as defined by this objective reference standard, had significantly lower NEI VFQ-25 Rasch-calibrated scores than normal patients and glaucoma suspects, even after adjusting for confounding demographic and socioeconomic variables.

They concluded that the proposed objective criteria for the diagnosis of GON was significantly associated with patient-reported QoL outcomes. Thus, the utilization of this criterion may provide clinically relevant metrics, which could improve the comparability of study findings and validation of newly proposed diagnostic tools.