Screening for Glaucoma in High-Risk Populations Using Optical Coherence Tomography

Gisèle Li, MD,[1,2] Alvine Kamdeu Fansi, MD, PhD,[2] Jean-François Boivin, MD, ScD,[1] Lawrence Joseph, PhD,[1] Paul Harasymowycz, MD, MSc[2]

Objective: To estimate the diagnostic accuracy of Stratus optical coherence tomography (OCT) for glaucoma screening in high-risk populations.

Design: Cross-sectional evaluation of a diagnostic test for screening.

Participants: Three hundred thirty-three community-based volunteer participants with risk factors for glaucoma.

Methods: The optic nerve and peripapillary retinal nerve fiber layer (RNFL) of participants' eyes were scanned using the Stratus OCT. Based on an ophthalmologic examination and frequency doubling perimetry, eyes were classified into 4 categories: normal, possible glaucoma, probable glaucoma, and definitive glaucoma.

Main Outcome Measures: The sensitivities, specificities, positive and negative likelihood ratios of the RNFL, optic disc parameters, and their combinations were calculated.

Results: The right eyes were retained for analyses. After excluding eyes with missing data or with poor quality scans, the data of 210 right eyes were analyzed. Six eyes had definitive glaucoma. Combining the best performing optic nerve head parameters (cup diameter or cup/disc vertical ratio or cup/disc area ratio) and RNFL parameters (superior average or inferior average or overall average) using AND-logic resulted in a sensitivity of 67% (95% confidence interval [CI], 24%–94%), specificity of 96% (95% CI, 92%–98%), a positive likelihood ratio of 17.08 (95% CI, 7.06–41.4), and a negative likelihood ratio of 0.35 (95% CI, 0.11–1.08).

Conclusions: When adequate quality scans may be obtained, the Stratus has moderate sensitivity and high specificity for definitive glaucoma. Specificity is increased when parameters from both the optic nerve head and RNFL scans are combined.

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Glaucoma is the primary cause of irreversible blindness worldwide. In the United States, >2 million people were estimated to be affected in 2000 and the number affected is projected to increase to 3.6 million by 2020 as the population ages.[1]

Current recommendations for glaucoma screening remain equivocal.[2] The United States Preventive Services Task Force Recommendation Statement regarding screening for glaucoma cites insufficient evidence to "determine the extent to which screening would reduce impairment in vision related function or quality of life."[3,4] Meanwhile, the Recommendation Statement acknowledged the potential benefit of screening high-risk groups such as older African Americans.

Known risk factors for glaucoma include age, race, and family history. The prevalence rates of chronic open angle glaucoma increase from 1.5% in the 40- to 49-year-old age group to 5.1% in 70- to 79-year-olds.[1] The Los Angeles Latino Eye Study showed significantly higher prevalence rates among Hispanics of Mexican ancestry compared with whites particularly in those >70 years old.[5] The Baltimore Eye Survey showed a 3- to 4-fold higher prevalence for every age group in blacks compared with whites.[6] Having a first-degree relative (parent, sibling, or child) with glaucoma has been consistently associated with an increased risk of chronic open-angle glaucoma in prevalence surveys.[7–9] Selective screening in high-risk groups may be a more cost-effective option than comprehensive, population-based screening.

A recent systematic review of cost-effectiveness studies regarding glaucoma screening also cited insufficient evidence to reach a conclusion.[10] The uncertainty was partly attributed to technological advances in glaucoma diagnostic imaging devices, which had not been adequately evaluated for screening purposes.

Glaucoma diagnostic imaging with optical coherence tomography provides quantitative measurements of the optic nerve head and peripapillary retinal nerve fiber layer (RNFL). The earliest observable defect in glaucoma is atrophy of the RNFL.[11] Optic nerve cupping has also been shown to precede visual field (VF) loss.[12–14] Thus, imaging enables early detection of the disease and treatment initiation. Early treatment of glaucoma has been shown to reduce the incidence of VF loss.[15,16]

The Stratus optical coherence tomography (Stratus OCT; Carl Zeiss Meditec Inc., Dublin, CA) can provide high-

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resolution (8–10 μm), cross-sectional images of the RNFL and optic nerve head (Stratus OCT Software Version 4.0: Real Answers in Real Time. available: http://www.meditec.zeiss.com; accessed October 10, 2008). The RNFL parameters found to be most useful for detecting glaucoma were the overall average, inferior, and superior quadrants. These parameters were associated with area under the receiver operating curves (AUC) ranging from 0.86 to 0.89.[17,18] The best optic nerve head parameter in 1 study was the cup/disc area ratio with an AUCs of 0.88.[19] These and many previous studies on the diagnostic accuracy of the Stratus were conducted among eye clinic or glaucoma service patients.[17,20–23] The sensitivity and specificity of diagnostic tests have been shown to depend on the disease spectrum in the population in which they are used.[24] The severity of VF loss has been shown to significantly influence the sensitivity of glaucoma imaging devices. The sensitivity of the Stratus OCT and scanning laser polarimetry improve with more severe disease.[23] Patients seen in eye clinics or by glaucoma services likely have more advanced disease than volunteer participants from the community neither referred nor previously evaluated for glaucoma. The purpose of our study was to evaluate the performance of the Stratus fast RNFL and fast optic disc parameters to screen for glaucoma in high-risk populations neither referred nor followed by ophthalmologists.

Methods

The Standards for Reporting of Diagnostic Accuracy were reviewed and followed.[25]

Patient Population

This observational, cross-sectional study was performed in Montreal, Quebec, Canada. The study protocol was approved by the ethics committee of Maisonneuve-Rosemont Hospital, a University of Montreal affiliated hospital. Informed consent was obtained from all study participants and the research protocol adhered to the tenets of the Declaration of Helsinki. Data collection was planned before the date of enrollment and before testing was performed.

To be eligible, subjects had to fulfill ≥1 of the following inclusion criteria: (1) self-described Caribbean, African, or Hispanic origin, (2) >50 years of age, or (3) positive family history of glaucoma. For example, a 60-year-old Caucasian man with no family history of glaucoma would have been included as a case because he fulfilled 1 of the criteria. The exclusion criteria were an inability to give informed consent and an inability to complete an ophthalmic examination or OCT scan.

Participants were recruited and examined consecutively at the following locations: a Caribbean community church, an outdoor summer festival, a community park, the Judith Jasmin Chronic Care Nursing Centre, the Eye Clinic of Maisonneuve-Rosemont Hospital, and the Glaucoma Institute of Montreal between August 2003 and May 2008. Participants examined at the first 3 sites were recruited by setting up kiosks and recruiting passersbys. Participants examined at the Judith Jasmin Centre were approached on the ward and offered free glaucoma screening. At these 4 sites, participants were examined in a mobile clinic that included a Stratus OCT and underwent scanning the same day. Participants who were examined at Maisonneuve-Rosemont Hospital and the Glaucoma Institute of Montreal were volunteer participants who either responded to advertisements placed in clinic waiting areas, hospital circulars, and local newspapers, or were approached by study coordinators offering free screening tests for family members accompanying glaucoma patients. These participants were examined at the hospital or the Glaucoma Institute and underwent scanning the same day or, when an ophthalmic technician was unavailable, within 1 month of their examination.

After informed consent was obtained, an interviewer completed a questionnaire regarding family, medical, and ocular history. Family history of glaucoma was considered positive if the participant reported a first-degree relative (parent, sibling, or child) diagnosed with glaucoma.

Clinical Examination

Subjects underwent a complete eye examination by 1 of 2 glaucoma specialists (PH, GL) who were masked to the results of the Stratus scan and perimetry. The ocular examination included pachymetry, gonioscopy, slit-lamp examination, intraocular pressure (IOP), and a stereo examination of the optic nerve head, RNFL, and retina. The optic nerve head examination was performed using a 78-diopter lens and documented using the vertical cup-to-disc ratio and the Disc Damage Likelihood Scale,[26] where stage 0 represents no optic nerve damage and stage 7 represents advanced rim loss. Pupils were only dilated for the clinical examination when visualization of the optic nerve head was difficult undilated. Patients also underwent confocal scanning laser ophthalmoscopy of the optic nerve head with a Heidelberg Retina Tomograph (HRTII or HRTIII; Heidelberg Engineering, Heidelberg, Germany) for a separate ongoing study.[27] Based on the Disc Damage Likelihood Scale, individual eyes were then classified by the examiner as normal, glaucoma suspect, or glaucoma.

Frequency Doubling Technology

At the same visit, patients performed a VF test in both eyes using the frequency doubling technology (FDT) screening C-20-5 program (Humphrey Instruments, Dublin, CA) or the 24-2 FDT Matrix threshold program (FDT2, Humphrey Matrix; Carl-Zeiss Meditec). The test has been described previously.[28] Testing was performed in a dark room. Both eyes were tested according to the instrument protocol. The test was orally explained to each subject and a preview of the target stimuli was shown at the beginning. The test was administered by a physician-researcher trained in FDT testing or a VF technician with ≥1 year experience with the machine. For the C-20-5 program, 17 targets including sixteen 10° square stimuli (4 per quadrant) plus a central 5° diameter circular stimulus were presented to each eye.[28] The test printout classifications ('within normal limits,' 'mild relative loss,' 'moderate relative loss,' and 'severe loss') based on comparisons with an age-related normative database for each target were documented. An FDT with ≥2 adjacent squares of relative loss was considered abnormal using the C-20-5.[29] The FDT2 24-2 program consists of 54 test points covering the central field out to 24°, except nasally, where it extends to 30°. The 24-2 program printout shows the number and areas of decreased sensitivity, the glaucoma hemifield test results (within normal limits, borderline, or outside normal limits), the pattern standard deviation, and the mean deviation.[30] A glaucoma hemifield test outside normal limits or borderline was considered abnormal.

Final Diagnostic Classifications

The data of eyes classified as "glaucoma suspect" or "glaucoma" were reviewed in combination with the FDT results (but blinding to the Stratus scan results was maintained) to assess whether areas