Remote Screening for Optic Nerve Cupping Using Smartphone-based Nonmydriatic Fundus Photography

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Precis: Evaluation of nonmydriatic fundus photographs captured with a low-cost, smartphone-based camera facilitated remote screening of patients for enlarged optic nerve cup-to-disc ratio in the Independent Nation of Samoa, an underserved setting with one full-time ophthalmologist in the entire country.

Purpose: To investigate factors that impact inter-rater agreement of glaucoma suspect optic disc status using a low-cost, handheld nonmydriatic fundus camera.

Methods: Color fundus photographs were obtained using the PanOptic iExaminer attached to an iPhone 6S by a lay examiner on 206 participants in the Independent Nation of Samoa. Images were remotely graded by an ophthalmologist and optometrist, and images from participants identified as at-risk for glaucoma were escalated to a glaucoma subspecialist for review. Fundus photo brightness, contrast, and focus were measured using the cup, rim, and temporal regions of the disc. Stereoscopic image pairs were subsequently generated from a subset of individual nonmydriatic photographs.

Results: Features suggestive of glaucoma based on optic disc cupping were identified in 16.0% (33/206) of participants. There was moderately strong agreement between graders (90.3%) with κ=0.53 [95% confidence interval (CI) = 0.33-0.73]. The intraclass correlation coefficients for the cup-to-disc ratio (CDR) and its difference were 0.84 (95% CI = 0.81-0.87) and 0.68 (95% CI = 0.59-0.75). Of the 33 participants identified, 94% had clinical risk criteria for potential glaucoma when reviewed by a subspecialist. Color fundus photograph cup brightness was significantly associated with cup-to-disc (CDR) grade, R² = 0.36 (P < 0.001), in which a brighter disc yielded a higher CDR.

Conclusions: Smartphone-based screening is a simple, low-cost method capable of measuring the CDR of the optic nerve. When combined with testing for other glaucoma risk factors such as intraocular pressure, this method of measuring CDR may help identify those patients who should be referred for further ophthalmologic assessment. We are currently conducting studies to assess the sensitivity and specificity of smart phone-based remote screening.

Key Words: glaucoma, screening, imaging-posterior segment, optic nerve, stereo disc photography, telemedicine (J Glaucoma 2021;30:58–60)

Screening for vision-threatening conditions in resource-constrained settings remains a significant challenge in health care. Advances in handheld, battery-operated devices, however, have overcome difficulties associated with fundus photography outside of the traditional clinic. Recently, we reported on the feasibility of using the PanOptic iExaminer, a portable low-cost smartphone-based nonmydriatic fundus camera, to screen for signs of diabetes-associated eye disease in Samoans with elevated blood glucose levels. We found that clinically gradable images could be obtained from nearly 82% of eyes in a teleophthalmology program conducted throughout 12 remote villages in the Independent Nation of Samoa, a country where only one full-time ophthalmologist serves an island population of nearly 200,000 people. The purpose of our study is to evaluate the application of this ultraportable camera in a medically underserved setting to screen for potential signs of glaucoma in disc images. We also explore the impact of quantitative fundus photograph metrics, including image brightness, contrast, and focus, on inter-rater agreement of glaucoma suspect status.

METHODS

The present study was undertaken alongside an ongoing longitudinal study of the genetics of obesity and diabetes among Samoans: the Samoan Obesity, Lifestyle, and Genetic Adaptation Group’s Soifua Manuia (Good Health) study. After informed consent was obtained, a trained lay examiner used the PanOptic iExaminer attached to an iPhone 6S to obtain color fundus photographs from 206 participants. Fundus imaging was performed in traditional Samoan fales (open-sided houses). To overcome constriction...
of the pupil in outdoor daytime illumination, curtains were hung to construct a “tent” to block ambient light. All participants had either prediabetes or diabetes (HbA1c ≥ 5.7% or FBG ≥ 110 mg/dL) and were 30.5 to 50 years of age. Fewer than 1% of participants had undergone any eye examination in the past year. No participants reported a prior history of eye injections, laser, or surgery.

Images were remotely graded in the United States by an ophthalmologist and optometrist who were masked to participants’ demographic, visual acuity, and biometric data. Participants at risk for glaucoma (glaucoma suspects) were defined as having a vertical cup-to-disc ratio (CDR) in 1 or both eyes ≥ 0.6 or a difference in CDR between the 2 eyes ≥ 0.2. We chose to classify participants using this broad clinical standard, so as to capture as many participants as possible in this population in which the true prevalence of glaucoma is not yet known. Persons with type 2 diabetes mellitus are also more likely to have primary open-angle glaucoma, making a lower threshold for screening appropriate in our study population, which has a high prevalence of diabetes.6 Cohen κ statistic was used to assess the interobserver agreement for glaucoma suspect status by participant. Intrarater reliability between the grading ophthalmologist and optometrist was calculated using the intraclass correlation coefficient (ICC) based on a single-measures, absolute-agreement, 2-way mixed effects model. Images identified as at-risk were referred to a glaucoma subspecialist for review. Image brightness was measured by integrating the pixel intensity at the cup, rim, and temporal regions of the disc. Contrast was calculated as the ratio between these 2 regions of the disc. Focus was estimated by calculating the Laplacian operator for each image in Python 3.7. Participants with 2 high-quality, suitably aligned views of the optic disc were selected to be reconstructed into stereoscopic image pairs (40 eyes form 20 participants). All of these image sets were viewed in stereo with a stereo viewer (Pocket Stereo Viewer, Luminos Photo Corp, Yonkers, NY) placed over the iPhone 6S screen.

RESULTS

A total of 2758 fundus images were obtained for remote diagnostic review, averaging 7.0 ± 2.9 images per eye (range: 1 to 18 images). Most images captured views of the disc and surrounding posterior pole (Fig. 1). Participants averaged 45.4 ± 9.1 years, and 61.3% were female. Elevated CDR or intereye asymmetries were identified in 16.0% (33/206) of participants. No disc hemorrhages were observed. There was moderately strong agreement between graders (90.3%) with Cohen κ = 0.53 [95% confidence interval (CI) = 0.33-0.73]. The ICs for CDR and its difference were 0.84 (95% CI = 0.81-0.87) and 0.68 (95% CI = 0.59-0.75), respectively. Participants had an average CDR of 0.39 ± 0.11 and CDR asymmetry of 0.01 ± 0.06, and CDR showed no association with image quality as defined in the Feasibility of Nonmydriatic Ocular Fundus Photography (FOTO-ED) studies7 (F4,174 = 1.05, P = 0.382). Likewise, there was no significant association between image quality and glaucoma suspect status agreement (F4,378 = 0.85, P = 0.496), indicating that our observed interrater agreement was not limited by image quality variability. Of the 33 participants identified as having CDR parameters above threshold during the initial screening, 94% had clinical risk criteria for potential glaucoma when subsequently reviewed by a glaucoma specialist. Cup brightness was significantly associated with CDR grade (R² = 0.36, P < 0.001), in which a brighter disc yielded a higher CDR (Table 1). Image contrast was correlated to a lower degree with variation in CDR grade. All 33 study participants with criterion CDR
TABLE 1. Impact of Color Fundus Photograph Metrics on Cup-to-Disc Ratio Grading

| Fundus Photograph Metric* | $R^2$† | $P^2$  |
|--------------------------|--------|--------|
| Cup brightness           | 0.36   | <0.001 |
| Rim brightness           | 0.26   | <0.01  |
| Temporal brightness      | −0.14  | 0.01   |
| Cup:rim contrast         | 0.12   | 0.02   |
| Rim:temporal contrast    | 0.20   | <0.001 |
| Cup:temporal contrast    | 0.17   | <0.001 |
| Focus                    | −0.03  | 0.60   |

*Image brightness was calculated by integrating the pixel density at the cup, rim, and temporal regions of the disc using ImageJ software (NIH, Bethesda, MD). Nerve fibers were avoided while obtaining measurements. Contrast was calculated as the ratio between these 2 regions of the disc. Focus was estimated by calculating the Laplacian of each image in Python 3.7.

†$R^2$ represents the Pearson correlation coefficient. All coefficients were calculated by using intrarater measurements of photograph metrics and the cup-to-disc ratio.

‡For analysis of variance analyses, a 2-sided $P$ < 0.05 was considered the threshold of statistical significance.

This proof-of-concept study provides evidence that smartphone-based screening is a simple, low-cost method capable of reaching underserved populations who would otherwise lack access to primary eye care. Moreover, our study identifies a novel method of enhancing the utility of color fundus photographs by generating stereoscopic image pairs from individual nonmydriatic photographs. Future work will determine if this method of enhanced viewing allows more accurate detection of optic disc pathology. In conclusion, our study demonstrates that a portable low-cost smartphone-based nonmydriatic fundus camera can be successfully integrated into an eye screening program and that these images can identify patients with large CDR or CDR asymmetry. Together with assessment of other risk factors such as tonometry, smartphone-based CDR determination may help identify patients at risk for glaucoma and in need of additional ophthalmologic evaluation.

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findings were referred to a local ophthalmologist in Samoa. The outcomes of these ophthalmic examinations are not available for this study due to privacy considerations.

DISCUSSION

Risk of glaucoma based on features of the optic disc was readily identified with the PanOptic iExaminer. Interestingly, image brightness was associated with larger cup-to-disc grading among all graders, suggesting that color fundus photograph standardization may be important to reduce grader bias. Despite being an ultraportable device, image quality was sufficient to allow reproducible disc grading for a majority of participants and even allowed a subset of eyes to be evaluated as stereoscopic image pairs.

Cupping of the optic nerve head is a hallmark for glaucomatous optic neuropathy. However, there is wide variation within the human population, and no normative data for the Samoan population exist. Our study identified a relatively high prevalence of suspicious optic nerves (16.0%), similar to a rural US study based on optic nerve head cup size (10.5%). CDR asymmetry is another well-known hallmark of glaucoma and is by itself predictive of glaucoma prevalence. However, optic disc structural changes by themselves are not confirmatory of glaucoma, and this should be considered a limitation of our current study. The diagnosis of glaucoma requires comprehensive evaluation of the patient beyond the structure of optic disc, including accounting for other well-known risk factors for glaucoma such as intraocular pressure, family history, refractive error, and functional testing to identify characteristic defects indicative of a glaucomatous optic neuropathy. We are currently conducting comprehensive examinations and additional studies to assess the sensitivity and specificity of smart phone-based remote screening.