Long-term variability of retinal nerve fibre layer thickness measurement in patients with glaucoma of African and European descents

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Abstract

Background: To examine long-term retinal nerve fiber layer thickness (RNFLT) variability and associated clinical factors in African (AD) and European descent (ED) individuals with glaucoma.

Methods: This retrospective cohort study included glaucoma eyes of AD and ED from DIGS/ADAGES with 4-visits/2-years of follow-up. We calculated optic nerve head RNFLT variability per-exam/visit as the absolute error of its residuals across follow-up. Full, baseline, and parsimonious linear-mixed models were fit to evaluate the effects of clinical factors (demographics and ocular characteristics, prior/intervening glaucoma surgeries and cataract extraction (CE), RNFLT thinning rate, scan quality, visit/testing frequency, etc.) on RNFLT variability in both races.

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Results: There were 376 and 625 eyes (226 and 349 participants) of AD and ED, and the mean(95%CI) RNFLT variability was 1.62(1.52,1.71)μm and 1.42(1.34,1.50)μm, respectively (P=0.002). AD and ED had some shared predictors of RNFLT variability, including intraocular pressure fluctuation and scan quality, although the effects varied (P<0.05). In both races, intervening CE was most strongly correlated with higher RNFLT variability (β:0.24–0.92, P<0.05). After excluding eyes with intervening CE, RNFLT variability was reduced and the small racial difference was no longer significant (AD:1.40 [1.31, 1.48]μm vs. ED:1.34 [1.27, 1.40]μm; P=0.280).

Conclusions: Although some predictors were identified, long-term RNFLT variability appeared small for both AD and ED eyes. Moreover, the racial difference did not remain once intervening CE, the strongest predictor of variability, was eliminated. Our findings inform on strategies to optimize structural assessment and suggest that, when accounting for relevant factors, RNFLT is reliable across races.

PRECIS

While several factors may affect RNFLT measurement in AD and ED, the long-term variability was small for both races. Furthermore, no significant racial difference was found after the strongest predictor, intervening cataract extraction, was eliminated.

Keywords

glaucoma; OCT; RNFL thickness; variability; African descents

INTRODUCTION

Optical coherence tomography (OCT) is a routine component of the examination in the long-term follow-up for glaucoma. Clinicians have increasingly relied on serial OCT measurements, including the retinal nerve fiber layer thickness (RNFLT), to assess glaucomatous structural progression.[1] Although commonly used for progression detection, estimates of the variability of RNFLT varied widely across studies.[2–4] In addition to inter-instrument difference, individual difference in measurement fluctuation, which has not been thoroughly investigated previously, might also account for this observation. Furthermore, most prior studies analyzing RNFLT reproducibility were short-term, with limited data on long-term variability.[1] While largely unexplored, information on the long-term variability of RNFLT and its predictors may help to assess structural changes more reliably by OCT.

Many studies have found the ocular biometry to vary across races,[5–7] and have suggested such differences be considered when interpreting clinical tests to prevent inaccurate assessment for glaucoma management. For example, thinner temporal RNFLT has been reported in individuals of African descent (AD),[8–10] which can result in discrepant OCT diagnostic performances for glaucoma.[11] Such racial difference may also present in measurement variability, which can potentially affect the detection and intervention of glaucoma progression. Some prior studies have demonstrated a greater variability in visual field (VF) measurement in AD, which were subsequently found to result in delayed VF progression detection as compared to individuals of European descent (ED).[12 13]

However, information on whether AD might also have a greater RNFLT variability that could potentially impact structural progression detection remains limited.

Our prior work examining a general cohort of glaucoma patients has suggested that African American race is a risk factor for higher RNFLT variability.[14] Considering AD are originally at higher risk of adverse functional outcomes in glaucoma,[15 16] it is clinically important to verify if OCT may indeed be less reliable for progression detection in this population when compared directly against another race. Furthermore, the factors contributing to measurement variability across races, particularly the modifiable ones, should be identified. To answer these questions, in this follow-up study to our prior work, [14] we performed a race-stratified investigation on the long-term RNFLT variability and its clinical predictors among AD and ED individuals diagnosed with glaucoma.

METHODS

Participants

In this retrospective cohort study, we included primary open angle glaucoma (POAG) and glaucoma suspect individuals self-reported as AD and ED from the Diagnostic Innovations in Glaucoma Study (DIGS) / The African Descent and Glaucoma Evaluation Study (ADAGES)[11] with at least 2 years and 4 visits of OCT tests. Inclusion/Exclusion criteria and examination protocol for DIGS/ADAGES are detailed in Supplemental Method 1. POAG was defined as having repeatable and reliable (fixation losses ≤ 33; false negatives ≤ 33%; false positives ≤ 15%) 24–2 Swedish Interactive Thresholding Algorithm (SITA) VF test results showing the following abnormalities indicating glaucomatous damage: (1) a pattern standard deviation outside the 95% normal limits or (2) a glaucoma hemifield test result outside the normal limit. Glaucoma suspect was defined as having the following signs without repeatable glaucomatous VF damage: (1) an intraocular pressure (IOP) ≥ 22 mm Hg or (2) a suspicious appearance of optic disc. Considering the potential floor effect of OCT,[17] eyes with a baseline VF mean deviation (MD) worse than −14 dB were excluded from this study.

Ethics Statement

The study design was approved by the University of California San Diego (UCSD) Human Research Protection Program (NCT00221897) and the institution review boards of the participating ADAGES centers and adhered to the tenets of the Declaration of Helsinki and the Health Insurance Portability and Accountability Act. Written informed consent was obtained from all DIGS/ADAGES participants.

RNFLT variability calculation

The high resolution RNFL circle scan centered on the optic nerve head (ONH)-by Spectralis spectral domain-OCT (Heidelberg Engineering, GmbH, Heidelberg, Germany) was used to measure mean global RNFLT. Similar to our prior work,[14] we calculated the long-term RNFLT variability on a per-exam/visit basis as the longitudinal absolute error of RNFLT over time, with the time-varying residuals derived from a linear mixed-effects model. In this model, RNFLT measurements across follow-up time was fit using a linear mixed-effects

model, with a random slope accounting for longitudinal follow-up time.[14] The model was further fit with random intercepts to account for variability derived from within-subject eye correlation and different Spectralis OCT software versions. Using this method, we intended to capture RNFLT variability across all levels of progression and aging effects as in prior studies.[12 18] Two separate models were fit for AD and ED, in order to calculate and compare the individual RNFLT variability of the two races.

Selection of clinical factors

Following the established method,[14 19] we considered clinical factors in the following categories as candidate predictors of RNFLT variability (see Supplemental Method 2 for the complete list): (1) baseline variables (measurements obtained within 6 months of the first RNFLT included in the analysis): general demographics, systemic conditions, glaucoma diagnosis, baseline ocular measurements (e.g., central corneal thickness [CCT], IOP, , 24– 2 VF, RNFLT, etc.), glaucoma medications use, history of glaucoma surgeries/cataract extraction (CE); (2) longitudinal variables: slope of RNFLT thinning, IOP fluctuation, mean IOP during follow-up, intervening CE/glaucoma surgeries, frequency of visits/testing, scan quality (SQ), and more. [14 19] To prevent from multi-collinearity, we performed hierarchical cluster analyses (HCA) on all candidate factors separately for AD and ED, with the goal of securing a squared Spearman correlations rho^2 of 0.30 among the final set of clinical factors included for multivariable modeling.[14 19] As shown in Supplemental Figure 1, a final $rho^2 < 0.20$ was found among the factors eventually selected by HCA.

Model construction

To examine the effects of HCA-selected clinical factors on RNFLT variability within each race, linear mixed-effects models with random intercepts as described above and RNFLT variability as the dependent variable were constructed separately for AD and ED. [14 19] Supplemental Table 1–2 show the univariable models of the two races including all HCA-selected factors. Furthermore, we examined three types of multivariable models that included different subsets of HCA-selected factors:[12 14] (1) Full model, which included all HCA-selected factors; (2) Baseline model, which included HCA-selected baseline factors; (3) Parsimonious model, which included HCA-selected variables that were further included by least absolute shrinkage and selection operator (LASSO) regression. [20] The LASSO model produces sparse, parsimonious model selections, allowing for the identification of the key contributing factors with a higher prediction accuracy. For each model, we calculated the R^2 (total variance explained by the model) and performed 10-fold cross-validation to estimate the model performance in real-world.[12] The effect of each clinical factor is shown as β co-efficient, with a positive and negative β indicating increase and decrease in RNFLT variability, respectively

Statistical analysis

Demographics and clinical characteristic of AD and ED were compared, with categorical variables and continuous variables presented as count (%) and mean (95% confidence interval [CI]), respectively. Data imputation was not needed given the very low percentage (<2.5%) of missing data for all HCA-selected factors (Supplemental Figure 2). We performed statistical analyses using the R programming language packages "lme4", "nlme",

"lmerTest", and "performance" from version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) with. A P-value 0.05 indicates statistically significant.

RESULTS

Table 1 summarizes the clinical characteristics of the 376 AD eyes and 625 ED eyes (349 and 226 participants) included. The mean (95% CI) age of ED and AD participants was 66.8 (65.7, 67.8) and 63.4 (62.0, 64.8) years, respectively. A higher percentage of AD eyes were diagnosed with POAG (57% vs. ED:49%), while more ED eyes had prior history of CE (21% vs. AD:11%) and glaucoma surgeries (26% vs. AD:17%) (P<0.05). The mean follow-up duration of AD (7.0 [95%CI:6.7,7.4] years) was longer than that of ED (6.3 [6.0,6.6] years), although the mean visit/testing frequency of ED was slightly higher (1.7 vs. AD:1.5 times/year) (P<0.05). AD eyes also had thinner baseline CCT (533.8 [95%CI:528.3,539.4] μm vs. ED:551.6 [547.2,555.9] μm), worse baseline 24–2 VF MD (−2.7 [95%CI:−3.1,−2.3] dB vs. ED:−2.1 [−2.4,−1.8] dB), worse mean scan Automatic Real Time (ART)-function (55.7 [95%CI:53.4,57.9] vs. ED:60.3 [58.5,62.1]), and faster RNFLT thinning rate (−0.8 [95%CI:−0.9,−0.7] vs. ED:−0.6 [−0.7,−0.5]) (P<0.05). The overall mean (95% CI) RNFLT variability of AD (1.62 [1.52, 1.71] μm) was 0.2 μm higher than that of ED (1.42 [1.34, 1.50] μm, P=0.002).

Effects of clinical factors on RNFLT variability

The value of β presented in the results indicates the magnitude of RNFLT variability change associated with 1 unit increase in the clinical factor as specified in the corresponding tables.

Full models for AD and ED are shown in Figure 1 and supplemental Table 3. For AD, greater RNFLT variability was associated with higher IOP fluctuation (β[Standard error, SE]= 0.18[0.04]) and intervening CE (β[SE]= 0.92[0.14]), while older age (β[SE]= −0.01[0.01]), higher baseline IOP (β[SE]= −0.05[0.01]), and better SQ (β[SE]= −0.03[0.01]) were associated with smaller RNFLT variability (P<0.05). For ED, greater RNFLT variability was associated with higher IOP fluctuation (β[SE]= 0.13[0.03]), intervening CE (β[SE]= 0.24[0.10]) and thicker baseline RNFLT (β[SE]= 0.01[0.00]), while smaller RNFLT variability was associated with better SQ (β[SE]= −0.02[0.01]) and better VF MD (β[SE]= −0.04[0.01]) and higher IOP (β[SE]= −0.02[0.01]) at baseline (P<0.05).

Figure 2 and supplemental Table 4 show the baseline models. In AD, only the baseline history of glaucoma surgeries showed association with greater RNFLT variability (β[SE]= 0.38[0.18], P=0.036). No other clinical factors showed association with RNFLT variability. In ED, baseline history of glaucoma surgeries (β[SE]= 0.21[0.09]) and thicker baseline RNFLT (β[SE]= 0.01[0.00]) showed association with greater RNFLT variability, while smaller RNFLT variability was only associated with better VF MD at baseline (β[SE]= −0.05[0.01]) (P<0.05).

Parsimonious models of AD and ED are presented in Figure 3 and Supplemental Table 5. Intervening CE during follow-up was the only predictor selected for AD and was associated with greater RNFLT variability (β[SE]= 0.90[0.12], P<0.001). As for ED, intervening CE (β[SE]= 0.20[0.08]) and intervening glaucoma surgeries (β[SE]= 0.17[0.08])

showed association with greater RNFLT variability, while better baseline VF MD (β[SE]= −0.03[0.01]) and better SQ (β[SE]= −0.02[0.01]) showed association with smaller RNFLT variability (P<0.05).

Sub-analysis without intervening surgeries

Given that intervening CE was the strongest predictor of RNFLT variability in both races and a higher proportion (although not statistically significant) of AD than ED had intervening CE, we completed a sub-analysis excluding eyes with intervening CE (Table 2). In the subgroup including only eyes without intervening CE, the differences in RNFLT variability between AD and ED reduced and were no longer significant (mean [95%CI] variability: AD=1.40 [1.31,1.48]; ED=1.34 [1.27,1.40]; P=0.280). We also completed another sub-analysis excluding eyes with either intervening CE or glaucoma surgeries and found no racial differences in mean (95% CI) RNFLT variability (AD: 1.36 [1.27,1.44] μm, ED: (1.29 [1.23,1.36] μm; P=0.275). In the full models of eyes without intervening CE (Supplemental Table 6), greater IOP fluctuation and OCT SQ remained associated with increased and decreased RNFLT variability in AD, respectively (P<0.05), although IOP fluctuation was no longer a significant factor in ED (P=0.136). The R^2 decreased considerably after exclusion of intervening CE.

DISCUSSION

Following up our previous study,[14] we performed a race-stratified analysis comparing the long-term RNFLT variability in AD and ED glaucoma individuals and its associated clinical predictors. Although the overall RNFLT variability of AD was higher, the mean difference was small, and both races demonstrated low variability. Moreover, after excluding the effects of intervening CE, RNFLT variability reduced further in both races, and racial difference was no longer present. Several clinical factors were found to affect longitudinal RNFLT measurements, particularly intervening CE, which may reduce the ability to detect progressive thinning in glaucoma patients. To improve progression detection and RNFLT reliability across different races, these factors should be considered when assessing RNFLT thinning.

To our best knowledge, this is the first study to directly examine the long-term OCT variability of AD compared to another race. In general, both races demonstrated low RNFLT variability, although the overall variability of AD was around 0.2 μm (15%) higher than that of ED. Given the small difference observed, whether it is clinically meaningful and may impact RNFLT progression detection remains to be determined. Of note, underlying differences in baseline age and testing frequency were noticed between AD and ED. Since glaucomatous damage usually becomes more prominent with aging,[21] the older age of ED might have contributed to more prominent RNFLT changes. Similarly, the lower testing frequency in AD might cause slightly greater measurement variability.[14]

Interestingly, computer simulations have investigated how changes in VF variability may affect functional assessment. One study showed a 20% increase in the variability of standard automated perimetry would cause VF progression to be detected one visit later. [22] In another, the VF variability of AD was 30% higher than that of ED, which was

associated with a 3-year delay in progression detection.[13] Although the racial difference in OCT variability seemed smaller than that of VF, these studies provide a general idea on the potential negative consequences of a greater measurement variability on progression detection. It is also important to note that AD may be more susceptible to delayed progression detection in clinical practice for other reasons, such as the faster rate of progression and the lower visit frequency.[23] Therefore, clinicians should be aware of a greater racial difference in RNFLT variability and its possible associated impact on progression assessment in clinical practice.

Similar to prior finding on a general glaucoma cohort,[14] among the many factors examined, intervening CE showed consistent and the strongest associations with higher RNFLT variability in both AD and ED. Furthermore, as compared to visits without the effects of intervening CE, a higher RNFLT variability was found for visits after intervening CE (increase in variability: 0.26μm for AD, 0.15μm for ED; P<0.05 for both). The presence of lens opacity has been shown to attenuate OCT signal strength and affect eye-tracking and repositioning, leading to fluctuating measurements.[24 25] Similarly, the post-CE increase in OCT SQ, which was observed for both groups in our study (P<0.001), and post-CE refractive change may also cause thickness measurements to vary.[24–26] This was supported by the increase in RNFLT measurement after intervening CE in our cohort (difference between pre-CE and post-CE visit: 1.84μm, P=0.01). In general, our results suggest the need to more carefully assess RNFLT changes in glaucoma patients receiving CE during follow-up (e.g., by establishing a new imaging baseline after CE[14]). Additionally, modified practice standards, such as increasing imaging frequency or scan number, may also help improve progression assessment.[27 28]

Interestingly, while intervening CE also demonstrated a noticeable effect on RNFLT variability in ED (>0.2 μm), it seemed to affect AD more strongly, with an effect of >0.90 μm. To examine if the post-CE alteration in the aforementioned clinical factors vary based on races, we analyzed the changes in refractive power and SQ associated with intervening CE in our cohort. While the post-CE refractive change was insignificant in both groups (~−0.2 diopter), a greater improvement of mean SQ was noticed in AD (~5 units, P<0.001). Given the effect of scan quality on measurement accuracy, as aforementioned, it might be beneficial to establish a new imaging baseline after CE, especially in AD patients, in order to assess progression more reliably. Of note, in subgroup analysis on eyes without intervening CE, the racial difference in RNFLT variability became smaller and no longer statistically significant. Considering their similar measurement variability after elimination of intervening CE, our sub-analysis suggests OCT may demonstrate comparable reliability for patients of difference races once relevant factors contributing to RNFLT variability are accounted for, particularly modifiable ones.

Some other shared predictors were identified in individual models. Although not selected in the parsimonious model of AD, a better SQ predicted lower RNFLT variability in both races in the full models and sub-analysis excluding intervening CE. Therefore, our finding supports enhancing OCT SQ and excluding poor-quality scans when assessing structural progression, regardless of patient race. Another shared predictor noticed was IOP fluctuation, which in some but not all studies has been reported a risk factor for

functional and structural worsening.[29–31] Similar to that found for VF,[12] greater IOP fluctuation was associated with higher RNFLT variability in the full models. It also remained a significant predictor in AD after excluding intervening CE. One possibility is its potential association with ocular procedures,[32 33] as a minor but statistically significant decrease in mean IOP (~1.3 mmHg, P<0.001) was observed after intervening CE in both groups. Animal studies have also shown reversible RNFLT change associated with minor IOP variation.[34 35] Since maintaining a stable target IOP is important in managing glaucoma, for both AD and ED, optimizing IOP control will only benefit disease control, in addition to improving OCT evaluation.

There are several study limitations. First, we evaluated only Spectralis OCT, and other OCT devices might have different RNFLT variability profiles.[4 18 36] Additionally, measurement variability may be underestimated as images with poor scan quality and segmentation errors, the major factors driving variability in clinical practice, were excluded. Nonetheless, this further suggests the importance to investigate the predictors of RNFLT variability for a better real-world evaluation. Second, prior studies have demonstrated that reproducibility of sectors is worse than that of global metrics.[18 37–39] Investigation of the variability of sectoral RNFLT and how it may affect OCT progression across races is unknown and a subject for future study. Third, as most included eyes had mild glaucoma, our cohorts may not fully represent clinic populations with more advanced glaucoma. Last, given the limited case number of other races, only AD and ED were assessed. However, since this is a novel topic and AD and ED constitute a large proportion the United States population, our findings may serve as the basis for future investigation with a more diverse and comprehensive inclusion.

In conclusion, although several clinical factors were found to affect RNFLT measurements, the long-term RNFLT variability was generally low in both AD and ED. Moreover, the racial difference in RNFLT variability did not remain once the effect of intervening CE, the strongest predictor of higher variability, was eliminated. One should be cautious when assessing progression in glaucoma patients receiving intervening CE, particularly AD, for which altered practice standard should be considered. Our findings may improve structural assessment and suggest that, when accounting for relevant factors, the reliability of OCT-measured RNFLT is comparable across these races.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

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What is already known on this topic:

Prior studies have shown racial differences in the ocular structure and VF measurement variability between individuals of AD and ED. While largely unexplored, understanding the race-stratified long-term variability of OCT-measured RNFLT and its predictors will help to assess structural changes in AD more reliably.

What this study adds:

AD had a slightly higher RNFLT variability than ED, although the variability was generally low in both races. Among the few predictors identified, intervening cataract extraction was the strongest predictor of a higher RNFLT variability in both races; after eliminating this factor, RNFLT variability became smaller and similar for AD and ED.

How this study might affect research, practice, or policy:

Once relevant predictors are accounted for, longitudinal RNFLT assessment should be reliable for both AD and ED glaucoma patients.
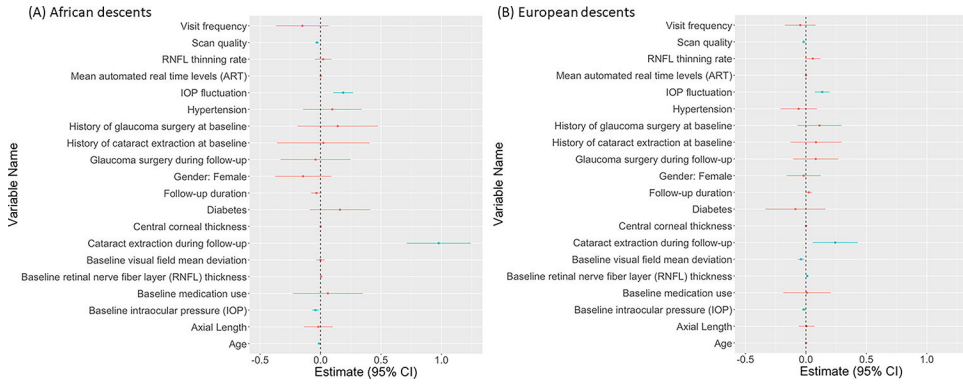
Figure 1.

Full models of (A) African descents and (B) European descents. On the x-axis of the forest plots, dots indicate the coefficient estimates and the bars indicate the 95% confidence intervals (CI). Blue and red indicates significant and insignificant effects, respectively. Estimates for the effects of continuous variables are reported for per 1-unit increase in the variable as indicated in the corresponding tables.
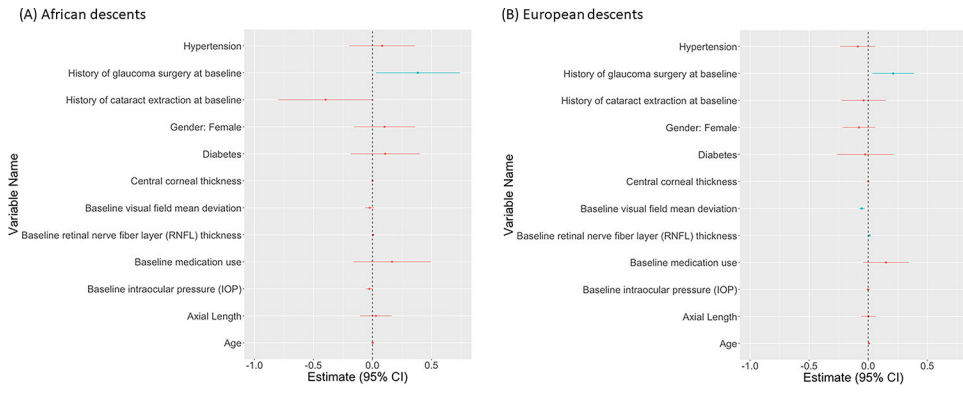
Figure 2.
Baseline models of (A) African descents and (B) European descents. On the x-axis of the forest plots, dots indicate the coefficient estimates and the bars indicate the 95% confidence intervals (CI). Blue and red indicates significant and insignificant effects, respectively. Estimates for the effects of continuous variables are reported for per 1-unit increase in the variable as indicated in the corresponding tables.
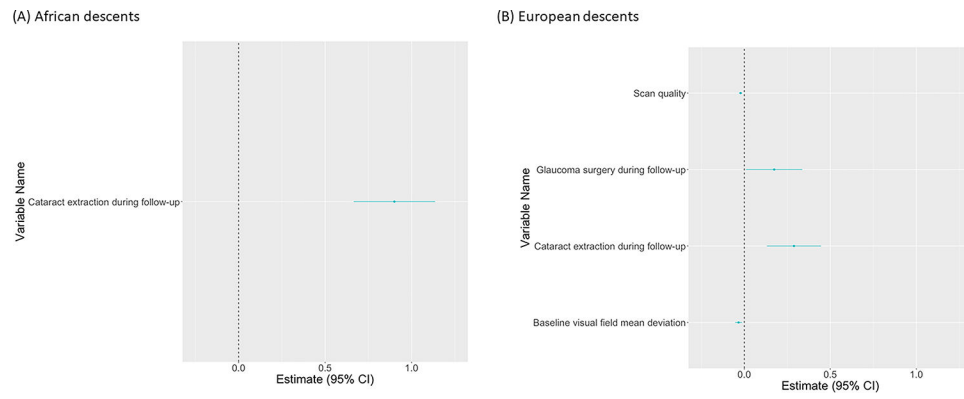
Figure 3.

Parsimonious models of (A) African descents and (B) European descents. On the x-axis of the forest plots, dots indicate the coefficient estimates and the bars indicate the 95% confidence intervals (CI). Blue and red indicates significant and insignificant effects, respectively. Estimates for the effects of continuous variables are reported for per 1-unit increase in the variable as indicated in the corresponding tables.

Table 1:

Characteristics of the included subjects and eyes

	AD (376 eyes, 226 participants)		ED (625 eyes, 349 participants)		
	Mean (95% CI)	Median (Range)	Mean (95% CI)	Median (Range)	P-value
Patient-level characteristics					
Age at baseline (years)	63.4 (62.0, 64.8)	62.5 (23.2, 90.5)	66.8 (65.7, 67.8)	67.4 (32.3, 95.9)	**<0.001**
Sex (Female, n)	138 (61.1%)	-	188 (53.9%)	-	0.102
Hypertension (Hypertensive, n)	146 (64.6%)	-	149 (42.7%)	-	**<0.001**
Diabetes (Diabetic, n)	48 (21.2%)	-	29 (8.3%)	-	**<0.001**
Eye-level characteristics					
Diagnosis (n)					
Glaucoma suspect	160 (42.6%)	-	317 (50.7%)	-	
POAG	216 (57.4%)		308 (49.3%)		
Baseline variables					
Baseline IOP (mmHg)	16.5 (15.9, 17.1)	16 (2, 32)	16.3 (15.8, 16.8)	16 (1, 34)	0.664
Baseline CCT (μm)	533.8 (528.3, 539.4)	531.3 (398.5, 654.0)	551.6 (547.2, 555.9)	552.7 (429.7, 694.0)	**<0.001**
Baseline axial length (mm)	24.0 (23.8, 24.1)	23.8 (19.4, 26.9)	24.0 (23.9, 24.1)	24.0 (17.9, 26.9)	0.699
Baseline 24–2 VF MD (dB)	−2.7 (−3.1, −2.3)	−1.8 (−14.0, 2.7)	−2.1 (−2.4, −1.8)	−1.0 (−13.9, 3.0)	**0.024**
Baseline 24–2 VF PSD (dB)	3.4 (3.1, 3.8)	2.2 (1.1, 16.7)	3.3 (3.1, 3.6)	1.9 (0.9, 15.3)	0.645
Baseline RNFLT (μm)	81.2 (79.2, 83.1)	81 (42, 124)	79.5 (77.9, 81.0)	79 (41, 131)	0.177
Baseline history of cataract extraction (n)	42 (11.2%)	-	129 (20.6%)	-	**<0.001**
Baseline history of glaucoma surgery (n)	62 (16.5%)	-	165 (26.4%)	-	**<0.001**
Glaucoma medication use at baseline	312 (83.0%)	-	520 (83.2%)	-	0.931
Longitudinal variables					
Mean IOP during follow-up (mmHg)	15.6 (15.1, 16.1)	14.9 (5.7, 30.0)	15.6 (15.2, 16.0)	15.4 (2.4, 28.6)	0.957
IOP fluctuation (mmHg)	2.6 (2.5, 2.8)	2.3 (0, 10.9)	2.5 (2.3, 2.6)	2.3 (0, 12.3)	0.155
RNFLT thinning rate (pm/year)	−0.8 (−0.9, −0.7)	−0.7 (−16.0, 13.0)	−0.6 (−0.7, −0.5)	−0.6 (−0.7, −0.5)	**0.025**
Intervening cataract extraction (n)	95 (25.3%)	-	125 (20.0%)	-	0.058

	AD (376 eyes, 226 participants)		ED (625 eyes, 349 participants)		
	Mean (95% CI)	Median (Range)	Mean (95% CI)	Median (Range)	P-value
Intervening glaucoma surgery (n)	78 (20.7%)	-	119 (19.0%)	-	0.513
Scan quality	28.1 (27.8, 28.4)	28 (10, 41)	27.9 (27.6, 28.1)	28 (10, 41)	0.171
Automatic Real Time (ART)-function	55.7 (53.4, 57.9)	65 (2, 100)	60.3 (58.5, 62.1)	71 (2, 100)	**0.002**
Number of follow-up visits	10.2 (9.5, 10.8)	12 (4, 30)	10.1 (9.6, 10.6)	11 (4, 29)	0.806
Follow-up time (years)	7.0 (6.7, 7.4)	9.1 (2, 12.3)	6.3 (6.0, 6.6)	7.1 (2.1, 12.3)	0.002
Frequency of visits/testing (times/year)	1.5 (15, 1.6)	1.5 (0.4, 4.4)	1.7 (16, 1.7)	1.7 (05, 4.2)	**<0.001**

Footnote: Unless otherwise indicated, values are shown in mean (95% CI) and median (range).

Abbreviations: POAG = primary open angle glaucoma; CCT = central corneal thickness; VF = visual field; MD = mean deviation; PSD = pattern standard deviation, IOP = intraocular pressure; RNFLT= RNFL thickness

Table 2.

RNFLT variability of AD and ED in subgroups without intervening surgeries

Subgroups	African descents		European descents		
	Counts of eyes (subjects)	RNFLT variability (μm)	Counts of eyes (subjects)	RNFLT variability (μm)	P-value
Eyes without intervening CE	281 (177)	1.40 (1.31, 1.48)	500 (293)	1.34 (1.27, 1.40)	0.280
Eyes without intervening CE and/or glaucoma surgeries	235 (154)	1.36 (1.27, 1.44)	427 (261)	1.29 (1.23, 1.36)	0.275

[*] Variability was presented in mean (95% confidence interval)

Abbreviation: RNFLT= retinal nerve fiber layer thickness; CE = cataract extraction