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Central Corneal Thickness in Northwestern American Indian/ Alaskan Natives and Comparison to White and African Americans

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Abstract

Purpose—To determine the demographic factors associated with central corneal thickness (CCT) in Northwestern American Indian/Alaskan Natives (AI/AN), and compare these CCT measurements to white and African Americans.

Design—Cross-sectional comparative observational study.

Methods—We performed ultrasonic pachymetry (DGH-500 Pachette; DGH Technologies, Exton, PA.) on a random sample of AI/AN subjects from 3 randomly selected AI/AN tribes in the Northwest United States (n=429). Pachymetry was also performed on a convenience sample of white (n=46) and African Americans (n=33). Our main outcome measure was the average of right and left eye CCT.

Results—Average AI/AN CCT was 554.8 +/- 33.9 microns. AI/AN CCT was found to be thicker than African Americans (528.5 +/- 33.2) but similar to Whites (551.9 +/-28.3). CCT was greater in AI/AN females than males (557.6 +/- 33.3 vs. 550.1 +/- 34.5, $p=0.03$). We found no difference in CCT based on percent AIAN heritage, age, and keratometry readings. We found no significant differences in mean CCT between AI/AN with glaucoma (556.2 microns) and those who did not have glaucoma (556.6 microns).

Conclusion—CCT measurements for the Northwest AI/AN population are similar to those of Whites but thicker than those of African Americans. While glaucoma is common in AI/AN, we did not find an association with thin CCT. We need future studies to explore the risk factors for glaucoma in AI/AN.

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Institutional Review Board (IRB): Both Legacy Health System and the Northwest Portland Area Indian Health Board Institutional Review Boards (IRB) approved this study. We obtained informed consent from all participants.

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INTRODUCTION

Thin central corneal thickness (CCT) is a risk factor for glaucomatous optic neuropathy.^{1, 2} One explanation may be that Goldmann applanation tonometry underestimates true intraocular pressure in cases of thin CCT. Alternatively, thin CCT may be an independent risk factor³ for glaucomatous disease and progression because it is a surrogate marker for other ocular structural features that predispose to glaucoma, such as a thin lamina cribrosa or a long axial length.^{4, 5}

While we do not clearly understand the nature of CCT and risk of glaucomatous disease, researchers need to identify ethnic groups with thin CCT because these groups may be at a higher risk for developing glaucoma. Studies identify African Americans as having a thinner CCT than Whites.⁶⁻⁸ Other studies have also shown thin CCT to be present in Japanese and Mongolian populations when compared to studies in Whites.^{6, 9}

To our knowledge, researchers have not published results of CCT in the American Indian and Alaskan Native (AI/AN) population. The purpose of this study is to characterize CCT in a random sample of AI/AN and identify demographic factors that correlate with CCT. Secondly, we determine whether CCT is thinner in AI/AN with glaucoma compared to AI/AN without glaucoma. Finally, we compare CCT of AI/AN to white and African American participants.

METHODS

Legacy Health System and the Northwest Portland Area Indian Health Board Institutional Review Boards (IRB) approved this study. We obtained informed consent from all participants.

Participants

We have published the methods, study design, recruitment, testing, and results elsewhere.¹⁰ Briefly, we randomly selected tribes from the Northwestern region of the United States (Oregon, Washington, and Idaho.) To be eligible, the tribal enrollment database must have included 400 adults over the age of 40 years. All selected tribes agreed to participate. We used the tribal enrollment databases to perform an age-stratified, random sampling of tribal members aged 40 years and older and excluded those who were deceased, seriously ill, or had dementia preventing them from participating in the study. For this ancillary study, we also excluded individuals with a history of refractive surgery or corneal disease.

To compare racial differences, we obtained a convenience sample of white and African American participants through voluntary participation in community glaucoma screenings in Portland, OR. Race was self-reported using a standardized questionnaire. We included consecutive participants with no history of corneal disease or refractive surgery. We recruited at least 33 white and African Americans based on a power analysis (see below).

Study Testing

In AI/AN, ophthalmic technicians performed automated refraction, keratometry, IOP with Tono-Pen XL (Medtronic Solan, Jacksonville, Fla.), and ultrasonic pachymetry (DGH-500 Pachette, DGH Technologies, Exton, PA.). We also performed manifest refraction, Frequency Doubling Technology (FDT) perimetry, confocal scanning laser ophthalmoscopy, and nonmydriatic photography; and will report these results in a separate manuscript.

Operators placed a drop of proparacaine 1%, then acquired ten automated sequential measurements of CCT from a single central location of the right eye, followed by the left eye. The pachymeter averaged these ten readings to provide a single CCT measurement for each

eye. We used the same ophthalmic technicians to perform pachymetry, and they used the same pachymeter to measure CCT in white and African American participants.

An ophthalmologist diagnosed glaucoma using the Foster Criteria categories (Category 1: cup-to-disc ratio $\geq .08$ or glaucomatous optic disc features and definite glaucomatous visual field loss; Category 2: cup-to-disc ratio $\geq .08$ or glaucomatous features and inability to complete visual field testing satisfactorily; Category 3: Visual field testing not possible and optic disc unable to be viewed, with either intraocular pressure (IOP) > 22 mm Hg or evidence of glaucoma surgery).¹¹ For this study, we defined glaucoma as the presence of any Foster Criteria category in one or both eyes.

For African American and white participants, we only performed pachymetry and frequency doubling technology perimetry as part of a community screening. Ophthalmic technicians performed pachymetry as described above.

Statistical Analysis

After confirming CCT had a normal distribution in all groups ($p > 0.05$, skewness and kurtosis), we used parametric univariate and multivariate statistical tests to characterize the association of demographic factors with CCT of AI/AN. We used an analysis of variance (ANOVA) model with Tukey post hoc honestly significant difference (HSD) as well as a multivariate linear regression equation to compare CCT differences by ethnicity. We averaged right and left eye CCT because the eyes had similar CCT (OD: 554.5 $\pm$ 36.0; OS 555.1 $\pm$ 34.4; $p = .56$). One patient only had monocular measurements secondary to prosthesis in the other eye, and this single measurement was used for CCT. Similarly, we averaged the mean keratometry of the right and left eye (OD: 786.3 $\pm$ 27.4; OS 785.2 $\pm$ 27.8; $p = 0.38$). We used SPSS (Version 10.0) for all statistical analyses.

We performed a power analysis ($\alpha = 0.05$, $\beta = 0.80$, and 15 micron difference, ANOVA with Tukey (HSD) to estimate the number of African Americans and white subjects needed to demonstrate a difference in CCT between AI/AN and these groups.⁸ The power analysis showed a sample size of 33 participants each in the African Americans and white groups.

RESULTS

American Indian/Alaskan Natives Recruitment

Of 631 randomly selected tribal members who were eligible to participate in the study, 74 (11.7%) declined and 118 (18.7%) agreed to participate but did not show up for the screening. We excluded one participant with a history of refractive surgery and an additional 8 participants who refused testing of pachymetry. This resulted in 429 AI/AN participants, with 68.0% participation.

We compared age and gender of participants to those that did not participate. Age and gender were similar ($p > 0.05$ for both age and gender) between participants, non-participants, and the tribes overall. We were unable to collect percentage AI/AN, income, and medical history from those who did not participate. Table 1 lists the demographic characteristics of the AI/AN participants.

American Indian/Alaskan Natives Central Corneal Thickness

Average CCT was 554.8 $\pm$ 33.9 microns. CCT was greater in females (557.6 $\pm$ 33.3) than males (550.1 $\pm$ 34.5, $p = 0.03$). There was no difference in CCT based on percent AIAN heritage ($p = 0.57$), age ($p = .14$), and keratometry readings ($R^2 = 0.004$; $p = 0.18$).

We found no difference in CCT for those AI/AN participants with glaucoma ($n = 52$, mean $\pm$ SD = 556.2 ± 38.5) when compared to those without glaucoma ($n = 377$, mean $\pm$ SD = 556.6 ± 33.4 , $p = .80$)

We categorized each eye into without glaucoma ($n = 384$ right eyes, and $n = 396$ left eyes); Foster's Category 1 ($n = 29$ right eyes, and $n = 20$ left eyes); or Foster's Category 2 ($n = 11$ right eyes, and $n = 11$ left eyes). We did not find an eye with Foster's Category 3. A participant could have any combination of the above results. In the right eye, CCT (mean $\pm$ SD) was 555.4 ± 35 , 564.7 ± 40 , and 556.0 ± 48 , respectively for eyes without glaucoma, Foster's Category 1, and Foster's Category 2. In the left eye, CCT (mean $\pm$ SD) was 557.3 ± 33 , 551.3 ± 45 , and 548.3 ± 21 , respectively for eyes without glaucoma, Foster's Category 1, and Foster's Category 2. We found no statistical difference when comparing the eyes without glaucoma, to those with a Foster's Category I or II in the right ($p \geq .53$) or left ($p \geq .76$) eye.

Differences in Central Corneal Thickness between American Indian/Alaskan Natives, African Americans, and whites

None of the African Americans or whites failed the FDT screening test. Table 1 shows AI/AN CCT to be thicker when compared to the African Americans participants ($p < 0.001$) but similar to the white participants ($p = .84$, ANOVA with Tukey post hoc HSD). Because small differences in age and gender occurred between AI/AN, African Americans, and whites, we used a multivariate linear regression equation with CCT as a dependent variable, and ethnicity, age, and gender as explanatory covariates to control for the effects of age and gender on ethnicity. This showed similar results when compared to the ANOVA model (Data not shown).

DISCUSSION

This study presents the first information regarding CCT in American Indian/Alaskan Natives (AI/AN). It represents a response rate of 68% and contains a large sample size ($n = 429$) that we randomly selected as part of a prevalence study. We show gender differences in CCT with females having thicker CCT than males. We show no associations of CCT with age, percentage AI/AN, or keratometry readings. AI/AN participants have similar CCT measurements when compared to whites, but thicker than African Americans. The CCT of AI/AN participants with glaucoma was similar to those without glaucoma. Overall, these results suggest that CCT is not the explanation for the higher prevalence of normal tension glaucoma in AI/AN.

Demographic associations with Central Corneal Thickness in American Indian/Alaskan Natives

The demographic results show both similarities and differences compared to studies in other ethnic groups. Studies suggest older age to be associated with thinner CCT,^{6, 7} but another study showed no association.⁸ Similar to the latter study, we showed no association with age. Studies show an association of higher keratometry measurements (steeper corneas) with thin CCT.^{8, 12} We did not show a significant relationship.

AI/AN women were associated with a decreased central corneal thickness when compared to men. Studies have had mixed results with women having thinner CCT in some studies,^{8, 12} but thinner CCT in men, or no association at all in other studies.^{6, 7} Overall, these heterogeneous results suggest that we need more information regarding the association of CCT with these demographic factors, and whether these different CCT results is related to ethnicity.

Ethnic differences in Central Corneal Thickness

Previous population studies show that African American, Japanese, Mongolian and Greenland Eskimo populations have thin CCT when compared to Whites.^{6, 9, 13} In the present study,

AI/AN had a CCT similar to white participants, but thicker than the African Americans participants, while other studies showed similar results (Table 2).^{6, 8} Overall, AI/AN had CCT most similar to the white participants.

One explanation for the similarity of AI/AN to the white participants, and the lack of thinner corneas such as seen in the Mongolian population, may be genetic admixture from contact with European settlers. We did not show any association with CCT when controlling for the proportion of AI/AN ethnicity. However, accuracy in estimating the proportion of ancestry is limited by cultural and political factors that may affect accuracy of self-reported ancestry. Genetic studies may help to determine the ethnic relationships with CCT.

Central Corneal Thickness and glaucoma

We hypothesized that thin CCT may explain the higher prevalence of glaucoma in AI/AN (8.1%¹⁰) when compared to whites (2.0%) and African Americans (6.2%). One prevalence study¹⁴ showed that 90% of Japanese glaucoma patients had IOP < 21 mm Hg and also had thin corneas (average CCT 521 microns). Similarly, we showed in AI/AN that 100% of glaucoma patients had intraocular pressure less than 21 mm Hg.¹⁰ In contrast, we did not show a thinner CCT in AI/AN when compared to white or African Americans. Similarly, we did not find AI/AN participants with glaucoma to have thinner CCT when compared to those without glaucoma. Therefore, CCT may not be an important explanatory factor for glaucoma in AI/AN, when compared to other risk factors for glaucoma such as diabetes or age. Future studies may identify unique risk factors for glaucomatous optic neuropathy in AI/AN when compared to other ethnic groups.

We collected CCT data from African American and white participants to compare the mean CCT in the AI/AN population. The same ophthalmic technicians collected the data for the white and African Americans using the same pachymeter. This study design is less likely to include instrument and operator error, such as ultrasonic frequency, angle of the probe to the cornea, and corneal location of the probe.¹⁵⁻¹⁷ Because a convenience sample was used for the African American and white populations, the possibility of bias is greater than a random sample. For example, our glaucoma screening at a health fair may increase the prevalence of ocular hypertension or prior suspicion of glaucoma. An over representation of ocular hypertension may skew results towards thicker CCT.^{6,7} An over representation of glaucoma suspect and glaucoma patients may skew towards thinner CCT.⁶ However, our CCT measurements are similar to other studies suggesting that these biases are probably minimal.^{6, 8}

This study reports CCT in AI/AN, which is data that is currently lacking in the literature. Thin CCT was not associated with glaucoma in AI/AN. CCT measurements for the Northwest AI/AN population are similar to those of whites but thicker than those of African Americans. Thin CCT does not explain the high prevalence of glaucoma and low-tension glaucoma in AI/AN.

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Table 1

Demographic and ocular characteristics of American Indian/Alaskan Natives (AI/AN), African American, and White participants.

	AI/AN (n=429)	African American (n=33)	White (n=46)
Age (range)	55.7 +/- 11.6 (40-88)	53.0 +/- 9.2 (40-76)	54.7 +/- 9.6 (41-81)
% Female	63%	53.6%	63.0%
% AIAN		N/A	N/A
Unknown	27 (6.1%)	-	-
<25%	55 (12.4%)	-	-
25% ≤ % < 50%	15 (3.4%)	-	-
50% ≤ % < 75%	76 (17.1%)	-	-
≥ 75%	271 (61.0%)	-	-
Mean * CCT (range)	554.8 +/- 33.9 (range= 451.5-646)	528.5 +/- 33.2 (range= 460.5-577.5)	551.9 +/- 28.3 (range= 502-615)
Mean * Keratometry (mm)	785.8 +/- 27.2	-	-

* Average of right and left eyes

N/A= Not applicable (not collected from African American and White participants)

Table 2

Summary of central corneal thickness measurements (in micrometers) between American Indian/Alaskan Natives (AI/AN), African American, White, Japanese, Eskimo, and Mongolian populations.

	Northwest AI/AN	African American	White	Japanese	Eskimo	Mongolian
Current Study [#]	554.8 SD 33.9 N=429	528.5 SD 33.2 n=33	551.9 SD 28.3 n=46	-	-	-
Aghaia E, et al ^{6#}	-	521.0 SE 3.9 n=107	550.4 SE 3.2 n=186	531.7 SE 4.1 n=121	-	-
Shimmyo et al ^{8#}	-	535.5 SD 33.4 n=116	552.6 SD 34.5 n=1466	-	-	-
Foster et al ^{9*}	-	-	-	-	-	504.5 SD 32 n=1129
Alsbirk et al ^{13*}	-	-	-	-	523.7 SD 30.5 N=839	-

[#] = Ultrasonic pachymetry

^{*} = Slit lamp optical pachymetry

SD= Standard deviation

SE= Standard error