The Characteristics of Glaucoma in Japanese Americans

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Objective: To determine the proportions of glaucoma subtypes and risk factors for glaucoma in a large Japanese American clinic population.

Methods: Medical records of patients of Japanese descent who visited 2 private ophthalmology clinics within the last 10 years were retrospectively reviewed. Glaucoma was diagnosed based on optic nerve findings and presence of visual field defects. Main outcome measures were distribution of glaucoma subtypes, characteristics of different glaucoma subtypes, and comparative results with Japanese American patients without glaucoma.

Results: Of 1732 patients, 112 had glaucoma (6.4%). Of these, 17% had high-tension glaucoma (HTG) and 70% had normal-tension glaucoma (NTG). There were 2 patients with primary angle-closure, 3 with mixed-mechanism, and 10 with secondary glaucoma. The presence of glaucoma was positively correlated with age, refractive error, visual acuity in logarithm of the minimum angle of resolution, and intraocular pressure, while there was a negative correlation between central corneal thickness and glaucoma. Controlling for age, intraocular pressure and visual acuity remained significantly correlated with glaucoma.

Conclusions: In this large Japanese American clinic population, the proportion of patients with glaucoma who had NTG was 4-fold higher than those with HTG. A prospective population-based study may be warranted to further define the spectrum of glaucoma and the reason for the high proportion of NTG in this population.


In Japanese adults, glaucoma was reported as the second most common reason for low vision.1 The Tajimi Study2 conducted in Japan reported a glaucoma prevalence of 5.0% and a glaucoma suspect prevalence of 2.5%. A total of 78% of all patients with glaucoma in this study had primary open-angle glaucoma (POAG). Of the patients with POAG, 92% had intraocular pressure (IOP) measurements of 21 mm Hg or less and were classified as having normal-tension glaucoma (NTG).2,3 There is no population-based study of Asian Americans conducted in the United States, and the data available are limited to studies from Asia that may not adequately reflect the true epidemiology in the United States.

According to the 2000 US Census,4 4.2% of the 281.4 million US residents were reported as Asian. Those classified as Japanese were among the 4 most numerous Asian subgroups. This study sought to define the proportions of glaucoma subtypes and risk factors for glaucoma in a large Japanese American clinic population.

Methods

Institutional review board approval was obtained from the University of California, San Francisco, and the California Pacific Medical Center. Patients who visited 2 private ophthalmology clinics with high numbers of patients of Japanese ancestry within the last 10 years were evaluated. One of the clinics specialized in glaucoma and the other was for general ophthalmology. Japanese American ethnicity in this study was defined by self-description in the initial new patient questionnaire. We excluded patients without a social security number (n=4) because they were noted to be tourists from Japan.

Medical records were reviewed for age, sex, ocular diagnoses, past medical history, previous ophthalmologic history, use of systemic and ophthalmic drugs, best-corrected visual acuity (BCVA), refractive errors, and slitlamp findings. Intraocular pressure measurements, central corneal thicknesses (CCT), cup-disk ratios (CDR), gonioscopy measurements, and visual fields were recorded when available. Visual field data were ordered by the physician when there was clinical suspicion of glaucoma. Van Herick grading of the anterior chamber angle was performed for all patients, and gonioscopy with a Zeiss-style lens was per-
formed in narrow-angle suspect eyes (≤ grade II by van Herick). Cup-disk ratios were clinically assessed by ophthalmologists (G.T. and D.H.) by indirect slitlamp biomicroscopy with a 90-diopter (D) handheld lens as recorded in the patients’ records. Some patients who were recorded as having a normal ratio had a CDR of 0.4 or less; however, they were not included in the analysis because no specific CDR was recorded. Central corneal thicknesses were measured by Corneo-Gage Plus (Sonogage Inc, Cleveland, Ohio), an ultrasound pachymeter, and mean values from the records were recorded. Visual fields were 30-2 Swedish Interactive Thresholding Algorithm (SITA) Standard fields by the Humphrey Field Analyzer II (Zeiss Meditec Inc, Dublin, California) until and including 2006. Later fields were 24-2 SITA-Standard Humphrey visual fields.

Glaucoma diagnoses were based on optic nerve head appearance and presence of glaucomatous visual field defects: (1) optic nerve head vertical CDR of 0.7 or more or a difference in the vertical CDR of 0.2 or more between both eyes; (2) the visual fields were judged to be abnormal when there were 3 or more nonedge contiguous points in the pattern deviation plot, with a probability of less than 5% in a reliable visual field. Reliable visual fields were those with fixation loss, false-negative, and false-positive values of 50% or less.

Glaucoma was diagnosed if both criteria were met. The patient was defined as a glaucoma suspect if only 1 was met. Also, for patients who did not have reliable visual fields, a CDR of 0.9 or higher was accepted as diagnostic for glaucoma. Patients were diagnosed as having glaucoma if they had a diagnosis of glaucoma in either eye.

Glaucoma was classified as primary or secondary and further subclassified as angle-closure (ACG) or open-angle glaucoma. Patients with glaucoma and a history of acute ACG and patients who had gonioscopy results showing a Schaffer grade of 2 or less in at least 3 quadrants were diagnosed as having ACG. When there was progressive glaucoma in patients with a history of narrow-angle and laser iridotomy, they were subclassified as having mixed-mechanism glaucoma. Patients with POAG who never had an IOP of more than 21 mm Hg were defined as having NTG, and those with a recorded IOP greater than 21 mm Hg were defined as having high-tension glaucoma (HTG).

For patients with glaucoma, we used the data from the date of diagnosis. In addition, 3 consecutive IOP measurements were recorded before initiating an IOP-lowering regimen. Moreover, the entire chart was reviewed for any IOP higher than 21 mm Hg. For the patients who were already treated with antiglaucoma medications, IOPs prior to treatment were gathered from the referral notes and histories in their records, when present, for their classification. Patients with an IOP higher than 21 mm Hg despite the medication were classified as having HTG. In the absence of these data, the patient was classified according to the diagnosis by the physician.

The BCVAs recorded as Snellen acuities were converted to logarithm of minimal angle resolution (logMAR) for statistical analysis. The spherical equivalents (SE) were calculated from the refractive errors by adding half of the cylindrical value to the spherical value.

The medical history of the patients was also recorded. If patients used medications for a chronic health condition (eg, antihypertensive drugs), they were considered to have the disease. Systemic diseases used in the analysis were hypertension, diabetes mellitus, coronary artery disease, pulmonary diseases, hypercholesterolemia, and hyperthyroidism.

All statistical analyses were performed with SPSS 12.0 (SPSS Inc, Chicago, Illinois) software. The Mann-Whitney U test was used for comparisons between diagnostic groups. Multiple regression analysis was performed to control for age. Correlations between continuous numerical and ordinal variables were calculated by Pearson correlation and χ²-tests. Suspects were not evaluated as a separate group in the analyses because they were a heterogeneous group, including those with physiologic cupping and potentially insignificant visual field defects. Statistical significance was described as a probability value of P < .05 in all analyses.

<table>
<thead>
<tr>
<th>Glaucoma Type</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td></td>
</tr>
<tr>
<td>OAG</td>
<td></td>
</tr>
<tr>
<td>HTG</td>
<td>19 (16.9)</td>
</tr>
<tr>
<td>NTG</td>
<td>78 (69.6)</td>
</tr>
<tr>
<td>MMG</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>ACG</td>
<td></td>
</tr>
<tr>
<td>Acute angle-closure</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Chronic angle-closure</td>
<td>1 (0.9)</td>
</tr>
</tbody>
</table>

Abbreviations: ACG, angle-closure glaucoma; HTG, high-tension glaucoma; MMG, mixed-mechanism glaucoma; NTG, normal-tension glaucoma; OAG, open-angle glaucoma.

Table 1. Distribution of Glaucoma Types Among Japanese Americans

There were 1732 Japanese American patients in this clinic population. A total of 624 (36%) were men. The mean (SD) age was 58.5 (20.6) years (range, 18-99 years). The mean (SD) BCVA was 0.13 (0.28) logMAR with a mean (SD) SE of −2.03 (3.29) D. The mean (SD) IOP was 16.49 (4.34) mm Hg and the mean (SD) CCT was 543.49 (38.66) µm. Right eyes were included in the analyses when both eyes had the same diagnosis, and left eyes were included when only the left eye had been diagnosed with glaucoma or glaucoma suspicion. There were 41 left eyes in the study. There were 112 (6.4%) patients with glaucoma and 181 (10.5%) with glaucoma suspect according to our study criteria. When we analyzed 1321 patients aged 40 years or older, 8.3% had glaucoma and 13.3% had glaucoma suspect.

Of the patients with glaucoma, 102 had primary and 10 had secondary glaucoma. Of the patients with primary glaucoma, 1 had chronic angle-closure, 1 had acute-angle closure, and 3 had mixed-mechanism glaucoma. Of the patients with POAG, 19.6% (19 of 97 patients) had HTG and 80.4% (78 of 97 patients) had NTG (Table 1).

There was only 1 secondary angle-closure glaucoma case that was due to previous ocular trauma. There were 2 neovascular glaucoma cases secondary to retinal vein occlusion and 1 pigmented, 1 aphakic, and 2 uveitic glaucomas. Bilateral glaucoma secondary to high-dose oral prednisone was seen in 1 patient while there were 2 unilateral cases secondary to intraocular and periocular steroid injections.
The glaucoma proportions in the subpopulations from the glaucoma and general ophthalmology clinics were 34.7% (25 of 72 patients) and 5.3% (87 of 1660 patients), respectively (P < .001). Distribution of glaucoma types was similar between the 2 subpopulations (P = .44) (data not shown). Normal-tension glaucoma comprised 76.2% (16 of 21 patients) and 81.6% (62 of 76 patients) of the patients with POAG in the glaucoma and general ophthalmology clinics, respectively (P = .58).

There were 16 patients with glaucoma who were on topical antiglaucoma medication from the first visit with the practitioner. After exclusion of those patients, who may be misclassified, the rate among all patients with POAG was 83.5% (71 of 85 patients) for NTG and 16.3% (14 of 85 patients) for HTG. The mean (SD) IOP of patients with glaucoma who were not receiving treatment was 19.56 (10.08) mm Hg.

The mean (SD) IOP in patients who had neither glaucoma nor glaucoma suspect (patients without glaucoma, n = 1260) was 15.92 (3.03) mm Hg. Patients with glaucoma (n = 112) have significantly higher mean (SD) IOPs (19.23 [9.59] mm Hg) than patients without (P < .001). The mean (SD) IOP of patients with HTG and NTG were 19.23 (9.59) mm Hg.

The mean (SD) CCTs in patients with HTG and NTG were 524.08 (38.97) µm and 554.79 (38.79) µm, respectively (P = .001). The mean (SD) SEs of patients with HTG and NTG were −0.81 (2.04) and −0.86 (2.78), respectively (P = .74). After the exclusion of aphakic and pseudophakic patients, SE remained positively correlated with diagnosis of glaucoma (P < .001).

The patients with glaucoma were older (mean [SD] age, 72.4 [11.7] years) than those without glaucoma (mean [SD] age, 55.9 [20.9] years; P < .001). The mean (SD) ages of the patients with HTG and NTG were 74.3 (7.3) and 72.2 (11.9), respectively (P = .76). Of the patients with glaucoma, 16.5% (18 of 109) had at least 1 other family member with glaucoma, while this rate was 7.1% (100 of 1402) for patients without glaucoma (P = .001). Familly history of glaucoma was present in 27.8% and 15.6% of patients with HTG and NTG, respectively (P = .22).

Medical history was available for 106 (94.6%) patients with glaucoma and 1393 (96.8%) without. The distribution of the systemic diseases other than hypertension and coronary artery disease were similar between patients with and without glaucoma. Hypertension was present in 53.8% and 26.5% of the patients with and without glaucoma, respectively. These rates were 4.7% and 1.3%, respectively, for coronary artery disease (P < .001 and P = .02). Controlling for age and sex, none of the systemic diseases showed significant correlation with the diagnosis (P = .12 and P = .09 for hypertension and coronary artery disease, respectively). Prevalence of all relevant systemic diseases were similar among patients with HTG and NTG (P > .05). The CCT values were positively correlated with diabetes mellitus (P = .02), while there was no correlation with other systemic diseases.

The presence of glaucoma was positively correlated with age, SE of the refractive error, IOP, and BCVA in logMAR, while there was a negative correlation between CCT and glaucoma. Controlling for age, IOP and BCVA in logMAR remained positively correlated with the presence of glaucoma (Table 2).

When the correlations between age and clinical parameters were evaluated in patients without glaucoma, older

### Table 2. Association of Clinical Parameters With Diagnosis of Glaucoma

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Glaucoma (Mean ± SD)</th>
<th>No Glaucoma (Mean ± SD)</th>
<th>P Value</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA, logMAR</td>
<td>0.30 (0.60)</td>
<td>0.11 (0.24)</td>
<td>&lt;.001</td>
<td>.04</td>
</tr>
<tr>
<td>SE, D</td>
<td>−0.62 (3.05)</td>
<td>−2.21 (3.28)</td>
<td>&lt;.001</td>
<td>.01</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>19.23 (9.59)</td>
<td>15.92 (3.03)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CCT, µm</td>
<td>524.08 (38.97)</td>
<td>554.79 (38.79)</td>
<td>&lt;.001</td>
<td>.07</td>
</tr>
</tbody>
</table>

Abbreviations: CCT, central corneal thickness; D, diopter; IOP, intraocular pressure; logMAR, logarithm of the minimum angle of resolution; SE, spherical equivalent of the refractive error; VA, visual acuity.

*P values are by Mann-Whitney U test. Multiple regression analysis controlled for age.
patients were found to have larger CDRs (correlation coefficient [CC] = 0.193; \( P < .001 \)). While there was no significant correlation between IOP and age (CC = 0.01; \( P = .72 \)), the reduction in CCT with age was borderline significant (CC = -0.166; \( P = .05 \)). Older patients had worse visual acuity by logMAR (CC = 0.312; \( P < .001 \)). Myopia decreased as age increased in this study population, with a correlation coefficient of 0.422 for SE and age (\( P < .001 \)). This correlation remained significant, even when we excluded patients who had undergone cataract surgery (CC = 0.433; \( P = .03 \)).

**COMMENT**

The proportion of patients with glaucoma (8.3%) in this study population is higher than that defined in population-based studies in Japan.\(^2\)\(^3\) The main reason is likely the selection bias introduced by choosing patients from a clinic—including one that is glaucoma-based—rather than a general population.

Previous studies\(^6\)\(^7\) described that optic nerve sizes and structures are different among different races. Uchida et al\(^1\) described the normal optic nerve structures of Japanese persons and found a mean (SD) CDR of 0.26 (0.12) (range, 0.007-0.595). The Tajimi Study used 0.7 and 0.9 for their cutoff values of CDR, but did not report the distribution in their study. We used diagnostic criteria similar to that of the Tajimi Study for comparison of our results.

In the Tajimi Study, 78% of all glaucomas were classified as POAG, whereas our proportion was 86.5%. The proportion of ACG in the Tajimi Study (12%) was substantially higher than our rate.\(^3\) Even with the inclusion of mixed-mechanism glaucoma in the angle-closure group, our percentage was 4.5%. In population-based studies, closed or narrow-angle diagnoses depend on gonioscopy, and not all patients in our study had gonioscopy documented, which may be a reason for underestimation of these diagnoses. Every patient had anterior chamber evaluation and assessment of the angle by the Van Herick method, which has been shown to have high sensitivity and specificity by many studies, including those conducted in Japanese populations.\(^9\)

Secondary glaucoma comprised only 9% of the glaucoma in our study, and this proportion is similar to that in the Tajimi Study,\(^3\) in which almost half of the secondary glaucomas were associated with exfoliation material, while pseudoxfoliative glaucoma was not diagnosed in our study. The pseudoxfoliation syndrome rate reported by a separate study was 3.4% in a Japanese population aged 50 years or older.\(^10\) Our participants were younger overall, but still there may be some underdiagnosis of exfoliative material because of undilated examination of some patients or lack of recording.

The most distinctive result in this study is the high proportion of NTG. In a previous review, it was found that maximum IOP levels varied significantly among NTG studies, but that 21 mm Hg was the most common.\(^11\) In the Tajimi Study, 92.3% of all patients with POAG had IOPs of less than 22 mm Hg and were classified as having NTG. In the present study, NTG comprised 80.4% of all POAG cases, with the same IOP cutoff. Also in the Tajimi Study, participants were classified as having HTG if they had an IOP higher than 21 mm Hg in either the screening or the definitive examination for the study. Although there was no diurnal monitoring done in our study, we reviewed the full medical records for any high pressures; this may have reduced the number of patients in our study characterized as having NTG.

The lower rate of NTG may also be owing to differences between Japanese Americans and Japanese people in mainland Japan, including differences in nutrition, environmental factors, and medical access. The recent census indicates that of the 6 largest specified Asian groups, Japanese persons were the most likely to report a second race in addition to Japanese.\(^4\) Interracial marriages may cause genetic heterogeneity, which we did not investigate in this retrospective study. Perhaps the most significant contributing factor to our lower rate of NTG is the selection bias because glaucoma may be underdiagnosed when the IOP is normal. Therefore it is more difficult for patients with NTG to be diagnosed unless they have significant optic nerve findings to cause physicians to order a visual field test that may show defects.

Classification of NTG and HTG depends on IOP, and our mean IOPs in all groups and overall in the study are higher than those in the Tajimi Study. This might contribute to the lower rate of NTG in this study. Difference in IOP can partially be explained by this population being Japanese American rather than mainland Japanese. In the absence of information regarding the generations of participants in United States and potential mixed ethnicity, this result should not be connected to environmental factors.

The average CCT of patients without glaucoma in our study is higher than those reported in previous Japanese studies.\(^2\)\(^12\) As the investigators in the Tajimi Study had discussed, CCT measurements by the noncontact specular microscopy (SP-2000P: Topcon, Hong Kong, China) were found to be approximately 20 µm lower than the measurements by ultrasound pachymetry.\(^13\) The patients without glaucoma in our study have measurements almost comparable with white persons.\(^14\) It is not clear from this study if this similarity with white persons is a consequence of similar environmental exposures or from potential inclusion of participants of mixed race in this study.

On the other hand, CCT of patients with glaucoma in our study was similar to that defined in the Tajimi Study. Patients with NTG were found to have thinner corneas than patients with HTG in the Tajimi Study. Although it was not significant, we found that patients with NTG have thicker corneas. This might be owing to higher suspicion of glaucoma in patients with NTG with thicker corneas and borderline pressures compared with patients with NTG with thin corneas and lower IOP.

We found a borderline significance for reduction of CCT with increasing age that is similar to some previous articles.\(^15\) Some studies defined a correlation between some systemic diseases and corneal thickness, while others did not.\(^16\)\(^20\) We found a slight positive correlation between corneal thickness and diabetes, while other systemic diseases were not correlated.
However, our results for corneal thickness comparisons should be evaluated with caution because not all of our patients had pachymetry measurements. Some patients were evaluated before having pachymetry in a physician’s office and, for the rest, pachymetry was used only when it was thought necessary, especially for patients with a family history of glaucoma or ocular hypertension.

The correlation between family history of glaucoma and diagnosis of glaucoma should also be viewed with caution. Because family history was learned by self-description, patients with glaucoma might have searched their family and had higher positive responses, while patients without glaucoma had less incentive to check their families for glaucoma history.

Patients with glaucoma in this study population seemed to be more hyperopic than patients without; this remained significant even after the exclusion of patients with previous lens surgery. In contrast, myopia was defined as a risk factor for glaucoma in the Tajimi Study.21 Most patients without glaucoma in our study were younger and visited the offices for refractive error-related reasons; this may have increased the myopia percentage in the group without glaucoma. In fact, controlling for age, there was no significant correlation between refractive error and glaucoma diagnosis.

Our study has some limitations because it is retrospective and clinic-based. The attendance of a private clinic depends on the subspecialty of the clinic and experts, referral patterns, symptoms of the patients, and other factors. For example, a small proportion of our patients were from a private glaucoma clinic. Predictably, the proportion of glaucoma was high (34.7%) in that group; however, the percentage of NTG among patients with POAG in the glaucoma clinic (76.2%) was very similar to that of the general ophthalmology practice (81.6%). Because we don’t know the generation data from our population, it was impossible to evaluate the effect of genetic and environmental factors on our results.

In summary, the prevalence and presentation of glaucoma among Japanese persons in the United States may be different from other American ethnicities and possibly mainland Japanese. Ophthalmic practices should be aware of the differences between various races and diagnostic protocols should be patient- and ethnicity-based. Future studies—particularly prospective, population-based investigations—on differences in glaucoma distribution among different Asian ethnicities will help improve health care delivery to minority populations.

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