Original Article

Is being female a risk factor for shallow anterior chamber? The associations between anterior chamber depth and age, sex, and body height

Wei-Cherng Hsu[1,2], Elizabeth P Shen[1,2,3], Yi-Ting Hsieh[1,2,3]

Aim of Study: To analyze the association between anterior chamber depth (ACD) and age, sex, and body height (BH). **Materials and Methods:** One thousand four hundred eighty eyes of 1480 adults 40 years of age and older receiving preoperative evaluation for cataract surgery were recruited consecutively from June 1, 2006, to December 31, 2010. ACD was measured with the Zeiss IOLMaster. Univariate and multivariate linear regression models were used to analyze the correlations, and receiving operator characteristic (ROC) curves and the area under the curve (AUC) were used for evaluating the predictability of an ACD less than 2.70 mm. **Results:** ACD was negatively correlated with age and positively correlated with BH in both univariate and multivariate regression analysis ($P < 0.001$). Sex was associated with ACD in univariate analysis, but not after adjustment with age and BH. In predicting an ACD less than 2.70 mm, the AUCs of ROC curves for 'age and sex', 'age and BH', and 'age, sex, and BH' were 0.687, 0.689, and 0.689, respectively.**Conclusion:** Age and BH were independent associating factors of ACD; however, sex was not. Older people and shorter ones likely had shallower ACD, and therefore were predisposed to Primary angle closure glaucoma (PACG). The predictability of ACD by age and BH solely was low, and adding sex did not increase it.

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Primary angle closure glaucoma (PACG) is a leading cause of blindness in Asian population.[1] Of the ocular risk factors for PACG, shallow anterior chamber (AC) is the most consistent.[2-5] Age, sex and race have been viewed as the main demographic risk factors for PACG,[3,6] and all these factors are directly associated with anterior chamber depth (ACD). Aging results in the increased thickness of lens, thus decreased ACD, while Asian and Eskimo people have a shallower AC than Caucasians.[4,5] With respect to sex, it is well documented that in various races, females have a shallower AC than males.[5,7-10] The reasons for this include females' shorter stature and possibly underlying genetic difference.[11] Several population-based studies have shown that sex is independently associated with ACD after the adjustment for body height (BH) in multivariate linear regression.[7,10,12,13] However, additional factors for adjustment varied in these studies, which could possibly affect the results of regression analysis. Therefore, we want to clarify the relationship between ACD and age, sex and BH.

The commercial introduction of noncontact partial coherence interferometry (PCI) has led to largely improved accuracy of intraocular lens (IOL) power calculation for patients receiving cataract surgery.[14-16] Accuracy of ACD measurement by the Zeiss IOLMaster (Carl Zeiss Meditec, Dublin, CA) has also been documented.[17] However, PCI has not been widely used in studies addressing the distribution and determinants of ocular biometric parameters.[10,18] In this study, we used the data of ACD measured by the IOLMaster to analyze the relationship between ACD and demographic as well as anthropometric parameters including age, sex, and BH. Because an ACD less than 2.70 mm including corneal thickness has been documented as an indicator for PACG,[19] we also analyzed the predictability of an ACD less than 2.70 mm.

Materials and Methods

Patients who received preoperative evaluation for cataract surgery from June 1, 2006 to December 31, 2010 in one hospital were recruited consecutively. Exclusion criteria included: Age less than 40, previous intraocular surgery, measurement failure of any ocular parameter by the IOLMaster, and the absence of BH records within 6 months of ocular parameter measurement. If both of the subject's eyes were eligible, one eye was selected randomly because of the correlation for ACD between right and left eyes (correlation coefficient = 0.70). A total of 1480 eyes from 1480 cases were enrolled for analysis. This research followed the tenets of the Declaration of Helsinki, and Institutional Review Board (IRB) approval was obtained. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

The ACD was measured as the distance between the anterior corneal surface and the anterior lens surface with the IOLMaster (Version 4.0). Age and sex were recorded by chart review. BH was measured at the first visit and at hospitalization for every patient in the hospital, and the closest record of BH within 6 months of ocular parameter measurement was taken by chart review.

Distribution for ACD was tested for normality using the Kolmogorov–Smirnov test. P value less than 0.01 was considered significantly different from normal. Linear regression models were used to analyze the associations between ACD and other

[1]Department of Ophthalmology, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei, Taiwan, [2]School of Medicine, Tzu Chi University, Hualien, Taiwan, [3]National Taiwan University Hospital, Taipei, Taiwan

Correspondence to: Dr. Yi-Ting Hsieh, Department of Ophthalmology, NationalTaiwan University Hospital, 7, Zhongshan S. Rd., Zhongzheng District, Taipei, 10002, Taiwan. E-mail: ythyth@gmail.com

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variables. Explanatory variables included age, sex, and BH. Both univariate and multivariate regression models were used for analysis. In multivariate analysis, Mallows' Cp criteria were used first to select the best-fitted model as Model 1, and then a full model was fitted as Model 2. Squared partial correlation coefficients (pr^2) using Type II sum of squares were calculated to indicate the percentage of remaining variance accounted for by each explanatory variable. R^2 as well as adjusted R^2 was compared between the full model and the best-fitted one. Residuals against explanatory variables were plotted to examine the linear trend of each variable, and the variance inflation factor (VIF) of each variable was examined to check for collinearity. The Wald test was conducted to examine the significance of parameter estimates, and regression coefficients with P values smaller than 0.05 were considered significant. The efficacy of predicting an ACD less than 2.70 mm was analyzed by using receiving operator characteristic (ROC) curves, and the area under the curve (AUC) was calculated.

Results

Of the 1480 subjects, all were of Asian descent, and 839 (56.7%) were female. The mean age of the subjects was 69.0 ± 10.5 years, and the mean BH was 157.9 ± 8.4 cm. The mean ACD was 2.96 ± 0.45 mm, ranging from 1.86 to 4.45 mm, and the distribution of ACD was normal (P = 0.07 by Kolmogorov–Smirnov test). The mean ACD of females and males were 2.93 ± 0.44 mm and 3.02 ± 0.47 mm, respectively (P < 0.001).

The results of regression analysis for ACD are shown in Table 1. In univariate analysis, males had deeper ACD than females. BH was positively correlated with ACD, while the age was negatively correlated. In multiple regression analysis with model selection by Mallows' Cp criteria (Model 1), age and BH stayed in the best-fitted model, but sex did not. In the full model that contained all three explanatory variables (Model 2), the regression coefficients of age and BH were significant (P < 0.001), while that of sex was not (P = 0.56). The pr^2 of sex in Model 2 was only 0.0002, and the R^2 for Models 1 and 2 differed by only 0.0002. The adjusted R^2 of the full model was even lower than that of the parsimonious best-fitted model. Residual plots showed that linear relationships with homoscedasticity remained for all explanatory variables in Models 1 and 2 both. The VIFs for explanatory variables in Models 1 and 2 were all less than 2.06, showing that the problem of collinearity was limited in our analysis.

Prediction for PACG

We used an ACD less than 2.70 mm as an indicator for PACG. The ROC curves of three different combinations of anthropometric parameters for predicting an ACD less than 2.70 mm were plotted. The AUC for 'age and sex', 'age and BH', and 'age, sex, and BH' were 0.687, 0.689, and 0.689, respectively.

Discussion

ACD is important for the screening of PACG. Devereux *et al*. showed that measurement of ACD can detect occludable angles and may play a role in population screening for PACG.[20] Even in eyes with plateau iris syndrome, the ACD is also shallower than in the normal population.[21] Kurita *et al.* showed that ACD, rather than anterior chamber angle, is a good predictor for primary angle closure (PAC).[22] All of these studies support the idea that ACD can be treated as a surrogate marker for PAC or PACG. The measurement of ACD, however, demands biometry that is not readily used even in ophthalmologists' clinics. Therefore, demographic or anthropometric risk factors, if they exist, are more practical for population screening for PACG.

Being female is traditionally viewed as a risk factor for PACG.[3,6,5] Although genetic difference may also play a role, BH is the most likely confounding factor. Several population-based studies have shown, however, that sex is independently associated with ACD after adjustment for BH.[7,10,12,13] In these studies, multivariate linear regression was used for analysis with or without model selection (stepwise or backward). Because collinearity often exists among the explanatory variables in multivariate regression analysis, it is sometimes difficult to choose the best-fitted model while adjusting for all possible confounding factors.[23,24] Moreover, some nonanthropometric covariates such as hypertension and education status also appeared in the multiple regression models of these studies. These complicated models made them more difficult to explain clinically. In our study, we recruited only age, sex, and BH as the explanatory variables in multivariate linear regression analysis, and tried to clarify whether sex is an independent associating factor of shallow ACD. First, we used Mallows' Cp criteria to choose the best-fitted model, and found that sex was excluded from the model. Second, we used Wald tests to examine the significance of regression coefficients in full models, and found that the regression coefficient of sex was not significant. The pr^2 of sex in Model 2 was only 0.0002 and the R^2 for Models 1 and 2 differed by only 0.0002, which means that sex added very little information in predicting or estimating an ACD besides age and BH. The adjusted R^2 of the full model was even lower than that of Model 1, which means that adding sex as a covariate reduced the goodness of fit of the regression model.

Table 1: Linear regression analysis for anterior chamber depth

	Univariate analysis			Multivariate analysis							
				Model 1 (R^2=0.2727, adjusted R^2=0.2717)				Model 2 (R^2=0.2729, adjusted R^2=0.2714)			
	Coefficient (mm)	P value	R^2	Coefficient (mm)	P value	pr^2	VIF	Coefficient (mm)	P value	pr^2	VIF
Age (year)	–0.0209	<0.001	0.2512	–0.0202	<0.001	0.2415	1.01	–0.0203	<0.001	0.2356	1.06
Sex (F:0, M:1)	0.0706	0.002	0.0063	NA	NA	NA	NA	0.0167	0.56	0.0002	2.06
Body height (cm)	0.0105	<0.001	0.0412	0.0077	<0.001	0.0287	1.01	0.0070	<0.001	0.0118	2.05

pr^2: Squared partial correlation coefficient; VIF: Variance inflation factor

All these results showed that age and BH were correlated with ACD; however, sex was not. We checked for the VIFs in our models and found that there were no problems of collinearity in our regression analysis. We also used the ROC curve to examine the predictability of ACD less than 2.70 mm by anthropometric factors. The AUC of 'age, BH, and sex was the same as that of 'age and BH', indicating that sex did not help in screening for shallow ACD. Although associated with ACD in univariate analysis, sex appeared to be confounded by BH and was not an independent associating demographic factor of ACD. This result seems to contradict some published reports.[7,10,12,13] However, the latter studies did not focus on the question of whether sex is an independent risk factor of shallow ACD. As previously stated, different methods of regression model selection may yield different results. We used several different means of exploring the relationship between sex and ACD and found the same result that, after BH is adjusted, sex is no longer associated with ACD. This result was the same as that of the Beaver Dam Eye Study,[25] which showed that adjustment for height accounted for all sex differences of ACD.

With respect to the relationship between BH and ACD, most studies have shown BH to be correlated with ACD.[10,12,13,26] Some, however, have not.[27] We found that BH was positively correlated with ACD after adjusting for age and sex, and the linear trend held through the whole spectrum of BH. For every 1 cm increment of BH, ACD increases by 0.0077 mm. We also found that 'age and BH' was a better predictor of shallow ACD than 'age and sex', although the difference of AUCs was only 0.002. Following these results, we propose that short stature, but not being female, is independently associated with shallow ACD and should be considered an anthropometric risk factor of PACG.

The association between age and ACD was the same as has been previously reported.[4-9] By adjusting for sex and BH, we found a 0.02 mm decrement in ACD for every 1 year increment in age. The residual plot showed that such a linear relationship remained for patients between 40 and 94 years old. Because our study is cross sectional, we cannot conclude that one's ACD will continue to grow shallower at the same rate after 40 years of age. A longitudinal study would be required to explore the relationship between ACD and aging.

The R^2 of Model 1 and Model 2 in our study were both less than 0.3. This means that age, sex, and BH could only partially explain the between-individual differences of ACD. The AUCs of ROC curves for predicting an ACD less than 2.70 mm with age, sex, and BH were all less than 0.7. Although old age and short stature were significant associating factors of shallow ACD, they cannot be used solely to predict the ACD. Nevertheless, the relationships between ACD and demographic and anthropometric factors are still valuable to epidemiological research and population education for PACG.

The most significant drawback of this study is that it was hospital based and not population based. The participants were enrolled retrospectively from the medical records of a regional hospital. All had received examinations for preoperative evaluation of cataract surgery, and those with severe cataract were excluded due to failure of the IOLMaster examination. Therefore, only those with mild to moderate cataract are represented here. On the other hand, the confounding effect of cataract in statistical analysis might thus be reduced as a result. Because previous studies have shown that central ACD is not influenced by laser iridotomy,[28-30] in this study we did not exclude subjects who had received laser iridotomy. Still it is questionable that we can extrapolate the results to the general population. A population-based participant source should be considered in future research.

In conclusion, we found that age and BH were independent demographic and anthropometric associating factors of ACD; however, sex was not. Older people and shorter ones likely had shallower ACD, and therefore were predisposed to PACG. The predictability of ACD by age and BH was low; adding sex did not increase the predictability of ACD.

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