Cohort Study: Corneal Higher-Order Aberrations and Its Related Factors in Chinese People with Emmetropia

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Abstract

Purpose: To evaluate the association among age, gender, central corneal thickness (CCT), anterior chamber depth (ACD) and higher-order aberrations (HOAs) of cornea in Chinese people with emmetropia by Pentacam.

Methods: Prospective, a non-randomized population-based study. All subjects came spontaneously for consultation and were subdivided into six age-groups. One thousand two hundred and six candidates (605 male, 601 female) were tested and underwent anterior segment examination by Pentacam. These parameters were measured: 1) root mean-square HOA (RMS-HOA) from anterior and posterior cornea, 2) RMS of coma, secondary astigmatism and spherical aberration (SA) from anterior and posterior cornea, 3) CCT and ACD.

Results: For analysis of variance (ANOVA) between genders, there were statistical differences on: 1) anterior corneal HOAs of y-coma, y-coma and SA (F=5.643, P=0.018; F=16.971, P=0.000; F=23.443, P=0.000); 2) total corneal HOAs of y-coma and SA (F=12.906, P=0.000; F=111.590, P=0.000). There was significant different between y-second astigmatism of anterior corneal surface and age (r² =0.023, p<0.000), that of posterior corneal surface and age (r² =0.055, p=0.001), between RMS-HOAs of anterior corneal surface and age (r² =0.259, p<0.000), that of posterior corneal surface and age (r² =0.055, p=0.001), that of total corneal surface and age (r² =0.359, p<0.000).

Conclusion: a) For the ethnic, there was a significant difference on magnitude of corneal HOAs between Chinese people and the other people. b) Pentacam can provide a more precise data of posterior cornea HOAs which seldom reported before.

Keywords: Corneal Higher-Order Aberrants; Pentacam; Emmetropia; Age; Gender; Anterior Chamber Depth; Central Corneal Thickness

Introduction

Aberration as an element of vision quality assessment is defined as the difference between a real image and an ideal image and if it occurs, the quality of vision becomes poorer. Both the anterior corneal surface and the internal optics (the posterior cornea, crystalline lens) contribute to the aberration of a wavefront passing through the eye. Although we are usually interested in the total wavefront aberration of the eye (ocular wavefront aberration), it is sometimes valuable to know the contribution that the cornea (or more strictly the anterior air–tear film interface; posterior corneal surface and total cornea surface) makes to the total aberration. This can be estimated from the surface height data provided by corneal topographers. Pentacam Instruments are now beginning to become available which combine an aberrometer with a corneal topographer and can thus yield the wavefront aberrations of both the whole cornea alone and anterior or posterior corneal aberration, respectively [1] (Figure 1).

Another fact is that corneal and ocular HOAs have been studied for many years; it is only relatively recently that the aberrational characteristics of large populations of normal subjects have been analyzed in Zernike terms [2-4]. While inevitably their results show some differences due to the slightly different ages and other characteristics of the populations involved, Salmon and van de Pol established the population norms of ocular aberrations in a large cohort of 2560 eyes; all but 134 eyes were from white populations (171 eyes, Spain; 2255 eyes, United States; 134 eyes, Japan) [5]. Higher order ocular aberrations of Chinese population with myopia were reported recently [6], but the parameters of HOAs were not completed and only reflected the population of ametropia. Basic data regarding corneal HOAs, such as the distribution in the population and changes with increasing aging, are essential for understanding the nature of each aberration and correcting it.

Hence, the purpose of this study were: firstly, to obtain information about characters of anterior and posterior corneal HOAs in the Asian eyes of Chinese people with emmetropia and to compare them with findings in other series in the literature; secondly, to determine their relationships with age, gender, CCT and ACD.

Materials and Methods

This study was designed as a prospective, randomized study and followed the tenets of the Declaration of Helsinki. Informed consent was obtained from each candidate.

A total of 1026 eyes of 1206 candidates, 605 male (50.2%), 601 female (49.8%) were examined, only right eyes were considered. Corneal HOAs were computed from the central 6.0 mm zone of the corneal topographic maps. All Subjects came spontaneously for consultation and were subdivided into six age groups. The subjects were submitted

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to ophthalmic examination in the Department of Excimer Laser Center from September 2009 to April 2010.

Patients’ examinations

The same ophthalmologist performed all ocular examination.

None of the subjects had any ocular disease other than lower refractive errors, such as myopia, hyperopia (spherical equivalent within the range -0.88D to +0.75D) and regular forms of astigmatism≤±1.00D.

Exclusion criteria were best-corrected visual acuity ≤20/25, dry eye, previous ocular surgery, irregular astigmatism or inferior asymmetry in the topography, contact lens users, history and presence of cataracts or other ocular opacities and systemic diseases. The Lens Opacities Classification System III was used to assess lens transparency. Only clear lens were accepted. Finally, 976 candidates (485 male, 491 female) of 976 eyes in the initial cohort met the inclusion criteria, mean age of 34.97 ± 20.74 years (range 16-83 years) (Table 1).

Pentacam Imaging Scan

Pentacam Instruction Manual measurement and Evaluation System guided measurement for the Anterior Eye Segment.

For all the candidates, Scanning was performed using a rotating Scheimpflug camera (Oculus Pentacam Rotating Scheimpflug Camera; Oculus, Wetzlar, Germany; Pentacam software version 1.09). The candidate is seated with his or her chin on a chin rest and forehead against the forehead strap and is asked to fixate straight ahead on a fixation target. The operator visualizes a real-time image of the candidate’s eye on a computer screen, with the machine marking the pupil edge and center and corneal apex. To reduce operator-dependent variables, the automatic release mode of the Pentacam was used to automatically determine when correct focus, alignment with the corneal apex had been achieved and then to capture an image.

The anterior surface of the cornea is calculated with no optical distortion and the tear film has no effect on measurements. Imaging was performed using the 50 scans setting obtained in 2 seconds and saved in jpeg format.

Zernike analysis

Clicking on [Display] in the upper menu bar and then on [Zernike Analysis] opens a screen with freely selectable color. They are useful for analyzing corneal wavefront aberration because they directly provide a series of data of corneal aberration co-efficient in a single screen, including Wavefront Aberration Cornea Front, Wavefront Aberration Cornea Back, Wavefront Aberration Cornea, RMS-Total, RMS-LOA and RMS-HOA.

Repeatability of the system

To determine the repeatability of this system, three Pentacam scans were performed on each eye, and three tomograms of anterior and posterior corneal surface were obtained. Each candidate was asked to sit back and relax for 3 minutes between scans. The average value of three measurements was regarded as analyzed data. The joystick
**Results**

**Comparison of corneal HOAs and gender**

Table 2 showed the mean and standard deviation of HOAs and RMS of cornea according to the gender. There were statistical differences on:

1. anterior corneal HOAs of x-coma, y-coma and SA (F=5.643, P=0.018; F=16.971, P<0.000; F=23.443, P<0.000); 2) total corneal HOAs of y-coma and SA (F=12.906, P=0.000; F=111.590, P=0.000). Based on the above results, x-coma, y-coma and SA were analyzed separately in accordance with gender.

1. **x-coma, y-coma and SA in female group:**

There was a correlation between A.C.D and x-coma (Figure 2). Compared with posterior and total corneal surface, a curve fitting relationship was found in anterior corneal surface for x-coma; linear regression showed statistic differences between x-coma of posterior corneal surface (y=0.250-0.329x, r²=0.108, p<0.000) and A.C.D, that of total corneal surface (y=0.076-0.317x, r²=0.091, p<0.000) and A.C.D.

There were correlation between age and y-coma for anterior and posterior corneal surface (Figure 3). There was also a curve fitting relationship for y-coma in anterior corneal surface compared with posterior one; linear regression showed statistic differences between y-coma of posterior corneal surface (y=0.324x-0.056, r²=0.105, p<0.000) and age, there was no relationship between that of total corneal surface and age.

There were positive correlation between age and SA for anterior and total corneal surface (Figure 4), there was no correlation between age and SA for posterior corneal surface. Line regression showed statistic differences between SA of anterior corneal surface (y=0.434x+0.284, r²=0.190, p<0.000) and age, that of total corneal surface (y=0.555x+0.027, r²=0.108, p<0.000) and age.

2. **x-coma, y-coma and SA in male group:**

There was a curve fitting relationship between A.C.D and x-coma for anterior corneal surface, a positive linear relationship between A.C.D and x-coma for posterior corneal surface and a negative linear relationship for total corneal surface (Figure 5).

There was a curve fitting relationship between A.C.D and y-coma for posterior corneal surface, however a positive linear relationship was found between age and y-coma for total corneal surface (Figure 6).

There were statistical correlation between age and SA, A.C.D and SA in Male group (Figure 7). Multiple linear regression showed statistic differences between SA of anterior corneal surface and age with A.C.D (y=0.236x+0.570x²-0.242, r²=0.203, p<0.000, 1=A.C.D, 2=age), that of total corneal surface and age with A.C.D (y=0.609x-0.149x²+0.246, r²=0.514, r²*=-0.301, p<0.000, 1=A.C.D, 2=age).

**Comparison of corneal HOAs and age**

There was significant different between y-second astigmatism of anterior corneal surface and age (r²=0.023, p<0.000), that of posterior corneal surface and age (r²=0.021, p=0.001) (Figure 8).

There was significant different between RMS-HOAs of anterior corneal surface and age (r²=0.259, p<0.000), that of posterior corneal surface and age (r²=0.055, p=0.001), that of total corneal surface and age (r²=0.359, p<0.000) (Figure 9).

**Comparison of corneal HOAs and A.C.D**
There was significant different between x-second astigmatism of posterior corneal surface and A.C.D (r²=0.212, p<0.000), that of total corneal surface and A.C.D (r²=0.014, p<0.001) (Figure 10).

Comparison of corneal HOAs and CCT

There were no correlation between any corneal HOAs and CCT.

Discussion

Our data of corneal HOAs by Pentacam

The anterior cornea with tear film is the first optics of the eye and the dominating structure in the optical power of the eye (mean approximately 70%). Accordingly, it is the main contributor to aberrations in the eye. The posterior corneal surface, as an integral
part of internal optics, has an effect on ocular aberrant and is seldom separately reported previously. However, as is known, posterior corneal surface plays an important role in cornea and may be the first abnormal in some corneal diseases. Some report showed that the best detector to differentiate between suspected keratoconus and normal corneas was vertical coma (Z3') (specificity 71.9%; sensitivity 89.3%) in the HOAs [7]. The maximum refractive power, elevation and thickness of corneal thinnest point of corneal posterior surface were significantly different between keratoconus patients and normal people [8].

Therefore, in our study, RMS- HOAs of anterior and posterior corneal surface according to age group were tested respectively by Pentacam, which can perform Zernike analysis for the anterior and posterior surface based on the measured height data (Table 3). Our study found RMS-HOAs of anterior, posterior and total corneal surface were all positive values. There were obviously different in RMS-HOAs of anterior corneal surface between age group, a little change in RMS-HOAs of posterior corneal surface between age group was found in our research. We supposed that RMS-HOAs of anterior corneal surface had a main effect on that of total corneal surface compared to posterior corneal surface.

We referred to the article of research on the variations of internal optics with age and evaluation of the degree of compensation that the internal optics provide for anterior corneal aberration [9], it represented compensation of HOAs for anterior corneal surface by posterior corneal surface when the values of HOAs for posterior corneal surface had the same sign for anterior corneal surface to produce an improved retinal image. It indicated that posterior corneal surface added aberrations to those of anterior corneal surface, and HOAs of total corneal surface would be much more than those of anterior corneal surface.

Experimental studies show that each HOA has a different impact on vision and can interact with other aberrations to positively or negatively influence visual performance [10]: spherical aberration, coma, secondary astigmatism have a greater effect on visual performance than other HOAs [11]. Therefore, in our study, HOAs of coma, spherical aberration and secondary astigmatism were selected to analyze (Table 4.5.6).

For the each corneal HOAs, the values varied widely from subject to subject in our research. This was shown by the large standard deviations, wide ranges, and much greater magnitude of the absolute mean values compared to the arithmetic mean values for each HOAs. For x- coma, less than 55 year old of values were negative values, more than 55 year old of that were positive (Table 4.5.6). For anterior corneal surface, the values of y- second astigmatism with less than 35 year old were positive, and those with more than 35 year old were negative (Table 4). SA was the only term with all positive values for anterior and total corneal surface, all negative values for posterior corneal surface. Therefore, SA of total corneal surface were more than those of anterior corneal surface, and again it had a large range, from 0.0288 to 0.5982μm (anterior corneal surface), -0.0045 to -0.5488μm (posterior corneal surface) and 0.0423 to 0.6842 μm (total corneal surface).

Our data of corneal HOAs with effect factors

In our study, each corneal HOAs was analyzed to find the relationship with gender, age, CCT and ACD.

The data showed that there were higher RMS of x- coma, y-coma and SA in female than male, but for secondary astigmatism, there were no significant differences on genders. Therefore, the relationship between SA and A.C.D, age, CCT; between coma and A.C.D, age, CCT were analyzed separately on the basis of genders.

The data showed that different relationship between corneal HOAs and effect factors:

x-coma: Compared with male group, there was a more obvious rule for female group between x-coma and A.C.D. Curve estimation showed there was significant different between x-coma of anterior corneal surface and A.C.D, linear regression showed statistic differences between x-coma of posterior corneal surface (y=0.250-0.329x, r² =0.108, p<0.000) and A.C.D, that of total corneal surface (y=0.076- 0.317x, r²=0.091, p<0.000) and A.C.D. From the Figure 2, we found posterior corneal surface took a more effect on x-coma for total corneal surface than anterior corneal surface. With the A.C.D decreasing, x-coma of posterior and total corneal surface would be increasing. Our fouding can be proved by which was reported the cortical cataract group had statistically significantly higher coma than the other groups, and SA predominated in the nuclear cataract group [12]. We known the relation between some corneal HOAs with age, but this could not explain coma and SA had different changes on two kind of age-relate cataract. However, posterior corneal surface like lens, as one part of internal optic, had a relationship with A.C.D. If cortical cataract made A.C.D decreased, x-coma would be increased. The association between x-coma and A.C.D we found in the present study therefore provides useful information for understanding increase of coma in cortical cataract patient.

Y-coma: In male group, we found the similar rule like x-coma in female group. However, the significant different relationship was between y-coma and age.

These findings on differences of genders might be the ACD values

<table>
<thead>
<tr>
<th>Age group (Year)</th>
<th>Y- coma</th>
<th>X- coma</th>
<th>Y- second Astigmatism</th>
<th>SA</th>
<th>X- second Astigmatism</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-25</td>
<td>-0.010±0.088</td>
<td>-0.026±0.205</td>
<td>-0.035±0.099</td>
<td>-0.109±0.35</td>
<td>-0.040±0.020</td>
</tr>
<tr>
<td>26-35</td>
<td>-0.019±0.036</td>
<td>-0.020±0.056</td>
<td>-0.012±0.018</td>
<td>-0.125±0.57</td>
<td>0.060±0.025</td>
</tr>
<tr>
<td>36-45</td>
<td>-0.020±0.014</td>
<td>-0.009±0.049</td>
<td>-0.142±0.065</td>
<td>0.121±0.33</td>
<td>-0.002±0.014</td>
</tr>
<tr>
<td>46-55</td>
<td>-0.014±0.018</td>
<td>-0.021±0.030</td>
<td>-0.075±0.058</td>
<td>0.160±0.42</td>
<td>0.005±0.066</td>
</tr>
<tr>
<td>&gt;55</td>
<td>0.025±0.070</td>
<td>0.068±0.130</td>
<td>-0.035±0.027</td>
<td>0.131±0.63</td>
<td>0.000±0.031</td>
</tr>
<tr>
<td>Total</td>
<td>0.069±0.092</td>
<td>0.002±0.078</td>
<td>-0.002±0.031</td>
<td>0.162±0.088</td>
<td>0.000±0.031</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age group (Year)</th>
<th>Y- coma</th>
<th>X- coma</th>
<th>Y- second Astigmatism</th>
<th>SA</th>
<th>X- second Astigmatism</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-25</td>
<td>-0.018±0.088</td>
<td>0.003±0.149</td>
<td>-0.003±0.059</td>
<td>0.180±0.083</td>
<td>-0.003±0.035</td>
</tr>
<tr>
<td>26-35</td>
<td>-0.013±0.158</td>
<td>0.013±0.153</td>
<td>-0.020±0.028</td>
<td>0.199±0.108</td>
<td>0.010±0.090</td>
</tr>
<tr>
<td>36-45</td>
<td>0.022±0.096</td>
<td>0.028±0.074</td>
<td>-0.050±0.195</td>
<td>0.304±0.115</td>
<td>-0.016±0.113</td>
</tr>
<tr>
<td>46-55</td>
<td>-0.062±0.000</td>
<td>0.056±0.014</td>
<td>-0.013±0.153</td>
<td>0.317±0.015</td>
<td>0.20±0.006</td>
</tr>
<tr>
<td>56-65</td>
<td>-0.091±0.251</td>
<td>0.166±0.479</td>
<td>-0.030±0.049</td>
<td>0.325±0.156</td>
<td>0.075±0.122</td>
</tr>
<tr>
<td>&gt;65</td>
<td>-0.110±0.330</td>
<td>0.146±0.867</td>
<td>0.035±0.024</td>
<td>0.221±0.000</td>
<td>-0.027±0.152</td>
</tr>
<tr>
<td>Total</td>
<td>-0.033±0.149</td>
<td>0.012±0.257</td>
<td>-0.030±0.102</td>
<td>0.267±0.130</td>
<td>0.032±0.083</td>
</tr>
</tbody>
</table>
Figure 5: There was a curve fitting relationship between A.C.D and x-coma for anterior corneal surface, linear regression showed statistic differences between x-coma of posterior corneal surface \(y=0.329x-0.185\), \(r^2=0.083\), \(p<0.000\) and age, that of total corneal surface \(y=0.982-0.317x\), \(r^2=0.176\), \(p<0.000\) and A.C.D.

Figure 6: There was a curve fitting relationship between A.C.D and y-coma for posterior corneal surface, linear regression showed statistic differences between y-coma of anterior corneal surface \(y=0.211x-0.354\), \(r^2=0.045\), \(p<0.000\) and A.C.D, that of total corneal surface \(y=0.430x-0.954\), \(r^2=0.180\), \(p<0.000\) and A.C.D.

Figure 7: There were statistical correlations between age and SA, A.C.D and SA in Male group, multiple linear regression showed statistic differences between SA of anterior corneal surface and age with A.C.D \(y=0.236x+0.570x^2-0.242\), \(r_1^2=0.02\), \(r_2^2=0.203\), \(p<0.000\), 1=A.C.D, 2=age), that of total corneal surface and age with A.C.D \(y=0.609x-0.149x^2+0.246\), \(r_1^2=0.514\), \(r_2^2=0.301\), \(p<0.000\), 1=A.C.D, 2=age).
for men and women were significantly different [13] : 2.59 mm (95% confidence interval [CI], 2.56 – 2.62) and 2.42 mm (95% CI, 2.39 – 2.44) respectively. The regression coefficients of ACD with age in males and females were $\mu_{0.010}$ ($P<0.001$) and $\mu_{0.009}$ ($P<0.001$) mm per year, respectively. Therefore, we supposed that coma of female were greater than that of male because of different A.C.D on genders.

For second astigmatism, we found the same rule like coma although there was no statically different between genders. Horizon HOAs seemed to have a relationship with A.C.D; however, Vertical HOAs seemed to have a relationship with age. There must be some reasons for this kind of phenomenon to need us research further.

In our research, we found there were a positive correlation between age and RMS-HOA in the anterior and total cornea (Figure 8), which was consistent with the findings of Oshika [14] and coauthors, and Guirao and coauthors, the RMS of total HOAs correlated positively with increasing age. For the posterior corneal surface, there were a negative relationship for posterior corneal surface ($r=-0.235, P=0.018$) (Figure 9).
relationship between age and RMS-HOAs. If the hypothesis [15] that changes in the shape of the anterior cornea throughout life may explain the corneal aberration changes with age were established, there would be a correlation between age and RMS-HOA of the posterior cornea as the same as the anterior and total cornea. For regarding shape changes, a “flat meridian toward a more vertical orientation” trend with increasing age for both the anterior and posterior corneal surfaces was observed (mean changes of 0.0295 and 0.0224 mm/5 years, respectively) [16].

For further study the factors of corneal HOAs, we estimated the relationship CCT with corneal HOAs, since CCT was associated with younger age [17]. To be disappointed, our study just found no correlation of CCT with any corneal HOAs.

The ethnic characteristics of our data of corneal HOAs

Using the large population study by Salmon and van de Pol as the reference norm for HOAs in a healthy population [5], we found the similarities in the distribution of predominant aberrations but distinct differences in the magnitude of aberrations. For the corneal RMS-HOA, the normal United States people were 0.479±0.124 µm (KL & HB 2009); the Malaysia (ethnic Chinese) people were 0.591±0.256 µm [18], RMS-HOAs of anterior corneal surface in our research were 0.598±0.125 µm, more than that of Caucasian.

Coma, secondary astigmatism and SA of the anterior cornea estimated in our research were seemed to be obviously different with Malaysia (ethnic Chinese) [13] and the White’s. The mean values of x-coma, x-secondary astigmatism and SA in supernormal vision of Korean were 0.137±0.091 µm, 0.036±0.057 µm, and 0.091±0.059 µm, respectively (Kim et al.2007). The anterior corneal co-efficient of SA in our research was 0.267+/−0.128 µm, was less than corneal SA of Canadian (0.274+/−0.089 µm) (RH et al.2010), was greater than ocular spherical aberation (0.23+/−0.14 µm) of Chinese people with myopia [19]. Other HOAs can’t be compared due to shortage of adequately statistics information.

Although direct comparison of values is not applicable for these studies since different method were used for measuring the corneal HOAs, different pupil diameters and different subjects were performed, we also had reason to believe that our results have some differences compared with previous study in the values.

1. We think there are at least 2 important reasons of the findings different from previous study in our research. This is the first time that Pentacam was performed to measure the corneal HOAs, including anterior and posterior corneal surface. As mentioned, the whole optical performance of the normal eye is governed by combination of aberrations in the corneal and intraocular optics. Corneal aberrations were divided into an anterior corneal aberration that were paid more attentions and posterior corneal aberration which were thought to be one part of internal optics aberration. In our study, we estimated the corneal aberrations separately according to the anterior and posterior surface. (Table 4.6.7)

2. The subjects of our study came from Asia, exactly the mainland of Chinese people. As far as the subjects of study were concerned, there were only several reports on wavefront aberrations mentioned Asian people, including Malaysia, Japan, India [20], Korean and Singapore [21]. Compared with Malaysia and Singapore, corneal HOAs and CCT were significantly different in Chinese people.

Limitations of this study include that the corneal HOAs in our study provide an incomplete characterization of corneal aberrations; wavefront aberrations were calculated for corneal surface only, whereas the optical performance of the eye obviously depends on total ocular aberrations.

In our research, we measured corneal HOAs of Chinese people with emmetropia for the first time and evaluated their relationships with age, gender, CCT and ACD. This kind of study for ethnic will make a greater understanding of the impact of aberrations on different people. The posterior corneal HOAs seldom reported but not negligible were also recorded. With the increasing number of patients receiving refractive surgical procedures and development of Interventional methods to reduce impacts of HOAs for visual quality, the knowledge of corneal HOAs are still acquired to study more precisely.

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b. Financial Disclosures: None
c. Contributions of Authors: Design of the study (yifei Huang); Conduct of the study (Jing Song, Yifei Huang); Analysis and interpretation (Jing Song); Data Collection (Mei Ge, Haipeng Zhao); Provision of materials (Jifeng Yu, Gaiping Du, Yifei Huang)
d. Other Acknowledgments: None

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