Original Article

Age-related variation in corneal biomechanical parameters in healthy Indians

Vaishal P Kenia, Raj V Kenia[1], Onkar H Pirdankar[2]

Purpose: To report age-related variations in corneal biomechanical parameters in healthy Indians. **Methods:** A retrospective study where healthy Indian individuals aged between 5 and 70 years having undergone corneal biomechanics assessment using Corvis ST between January 2017 and December 2018 and having best corrected visual acuity of 20/20 were enrolled. Subjects with central corneal thickness <500 microns, intra-ocular pressure (IOP) ≥ 22 mmHg, refractive error ≥ 6.00D, history of any systemic and ocular disease, previous ocular surgery, poor scans quality, and subjects with any missing data were also excluded. Corneal biomechanical parameters were noted and compared across different age groups. **Results:** Total of 3125 eyes had undergone the Corvis ST analysis. After applying exclusion criteria, 718 right eyes of 718 patients were included for the analysis and were further divided into different age groups as per each decade (sample size), such as 5-10 (37), 11-20 (113), 21-30 (396), 31-40 (116), 41-50 (39), 50 and above (17). All the subjects were matched for IOP and central corneal thickness (p > 0.05). A total of 19 out of 26 corneal biomechanical parameters were significantly different across age groups ($p < 0.05$). Vinciguerra screening parameters, such as deformation amplitude ratio max, biomechanically corrected IOP, and stiffness parameter A1 were significantly different across different age groups ($p < 0.05$). **Conclusion:** Corneal biomechanical parameters are affected by age as cornea becomes progressively stiffer. The information reported here would serve as a reference for future corneal biomechanical researches and would help in differentiating the abnormal eyes from normal healthy eyes.

Key words: Corneal biomechanical parameters, Corvis ST

Access this article online
Website:
www.ijo.in
DOI:
10.4103/ijo.IJO_2127_19
Quick Response Code:

Assessment of corneal biomechanical parameters in clinical settings is challenging, yet crucial in clinical and surgical interventions.[1-4] Cornea is a viscoelastic structure however there is limited knowledge of corneal biomechanics. Corneal biomechanical parameters are affected in ocular diseases, such as keratoconus,[5-10] Fuchs Dystrophy,[5,11] ocular surgeries like cataract[12,13] and refractive surgeries[5,7,14,15] systemic diseases like systemic lupus erythmatous,[16] diabetes,[17] and various corneal treatments like corneal cross linking treatment, SMILE lenticule implantation.[17]As corneal biomechanical changes precede topographical changes,[1] their assessment can be of great benefit in screening patients for refractive surgeries, thereby reducing the risk for post refractive surgical ectasia.

In clinical settings, corneal biomechanical properties were earlier assessed using ocular response analyzer (ORA) (Reichert, Buffalo, NY, USA). It is based on bidirectional dynamic applanation process where biomechanical properties are characterized by corneal hysteresis (CH) and the corneal resistance factor (CRF); however, theses parameters are less sensitive and specific in differentiating suspected cases of KC as compared to normal. In contrast, Corneal Visualization Scheimpflug Technology (Corvis ST) (Oculus Optikgerate GmbH, wetzlar, Germany) has been recently introduced which uses ultra-high speed Scheimpflug camera that images the corneal dynamic response and measures as many as 32 parameters.[3] Further compared, ORA derives the CCT corrected intra-ocular pressure (IOP) known as corneal compensated IOP (IOPcc), whereas Corvis ST gives biomechanically corrected IOP (bIOP) which is independent of central corneal thickness, age, and dynamic corneal response (DCR); ORA uses a variable pressure whereas Corvis ST uses a fixed puff of air to applanate the cornea; ORA has an electro optical infrared radiation sensor to records the signal of corneal applanation, whereas Corvis ST measures the complete corneal deformation process, thus, providing much more information on biomechanical properties as compared to ORA.[4]

Corneal biomechanical parameters are good predictor for detecting early ectasia.[6] Use of Corvis ST as a corneal biomechanics assessment tool may help differentiate abnormal corneas in the healthy population and help in predicting long-term outcomes of refractive and cataract surgeries. This warrants the knowledge about the normal corneal biomechanical properties among normal healthy population across different age groups. To the best of our knowledge, this particular information is missing among Indian subjects. Thus, we aim to study the corneal biomechanical parameters in healthy Indian subjects across various age groups.

Kenia Eye Hospital, [1]Kenia Foundation, [2]Kenia Medical and Research Foundation, Mumbai, Maharashtra, India

Correspondence to: Prof. Onkar H Pirdankar, Clinical Researcher and Faculty, Kenia Medical and Research Foundation, Maharashtra, India. E-mail: pirdankar_onkar@yahoo.com

Received: 25-Nov-2019 Revision: 13-May-2020
Accepted: 25-Jun-2020 Published: 23-Nov-2020

Cite this article as: Kenia VP, Kenia RV, Pirdankar OH. Age-related variation in corneal biomechanical parameters in healthy Indians. Indian J Ophthalmol 2020;68:2921-9.

Methods

In this retrospective study, visually normal subjects (with best corrected visual acuity of 20/20) aged 5-70 years who had undergone corneal biomechanics measurements using Corvis ST between January 2017 and December 2018 were analyzed. Subjects with ocular corneal diseases, history of previous ocular surgery, central corneal thickness <500 microns, IOP ≥22 mm of Hg, refractive error ≥6.00D, systemic diseases, such as systemic lupus erythematosus, diabetes, Steven Johnson Syndrome, graft versus host disease, hypothyroidism, poor quality Corvis ST scans, or missing data were excluded from the study.[18] The study was approved by Institutional Ethics Committee (EC reg. details: ECR/1088/Inst/MH/2018; EC approval ref. no. 2018/01) and adheres to tenets of declaration of Helsinki. As this was retrospective study, informed consent was not obtained.

The demographic and clinical variables, such as age, gender, eye, refractive error, best corrected visual acuity, scan quality, and 32 parameters of corneal biomechanical properties from Corvis ST assessment, were noted. The Corvis ST parameters comprised of 26 dynamic corneal response parameters and 6 Vinciguerra screening parameters. Fig. 1 demonstrates the complete corneal deformation process and shows the various vinciguerra screening parameters. The Corvis ST records the reaction of the cornea to a defined air pulse using ultra high-speed Scheimpflug-camera. The camera takes over 4300 images per second and 576 points per image. IOP and corneal thickness can be measured with great precision on the basis of the Scheimpflug images.

Corneal Deformation Parameters (Dynamic Corneal Response)

Dynamic corneal response parameters are assessed in three phases: 1. At first applanation (A1) 2. At second applanation (A2) 3. At highest concavity (HC). In the present study, following variables, measured by Corvis ST were analyzed.

(a) A1/A2 time (A1T/A2T): Time from start to first (A1)/second applanation (A2),
(b) A1/A2 velocity (A1V/A2V): velocity of corneal apex at A1/A2,
(c) A1/A2 deformation amplitude (A1DA/A2DA): Moving distance of the corneal apex from the initial position to that at the A1T/A2T,
(d) A1/A2 deflection length (A1DL/A2DL): Length of the flattened cornea at A1/A2,
(e) A1/A2 deflection amplitude (A1DeflA/A2 DeflA): Similar to A1DA/A2DA but without whole eye movement,
(f) A1/A2 delta Arc length (A1dArclength/A2dArclength): Change in arc length from initial state to A1/A2, in a defined 7-mm zone,
(g) HC time (HCT): Time to reach the maximum deformation,
(h) Radius (Rad): Central curvature radius at the highest concavity,
(i) HC deformation amplitude (HCDA): Distance of the corneal apex movement from the initiation of the deformation to the highest concavity,
(j) HC deflection length (HCDL): Length of the flattened cornea at highest concavity,
(k) HC deflection amplitude (HCDeflA): Similar to HCDA without whole eye movement,
(l) Peak distance (PD): Distance between the two surrounding peaks of the cornea at the highest concavity,
(m) HC delta Arc length (HC dArclength): Change in arc length during the highest concavity moment from the initial state, in a defined 7-mm zone.

Vinciguerra screening parameters

Vinciguerra screening display describes six parameters that are most helpful for differentiating normal corneas from keratoconic corneas and are described here.

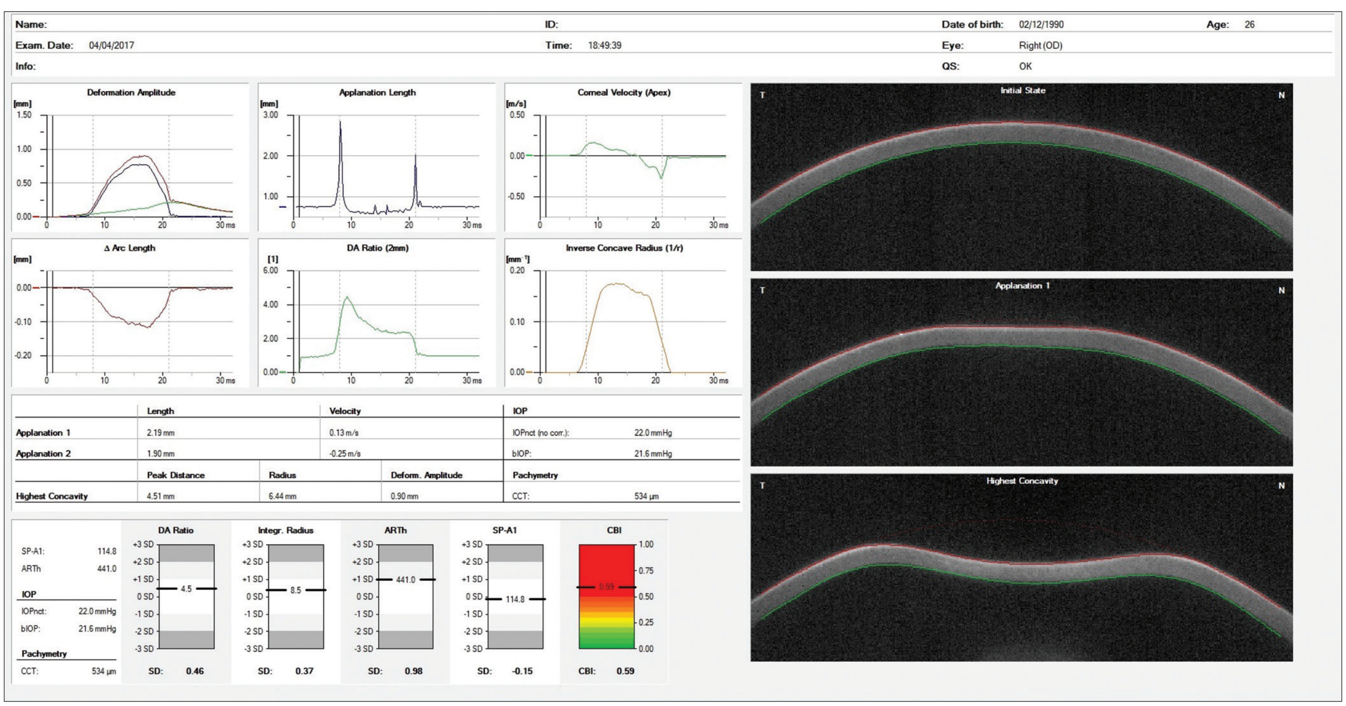

Figure 1: Demonstrates the complete corneal deformation process and shows the various Vinciguerra screening parameters

1. Deformation amplitude ratio max (2 mm) (DA ratio max) is the ratio between the deformation amplitude at the apex and the average deformation amplitude measured at 2 mm from the center
2. Ambrósio's relational thickness to the horizontal profile (ARTh) describes thickness profile in the temporal-nasal direction and defined as corneal thickness thinnest to pachymetric progression
3. Integrated radius (INR) is the area under the inverse concave radius versus time curve
4. Stiffness parameter at A1 (SP A1) describes corneal stiffness as defined by resultant pressure (Pr) divided by deflection amplitude at A1
5. Corvis Biomechanical Index (CBI) is the overall biomechanical index for keratoconus detection which is constructed using stepwise regression formula and uses parameters, such as A1 velocity, ARTh, Stiffness parameter, and DA ratio and deflection amplitude
6. Biomechanically corrected Intraocular Pressure (bIOP) is derived by finite element simulations that take into account the influence of central corneal thickness, age, and DCR parameters.

Statistical analysis

Data were entered in MS Excel (Microsoft Corporation) and analyzed using Minitab Software (Minitab LLC, State University, PA, USA). Means and standard deviation were calculated for continuous variables and proportions for the categorical variables. Further, the subjects were divided into different age groups as per each decade, such as 5-10, 11-20, 21-30, 31-40, 41-50, 50, and above. The means among genders were compared using two sample t-test whereas means among the different age groups were compared using analysis of variance. Post hoc analysis was done using Tukey test to understand the differences across groups. Univariate and stepwise multivariate analysis was done to obtain the association between independent variables, such as age, spherical equivalent refractive error, IOP, pachymetry, and dependent variables that are corneal biomechanical parameters.

Results

Demographics

Corvis ST records of total of 3125 eyes were retrospectively analyzed. Out of which 572 eyes had missing data, 553 eyes had corneal thickness less than 500 microns, 94 eyes had IOP ≥22 mm of Hg, 412 eyes had refractive error greater than -6.00 D and were excluded. After exclusion of this data, we had 1494 eyes out of which left eye data were excluded and finally 718 right eyes of 718 patients were included for the analysis.

In all 718 eyes, with mean ± SD (ranges) age, spherical equivalent refraction, intraocular pressure, and pachymetry were 26.36 ± 9.64 (5 to74) years, -2.63 ± 2.10 (3.38 to -6.00) diopter, 16.76 ± 2.11 (11.5 to 22.5) mm of Hg and 539.62 ± 26.27 (500 to 618) microns respectively. There were 320 were males and 398 were females. Age, spherical equivalent refraction, IOP and pachymetry were similar in both males and females ($p > 0.05$) [Table 1]. To understand the impact of age on corneal biomechanical parameters, eyes were divided into different age groups (sample size), such as 5-10 (37), 11-20 (113), 21-30 (396), 31-40 (116), 41-50 (39), 50, and above (17). The IOP and central corneal thickness which has an impact on corneal biomechanical parameters were similar across different age groups (IOP: $F = 0.57$, $P = 0.72$; central corneal thickness: $F = 1.40$, $P = 0.22$).

Corneal biomechanical parameters

Out of 32 corneal biomechanical parameters 25 were similar among males and females ($p > 0.05$) however peak distance, A1 deformation amplitude, A2 deformation amplitude, A1 deflection amplitude, HC deflection amplitude, HC deflection area, A1 dArc length, ARTh were significantly different among males and females ($p < 0.05$) [Table 1]. Out of 32 corneal biomechanical parameters, 26 are dynamic corneal response parameters, whereas 6 are Vinciguerra screening parameters and have been studied across different age groups and described below in detail.

Dynamic corneal response parameters in different age

Out of 26 dynamic corneal response parameters, 19 parameters were significantly different across age groups ($p < 0.05$). At first applanation, A1 time and A1 Velocity were similar across different age group ($p > 0.05$), whereas A1 deformation amplitude, A1 deflection amplitude, A1 deflection length, A1 deflection area and A delta arc length were significantly different across age groups ($p < 0.05$). At second applanation A2, all the parameters were significantly different ($p < 0.05$) except A2 time and A2 deflection length ($p > 0.05$). At highest concavity, HC time and HC deflection length were similar ($p > 0.05$), whereas other parameters, such as radius, HC deformation amplitude, HC deflection amplitude, peak distance, HC deflection area, and delta arc length were significantly different ($p < 0.05$). Maximum deformation and deflection amplitude, maximum delta arc length was significantly different, whereas maximum inverse radius was similar across age groups. Table 2 describes mean ± SD and 95% confidence interval of corneal biomechanical parameters in different age groups.

Vinciguerra screening parameters in different age

Out of six Vinciguerra screening parameters, three parameters, such as ARTh, integrated radius and corvis biomechanical index were similar in all age group (ARTh: $F = 1.32$, $P = 0.25$; integrated radius: $F = 2.04$, $P = 0.07$; corvis biomechanical index: $F = 0.66$, $P = 0.66$), whereas other three parameters, such as DA ratio at 2 mm, bIOP and SP A1 ($F = 2.97$, $P = 0.012$) were significantly different across age groups ($p < 0.05$). Mean deformation amplitude ratio was found to be lower in age group of 5-10 years and higher in age group of 50 years and older ($F = 3.15$, $P = 0.008$). On the other hand, biomechanically corrected IOP was significantly higher in the age group of 5-10 years, whereas lower in the age group of 50 years and older ($F = 3.66$, $P = 0.003$). Table 2 describes the mean ± SD and 95% confidence interval of vinciguerra parameters in different age groups.

Univariate and stepwise multivariate analysis

Univariate analysis revealed 21 out of 32 parameters were significantly associated with age, 11 out of 32 were significantly associated with spherical equivalent refractive error and 30 out of 32 parameters were significantly associated with IOP and central corneal thickness each [Table 3]. Stepwise multivariate analysis revealed that 22 out of 32, 16 out of 32, 28 out of 32 and 22 out of 32 were significantly associated with age, spherical equivalent refraction, IOP and central corneal thickness respectively [Table 4].

Table 1: Describes the mean±SD various corneal biomechanical parameters in different gender

Variable	Males (320)	Females (398)	*P*
Demographics			
Age	26.0±10.0	26.65±9.34	0.37
SER	2.48±2.06	-2.75±2.12	0.08
IOP	16.61±2.06	16.88±2.15	0.08
Pachymetry	539.0±25.1	540.1±27.2	0.57
First applanation A1			
A1 time (ms)	7.438±0.23	7.470±0.24	0.06
A1 velocity (m/s)	0.150±0.02	0.151±0.02	0.54
A1 deformation amplitude	0.128±0.01	0.129±0.01	0.002
A1 deflection length	2.38±0.22	2.40±0.22	0.20
A1 deflection amplitude	0.097±0.01	0.098±0.01	0.002
A1 deflection area	0.167±0.02	0.171±0.02	0.006
A1 delta arc length	-0.016±0.003	-0.017±0.002	0.001
Second applanation A2			
A2 time (ms)	21.74±0.34	21.77±0.35	0.22
A2 velocity (m/s)	-0.266±0.03	-0.264±0.02	0.20
A2 deformation amplitude	0.35±0.06	0.36±0.05	0.04
A2 deflection length	4.48±1.60	4.56±1.61	0.48
A2 deflection amplitude	0.109±0.01	0.109±0.01	0.46
A2 deflection area	0.240±0.01	0.239±0.05	0.76
A2 delta arc length	-0.024±0.001	-0.024±0.001	0.64
Highest concavity			
HC time	16.53±0.44	16.57±0.38	0.21
Radius (mm)	6.57±0.59	6.58±0.64	0.84
HC deformation amplitude	1.052±0.09	1.046±0.09	0.34
HC deflection length	5.89±1.07	5.85±1.05	0.62
HC deflection amplitude	0.90±0.09	0.89±0.09	0.04
Peak distance	4.98±0.25	4.93±0.24	0.001
HC deflection area	3.26±0.48	3.18±0.45	0.02
HC delta arc length	-0.129±0.03	-0.129±0.02	0.83
Maximum			
Max deformation amplitude	1.052±0.09	1.046±0.09	0.34
Max deflection amplitude	0.91±0.09	0.90±0.08	0.007
Max delta arc length	-0.144±0.03	-0.145±0.03	0.87
Max inverse radius	0.186±0.01	0.187±0.02	0.36
Vinciguerra screening parameter			
Deformation amplitude ratio max (2mm)	4.49±0.42	4.46±0.40	0.32
Ambrósio's relational thickness to the horizontal profile	443.4±79.1	426.9±76.8	0.005
bIOP	16.56±1.93	16.76±1.91	0.16
Integrated radius	8.90±0.96	8.93±0.97	0.69
Stiffness parameter at A1	104.6±12.90	104.3±13.1	0.72
Corvis Biomechanical Index	0.094±0.20	0.113±0.21	0.23

Two sample *t*-test, $P<0.05$ is considered as statistically significant

Discussion

Corneal biomechanics is a rapidly advancing field that has changed clinicians' understanding towards corneal diseases. Understanding of these parameters would definitely help clinicians to improve and provide quality care to the patient in terms of corneal diagnostics and surgical management. Earlier, corneal biomechanics was assessed only *in vitro* studies with isolated corneas by measuring stress, strain, and modulus of elasticity. Also, in clinical setting, ORAwas used enormously; however, its ability to differentiate early keratoconic corneas from normal cornea was poor.[2] In the present study we used Corvis ST which has shown a good repeatability and reproducibility for measuring dynamic corneal response parameters in healthy eyes.[19] In the present study, we have reported corneal biomechanical parameters in

Table 2: Describes mean±SD corneal biomechanical parameters and Vinciguerra screening parameters in different age groups

Variable	5-10 (37) Mean±SD (95% CI)	11-20 (113) Mean±SD (95% CI)	21-30 (396) Mean±SD (95% CI)	31-40 (116) Mean±SD (95% CI)	41-50 (39) Mean±SD (95% CI)	Above 50 (17) Mean±SD (95% CI)	*F, P*
First applanation A1							
A1 time (ms)	7.50±0.25 (7.43, 7.58)	7.46±0.21 (7.41, 7.50)	7.45±0.23 (7.43, 7.47)	7.46±0.24 (7.42, 7.50)	7.43±0.27 (7.36, 7.50)	7.52±0.28 (7.41, 7.63)	0.71, 0.61
A1 velocity (m/s)	0.15±0.02 (0.14, 0.15)	0.15±0.015 (0.15, 0.15)	0.15±0.02 (0.15, 0.15)	0.15±0.02 (0.15, 0.15)	0.15±0.02 (0.14, 0.15)	0.15±0.02 (0.14, 0.15)	1.31, 0.26
A1 deformation amplitude	0.13±0.01 (0.12, 0.13)	0.13±0.01 (0.13, 0.13)	0.13±0.01 (0.13, 0.13)	0.13±0.01 (0.13,0.13)	0.13±0.01 (0.13, 0.13)	0.14±0.01 (0.13, 0.14)	4.54, <0.001
A1 deflection length	2.41±0.21 (2.34, 2.48)	2.38±0.26 (2.34, 2.42)	2.38±0.22 (2.36, 2.40)	2.42±0.14 (2.38, 2.46)	2.47±0.26 (2.40, 2.54)	2.50±0.26 (2.40, 2.60)	2.50, 0.029
A1 deflection amplitude	0.096±0.01 (0.1, 0.1)	0.096±0.01 (0.1, 0.1)	0.097±0.01 (0.1, 0.1)	0.098±0.01 (0.1, 0.1)	0.098±0.01 (0.1, 0.1)	0.102±0.01 (0.1, 0.1)	3.93, 0.002
A1 deflection area	0.17±0.022 (0.16, 0.18)	0.16±0.02 (0.16, 0.17)	0.17±0.02 (0.17, 0.17)	0.17±0.02 (0.17, 0.17)	0.17±0.03 (0.17,0.18)	0.18±0.02 (0.17,0.19)	2.31, 0.043
A1 delta arc length	-0.02±0.00 (-0.02, -0.01)	-0.02±0.00 (-0.02,-0.01)	-0.02±0.00 (-0.02,-0.02)	-0.02±0.00 (-0.02,-0.02)	-0.02±0.00 (-0.02,-0.02)	-0.02±0.00 (-0.00,-0.02)	4.78, <0.001
Second applanation A2							
A2 time (ms)	21.69±0.34 (21.59, 21.81)	21.81±0.29 (21.75, 21.87)	21.76±0.34 (21.73, 21.80)	21.71±0.34 (21.65,21.77)	21.77±0.43 (21.67,21.89)	21.59±0.45 (21.42,21.75)	2.14, 0.059
A2 velocity (m/s)	-0.25±0.025 (-0.26,-0.24)	-0.26±0.02 (-0.27,-0.26)	-0.27±0.02 (-0.27,-0.26)	-0.27±0.03 (-0.27,-0.26)	-0.27±0.04 (-0.27,-0.26)	-0.27±0.02 (-0.28,-0.26)	2.63, 0.023
A2 deformation amplitude	0.36±0.05 (0.35, 0.38)	0.35±0.059 (0.34, 0.36)	0.35±0.05 (0.35, 0.36)	0.35±0.05 (0.34, 0.36)	0.38±0.07 (0.37, 0.40)	0.39±0.06 (0.37, 0.42)	4.01, 0.001
A2 deflection length	4.23±1.59 (3.71, 4.75)	4.26±1.72 (3.96, 4.55)	4.58±1.61 (4.42, 4.74)	4.66±1.55 (4.37, 4.96)	4.61±1.49 (4.11, 5.12)	4.58±1.51 (3.82, 5.35)	1.17, 0.324
A2 deflection amplitude	0.10±0.01 (0.10, 0.11)	0.11±0.01 (0.10, 0.11)	0.11±0.01 (0.11, 0.11)	0.11±0.01 (0.11, 0.11)	0.11±0.01 (0.11, 0.12)	0.12±0.01 (0.11, 0.12)	4.57, <0.001
A2 deflection area	0.23±0.042 (0.22, 0.24)	0.23±0.03 (0.22, 0.24)	0.24±0.04 (0.24, 0.24)	0.24±0.04 (0.23, 0.25)	0.25±0.043 (0.24, 0.27)	0.27±0.05 (0.26, 0.29)	4.27, 0.001
A2 delta arc length	-0.02±0.01 (-0.02,-0.02)	-0.02±0.00 (-0.02,-0.02)	-0.02±0.01 (-0.02,-0.02)	-0.02±0.00 (-0.03,-0.02)	-0.03±0.01 (-0.03,-0.02)	-0.03±0.01 (-0.03,-0.03)	5.37, <0.001
Highest concavity							
HC time	16.59±0.47 (16.46, 16.72)	16.55±0.43 (16.47, 16.63)	16.55±0.39 (16.51,16.60)	16.54±0.43 (16.46,16.61)	16.60±0.39 (16.47,16.72)	16.58±0.50 (16.38,16.77)	0.18, 0.971
Radius (mm)	6.29±0.69 (6.09, 6.48)	6.40±0.49 (6.29, 6.52)	6.64±0.62 (6.58, 6.69)	6.55±0.55 (6.44, 6.66)	6.72±0.74 (6.53, 6.91)	6.61±0.79 (6.32, 6.90)	4.82, <0.001
HC deformation amplitude	1.00±0.09 (0.97, 1.03)	1.05±0.08 (1.03,1.07)	1.05±0.08 (1.04, 1.06)	1.05±0.09 (1.03, 1.07)	1.08±0.12 (1.05, 1.11)	1.08±0.09 (1.03, 1.12)	4.03, 0.001
HC deflection length	5.48±1.26 (5.14, 5.82)	5.79±1.18 (5.59, 5.98)	5.90±1.04 (5.80, 6.01)	5.99±0.84 (5.80, 6.18)	5.87±0.99 (5.53, 6.19)	5.69±1.374 (5.19, 6.19)	1.64, 0.148
HC deflection amplitude	0.82±0.09 (0.79, 0.85)	0.89±0.08 (0.88, 0.91)	0.90±0.09 (0.89, 0.91)	0.90±0.08 (0.88, 0.91)	0.91±0.14 (0.89, 0.94)	0.89±0.093 (0.85,0.93)	5.41, <0.001
Peak distance	4.76±0.28 (4.68, 4.84)	4.97±0.22 (4.92, 5.01)	4.96±0.23 (4.94, 4.99)	4.95±0.23 (4.90, 4.99)	4.99±0.36 (4.92, 5.07)	4.88±0.20 (4.76, 4.99)	5.44, <0.001
HC deflection area	2.83±0.44 (2.68, 2.98)	3.20±0.40 (3.12, 3.28)	3.24±0.43 (3.19, 3.28)	3.20±0.42 (3.12, 3.29)	3.37±0.79 (3.22, 3.51)	3.17±0.41 (2.95, 3.39)	6.46, <0.001
HC delta arc length	-0.11±0.02 (-0.11,-0.10)	-0.12±0.02 (-0.13,-0.12)	-0.13±0.02 (-0.13,-0.13)	-0.13±0.02 (-0.13,-0.12)	-0.14±0.03 (-0.15,-0.13)	-0.13±0.03 (-0.14,-0.12)	11.95, <0.001
Maximum							
Max deformation amplitude	0.10±0.09 0.97,1.02)	1.050±0.08 (1.03, 1.07)	1.05±0.08 (1.04, 1.06)	1.05±0.09 (1.03, 1.07)	1.08±0.12 (1.05, 1.11)	1.07±0.10 (1.03, 1.12)	4.03, 0.001
Max deflection amplitude	0.83±0.085 (0.81, 0.86)	0.90±0.08 (0.88, 0.92)	0.91±0.08 (0.90, 0.91)	0.91±0.08 (0.89, 0.92)	0.92±0.14 (0.90, 0.95)	0.90±0.09 (0.86, 0.95)	5.40, <0.001

Contd...

Table 2: Contd...

Variable	5-10 (37) Mean±SD (95% CI)	11-20 (113) Mean±SD (95% CI)	21-30 (396) Mean±SD (95% CI)	31-40 (116) Mean±SD (95% CI)	41-50 (39) Mean±SD (95% CI)	Above 50 (17) Mean±SD (95% CI)	*F, P*
Max delta arc length	-0.12±0.02 (-0.13,-0.12)	-0.14±0.02 (-0.14,-0.13)	-0.15±0.02 (-0.15,-0.14)	-0.14±0.03 (-0.15,-0.14)	-0.16±0.03 (-0.16,-0.15)	-0.15±0.03 (-0.17,-0.14)	8.79, <0.001
Max inverse radius	0.19±0.02 (0.18, 0.20)	0.19±0.02 (0.19, 0.19)	0.19±0.02 (0.18, 0.19)	0.19±0.02 (0.18, 0.19)	0.18±0.02 (0.18, 0.19)	0.19±0.02 (0.18, 0.20)	2.22, 0.051
Vinciguerra screening parameter							
Deformation amplitude ratio max (2mm)	4.30±0.41 (4.17, 4.43)	4.40±0.35 (4.32, 4.47)	4.48±0.40 (4.44, 4.52)	4.55±0.42 (4.48, 4.62)	4.46±0.41 (4.32, 4.58)	4.53±0.59 (4.33, 4.72)	3.15, 0.008
Ambrósio's relational thickness to the horizontal profile	450.0±86.9 (424.8,475.2)	428.51±71.45 (414.1,442.94)	430.17±74.43 (422.5,437.87)	440.46±81.66 (426.22,454.69)	448.6±105.7 (424.0, 473.1)	457.0±87.2 (418.7,495.4)	1.32, 0.253
bIOP	17.41±1.94 (16.80,18.027)	16.89±1.75 (16.54,17.24)	16.68±1.84 (16.50,16.88)	16.60±1.95 (16.26,16.95)	15.82±2.52 (15.22,16.42)	15.84±2.25 (14.94,16.75)	3.66, 0.003
Integrated radius	9.13±1.13 (8.82,9.44)	9.13±0.80 (8.95,9.30)	8.85±0.97 (8.75,8.94)	8.96±0.92 (8.78,9.13)	8.80±1.08 (8.49,9.10)	8.84±1.33 (8.38,9.29)	2.04, 0.07
Stiffness parameter at A1	103.25±12.44 (99.08,107.41)	103.59±11.07 (101.20,105.97)	103.90±13.37 (102.62,105.17)	104.51±13.05 (102.16,106.86)	109.37±12.32 (105.32,113.43)	113.07±13.99 (106.93,119.21)	2.97, 0.012
Corvis Biomechanical Index	0.08±0.15 (0.01, 0.14)	0.09±0.18 (0.05,0.13)	0.12±0.22 (0.09, 0.14)	0.09±0.17 (0.05, 0.13)	0.11±0.26 (0.047, 0.18)	0.08±0.16 (-0.02, 0.18)	0.66, 0.656

One-way analysis of variance, $P<0.05$ is considered as statistically significant. *F* value stands for F ratio which is ratio of explained variance to unexplained variance. If calculated F value is greater than critical *F* value (found on F statistics table) then that suggests there is significant variation among group means

Indian healthy population across different age groups. To the best of our knowledge this is the first report with large sample size that describes the corneal biomechanical parameters in normal Indian eyes. Our chief observations were: 1. Increase in corneal stiffness as function of age. 2. Most of the corneal biomechanical parameters were similar for both genders. 3. A total of 19 out of 26 dynamic corneal response parameters were significantly different across different age groups. 4. Decrease in biomechanically corrected IOP as a function of age. Here we discuss these observations in detail.

Dynamic corneal response

In the present study, we noted that A1 time and A1 velocity were similar across different age group; however, previous study have noted significant difference in A1 time and A1 velocity across different age group involving adult subjects.[18] We noted higher A1 time and lower A1 velocity in Indian adult subjects as compared to Chinese adult subjects; however, we noted similar values in pediatric groups.[18,20] A1 deformation amplitude was significantly different across adult age group which is in agreement with previous study[18] and was higher in Indian subjects as compared to Chinese subjects.[18,20] Maximum deformation and deflection amplitude, maximum delta arc lengths were significantly different across age groups. In the present study, deformation amplitude at A1 and A2 were significantly different among males and females. Also, we noted significantly lower peak distance in females as compared to males. However, a study by Wang *et al.* did not find significant difference in the deformation amplitude, peak distance among males and females.

Vinciguerra screening parameter

To our knowledge, this is the first study which describes the Vinciguerra parameters in different Indian age groups. Recently developed Vinciguerra screening parameters are constructed using algorithm that comprises optimal combination of selected biomechanical and ocular parameters and they provide accurate information in differentiating ectatic corneas from normal corneas;[21] therefore, information about these parameters across different age groups will serve as a reference and help differentiate ectatic corneal conditions. Parameters such as ARTh, integrated radius, CBI were found to be similar across different age groups. As ARTh is based on corneal thickness profile and the observations noted could be explained by similar corneal thickness across all age groups. CBI is much more sensitive in predicting the ectasia or early keratoconus.[21] CBI value ranges between 0 and 1 and values closer to 0 and 1 is associated with biomechanically healthy and weaker corneas respectively.[22] As per CBI scale, value up to 0.1 is considered as normal and values above 0.25 are considered as abnormal. In the present study the mean value of CBI was ranging between 0.08 and 0.12 across all age groups. In a previous study of normals of age group (7-90 years) the mean CBI reported was 0.06 which is similar to present data.[22]

The bIOP has been validated both experimentally and clinically previously[19] and therefore could serve as an alternative to IOP measurement. As bIOP is calculated by considering various factors, such as age, corneal thickness, and corneal deformation parameters, this could be superior to corneal thickness corrected IOP. In the present study, bIOP was found to decrease with age. This could be attributed to age and corneal deformation parameter since corneal thickness and IOP were similar across different age groups. In the present study mean ± SD DA ratio at 2 mm in age group of 5-10 years was 4.30 ± 0.41, whereas in older subjects (50 and above) it was 4.53 ± 0.59 respectively which is comparable to normal eyes

Table 3: Describes the results of univariate linear regression model

Variable	Age		Spherical equivalent		IOP		Pachymetry	
	Coef (β)	*P*	Coef (β)	*P*	Coef (β)	*P*	Coef (β)	*P*
A1 time (ms)	-0.0006	0.487	-0.0065	0.117	0.1085	<0.001	0.0021	<0.001
A1 velocity (m/s)	0.0001	0.322	-0.0001	0.623	-0.0063	<0.001	-0.0002	<0.001
A1 deformation amplitude	0.0001	<0.001	- 0.0001	0.494	0.0015	<0.001	0.0000	<0.001
A1 deflection length	0.0021	0.013	0.0029	0.453	0.0223	<0.001	0.0012	<0.001
A1 deflection amplitude	0.0001	<0.001	-0.0000	0.641	0.0006	<0.001	0.0000	<0.001
A1 deflection area	0.0002	0.014	-0.0004	0.301	0.0015	<0.001	0.0001	<0.001
A1 delta arc length	-0.0000	<0.001	0.0000	0.914	-0.0003	<0.001	-0.0000	<0.001
A2 time (ms)	-0.0016	0.215	0.0126	0.039	-0.1358	<0.001	-0.0009	0.058
A2 velocity (m/s)	-0.0002	0.042	0.0018	<0.001	0.0064	<0.001	0.0001	<0.001
A2 deformation amplitude	0.0007	0.001	0.0059	<0.001	-0.0022	0.020	0.0001	0.107
A2 deflection length	0.0107	0.085	0.0064	0.823	-0.0992	<0.001	-0.0053	0.020
A2 deflection amplitude	0.0002	<0.001	0.0002	0.310	0.0006	0.005	0.0001	<0.001
A2 deflection area	0.0006	<0.001	0.0014	0.064	0.0003	0.634	0.0004	<0.001
A2 delta arc length	-0.0001	<0.001	-0.0002	0.022	-0.0002	0.067	-0.0001	<0.001
HC time	0.0005	0.748	0.0169	0.02	-0.0239	0.001	-0.0001	0.825
Radius (mm)	0.0061	0.010	0.0014	0.902	0.0638	<0.001	0.0070	<0.001
HC deformation amplitude	0.0013	<0.001	-0.0025	0.107	-0.0319	<0.001	-0.0007	<0.001
HC deflection length	0.0076	0.061	-0.0072	0.703	-0.1075	<0.001	-0.0033	0.029
HC deflection amplitude	0.0011	0.002	-0.0070	<0.001	-0.0318	<0.001	-0.0008	<0.001
Peak distance	0.0017	0.075	-0.0168	<0.001	-0.0835	<0.001	-0.0017	<0.001
HC deflection area	0.0057	0.001	-0.0332	<0.001	-0.1569	<0.001	-0.0028	<0.001
HC delta arc length	-0.0004	<0.001	0.0015	<0.001	0.0023	<0.001	-0.0002	<0.001
Max deformation amplitude	0.0012	<0.001	-0.0025	0.107	-0.0319	<0.001	-0.0007	<0.001
Max deflection amplitude	0.0011	0.001	-0.0064	<0.001	-0.0316	<0.001	-0.0008	<0.001
Max delta arc length	-0.0005	<0.001	0.0015	0.001	0.0036	<0.001	-0.0001	<0.001
Max inverse radius	-0.0000	0.420	0.0003	0.393	-0.0013	<0.001	-0.0002	<0.001
Deformation amplitude ratio max (2 mm)	0.0048	0.002	-0.0055	0.452	-0.1236	<0.001	-0.0075	<0.001
Ambrósio's relational thickness to the horizontal profile	0.4504	0.139	- 1.149	0.413	5.130	<0.001	0.9154	<0.001
bIOP	-0.0327	<0.001	-0.0752	0.028	0.8317	<0.001	-0.0093	0.001
Integrated radius	-0.0049	0.186	0.0174	0.312	-0.2530	<0.001	-0.0149	<0.001
Stiffness parameter at A1	0.1359	0.007	-0.1076	0.643	4.112	<0.001	0.3190	<0.001
Corvis Biomechanical Index	0.0003	0.733	0.0137	<0.001	-0.0359	<0.001	-0.0025	<0.001

β indicates regression coefficient and $P<0.05$ indicates statistical significance

4.30 ± 0.50 (age group: 7 to 90 years).[22] Higher deformation amplitude ratio suggests that the cornea is less resistant to deformation. We noted a higher deformation amplitude ratio in older subjects as compared to pediatrics. Deformation amplitude ratio at 2 mm is thought to be confounded by variables like scleral rigidity, retrobulbar fat, and extraocular muscle tone.[23] Thus, it does not represent true corneal biomechanics. We noted an increase in stiffness parameters at A1 (SP A1) as a function of age. Stiffness is generally described by resistance to deformation and comprises geometric and material stiffness. Material stiffness is due to tissue, whereas geometric stiffness is dependent on thickness, curvature, and diameter. In the present study IOP and CCT were similar across all age groups thereby negating the effect of geometric stiffness and solely describing corneal stiffness due to corneal microstructures, such as collagen fibrils arrangement and organization in the cornea. Also, since IOP and CCT were similar, the changes in other biomechanical parameters could also be attributed corneal microstructures (material stiffness), such as age-related changes in collagen fibrils crosslinking and reduction in interfibrillary spacing.[24] Also, it is noteworthy that the corneal interfibrillary linkage is less and the fibers are disorganized in keratoconic corneas.[25]

In our study, univariate and multivariate linear regression models suggest that most of the corneal deformation parameters are influenced by age, intraocular pressure, and central corneal thickness which is in agreement with previous studies.[12,26] Understanding corneal biomechanics would not only help in screening refractive surgery or corneal ectasia patients but also screening ocular hypertension or primary open angle glaucoma at early stage since it has been reported that some of the corneal deformation parameters are different in glaucoma subjects as compared to normals.[27]

Table 4: Describes the results of stepwise multivariate regression model

Variable	Age		Spherical equivalent		IOP		Pachymetry	
	Coef (β)	*P*	Coef (β)	*P*	Coef (β)	*P*	Coef (β)	*P*
First applanation A1								
A1 time (ms)					0.1084	<0.001		
A1 velocity (m/s)			-0.0005	0.008	-0.0061	<0.001	-0.0001	<0.001
A1 deformation amplitude	0.0001	<0.001			0.0015	<0.001		
A1 deflection length	0.0022	0.009			0.0199	<0.001	0.0008	0.010
A1 deflection amplitude	0.0001	<0.001			0.0006	<0.001	0.0000	0.008
A1 deflection area	0.0002	0.012			0.0012	0.002	0.0001	0.002
A1 delta arc length	-0.0000	<0.001			-0.0003	<0.001	-0.0000	<0.001
Second applanation A2								
A2 time (ms)	-0.0024	<0.001			-0.1424	<0.001	0.0020	<0.001
A2 velocity (m/s)	-0.0002	0.010	0.0023	<0.001	0.0065	<0.001		
A2 deformation amplitude	0.0006	0.005	0.0055	<0.001	-0.0024	0.014	0.0002	0.031
A2 deflection length					-0.0982	0.001		
A2 deflection amplitude	0.0002	<0.001					0.0001	<0.001
A2 deflection area	0.0006	<0.001					0.0004	<0.001
A2 delta arc length	-0.0001	<0.001	-0.0001	0.045			-0.0001	<0.001
Highest concavity								
HC time			0.0155	0.032	-0.0229	0.001		
Radius (mm)	0.0060	0.008			0.0454	<0.001	0.0060	<0.001
HC deformation amplitude	0.0011	<0.001	-0.0048	<0.001	-0.0321	<0.001		
HC deflection length					-0.1067	<0.001		
HC deflection amplitude	0.0011	<0.001	-0.0093	<0.001	-0.0318	<0.001		
Peak distance	0.0016	0.008	-0.0225	<0.001	-0.0846	<0.001		
HC deflection area	0.0057	<0.001	-0.0450	<0.001	-0.1589	<0.001		
HC delta arc length	-0.0004	<0.001	0.0019	<0.001	0.0031	<0.001	-0.0002	<0.001
Maximum								
Max deformation amplitude			0.0011	<0.001	-0.0049	<0.001	-0.0320	<0.001
Max deflection amplitude	0.0011	<0.001	-0.0087	<0.001	-0.0315	<0.001	-0.0002	0.043
Max delta arc length	-0.0005	<0.001	0.0020	<0.001	0.0044	<0.001	-0.0002	<0.001
Max inverse radius					-0.0006	0.033	-0.0002	<0.001
Vinciguerra screening parameters								
Deformation amplitude ratio max (2mm)	0.0049	<0.001	-0.0135	0.007	-0.1068	<0.001	-0.0054	<0.001
Ambrósio's relational thickness to the horizontal profile							0.867	<0.001
bIOP	-0.0263	<0.001	-0.0086	0.002	0.9160	<0.001	-0.0277	<0.001
Integrated radius					-0.2207	<0.001	-0.0104	<0.001
Stiffness parameter at A1	0.1376	<0.001			3.338	<0.001	0.2498	<0.001
Corvis Biomechanical Index			0.0123	<0.001	-0.0294	<0.001	-0.0019	<0.001

β indicates regression coefficient and $P<0.05$ indicates statistical significance

The strength of the study is that it describes the detailed assessment of corneal biomechanical parameters including Vinciguerra screening parameters in a large sample size which was possible due to latest software. The study suffers from the limitation that we could not retrieve the information about female individual hormonal status and information about their pregnancy and menstrual cycle due to retrospective study design and thereby could not explain these hormonal impact on corneal biomechanics;[28,29] nevertheless, in the present study most of corneal biomechanical parameters were similar in both male and female. Second, the sample size in extreme age groups (5-10 years and above 50 years) was smaller as compared to other groups which may have restricted a standard data reporting in this age group.

Conclusion

To conclude, the corneal biomechanical parameters are affected by age as cornea becomes progressively stiffer. The information reported here would serve as a reference for future corneal biomechanical researches and would help in differentiating the corneal biomechanically compromised eyes from biomechanically normal healthy eyes. Also, it would serve as a benchmark for Indian normative data in corneal biomechanics and will add value to current available literature in terms of enhancing diagnostic and therapeutic management in our clinical practice.

Acknowledgements

Authors would like to thanks Dr Saroj Sahdev for her useful suggestion towards the manuscript. They also thank Dr Merlin Saldanha for reviewing the manuscript and Mr Ganesh Sakharkar for technical help.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Roy A, Shetty R, Kummelil M. Keratoconus: A biomechanical perspective on loss of corneal stiffness. Indian J Ophthalmol 2013;61:392.
2. Fontes B M, Ambrosio R, Jardim D, Velarde GC, Nosé W. Corneal biomechanical metrics and anterior segment parameters in mild keratoconus. Ophthalmology 2010;117:673-9.
3. Kenia VP, Kenia RV, Pirdankar OH. Association between corneal biomechanical parameters and myopic refractive errors in young Indian individuals. Taiwan. Taiwan J Ophthalmol 2020;10:45-53.
4. Koprowski R, Lyssek-Boron A, Nowinska A, Wylegala E, Kasprzak H, Wrobel Z. Selected parameters of the corneal deformation in the Corvis tonometer. Biomed Eng Online 2014;13:55.
5. Luce DA. Determining *in vivo* biomechanical properties of the cornea with an ocular response analyzer. J Cataract Refract Surg 2005;31:156-62.
6. Tian L, Huang Y-F, Wang LQ, Bai H, Wang Q, Jiang JJ, *et al.* Corneal biomechanical assessment using corneal visualization Scheimpflug technology in keratoconic and normal eyes. J Ophthalmol 2014;2014:1–8. doi: 10.1155/2014/147516.
7. Ortiz D, Piñero D, Shabayek MH, Arnalich-Montiel F, Alió JL. Corneal biomechanical properties in normal, post-laser *in situ* keratomileusis, and keratoconic eyes. J Cataract Refract Surg 2007;33:1371–5.
8. Bao F, Geraghty B, Wang Q, Elsheikh A. Consideration of corneal biomechanics in the diagnosis and management of keratoconus: Is it important?. Eye Vis 2016;3:18.
9. Elham R, Jafarzadehpur E, Hashemi H, Amanzadeh K, Shokrollahzadeh F, Yekta A, *et al.* Keratoconus diagnosis using Corvis ST measured biomechanical parameters. J Curr Ophthalmol 2017;29:175–81.
10. Kerautret J, Colin J, Touboul D, Roberts C. Biomechanical characteristics of the ectatic cornea. J Cataract Refract Surg 2008;34:510-3.
11. Clemmensen K, Hjortdal J. Intraocular pressure and corneal biomechanics in Fuchs' endothelial dystrophy and after posterior lamellar keratoplasty. Acta Ophthalmol 2014;92:350–4.
12. Valbon BF, Ambrósio R, Fontes BM, Alves MR. Effects of age on corneal deformation by non-contact tonometry integrated with an ultra-high-speed (UHS) scheimpflug camera. Arq Bras Oftalmol 2013;76:229–32.
13. Kato Y, Nakakura S, Asaoka R, Matsuya K, Fujio Y, Kiuchi Y. Cataract surgery causes biomechanical alterations to the eye detectable by Corvis ST tonometry. PLoS One 2017;12:1–12.
14. Pepose JS, Feigenbaum SK, Qazi MA, Sanderson JP, Roberts CJ. Changes in corneal biomechanics and intraocular pressure following LASIK using static, dynamic, and noncontact tonometry. Am J Ophthalmol 2007;143:39–48.
15. Medeiros FW, Sinha-Roy A, Alves MR, Dupps WJ Jr. Biomechanical corneal changes induced by different flap thickness created by femtosecond laser. Clinics 2011;66:1067–71.
16. Yazici AT, Yüksel K, Altinkaynak H, Baz O, Bozkurt E, Demirok A. The biomechanical properties of the cornea in patients with systemic lupus erythematosus. Eye 2011;25:1005-9.
17. Kling S, Hafezi F. Corneal biomechanics – A review. Ophthalmic Physiol Opt 2017;37:240–52.
18. Wang W, He M, He H, Zhang C, Jin H, Zhong X. Corneal biomechanical metrics of healthy Chinese adults using Corvis ST. Contact Lens Anterior Eye 2017;40:97–103.
19. Lopes BT, Roberts CJ, Elsheikh A, Vinciguerra R, Vinciguerra P, Reisdorf S, *et al.* Repeatability and reproducibility of intraocular pressure and dynamic corneal response parameters assessed by the corvis ST. J Ophthalmol 2017;2017:4–8. doi: 10.1155/2017/8515742.
20. He M, Ding H, He H, Zhang C, Liu L, Zhong X. Corneal biomechanical properties in healthy children measured by corneal visualization scheimpflug technology. BMC Ophthalmol 2017;17:1–7.
21. Vinciguerra R, Ambrósio R Jr, Elsheikh A, Roberts CJ, Lopes B, Morenghi E, *et al.* Detection of keratoconus with a new biomechanical index. J Refract Surg 2016;32:803–10.
22. Ambrósio R, Lopes BT, Faria-Correia F, Salomão MQ, Bühren J, Roberts CJ, *et al.* Integration of Scheimpflug-based corneal tomography and biomechanical assessments for enhancing ectasia detection. J Refract Surg 2017;33:434–43.
23. Francis M, Pahuja N, Shroff R, Gowda R, Matalia H, Shetty R, *et al.* Waveform analysis of deformation amplitude and deflection amplitude in normal, suspect, and keratoconic eyes. J Cataract Refract Surg 2017;43:1271–80.
24. Blackburn BJ, Jenkins MW, Rollins AM, Dupps WJ. A review of structural and biomechanical changes in the cornea in aging, disease, and photochemical crosslinking. Front Bioeng Biotechnol 2019;7:66.
25. Pahuja N, Kumar NR, Shroff R, Shetty R, Nuijts RMMA, Ghosh A, *et al.* Differential molecular expression of extracellular matrix and inflammatory genes at the corneal cone apex drives focal weakening in keratoconus. Investig Ophthalmol Vis Sci 2016;57:5372–82.
26. Kotecha A, Elsheikh A, Roberts CR, Zhu H, Garway-heath DF. Corneal thickness- and age-related biomechanical properties of the cornea measured with the ocular response analyzer. Invest Ophthalmol Vis Sci 2006;47:5337–47.
27. Wang W, Du S, Zhang X. Corneal deformation response in patients with primary open-angle glaucoma and in healthy subjects analyzed by corvis ST. Invest Ophthalmol Vis Sci 2015;56:5557–65.
28. Goldich Y, Barkana Y, Pras E, Fish A, Mandel Y, Hirsh A, *et al.* Variations in corneal biomechanical parameters and central corneal thickness during the menstrual cycle. J Cataract Refract Surg 2011;37:1507–11.
29. Tabibian D, de Tejada BM, Gatzioufas Z, Kling S, Meiss VS, Boldi MO, *et al.* Pregnancy-induced changes in corneal biomechanics and topography are thyroid hormone related. Am J Ophthalmol 2017;184:129–36.