

# Evaluation of corneal topography and tomography in fellow eyes of unilateral keratoconus patients for early detection of subclinical keratoconus

Mithun Thulasidas, Prateek Teotia

**Purpose:** To analyse topographic and tomographic changes in fellow eyes of unilateral keratoconus patients by comparing them with normal eyes. **Methods:** This five-year retrospective observational comparative case study included 15 advanced keratoconus eyes of unilateral keratoconus (KCN group), 15 normal fellow eyes of unilateral keratoconus (Fellow eye group) and 34 eyes of normal refractive surgery candidates (Normal group). Topographic and tomographic data, data from enhanced elevation maps, and keratoconus indices were measured in all study eyes using Pentacam. Receiver operating characteristic (ROC) curves were used to evaluate the area under the curve (AUC), sensitivity and specificity of each parameter and identify cut-off points in discriminating between the fellow and normal eyes. **Results:** Corneal thickness at the apex (CTA,  $P = 0.001$ ) and at the thinnest point (CTT,  $P < 0.001$ ), corneal volume (CV,  $P = 0.007$ ), Belin/Ambrosio Enhanced Ectasia Display (BAD) - thinnest point (Dt,  $P = 0.002$ ) and thinnest point displacement (Da,  $P = 0.002$ ) were significantly lower in the fellow group compared to eyes of normal subjects. On ROC curve analysis, the most efficient distinguishing indices between the fellow group and normal controls were BAD - overall D value (AUC = 0.859), Dt (AUC = 0.827), Da (AUC = 0.789) followed by pachymetric progression index maximum (AUC = 0.741). **Conclusion:** BAD-D value and pachymetric progression index could be useful in detecting the earliest form of subclinical keratoconus. However, every single parameter alone is not enough to detect early changes; a combination of different data is required to distinguish subclinical keratoconus.

**Key words:** Belin/Ambrosio enhanced ectasia display, Pentacam, tomography, topography, unilateral keratoconus

Detecting keratoconus in its earliest stage is one of the most important aspects of avoiding iatrogenic corneal ectasia after refractive surgery. Based on a large series of cases reported in the literature, Randleman *et al.* proposed a score that can be used to predict the risk of ectasia (Ectasia Risk Score) to prevent the development of post-refractive surgery corneal ectasia. This score takes into account the preoperative topographic appearance, the preoperative central corneal thickness, the residual posterior wall, the patient's age, and the planned correction.<sup>[1]</sup> Among these various parameters, the presence of undiagnosed early keratoconus is the leading risk factor for post-refractive surgery ectasia.<sup>[2]</sup> Studies suggest that subclinical or clinical keratoconus is found in 1-6% of myopic patients undergoing refractive surgery.<sup>[3-5]</sup> Advanced keratoconus can be diagnosed with typical biomicroscopic, retinoscopic, and topographic findings. However, detection of the disease in the preclinical stage is difficult.

In literature, there were multiple terms referring to the earliest stage of keratoconus, which were frequently misused and caused confusion, including subclinical keratoconus, keratoconus suspect (KCS), and forme fruste keratoconus (FFKC).<sup>[6-9]</sup> The term KCS was reserved for the cornea with

some anterior topographic changes of keratoconus but without evidence of clinical keratoconus in either eye. The term FFKC was first described by Amsler as an incomplete, abortive, or unusual form of a syndrome of disease, meaning corneas that have subtle topographic characteristics but do not reach the threshold of keratoconus suspect.<sup>[7]</sup> However, due to the ambiguity of definition and significant overlap between these terms, there are no definitive criteria to distinguish subclinical keratoconus from normal.

Pentacam is considered to be the most sensitive device for detecting the early form of keratoconus using various parameters such as corneal thickness spatial profile, the percentage of thickness increase, and Belin/Ambrosio Enhanced Ectasia Display (BAD).<sup>[10-14]</sup> The purpose of this study was to evaluate the characteristics of the subtle changes in subclinical keratoconus and compare it with normal eyes. Previous research shows that true unilateral keratoconus is rare and that the normal fellow eye is believed to have subclinical keratoconus.<sup>[14]</sup> Hence, the normal fellow eye in unilateral keratoconus may be the ideal model for the earliest form of

## Access this article online

### Website:

www.ijo.in

### DOI:

10.4103/ijo.IJO\_2129\_19

## Quick Response Code:



Cornea, Cataract and Refractive Surgery Services, Centre for Sight Eye Institute, New Delhi, India

**Correspondence to:** Dr. Mithun Thulasidas, Centre for Sight Eye Institute, Plot No 9, Sector 9, Dwarka, New Delhi - 110 075, India. E-mail: mithun.thulasidas@gmail.com

Received: 18-Nov-2019  
Accepted: 17-May-2020

Revision: 15-May-2020  
Published: 26-Oct-2020

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_reprints@wolterskluwer.com

**Cite this article as:** Thulasidas M, Teotia P. Evaluation of corneal topography and tomography in fellow eyes of unilateral keratoconus patients for early detection of subclinical keratoconus. Indian J Ophthalmol 2020;68:2415-20.

subclinical keratoconus. In the present study, normal fellow eyes in unilateral keratoconus patients were considered as the mildest form of subclinical keratoconus, and topographic and tomographic parameters were compared with normal eyes using Pentacam.

## Methods

This 5-year retrospective observational comparative case study included patients with unilateral keratoconus diagnosed by Pentacam and candidates for refractive surgery with normal corneas. Clinical records of 49 patients (64 eyes) were retrospectively analysed at our eye institute between January 2014 and December 2018. The ethical committee approval was obtained, and the tenets of the Declaration of Helsinki were followed for all study procedures. The study was registered in Clinical Trials Registry - India (CTRI).

The study subjects were divided into 3 groups: 15 advanced keratoconus eyes of unilateral keratoconus patients (KCN group), 15 normal fellow eyes of unilateral keratoconus patients (Fellow eye group) and 34 eyes of normal refractive surgery candidates (Normal group). Eyes were diagnosed as keratoconus based on Pentacam rotating Scheimpflug camera-derived topographic/tomographic parameters and criteria used in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) study.<sup>[15]</sup> Patients with advanced keratoconus in 1 eye and a normal fellow eye were defined as unilateral keratoconus. In this study, fellow eyes in unilateral keratoconus should not only be clinically normal but also satisfy all of the following criteria determined by the Pentacam: normal index of topographic and tomographic keratoconus classification with final D value <1.6 standard deviation (SD) from the BAD. Normal control patients were myopic or myopic astigmatism candidates for refractive surgery with clinically normal corneas and topographic/tomographic characteristics within normal limits determined by the Pentacam. All normal control patients underwent uncomplicated refractive surgery, either Small incision lenticule extraction (SMILE) or Femto-laser-assisted *in situ* keratomileusis (LASIK) and had a 6-month follow-up without any evidence of ectatic corneal changes. In the normal group, only left eyes were used in the study analysis.

Exclusion criteria included a history of ocular surgery, history of ocular trauma, any other ocular pathology and significant corneal scarring that might potentially affect the outcomes.

All patients were asked to stop wearing soft contact lenses for at least 1 week and rigid gas-permeable contact lenses for at least 3 weeks before the examination. A complete ocular examination including slit lamp biomicroscopy, cycloplegic refraction, best corrected distance visual acuity (BCVA) using Snellen acuity chart, keratometry readings, intraocular pressure measurement and dilated fundus examination was performed.

Topographic and tomographic examinations were performed using the Pentacam rotating Scheimpflug camera (Oculus, Wetzlar, Germany). Image quality was checked, and for each eye, only one examination with a good quality factor was recorded. Various parameters were derived from topographic and topometric maps and the BAD, as described below.

Data from topographic maps: flat keratometry (K1), steep keratometry (K2), mean keratometry (Km) for the central 3.0 mm of the cornea, maximum keratometry (Kmax), topographic astigmatism (A), asphericity for the anterior corneal surfaces (Q), keratometric asymmetry: inferior-superior asymmetry at 4 and 6 mm (4 mm I-S and 6 mm I-S), superotemporal-inferonasal asymmetry at 4 and 6 mm (4 mm ST-IN and 6 mm ST-IN), and superonasal-inferotemporal asymmetry at 4 and 6 mm (4 mm SN-IT and 6 mm SN-IT) radius ring of the cornea, corneal volume (CV) in 7 mm diameter centred on the anterior corneal apex, corneal thickness at the apex (CTA) and at the thinnest point of the cornea (CTT) with y coordinate of the thinnest local (Y).

Data from elevation maps: maximum elevations on anterior (AEmax) and posterior cornea (PEmax), minimum elevations on anterior (AEmin) and posterior cornea (PEmin), elevation differences (maximum-minimum) on anterior (AEdif) and posterior cornea (PEDif) in the central 3 mm zone.

Data from topometric maps: index of surface variance (ISV), index of vertical asymmetry (IVA), keratoconus-index (KI), centre keratoconus-index (CKI), index of height asymmetry (IHA), index of height decentration (IHD), and radii minimum (Rmin).

Data from the BAD: D values representing the front surface (Df), back surface (Db), pachymetric progression (Dp), thinnest point (Dt), thinnest point displacement (Da), and final (D), pachymetric progression indices – maximum (PImax), minimum (PImin) and average (PIavg).

## Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean  $\pm$  SD. The normality of data was tested by the Kolmogorov Smirnov test. Qualitative variables were compared using Pearson's Chi-Square test/Fisher's exact test. One way ANOVA was used to test the mean values between the 3 groups, followed by Tukey HSD Post-hoc test for multiple comparisons. The receiver operating characteristic (ROC) curve with area under the curve (AUC) was plotted for Pentacam parameters between the 3 groups. The diagnostic specificity and sensitivity of the main parameters (AUC >0.7) for distinguishing fellow eyes from normal eyes were evaluated, and cut-off points were presented. A probability value (P value) less than 0.05 was considered as significant at 95% confidence level. The statistical package for social sciences (SPSS) version 24.0 was used in the analysis.

## Results

Fifteen eyes of 15 unilateral keratoconus patients (10 males and 5 females) and 34 eyes of 34 normal refractive surgery candidates were analysed (17 males and 17 females). Out of 15 unilateral keratoconus eyes, advanced keratoconus manifested in 11 left eyes and 4 right eyes, which was statistically significant ( $P < 0.001$ ). The ratio of male to female patients was 2:1 in the unilateral KCN group and 1:1 in the Normal group, respectively. The mean age was  $26.4 \pm 4.08$  (range: 18-33) years in the unilateral KCN and  $25.22 \pm 4.24$  (range: 18-35) years in the normal, which was not statistically different.

KCN vs. Fellow eye group: There were significant differences ( $P \leq 0.001$ ) between the KCN and fellow eye group in almost all measured parameters except for corneal

volume (CV), superotemporal-inferonasal asymmetry at 4 mm (4 mm ST-IN) and y coordinate of the thinnest local point (Y) [Tables 1 and 2].

KCN vs. Normal group: There were significant differences ( $P \leq 0.001$ ) between the KCN and normal eye group in all measured parameters [Tables 1 and 2].

**Table 1: Mean pentacam parameters in KCN, fellow eye, and normal groups**

Pentacam parameters	KCN group (n=15), mean (SD)	Fellow eye group (n=15), mean (SD)	Normal group (n=34), mean (SD)
K1	45.8 (4.11)	42.73 (0.99)	42.95 (1.37)
K2	49.89 (5.15)	43.68 (1.11)	44.03 (1.49)
Km	47.74 (4.52)	43.21 (1.02)	43.47 (1.4)
Kmax	57.68 (8.1)	44.39 (1.15)	44.57 (1.47)
A	4.09 (2.02)	0.95 (0.47)	1.08 (0.64)
Q	-0.76 (0.44)	-0.3 (0.14)	-0.29 (0.09)
4 mm I-S	12.64 (5.91)	0.27 (0.94)	0.06 (0.69)
6 mm I-S	6.45 (4.83)	0.58 (1.07)	0.03 (1.09)
4 mm ST-IN	-3.07 (5.92)	-0.04 (0.64)	-0.08 (0.54)
6 mm ST-IN	-2.69 (4.39)	0.28 (0.59)	0.1 (0.72)
4 mm SN-IT	-9.12 (6.77)	-0.35 (0.47)	-0.2 (0.59)
6 mm SN-IT	-5.41 (3.1)	-0.21 (2.64)	-0.41 (0.66)
CV	56.99 (2.74)	58.37 (3.13)	61.09 (2.62)
CTA	467.8 (28.41)	515.07 (26.64)	546.24 (23.99)
CTT	455.13 (29.28)	512.2 (26.79)	544.12 (23.46)
Y	-0.64 (0.47)	-0.45 (0.18)	-0.3 (0.18)
AEmax	29.67 (16.76)	3.13 (0.92)	2.82 (1.03)
PEmax	57.27 (28.14)	5.27 (2.89)	4.12 (2.28)
AEmin	-10.93 (7.91)	-0.47 (1.64)	-0.26 (0.99)
PEmin	-17.87 (14.98)	-1.67 (2.69)	-2.18 (3.5)
AEdif	40.6 (20.24)	3.6 (1.55)	3.09 (1.36)
PEdif	75.13 (32.07)	6.93 (3.28)	6.29 (3.08)
ISV	102.8 (47.69)	16.13 (2.47)	15.62 (4.05)
IVA	1.16 (0.56)	0.11 (0.04)	0.11 (0.04)
KI	1.28 (0.18)	1.02 (0.02)	1.02 (0.02)
CKI	1.08 (0.07)	1 (0.01)	1 (0.01)
IHA	32.13 (34.55)	5.43 (5.43)	6.9 (3.23)
IHD	0.15 (0.09)	0.01 (0.01)	0.01 (0)
Rmin	5.96 (0.8)	7.58 (0.18)	7.58 (0.26)
Plmax	3.94 (2.34)	1.31 (0.16)	1.17 (0.16)
Plmin	1.35 (0.66)	0.73 (0.11)	0.65 (0.16)
Plavg	2.3 (1.11)	1.03 (0.13)	0.93 (0.12)
Df	10.92 (7.14)	0.21 (0.93)	-0.08 (1.04)
Db	8.01 (5.78)	-0.04 (0.56)	-0.36 (0.82)
Dp	9.43 (7.5)	0.83 (0.87)	0.16 (0.83)
Dt	2.87 (1.19)	0.81 (0.85)	-0.15 (0.65)
Da	3.1 (0.68)	0.82 (0.52)	0.13 (0.64)
D	9.18 (4.06)	1.18 (0.32)	0.54 (0.54)

SD=Standard deviation, n=Number of eyes, KCN=Keratoconus, K1=Flat keratometry, K2=Steep keratometry, Km=Mean keratometry, Kmax=Maximum keratometry, A=Topographic astigmatism, Q=Asphericity for the anterior corneal surface, 4 mm I-S=Keratometry inferior-superior asymmetry at 4 mm, 6 mm I-S=Keratometry inferior-superior asymmetry at 6 mm, 4 mm ST-IN=Superotemporal-inferonasal asymmetry at 4 mm, 6 mm ST-IN=Superotemporal-inferonasal asymmetry at 6 mm, 4 mm SN-IT=Superonasal-inferotemporal asymmetry at 4 mm, 6 mm SN-IT=Superonasal-inferotemporal asymmetry at 6 mm, CV=Corneal volume, CTA=Corneal thickness at the apex, CTT=Corneal thickness at the thinnest point, Y=Y coordinate of the thinnest local, AEmax=Maximum elevation on anterior cornea, PEmax=Maximum elevation on posterior cornea, AEmin=Minimum elevation on anterior cornea, PEmin=Minimum elevation on posterior cornea, AEdif=Elevation differences on anterior cornea, PEdif=Elevation differences on posterior cornea, ISV=Index of surface variance, IVA=Index of vertical asymmetry, KI=Keratoconus-index, CKI=Centre keratoconus-index, IHA=Index of height asymmetry, IHD=Index of height decentration, Rmin=Radii minimum, Df=Belin/Ambrosio enhanced ectasia display value representing the front surface, Db=Back surface, Dp=Pachymetric progression, Dt=Thinnest point, Da=Thinnest point displacement, D=Overall deviation, Plmax=Pachymetric progression index maximum, Plmin=Pachymetric progression index minimum, Plavg=Pachymetric progression index average.

**Table 2: Comparison of Pentacam parameters between KCN, Fellow eye and Normal groups**

Pentacam parameters	KCN vs Fellow eye P	KCN vs Normal P	Fellow eye vs Normal P
K1	0.001	<0.001	0.949
K2	<0.001	<0.001	0.912
Km	<0.001	<0.001	0.934
Kmax	<0.001	<0.001	0.989
A	<0.001	<0.001	0.931
Q	<0.001	<0.001	0.999
4 mm I-S	<0.001	<0.001	0.97
6 mm I-S	<0.001	<0.001	0.756
4 mm ST-IN	0.15	0.001	0.999
6 mm ST-IN	0.001	<0.001	0.962
4 mm SN-IT	<0.001	<0.001	0.988
6 mm SN-IT	<0.001	<0.001	0.947
CV	0.366	<0.001	0.007
CTA	<0.001	<0.001	0.001
CTT	<0.001	<0.001	<0.001
Y	0.138	<0.001	0.189
AEmax	<0.001	<0.001	0.992
PEmax	<0.001	<0.001	0.96
AEmin	<0.001	<0.001	0.985
PEmin	<0.001	<0.001	0.975
AEdif	<0.001	<0.001	0.984
PEdif	<0.001	<0.001	0.99
ISV	<0.001	<0.001	0.997
IVA	<0.001	<0.001	0.999
KI	<0.001	<0.001	0.98
CKI	<0.001	<0.001	0.997
IHA	<0.001	<0.001	0.958
IHD	<0.001	<0.001	0.995
Rmin	<0.001	<0.001	1
PImax	<0.001	<0.001	0.918
PImin	<0.001	<0.001	0.697
Plavg	<0.001	<0.001	0.828
Df	<0.001	<0.001	0.963
Db	<0.001	<0.001	0.93
Dp	<0.001	<0.001	0.826
Dt	<0.001	<0.001	0.002
Da	<0.001	<0.001	0.002
D	<0.001	<0.001	0.552

Fellow eye vs Normal group: There were significant differences between the fellow eye and normal group in 5 parameters: corneal thickness at the apex (CTA,  $P = 0.001$ ) and at the thinnest point of the cornea (CTT,  $P < 0.001$ ), corneal volume (CV,  $P = 0.007$ ), BAD - thinnest point (Dt,  $P = 0.002$ ) and thinnest point displacement (Da,  $P = 0.002$ ) [Tables 1 and 2].

#### Receiver operating characteristic (ROC) curve analysis

When discriminating Fellow eye group from Normal group, the D value showed the highest AUC (0.859), followed by Dt (0.827) and Da (0.789) [Table 3]. In discriminating between KCN group and Normal group, most parameters had high AUCs [Table 3].

Table 4 shows the cut-off points and sensitivity and specificity values of the main Pentacam parameters derived from ROC curve analysis used to discriminate between Fellow eye in unilateral keratoconus and Normal groups. Fig. 1 presents the graphical representation of the ROC curve of Pentacam parameters between Fellow eye and Normal groups.

## Discussion

Many studies investigated early screening and diagnosis of keratoconus using the Pentacam device in different ethnic populations.<sup>[9-11,16-26]</sup> Results varied in different populations related to race, geographic location, and size of the study population. Most such studies differed from each other by the criteria used to diagnose subclinical/FFKC.<sup>[11,16-20,25,26]</sup> To the best of our knowledge, the present study is the first and only study to identify characteristics of the subtle morphologic changes in the fellow eyes of unilateral keratoconus patients in Indian population.

In the present study, fellow eyes of unilateral keratoconus patients showed normal values with respect to not only topographic but also tomographic parameters in Pentacam. This may be explained by the fact that fellow eye in our study was defined as the earliest form, with normal elevation and pachymetric values, including the final D value in BAD.

The preponderance towards males in the population in this study is consistent with other keratoconus incidence studies.<sup>[21,24]</sup> CTA, CTT, CV, BAD-Dt, and Da were significantly different in the fellow group and normal group; these results are very comparable to those of other studies.<sup>[9,11,16,17,19,20,25]</sup> However, the fellow eye in the present study was defined as normal, not only in the anterior curvature, but also in the elevation, pachymetric, and BAD maps.

In this study, D value was the most characteristic index between the fellow and normal groups and showed the highest area under the ROC curve. The cut-off for D value to differentiate fellow eyes from normal eyes was found to be 0.835, with 93.3% sensitivity but limited specificity. On the other hand, the cut-off for D value in differentiating keratoconus from normal eyes was found to be 1.965, with a sensitivity of 100%. The D value is a multimetric combination parameter composed of keratometric, pachymetric, pachymetric progression, and posterior elevation parameters. Similar to this study, D value had the highest area under the ROC curve to differentiate between subclinical keratoconus eyes and control eyes in the studies done by Muftuoglu *et al.*, Ruisenor Vazquez *et al.*, and Huseynli *et al.*<sup>[17,19,25]</sup> This result suggests that the D index can be useful as a sole parameter in diagnosing early subclinical keratoconus.

Pachymetric progression index maximum (PImax) was also considered as a valuable parameter in discriminating fellow eyes with normal eyes in this study, consistent with the reports by Uçakhan *et al.*, Ruisenor Vazquez *et al.*, and Huseynli *et al.*<sup>[16,19,25]</sup> The cut-off for PImax to differentiate fellow eyes from normal eyes was found to be 1.155, with 93.3% sensitivity but limited specificity.

Pinero *et al.* reported progressively lower pachymetric readings in eyes with subclinical, early, or moderate keratoconus ( $P < 0.01$ ) and significantly lower CV in the moderate keratoconus group than in the subclinical and mild groups ( $P = 0.04$ ). A possible explanation for this finding may



**Table 3: Receiver operating characteristic curve (ROC) analysis for KCN and Fellow eye versus Normal groups**

Pentacam parameters	KCN vs Normal AUC (CI 95%)	Fellow eye vs Normal AUC (CI 95%)
K1	0.74 (0.562-0.919)	0.431 (0.266-0.597)
K2	0.892 (0.77-1.014)	0.411 (0.244-0.577)
Km	0.833 (0.692-0.975)	0.427 (0.261-0.593)
Kmax	0.981 (0.946-1.016)	0.45 (0.281-0.619)
A	0.969 (0.928-1.01)	0.457 (0.274-0.639)
Q	0.148 (-0.13-0.309)	0.387 (0.204-0.571)
4 mm I-S	1 (1)	0.519 (0.334-0.703)
6 mm I-S	0.989 (0.969-1.01)	0.629 (0.46-0.799)
4 mm ST-IN	0.206 (0.004-0.407)	0.512 (0.325-0.698)
6 mm ST-IN	0.195 (0.018-0.372)	0.598 (0.432-0.764)
4 mm SN-IT	0.005 (-0.007-0.017)	0.457 (0.287-0.627)
6 mm SN-IT	0.025 (-0.022-0.073)	0.377 (0.185-0.57)
CV	0.138 (0.035-0.242)	0.249 (0.1-0.398)
CTA	0.008 (-0.01-0.026)	0.187 (0.05-0.324)
CTT	0 (0)	0.171 (0.036-0.305)
Y	0.233 (0.089-0.378)	0.28 (0.13-0.431)
AEmax	1 (1)	0.605 (0.435-0.775)
PEmax	1 (1)	0.636 (0.452-0.821)
AEmin	0.005 (-0.008-0.018)	0.485 (0.291-0.679)
PEmin	0.122 (-0.003-0.246)	0.544 (0.369-0.719)
AEdif	1 (1)	0.584 (0.407-0.762)
PEdif	1 (1)	0.564 (0.382-0.745)
ISV	0.998 (0.992-1.004)	0.605 (0.435-0.775)
IVA	1 (1)	0.508 (0.322-0.694)
KI	1 (1)	0.589 (0.418-0.76)
CKI	0.846 (0.682-1.01)	0.533 (0.342-0.724)
IHA	0.846 (0.689-1.004)	0.327 (0.131-0.524)
IHD	0.989 (0.966-1.013)	0.336 (0.133-0.54)
Rmin	0.017 (-0.15-0.048)	0.53 (0.363-0.698)
Plmax	0.997 (0.989-1.005)	0.741 (0.602-0.88)
Plmin	0.947 (0.882-1.012)	0.689 (0.532-0.846)
Plavg	0.998 (0.992-1.004)	0.693 (0.536-0.851)
Df	0.986 (0.957-1.015)	0.598 (0.432-0.764)
Db	0.988 (0.963-1.013)	0.648 (0.495-0.801)
Dp	0.998 (0.992-1.004)	0.695 (0.538-0.852)
Dt	1 (1)	0.827 (0.693-0.962)
Da	0.998 (0.992-1.004)	0.789 (0.66-0.919)
D	1 (1)	0.859 (0.756-0.961)

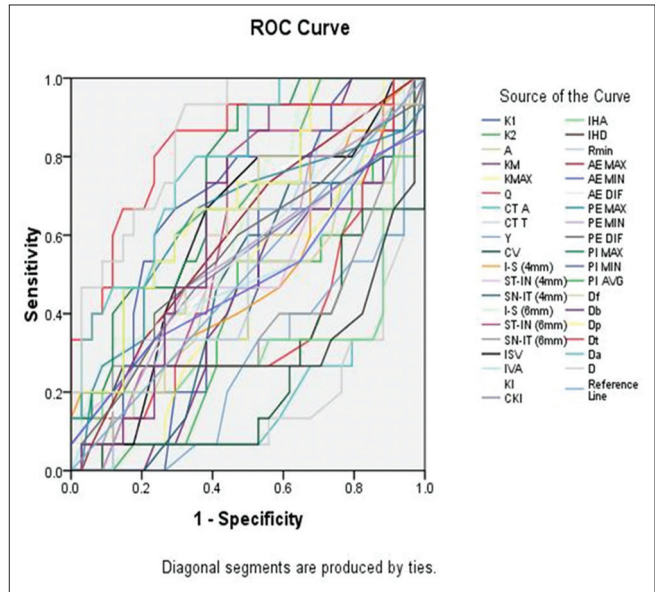
AUC=Area under the receiver operating characteristic curve; CI=Confidence interval

be that at the early stages of keratoconus, a redistribution of CV occurs with no loss of tissue.<sup>[11]</sup> As discussed, we found significant differences in CCT, CTA, and CV between normal eyes and fellow eyes of unilateral keratoconus.

Uçakhan *et al.* evaluated Pentacam parameters in mild to moderate keratoconus, subclinical keratoconus, and normal eyes with myopic astigmatism. They defined subclinical keratoconus as the fellow eye of keratoconus with abnormal topographic features (inferior-superior asymmetry or bow-tie pattern with skewed radial axis) and found that corneal

**Table 4: Cut-off points, sensitivity, and specificity of the main Pentacam parameters derived from receiver operating characteristic curve (ROC) analysis used to discriminate between Fellow eye in unilateral keratoconus and Normal groups**

Pentacam parameters (AUC >0.7)	Cut-off value	Sensitivity	Specificity
D	0.835	0.933	0.324
Dt	0.105	0.867	0.294
Da	0.515	0.8	0.353
Plmax	1.155	0.933	0.471



**Figure 1: Receiver operating characteristic (ROC) curve of Pentacam parameters between Fellow eye and Normal groups**

thickness distribution indices and posterior elevation data were more helpful than anterior elevation data in identifying eyes with subclinical keratoconus.<sup>[16]</sup> This is similar to the observations of the present study. Bae *et al.*, on the other hand, found that keratometric asymmetry, topometric index and anterior/posterior elevation difference had a higher discriminative ability than pachymetric parameters in detecting the earliest form of subclinical keratoconus.<sup>[18]</sup>

Huseynli *et al.* evaluated scheimpflug tomography parameters in subclinical keratoconus, clinical keratoconus, and normal Caucasian eyes. They defined subclinical keratoconus as clinically normal eyes with abnormal topographic features and observed that D value, elevation parameters, and pachymetric progression indices could effectively differentiate subclinical keratoconus from normal corneas in a Caucasian population.<sup>[25]</sup> This is in comparison with the results of the present study.

As discussed above, our study is the first and only study to identify early topometric and tomographic changes in the fellow eyes of unilateral keratoconus patients in the Indian population, and we had included only those fellow eyes which were normal in the anterior curvature, elevation, pachymetric, and the BAD maps.

The limitation of this study was its relatively small sample size. The incidence of true unilateral keratoconus is rare, and thus, this is unlikely to skew the results of this study. Further studies with larger sample size and simultaneous evaluation of the corneal biomechanics and wave front aberrations may be more useful for early detection of subclinical keratoconus.

## Conclusion

Our study showed that the BAD-D value and pachymetric progression index were more effective than other Pentacam parameters in detecting the earliest form of subclinical keratoconus. The present study supports findings previously reported on the usefulness of Scheimpflug imaging to assess subclinical keratoconus in different populations and confirms results indicating that any single parameter alone is not enough to detect early changes. A combination of different data is required to distinguish subclinical keratoconus.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

- Randleman JB, Trattler WB, Stulting RD. Validation of the ectasia risk score system for preoperative laser *in situ* keratomileusis screening. *Am J Ophthalmol* 2008;145:813-8.
- Binder PS, Trattler WB. Evaluation of a risk factor scoring system for corneal ectasia after LASIK in eyes with normal topography. *J Refract Surg* 2010;26:241-50.
- Ambrósio R Jr., Klyce SD, Wilson SE. Corneal topographic and pachymetric screening of keratorefractive patients. *J Refract Surg* 2003;19:24-9.
- Nesburn AB, Bahri S, Salz J, Rabinowitz YS, Maguen E, Hofbauer J, *et al.* Keratoconus detected by videokeratography in candidates for photorefractive keratectomy. *J Refract Surg* 1995;11:194-201.
- Varssano D, Kaiserman I, Hazarbassanov R. Topographic patterns in refractive surgery candidates. *Cornea* 2004;23:602-7.
- Gatinel D, Saad A. The challenges of the detection of subclinical keratoconus at its earliest stage. *Int J Keratoco Ectatic Corneal Dis* 2012;1:36-43.
- Amsler M. The "forme fruste" of keratoconus. *Wien Klin Wochenschr* 1961;73:842-3.
- Klyce SD. Chasing the suspect: Keratoconus. *Br J Ophthalmol* 2009;93:845-7.
- Saad A, Gatinel D. Topographic and tomographic properties of forme fruste keratoconus corneas. *Invest Ophthalmol Vis Sci* 2010;51:5546-55.
- De Sanctis U, Loiacono C, Richiardi L, Turco D, Mutani B, Grignolo FM. Sensitivity and specificity of posterior corneal elevation measured by Pentacam in discriminating keratoconus/subclinical keratoconus. *Ophthalmology* 2008;115:1534-9.
- Pinero DP, Alio JL, Aleson A, Escaf Vergara M, Miranda M. Corneal volume, pachymetry, and correlation of anterior and posterior corneal shape in subclinical and different stages of clinical keratoconus. *J Cataract Refract Surg* 2010;36:814-25.
- Ambrosio R Jr, Alonso RS, Luz A, Coca Velarde LG. Corneal-thickness spatial profile and corneal-volume distribution: Tomographic indices to detect keratoconus. *J Cataract Refract Surg* 2006;32:1851-9.
- Ambrosio R Jr, Caiado AL, Guerra FP, Louzada R, Sinha RA, Luz A, *et al.* Novel pachymetric parameters based on corneal tomography for diagnosing keratoconus. *J Refract Surg* 2011;27:753-8.
- Li X, Rabinowitz YS, Rasheed K, Yang H. Longitudinal study of the normal eyes in unilateral keratoconus patients. *Ophthalmology* 2004;111:440-6.
- Zadnik K, Barr JT, Edrington TB, Everett DF, Jameson M, McMahon TT, *et al.* Baseline findings in the collaborative longitudinal evaluation of keratoconus (CLEK) study. *Invest Ophthalmol Vis Sci* 1998;39:2537-46.
- Uçakhan ÖÖ, Cetinkor V, Özkan M, Kanpolat A. Evaluation of scheimpflug imaging parameters in subclinical keratoconus, keratoconus and normal eyes. *J Cataract Refract Surg* 2011;37:1116-24.
- Muftuoglu O, Ayar O, Hurmeric V, Orucoglu F, Kılıç I. comparison of multimetric D index with keratometric, pachymetric and posterior elevation parameters in diagnosing subclinical keratoconus in fellow eyes of asymmetric keratoconus patients. *J Cataract Refract Surg* 2015;41:557-65.
- Bae GH, Kim JR, Kim CH, Lim DH, Chung ES, Chung TY. Corneal topographic and tomographic analysis of fellow eyes in unilateral keratoconus patients using Pentacam. *Am J Ophthalmol* 2014;157:103-9.
- Ruisenor Vazquez PR, Galletti JD, Minguez N, Delrivo M, Fuentes Bonthoux F, Pfortner T, *et al.* Pentacam scheimpflug tomography findings in topographically normal patients and subclinical keratoconus cases. *Am J Ophthalmol* 2014;158:32-40.
- Hashemi H, Beiranvand AA, Yekta A, Maleki A, Yazdani N, Khabazkhoob M. Pentacam top indices for diagnosing subclinical and definite keratoconus. *J Curr Ophthalmol* 2016;28:21-6.
- Kanellopoulos AJ, Asimellis G. Revisiting keratoconus diagnosis and progression classification based on evaluation of corneal asymmetry indices derived from Scheimpflug imaging in keratoconic and suspect cases. *Clin Ophthalmol* 2013;7:1539-48.
- Du XL, Chen M, Xie LX. Correlation of basic indicators with stages of keratoconus assessed by Pentacam tomography. *Int J Ophthalmol* 2015;8:1136-40.
- Kamiya K, Ishii R, Shimizu K, Igarashi A. Evaluation of corneal elevation, pachymetry and keratometry in keratoconic eyes with respect to the stage of Amsler-Krumeich classification. *Br J Ophthalmol* 2014;98:459-63.
- Lim HB, Tan GS, Lim L, Htoon HM. Comparison of keratometric and pachymetric parameters with scheimpflug imaging in normal and keratoconic Asian eyes. *Clin Ophthalmol* 2014;128:2215-20.
- Huseynli S, Abdulaliyeva F. Evaluation of scheimpflug tomography parameters in subclinical keratoconus, clinical keratoconus and normal caucasian eyes. *Turk J Ophthalmol* 2018;48:99-108.
- Değirmenci C, Palamar M, İsmayilova N, Eğrilmez S, Yağcı A. Topographic evaluation of unilateral keratoconus patients. *Turk J Ophthalmol* 2019;49:117-22.