Comparison of Scheimpflug Derived Biomechanical and Tomographical Indices to Detect Corneal Ectasia - A Cross Sectional Study

Fazla Younis, Omar Zafar

Armed Forces Institute of Ophthalmology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSRTACT

Objective: To compare Corvis ST (Oculus Wetzlar, Germany) and Pentacam (Oculus) derived indices to detect normal cornea, keratoconus and for mefruste keratoconus.

Study Design: Comparative cross sectional study.

Place and Duration of Study: Armed Forces Institute of Ophthalmology (AFIO), Rawalpindi, from Feb to Jul 2019.

Methodology: Following strict inclusion criteria 90 patients were enrolled that were divided into 3 equal groups of normal, Keratoconus and Formefruste kertoconus. One eye of the patient was selected and underwent ophthalmic examination followed by assessment of Corvis ST (Oculus Wetzlar, Germany) and Pentacam (Oculus). Classification analysis between normal, keratoconus and formefruste keratoconus was evaluated using receiver operating characteristic (ROC) curves. The area under the ROC curve (AUC) was compared.

Results: Several corneal response parameters generated by Corvis St (Oculus Wetzlar, Germany) were statistically significant (p-value <0.05) in keratoconus group. The Area under the curve (AUC) ROC values for the keratoconus and normal comparison were 0.84(SPA1), 0.864 (BAD-D), 0.865 (PRFI), 0.92 (CBI), 0.96 (TBI). Among the combined indices TBI showed increase sensitivity of 98.3 % and 94.7% specificity to detect keratoconus. The AUC ROC value for the formefruste and normal control comparison were 0.75 (SPA1), 0.81 (BAD-D), 0.82 (PRFI), 0.81 (CBI), 0.91 (TBI) with 94% sensitivity and 90% specificity to detect formefruste keratoconus.

Conclusion: Our study concluded that among the combined indices TBI demonstrated greater precision to detect keratoconus and formefruste keratoconus thus aiding and augmenting the recent technology.

Keywords*:* Corvis ST, Keratoconus, Pentacam, TBI.

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INTRODUCTION

The demand for refractive surgery has increased globally owing to its ability to improve the quality of life of patients with milderrisks. Being an elective procedure all precautions must be taken to prevent technical hitches.[1,2] Refractive surgery involves removal of tissue which weakens the cornea biomechanically thus predisposing to iatrogenic ectasia in already susceptible cornea.[3] The first case of ectasia after Lasik occurred in forme fruste keratoconus.[4] Thus, to prevent ectasia it'sparamount to detect these biomechanically weakened cornea.

In the past placido disk based topography has been a crucial step in recognition of ectasia and planning of refractive procedures, however its limitations has compelled the development of innovative equipment to gauge the cornea more carefully.[5] These technologies can perceive ectasia at an earlier phase and with greater precision but still appreciation of formefruste keratoconus is a challenging task for the ophthalmologists. Roberts and Dupps,[6] proposed that changes in ectatic corneal diseases are secondary to main abnormalities in the biomechanics of cornea. Thus these changes should be perceived early to detect such cases to prevent the risk of postoperative ectasia after laser procedure.

Studies involving Corvis ST (oculus optikgerate GmbH) and Ocular response analyser (Reichert technologies) have demonstrated changes in biomechanical properties between normal and ectatic corneas however they are not sensitive and specific to detect early subclinical cases.[7]

Newer parameters have been formulated to identify keratoconus with superior sensitivity. The novel parameters include Corvisbiomechanical index (CBI) that is a combination of corvis parameters (DA ratio, A1V, SD of HCDA and SPA1),[8] tomographic and bio-mechanical index (TBI) and Pentacam random forest index (PRFI).[3] and BAD-D.

The objective of the study was to compare the specificity and sensitivity of these parameters (SPA1,

Correspondence: Dr Fazla Younis, House No. 223, Askari 11 Rawalpindi-Pakistan

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CBI, TBI, PRFI and BAD-D) to diagnose formefruste keratoconus and clinical keratoconus in Population of Pakistan.

METHODOLOGY

This was a comparativecross-sectional study conducted at Armed Forces Institute of Ophthalmology from February to July 2019. The study was approved by the ethical committee at AFIO IERB approval certificate number 210/ERC/AFIO. All participants volunteered for the study and consented to take part. Sample size calculations were based on a recent keratoconus pre-valence survey,[9] where the prevalence rate has been reported to So, keeping power of study 80%, alpha of 0.05, prevalence 0.0479 the minimum sample size was calculated to be 73, using sample size formula i.e., n=z2x(*p*)(1-*p*)/ α2. Non-probability-consecutive samp-ling technique was used.

Inclusion Criteria: Total of 90 patients were assessed that were divided in three groups.30 patients in each group Normal group consisted of patients that had normal cornea who came for refractive surgery. Keratoconus group had patients with bilateral keratoconus, one eye was selected at random from both above groups .The third group Forme Fruste keratoconus had clinical keratoconus in one eye and other eye was topographically normal.

Exclusion Criteria: All the patients who had undergone any procedure for keratoconus such as CXL,ICRS were excluded from the study along with patients that were glaucomatous, diabetics or had any other systemic illness.

All patients underwent complete ophthalmic examination for visual acuity, best corrected visual acuity (BCVA) along with corneal topography, Corvis St (Oculus Optikgeräte) and Pentacam (Oculus Optikgeräte, Wetzlar, Germany).

Normal group composed of patients that had BCVA of 6/6, normal slit lamp findings , topography and tomography. Keratoconus was diagnosed on clinical signs (Munson sign, Rizzuti sign, Vogts striae, scissoring reflex on retinoscopy, oil droplet sign) as well as topographical findings. Forme fruste keratoconus consisted of patients with diagnosis of keratoconus in one eye based on above mentioned criteria and the other eye showed a normal front surface curvature. All cases were clinically evaluated by the refractive surgeon.

Data were entered and analysed by using IBM SPSS (version 23.0) software. First, normality of data was checked by using normality graphs and shapiro wilk test. Quantitative normal data were described by using mean and standard deviation, while median and IQR was used for non-normal data. Percentage and frequencies were reported for qualitative data. Group comparisons were done by using Analysis of variance (one-way ANOVA) test. Sensitivity and specificity of diagnostic parameters were assessed and compared by using ROC analysis test and curves. The *p*-value of ≤0.05 was considered to be statistically significant.

RESULTS

Total number of patients enrolled in the study was 90, with 30 patients in each group, which means ninety eyes of the patients were assessed out of which thirty belonged to each normal, keratoconus and forme fruste group. There were 59 (65.5%) males while 31 (34.5%) females and overall mean age was 23.86 ± 6.99 years for study participants. Comparison of baseline clinical characteristics among three groups in given in Table-I, which shows that age and gender were evenly distributed among all study groups.

Table-I: Comparison of baseline clinical characteristics among study groups.

Parameters	Study Groups			*p*-value
	Normal (n=30)	Kerato-conus (n=30)	Forme Fruste (n=30)	
Age (years) (mean ± SD)	26.17 ± 5.68	22.17 ± 9.08	23.23 ± 5.16	0.071
Gender n (%)				
Male	19 63.3%)	22 (73.3%)	18 (60.0%)	0.527
Female	11 36.7%)	8 (26.7%)	12 (40.0%)	

*One-way ANOVA. *significant p values*

Various corneal response parameters were found to be significantly different among three study groups, the means, standard deviations and *p*-values for which are given in Table-II. Similarly, the Table-III shows significant difference in terms of diagnostic indices including SPA, BAD D, CBI, TBI and PRFI among normal eyes, keratoconus and forme fruste groups.

In comparison of normal eye group with both keratoconus and forme fruste group, TBI parameter was found to have highest predictive accuracy in terms of area under the curve to capture the disease, while on the other hand, BAD D, CBI, SPA and PRFI had relatively lower predictive accuracy, but yet signi-ficant. Table-IV provides detail comparison of predic-tive accuracy of different diagnostic parameters between normal eyes vs keratoconus and normal eyes vs forme fruste groups. The area under the curve values for first comparison i.e., normal eyes vs kera-toconus group for TBI, CBI, BAD D, SPA and PRFI were 0.96, 0.92, 0.86,

Table-II: Comparison of dynamic corneal response parameters among study groups.

Parameters	Study Groups			*p*-value
	Normal (n=30)	Keratoconus (n=30)	Forme Fruste (n=30)	
Applantation Length (Mean ± SD)	2.27 ± 0.33	2.02 ± 0.29	2.06 ± 0.35	0.01*
Applantation velocity (Mean ± SD)	-0.29 ± 0.02	-0.34 ± 0.06	-0.33 ± 0.05	0.002*
Peak distance (Mean ± SD)	5.05 ± 0.28	5.03 ± 0.39	5.12 ± 0.28	0.529
Radius (Mean ± SD)	7.34 ± 0.81	5.57 ± 0.82	6.23 ± 0.89	<0.001*
Deformation ampli (Mean ± SD)	1.05 ± 0.98	1.16 ± 0.18	1.14 ± 0.12	0.010*
Pachymetry (Mean ± SD)	541.13 ± 27.7	455.23 ± 24.4	504.50 ± 25.65	<0.001*
Integrated radius (Mean ± SD)	8.15 ± 0.95	11.85 ± 2.11	9.51 ± 1.14	<0.001*
ARth (Mean ± SD)	526.06 ± 132.78	184.15 ± 41.4	315.95 ± 73.67	<0.001*
DA Ratio (Mean ± SD)	4.27 ± 0.31	5.51 ± 0.93	4.76 ± 0.58	<0.001*
B IOP (Mean ± SD)	15.45 ± 1.65	13.7 ± 2.7	14.04 ± 1.75	0.005*
K max (Mean ± SD)	45.05 ± 2.08	55.8 ± 5.54	47.92 ± 2.10	<0.001*
IS value (Mean ± SD)	0.003 ± 0.65	5.71 ± 2.51	1.89 ± 2.85	<0.001*

*One-way ANOVA. Arth=, DA=, IOP=Intraoccular pressure, K=, IS=, *Significant p values*

Table-III: Comparison of combined indices among study groups.

Parameters	Study Groups			*p*-value
	Normal (n=30)	Keratoconus (n=30)	Forme Fruste (n=30)	
SPA (Mean ± SD)	96.66 ± 12.94	67.23 ± 25.86	81.26 ± 15.35	<0.001*
BAD D (Mean ± SD)	4.79 ± 2.79	8.67 ± 2.34	7.50 ± 1.61	<0.001*
CBI (Mean ± SD)	0.42 ± 0.14	0.72 ± 0.12	0.59 ± 0.10	<0.001*
TBI (Mean ± SD)	0.29 ± 0.15	0.72 ± 0.16	0.61 ± 0.13	<0.001*
PRFI (Mean ± SD)	0.15 ± 0.15	0.45 ± 0.19	0.41 ± 0.16	<0.001*

*One-way ANOVA. SPA=stiffness parameter at first applanation, BAD D=Belin-Ambrosio enhanced ectasia total deviation index, CBI=Cor-vis biomechanical index, TBI=tomography and biomechanicalindex, PRFI=Pentacam random forest index, *significant p-values.*

Table-IV: Comparison of ROC curve analysis among study groups.

Groups	Parameters	Indices					
		AUC & SE	95% CI	*p*-value	Cut-off score	Sensitivity	Specificity
Normal vs Keratoconus	SPA	0.846 ± 0.51	0.76-0.96	<0.001	≤90.11	89.2%	86.6%
	BAD D	0.864 ± 0.050	0.76-0.96	<0.001	<6.0	89.5%	84.7%
	CBI	0.923 ± 0.032	0.86-0.98	<0.001	<0.21	93.4%	89.6%
	TBI	0.960 ± 0.022	0.91-0.99	<0.001	<0.62	98.3%	94.7%
	PRFI	0.865 ± 0.051	0.91-1.00	<0.001	<0.45	90.1%	87.2%
Normal vs Forme Fruste	SPA	0.75 ± 0.64	0.63-0.88	<0.001	≤89.76	84.2%	82.4%
	BAD D	0.81 ± 0.061	0.69-0.93	<0.001	<6.1	83.3%	73.3%
	CBI	0.80 ± 0.056	0.69-0.91	<0.001	<0.18	90.4%	88.25
	TBI	0.91 ± 0.037	0.84-0.98	<0.001	<0.57	94.0%	90.4%
	PRFI	0.82 ± 0.055	0.72-0.93	<0.001	<0.18	83.3%	73.3%

0.84 and 0.86 respectively, while for second comparison between normal eyes and forme fruste group were 0.91, 0.80, 0.81, 0.75 and 0.82 respectively. The TBI with a cut off value of <0.62 had a sensitivity of 98.3% and specificity of 94.7% while comparing normal eyes with keratoconus eyes, whereas with cut off value of <0.57 the TBI has a sensitivity of 94.0% and specificity of 90.4% when normal eyes were compared with forme fruste eyes.

Figure showed comparative ROC curves for all diagnostic indices including TBI, CBI, SPA, BAD D and PRFI among normal eyes vs keratoconus and forme fruste groups respectively. It is clearly seen in the ROC curves that TBI can predict the disease with more accuracy and power as compared to all other indices as it has demonstrated maximum area under the curve in both the comparisons.

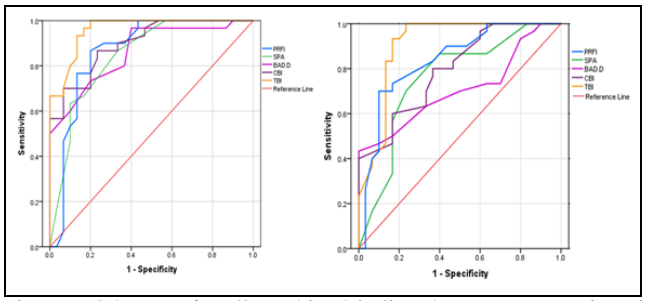

Figure: ROC curve for all combined indices between groups i.e. A) Normal vs Keratoconus group, B) Normal vs Forme Fruste group SPA =stiffness parameter at first applanation, BAD D=Belin-Ambrosio enhanced ectasia total deviation index, CBI=Corvis biomechanical index, TBI= tomography and biomechanical index, PRFI=Pentacam random forest index; IOP=Intraoccular pressure.

DISCUSSION

The increasing demand ofrefractive procedures has led to the necessity of identifying the biomechanically weak cornea that could lead to potentially debilitating condition of ectasia.[2] Forme fruste keratoconus is such an entity that could lead to iatrogenic ectasia.[10,11] No specific definition has been coined for this condition and the terms forme fruste ,subclinical and keratoconus suspect are inter-changing being used.[3] Forme Fruste cases were first reported by Amsler on the basis of pacidodisk mechanism,[11] whereas Kyle defined it as topographic normal eye of a patient with clinically evident keratoconus in other eye.[12] Thus a perplexing task has been to fashion indices that couldidentify the susceptible cornea that has tendency of ectasia if mechanically transformed.[13]

Multiple parameters has been established to detect normal eyes from keratoconus and forme fruste keratoconus including topographic, tomographic,[14] Corvis parameters and combined indices.[15,16] Recently introduced devices such as Ocular response analyser and corvis ST are being used to derive the parameters and assess changes that could help in screening out these corneas.Ocular response analyser uses infra-red rays reflection and Corvis ST make use of scheimpflug images to detect biomechanical properties of cor-nea.[17] In our study, we found thatdynamic corneal response parameters by Corvis ST were statistically significant between keratoconus and normal in consensus with study by salomoa *et al*,[18] and some dynamic corneal response parameters came out different between the normal and forme fruste keratoconus in accordance with study of koc *et al*.[19] However their discriminative power was less as stated by Steinberg *et al,* to differentiate normal and subclinical casesas all parameters have *p*-value ≤0.05, with A2 length showing the highest discriminative power sensitivity/specificity ratio of 67%/67% to differentiatebetween normal and KC suspect eyes,[20] thus combined indices has been generated to improve screening.

Ourstudy showed that Area under the curve (AUC) of Stiffness parameter A1 (SPA1) was0.86 and showed increased efficacys to detect keratoconus as demonstrated by Robert et al that has an AUC of 0.89.[21,22] Our study also demonstrated that TBI has greater AUC 0.960 and increase sensitivity of 98.3 % and 94.7% specificity to detectbetween normal and keratoconusas supported by sedaghat et alwith AUC 1 and sensitivity and specificity of 100 percent,[23] and AUC of 0.91 with 94% sensitivity and 90% specificity of TBI to detect between normal and forme fruste keratoconus which is higher than the other indices .Our results are comparable to study by kataria et althat showed thatTBI has 99% sensitivity and 100% specificity to detect normal from forme fruste keratoconus, Ambrosio *et al*. The AUROCs for the TBI, BAD-D, and CBI were 0.985, 0.839, and 0.822 in the VAE-NT group,koc et al demonstrated the TBI to have the highest area under the curve (0.790; sensitivity: 67%; specificity: 86%) in the receiver operating characteristic analysis., chan *et al,* stated that For differentiating normal and SCKC eyes, TBI demonstrated the highest AUC (0.925) 84.4% sensitivity and 82.4% specificity.[10,19,24,25] Thus our results are comparable to international studies demonstrating that in Pakistani population TBI has greater sensitivity to detect forme fruste keratoconus .

Our study period was 06 months in which we could not find any postoperative ectasia on follow up hence no such group of patients were studied that could tell us what biomechanically changes were present before surgery that eventually led to the development of ectasia.

CONCLUSION

Our study concluded that TBI was a novel parameter that has high ability to perceiveforme fruste keratoconus assisting and augmenting other technology for safe and effective laser surgery.Our study added that in Pakistani population TBI has 94% sensitivity to detect forme fruste keratoconus.

Conflict of Interest: None.

Authors' Contribution

FY: Data acqustion analysis, OZ: Concept design.

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