Validation and Repeatability of Inferior minus Superior Value and its Cut-off Value in Anterior Sagittal Curvature Map Using Pentacam in Early Keratoconus

Thesis

Submitted for Partial Fulfilment of
Master Degree in **Ophthalmology**

By

Mohammed El Sharkawy Mohammed Yousef
M. B. B. Ch. Faculty of Medicine, Ain Shams University

Under Supervision of

Prof. Dr. Khaled Abdel Wahab Eltagoury
Professor of Ophthalmology
Faculty of Medicine, Ain Shams University

Prof. Dr. Maged Maher Salib Roshdy
Professor of Ophthalmology
Faculty of Medicine, Ain Shams University

Prof. Dr. Rania Serag Elkitkat
Assistant Professor of Ophthalmology
Faculty of Medicine, Ain Shams University

Faculty of Medicine, Ain Shams University
2020

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to ***Allah*** *the Most Beneficent and Merciful.*

I wish to express my deepest thanks, gratitude and appreciation to ***Prof. Dr. Khaled Abdel Wahab Eltagoury****, Professor of Ophthalmology, Faculty of Medicine, Ain Shams University, for his meticulous supervision, kind guidance, valuable instructions and generous help.*

Special thanks are due to ***Prof. Dr. Maged Maher Salib Roshdy****, Professor of Ophthalmology, Faculty of Medicine, Ain Shams University, for his sincere efforts, fruitful encouragement.*

I am deeply thankful to ***Prof. Dr. Rania Serag Elkitkat****, Professor of Ophthalmology, Faculty of Medicine, Ain Shams University, for his great help, outstanding support, active participation and guidance.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Mohammed El Sharkawy Mohammed

List of Contents

Title	Page No.
List of Tables	5
List of Figures	6
List of Abbreviations	7
Introduction	- 1 -
Aim of the Work	13
Review of Literature	
Anatomy of the Cornea and Pathological Changes with KC	14
Ocular Surface Influences on the Corneal Topography	20
The Topometric Indices Available in the Pentacam HR	23
Patients and Methods	30
Results	34
Discussion	43
Summary	48
Conclusion	49
References	50
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table 1:	Showing Amsler-Krumeich Classification	10
Table 2:	Showing ABCD Grading System	11
Table 3:	Showing Forme Fruste KC.	12
Table 4:	The summary of the Cut off Values of the topometric indices values.	27
Table 5:	Shows Randleman ectasia score system	29
Table 6:	Demographic data of the two studied groups	34
Table 7:	Comparison between control and cases group regarding CDVA and IOP	36
Table 8:	Comparison between control and patients group regarding IS Scans	38
Table 9:	Correlation and Bland-Altman comparison between first reading and the other four readings in cases group	40
Table 10:	Correlation and Bland-Altman comparison between first reading and the other four readings in control group	41
Table 11:	Showing the AUROC among different parameters.	41
Table 12:	Showing the cut-off point, AUROC, sensitivity, and specificity between the control and patients groups.	42
Table 13:	The summary of previous studies and our study	47

List of Figures

Fig. No.	Title	Page No.
Fig. 1:	Showing six different corneal layers	15
Fig. 2:	Histopathology of corneal epithelium and Bowman's membrane	15
Fig. 3:	Electron Microscope image of a corneal graft, after researchers injected air in it, to separate the different layers of the cornea	17
Fig. 4:	Showing pathological changes in KC	19
Fig. 5:	Showing illustrative Placido projection	23
Fig. 6:	Showing 4 Maps (Ant sagittal curvature map, Ant and Post elevation map, and Pachymetry map)	24
Fig. 7:	Showing Topometric Indices of Pentacam	25
Fig. 8:	IS-value calculation	27
Fig. 9:	WaveLight, GmbH, Erlangen, Germany) with software version 1.20r20.	32
Fig. 10:	Bar chart between two groups according to sex	35
Fig. 11:	Bar chart between two groups according to sex	35
Fig. 12:	Bar chart between two groups according to BCVA	37
Fig. 13:	Bar chart between two groups according to IOP	37
Fig. 14:	Bar chart between two groups according to average IS scans.	39
Fig. 15:	Showing the cut-off point between the control and patients group.	42

List of Abbreviations

Abb.	Full term
3D	*Three-dimensional*
ABT	*Asymmetric bow-tie*
AK	*Amsler-Krumeich*
ARC	*Ant radius of curvature*
AST	*Astigmatism index*
AUROC	*Area under the receiver operating characteristic*
BCVA	*Best correction visual acuity*
CT	*Corneal thickness*
D	*Diopter*
ECM	*Extracellular matrix*
ERSS	*Ectasia Risk Score System*
FFKC	*Forme Fruste Keratoconus*
IHA	*Index of Height Asymmetry*
IHD	*Index of Height Decentration*
IS	*Inferior minus superior*
ISV	*Index of Surface Variance*
IS-Value	*Inferior minus Superior Value*
IVA	*Index of Vertical Asymmetry*
KC	*Keratoconus*
KISA%	*Keratoconus percentage index*
MMPs	*Matrix metalloproteinases*
MRSE	*Spherical equivalent manifest refraction*
PDCT	*Placido disk corneal topography*
PRC	*Post radius of curvature*
RSB	*Residual stromal bed*
SBT	*Symmetric bow-tie*
SD	*Standard deviation*
SRA	*Skewed radial axis*
TKC	*Topographic Keratoconus*

INTRODUCTION

Keratoconus (KC), the most common primary corneal ectasia, is a bilateral asymmetric corneal degeneration accompanied with local corneal thinning. It occurs most commonly in the inferior and central parts of the cornea.[1] Initiating at puberty, KC often progresses until the fourth decade of life.[2] KC usually causes high myopia and irregular astigmatism which results in a poor quality of vision.[2,3]

KC occurs more commonly in association with some systemic and ocular conditions. Systemic disorders include Down's syndrome, Turner syndrome, Ehlers-Dunlos syndrome, Marfan syndrome, atopy, and mitral valve prolapse, while ocular associations include vernal keratoconjuctivitis, retinitis pigmentosa, blue sclera, aniridia, ectopia lentis and mechanical eye rubbing.[3]

Incidence and prevalence of KC:

The burden of a disease is determined by its incidence and prevalence, which in turn describe the provision of relevant healthcare services, including screening programs, primary and specialist medical care.[4]

The reported prevalence of KC varies widely depending upon the geographic location, diagnostic criteria used, and the patients selected. The prevalence mentioned in studies ranges from 0.3 per 100 000 in Russia to 2300 per 100 000 in central

India.[5] Environmental factors may contribute to the wide variation in prevalence. Geographical locations with plenty of sunshine and hot weather such as India[5] and the Middle East[6] have a higher prevalence than locations with cooler climates and less sunshine such as Finland,[7] Denmark,[8] Minnesota, Russia, and Japan.[9]

Classification of KC:

The most widely used Amsler-Krumeich (AK) system fails to make use of the technological advances in corneal imaging. Specifically, the posterior corneal surface and full pachymetric data are not utilized. In the AK system, the severity of KC is graded from stage 1 to 4 using spectacle refraction, central keratometry, presence or absence of scarring, and central corneal thickness as shown in table 1.[10]

Table 1: Showing Amsler-Krumeich Classification[10]

Stage 1	-Eccentric steeping. -Myopia and astigmatism <5.00D. -Mean central K reading <48.00D.
Stage 2	-Myopia and astigmatism from 5.00 to 8.00D. -Mean central K reading <53.00D. -Absence of scarring. -Minimum corneal thickness>400 μm.
Stage 3	-Myopia and astigmatism from 8.00 to 10.00D. -Mean central K reading >53.00D. -Absence of scarring. -Minimum corneal thickness of 300 to 400 μm.
Stage 4	-Refraction not measurable. -Mean central K reading >55.00D. -Central corneal scarring. -Minimum corneal thickness of 200 μm.

The newly described ABCD Keratoconus Grading System uses the anterior and posterior radii of curvatures, which are obtained from the 3 mm zone centered on the thinnest point ("A" for anterior, "B" for back surface) and the corneal thickness at the thinnest point ("C" for corneal thickness) as well as best-corrected distance visual acuity ("D" for distance visual acuity). This new classification/grading system has advantages in that it recognizes the importance of the posterior corneal surface and each component (anterior,

posterior, thickness, and visual acuity) is individually graded[1,11] as shown in table 2.

Table 2: Showing ABCD Grading System[11]

ABCD Grading System	A	B	C	D	
	ARC (3mm zone)	PRC (3mm zone)	Thinnest pachymetry	BCVA	Scarring
Stage 0	>7.25mm (<46.5D)	>5.90mm (<57.25D)	>490 µm	>1.0	-
Stage I	>7.05mm (<48.0D)	>5.70mm (<59.25D)	>450 µm	<1.0	-,+,++
Stage II	>6.35mm (<53.0D)	>5.15mm (<62.5D)	>400 µm	<0.5	-,+,++
Stage III	>6.15mm (<55.0D)	>4.95mm (<65.5D)	>300 µm	<0.2	-,+,++
Stage IV	<6.15mm (>55.0D)	<4.95mm (>68.5D)	<300 µm	<0.05	-,+,++

ARC= ant radius of curvature; PRC=post radius of curvature; BCVA= best correction visual acuity

Although the clinical diagnosis of advanced KC is relatively easy with biomicroscopic and keratometric data, it is rather complicated to rule out forme fruste KC (FFKC) before refractive surgeries. Corneal tomography provided a better means of evaluating the morphological changes in patients with early KC.[12] With the introduction of rotating Scheimpflug devices for corneal tomography, many indices have been proposed for discriminating corneas with FFKC from normal corneas,

including curvature, pachymetric, elevation, and, most recently, biomechanical indices.[12] The highly reputable Randleman's Ectasia Risk Score System (ERSS) [13] uses the topographic asymmetry decentration index, inferior minus superior (IS) value, which is not presented as a single numerical value in the Pentacam HR software displays up to version 1.20. Recently, The Pentacam HR (OCULUS Optikgerate) with software version 1.21r24 displays IS value as a single numerical value.[14]

Emanating treatments that increase the effectiveness in halting early KC progression and preserving visual quality require highly specific diagnostic equipment to avoid applying unnecessary treatments in false positives. Detection of IS value and its cut-off value can help in the detection of early KC.

To assess early KC, it is necessary to use multiple parameters, algorithms and predictive models[15] as shown in table 3.

Table 3: Showing Forme Fruste KC.[15]

Diagnostic criteria for subclinical Keratoconus	
Main Signs (must be met)	-Corneal topography with abnormal localized steepening or an asymmetric bow–tie pattern
	-Normal–appearing cornea on slit-lamp biomicroscopy
Complementary Signs (at least 1 must be met)	-Keratometric power>47.0D -Oblique cylinder>1.50D -Central corneal thickness<500mm -Clinical Keratoconus in the fellow eye

AIM OF THE WORK

Detection of Inferior minus Superior (IS) value and its Cut-off Value which is clinically important in early KC detection.

Chapter 1

ANATOMY OF THE CORNEA AND PATHOLOGICAL CHANGES WITH KC

The cornea is a transparent avascular tissue that acts as a structural barrier and protects the eye against infections.[16] It provides an anterior refractive surface for the eye. The cornea contributes to about 40–44 D of the refractive power and accounts for approximately 70% of the total refraction. Its refractive index is 1.376.[17]

It is horizontally oval, measuring 11–12 mm horizontally and 9–11 mm vertically.[18] It is convex and aspheric. The radius of the anterior curvature is around 7.8 mm and that of the posterior curvature is around 6.5 mm. There is a gradual increase in thickness from the central cornea to the periphery.[19]

The cornea is made up of cellular and acellular components. The cellular components include the epithelial cells, keratocytes, and endothelial cells, while the acellular components include collagen and glycosaminoglycans. The epithelial cells are derived from ectoderm, while the keratocytes and endothelial cells are derived from the neural crest. The corneal layers include epithelium, Bowman's layer, stroma, Dua's layer[20], Descemet's membrane, and endothelium as shown in figure 1.[21]

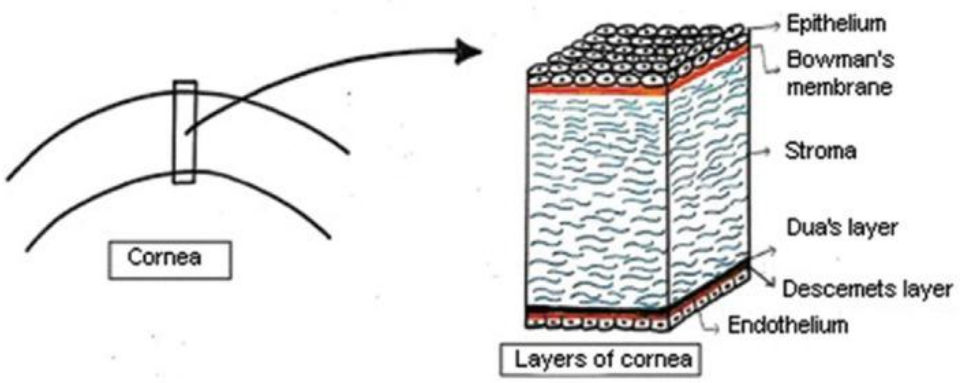

Fig. 1: Showing six different corneal layers[21]

The corneal epithelium is composed fairly uniformly of 5–7 layers of cells. It is about 50 μm in thickness. The epithelium is uniform to provide a smooth regular surface and is made up of nonkeratinized stratified squamous epithelium as shown in Figure 2.

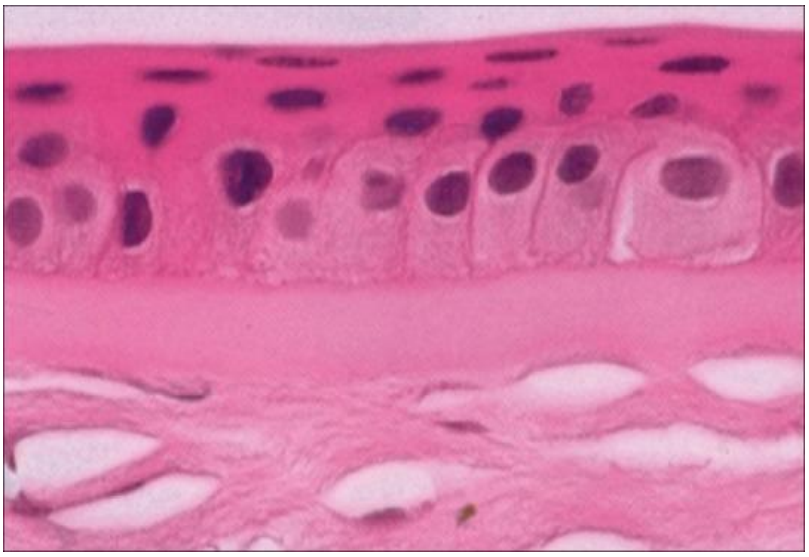

Fig. 2: Histopathology of corneal epithelium and Bowman's membrane.[22]