Association between Keratoconus Severity and Optical Densitometry

SOUTHERN COLLEGE OF OPTOMETRY

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PURPOSE

This study aimed to evaluate associations between optical densitometry (OD) and various tomography indices from Oculus Pentacam® AXL and the Amsler-Krumeich (A-K) classification.

METHODS

This retrospective study, included keratoconic eyes from subjects of any age, with Pentacam AXL good quality specification (QS) scores. Subjects were excluded with a history of ocular surgery, including corneal cross-linking, infection, trauma; or poor-quality specification (QS) scores. A total of 35 topographic, aberrometry, optical densitometry, and pachymetry values were extracted. Indices from Pentacam were analyzed using the Kruskal-Wallis test and linear regression ($p < 0.05$).

RESULTS

The study group included N = 146 eyes from 108 subjects (female = 54.8%; male = 45.2%); mean age 42.5 ± 12.8 yrs. (range 17-72 yrs.) at the time of a scan. OD variables anterior (rs= 0.03); posterior (rs= -0.13), center (rs= -0.06) and total (rs= -0.04) values were poorly correlated with A-K scale. The curvature, pachymetry, and elevation variables with the highest correlations included KFlat (rs= 0.82), KSteep (rs= 0.88), KMax (rs= 0.80), Deviation (rs= 0.73), Deviation of thickness (rs= -0.71), Thinnest pachymetry (rs= 0.71), Deviation in mean posterior thickness (rs= 0.70), Deviation in mean anterior thickness (rs= 0.70), Q-value (rs= -0.68), Deviation pachymetry progression (rs= 0.66), Average pachymetric progression (rs= 0.66), Posterior elevation (rs= 0.52), and Anterior elevation (rs= 0.51). HOA's weakly correlated with A-K stage including Total RMS (rs= 0.40), Z3+1 (rs= 0.21), Z3+3 (rs= 0.03), Z3-3 (rs= 0.01), and Z3-1 (rs=-0.27). SA (rs= -0.70) was the exception. Kruskal-Wallace comparisons found statistically significant differences between A-K stages for High RMS (P< 0.0001), Total RMS (P= 0.0001), Z3+1 (P= 0.02), Z3-1 (P< 0.001), and SA (P< 0.0001). Comparisons of OD (P= 0.94), OD anterior (P= 0.85), OD center (P= 0.91), and OD posterior (P= 0.28), did not vary significantly by stage. Race (P= 0.63) and Gender (P= 0.98) did not vary significantly by stage.

TABLE 1.
Aberrometric and optical densitometric indices by Amsler-Krumeich stage

	Stage (Amsler-Krumeich)				
	I	II	III	IV	P value
Count (N)	53 (36.3%)	56 (38.4%)	15 (10.3%)	22 (15.1%)	
Kmax	51.36 ± 3.29 (50.45 to 52.27)	56.38 ± 4.38 (55.21 to 57.55)	60.85 ± 3.58 (58.87 to 62.83)	68.23 ± 5.90 (65.61 to 70.84)	**<0.0001**
Q-value	-0.494 ± 0.308 (-0.570 to -0.409)	-0.878 ± 0.380 (-0.980 to -0.776)	-1.157 ± 0.687 (-1.537 to -0.776)	-1.415 ± 0.380 (-1.583 to -1.246)	**<0.0001**
HOA RMS	1.9248 ± 0.9540 (1.6618 to 2.1877)	2.4473 ± 1.1670 (2.1348 to 2.7598)	2.8043 ± 0.9251 (2.2920 to 3.3166)	4.2254 ± 1.6136 (3.5099 to 4.9408)	**<0.0001**
Total RMS	7.1488 ± 3.4010 (6.2113 to 8.0862)	9.0330 ± 4.6369 (7.7912 to 10.2748)	10.0677 ± 4.7353 (7.4454 to 12.6900)	13.8580 ± 5.7795 (11.2955 to 16.4204)	**<0.0001**
SA	0.0999 ± 0.3905 (-0.0077 to 0.2075)	-0.4613 ± 0.5031 (-0.5961 to -0.3266)	-0.9473 ± 0.9333 (-1.4642 to -0.4305)	-1.5360 ± 0.9520 (-1.9582 to - 1.1139)	**<0.0001**
Z31	-0.1066 ± 0.7113 (-0.3027 to 0.0895)	-0.0653 ± 1.1670 (-0.3778 to 0.2472)	0.2322 ± 1.2709 (-0.4716 to 0.9360)	0.8288 ± 1.6490 (0.0977 to 1.5600)	**0.0217**
Z3-1	-1.4599 ± 1.0695 (-1.7547 to -1.1651)	-1.7929 ± 1.1743 (-2.1074 to -1.4785)	-1.6888 ± 1.0539 (-2.2724 to -1.1052)	-3.0012 ± 1.7828 (-3.7917 to -2.2108)	**0.0012**
Z33	-0.0115 ± 0.3037 (-0.0952 to 0.0723)	0.0148 ± 0.4517 (-0.1062 to 0.1358)	-0.0614 ± 0.7365 (-0.4692 to 0.3464)	0.0323 ± 0.5907 (-0.2296 to 0.2942)	0.6518
Z3-3	-4.8180 ± 0.4615 (0.0347 to 0.2891)	-0.0473 ± 0.9092 (-0.2908 to 0.1962)	0.2281 ± 0.5945 (-0.1011 to 0.5573)	0.2944 ± 0.6905 (-0.0118 to 0.6005)	0.3463
Densit Ant	28.19 ± 4.50 (26.95 to 29.43)	28.35 ± 5.74 (26.81 to 29.88)	28.33 ± 5.02 (25.55 to 31.11)	29.06 ± 5.48 (26.63 to 31.49)	0.8502
Densit Post	15.15 ± 2.39 (14.49 to 15.81)	15.13 ± 2.37 (14.49 to 15.76)	14.37 ± 1.89 (13.32 to 15.42)	14.16 ± 2.02 (13.27 to 15.06)	0.2843
Densit Cent	17.94 ± 2.40 (17.28 to 18.60)	17.89 ± 2.70 (17.17 to 18.62)	17.83 ± 2.64 (16.36 to 19.29)	17.58 ± 2.33 (16.55 to 18.62)	0.9099
Densit Total	20.422 ± 2.777 (19.657 to 21.188)	20.459 ± 3.402 (19.548 to 21.370)	20.167 ± 2.868 (18.578 to 21.755)	20.255 ± 3.077 (18.890 to 21.619)	0.9355

TABLE 2.
Subject counts by race and gender

	N
Race	
African American	110 (75.34%)
Hispanic	10 (6.84%)
Caucasian	24 (16.43%)
Unspecified	2 (1.37%)
Gender	
Female	80 (54.79%)
Male	66 (45.21%)

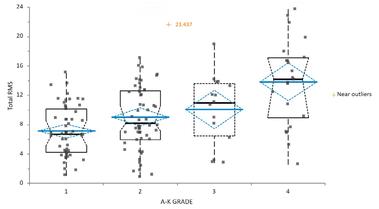

FIGURE 1. *Total RMS vs. A-K stage*

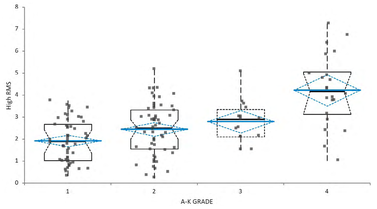

FIGURE 2. *HOA RMS vs. A-K stage*

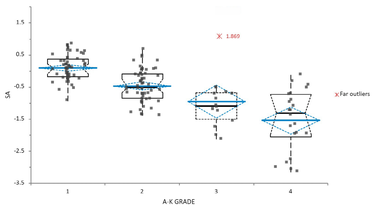

FIGURE 3. *SA vs. A-K stage*

DISCUSSION

This retrospective study identified few individual indices that predict keratoconus severity by A-K stage. In addition, it examined the novel approach of using optical densitometric values to find a correlation between keratoconus eyes by A-K stage.

Kmax represents the steepest front surface keratometry value that helps with the diagnosis.[1] Predictably, Kmax showed a strong positive correlation with A-K stages ($p < 0.0001$) in our study. This may be explained by the incorporation of mean keratometry (Km) into the A-K classification stage. Kmax is a generally accepted parameter to monitor ectatic progression after corneal crosslinking and to assess the efficacy of the procedure, and ≥1.0D of increase in Kmax represents a significant progression.[2] Nevertheless, a past study indicated that Kmax alone poorly detects disease progression.[3] Cunha et al. tested the performance of Kmax in predicting keratoconus progression and found a low sensitivity of 49% and a specificity of 100%.[4]

Q-value is an asphericity coefficient (conic constant) that describes the corneal curvature changes from center to periphery with a normative value of -0.20±0.12.[5] Higher magnitude corresponds to higher eccentricity while the direction indicates whether the corneal surface is prolate or oblate; negative Q-value indicates a prolate corneal surface whereas positive Q-value indicates an oblate surface. The more severe the degree of keratoconus the greater the anterior protrusion, which makes the corneal surface more prolate and results in increased magnitude of minus Q-value. Our study also found a negative correlation of Q-value with A-K stage ($p < 0.0001$). This agrees with a study where it found an inverse correlation of Q-value with the grade of keratoconus.[6] Interestingly, only the stage 4 group failed to reach statistical significance for the Q-value in this study. Torquetti provides an explanation for this finding that deformity of the cornea does not provide a reliable definition on true prolate shape of the cornea, because asphericity profile is lost in highly irregular cornea.[6]

Among the aberrometric indices, HOA RMS, Total RMS, and SA showed the strongest correlations ($p < 0.0001$) with A-K stage; higher A-K stage directly correlates with increasing mean indices. This agrees with findings by Kaşıkcı et al. where they found SA and HOA RMS significantly differ not only between A-K stages but also between keratoconus and normal eyes.[7] Another study theorized that HOA changes are the main cause of visual impairment in keratoconus.[8] In addition, vertical coma (Z3-1) among Zernike polynomials highly correlated ($p = 0.0012$) with A-K stages. This is not surprising, especially that past studies have reported that vertical coma is the best differentiator between keratoconus and normal eyes.[9,10]

This study found no statistical significance for optical densitometric values ($p > 0.05$) in predicting the severity of keratoconus or A-K stage. Optical densitometry parameters from the Pentacam have been successfully employed to detect and monitor corneal scarring after pterygium excision surgery.[11,12] This finding may indicate that keratoconus does not result in significant corneal opacification detectable by Pentcam until a complication such as hydrops occurs. Investigating the change in corneal density in hydrops with optical densitometry and establishing its sensitivity would be interesting topics for a next study. However, recruiting study subjects may be challenging because of the rarity of hydrops cases in keratoconus (incidence rate 0.143%).[13]

The limitations of our study are unequal distribution of patient counts in each A-K stage. Stage III and IV groups (15, 10.3%; 22, 15.1%) included lower patient counts compared to other patient groups in this study. Skewed distribution to African American patient population also could contribute to lack of significance found in Q-value variations across races. Logistic regression and multivariate analysis were not performed to assess the potential value of combining variables to increase the predictability of staging keratoconus.

CONCLUSIONS

Poor correlation was found between optical densitometric values and A-K stage. Kmax and Q-value changes are directly correlated with increasing severity of Keratoconus. The indices themselves are not strong predictors for keratoconus progression or disease severity consistent with other studies. Vertical coma, HOA RMS, Total RMS, and SA were best correlated with A-K stage.

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DISCLOSURES

Neither author has any disclosures.