# ORIGINAL RESEARCH AvaGen Genetic Testing versus Ocular Screening Assessments Including the Keratoconus Severity Score (KSS) and Randleman Ectasia Risk Score System (ERSS) in Refractive Surgery Candidates

Majid Moshirfar 1<sup>-3</sup>, Shreya Pandya<sup>4</sup>, Stephanie Zhang<sup>5</sup>, Isabella M Stoakes<sup>1,6</sup>, Azraa Ayesha<sup>7</sup>, Phillip C Hoopes

<sup>1</sup>Hoopes Vision Research Center, Hoopes Vision, Draper, UT, USA; <sup>2</sup>John A. Moran Eye Center, University of Utah School of Medicine, Salt Lake City, UT, USA; <sup>3</sup>Utah Lions Eye Bank, Murray, UT, USA; <sup>4</sup>University of Louisville School of Medicine, Louisville, KY, USA; <sup>5</sup>University of Arizona College of Medicine-Phoenix, Phoenix, AZ, USA; <sup>6</sup>Pacific Northwest University of Health Sciences, Yakima, WA, USA; <sup>7</sup>University of Utah School of Medicine, Salt Lake City, UT, USA

Correspondence: Majid Moshirfar, Hoopes Vision Research Center, 11820 S. State St. #200, Draper, UT, 84020, USA, Tel +1 801-568-0200, Fax +1 801-563-0200, Email cornea2020@me.com

Purpose: To determine whether the AvaGen (AG) Genetic Eye Test provided additional information for screening for the presence of keratoconus (KC) and assessing KC risk in refractive surgery candidates, as compared to the Keratoconus Severity Score (KSS) and Randleman Ectasia Risk Score System (ERSS).

Methods: This retrospective study analyzed patients seeking refractive surgery at an eye clinic in the United States between January 2022 and July 2023. The inclusion criteria encompassed those with a family history of KC, positive KC indices, or both. Corneal evaluations and demographic information were recorded and analyzed. KSS and ERSS criteria were utilized to evaluate postoperative KC and ectasia risk, respectively. Patients were categorized on how the AG genetic test compared to KSS and ERSS criteria. Clinicians assessed topographic indices, criteria scoring, and AG testing to deliver a definitive surgical recommendation.

Results: Among the 19 patients evaluated for ectasia risk, AG testing showed lower KC risk than ocular screening in three patients (15.8%), equal risk in three patients (15.8%), and higher risk in 13 patients (68.4%). The mean AG scores were  $45.7 \pm 7.0, 49.0 \pm 3.46$ , and  $61 \pm 13.0$  for these respective categories. The most frequently identified KC risk genes were ADAMTS18, COL2A1, and COL4A1. The AG test modified the physician's recommendation for refractive surgery in nine cases (47.4%).

**Conclusion:** Despite the promising application of AG testing for assessing KC risk, further research and development are needed to enhance its applicability for screening refractive surgery candidates, in addition to standard ocular screening approaches.

Keywords: AvaGen, keratoconus, severity, corneal topography, Randleman, ectasia risk score system, keratoconus severity score

#### Introduction

Keratoconus (KC) is a progressive condition typically characterized by asymmetric steepening, thinning, and protrusion of the cornea, usually leading to myopia and irregular astigmatism, which may result in vision loss and even require corneal transplantation.<sup>1,2</sup> Contrary to earlier perceptions, keratoconus is no longer considered non-inflammatory, as numerous pro-inflammatory factors have been implicated in its etiopathogenesis.<sup>3–5</sup> This condition has been found to be influenced by both genetic factors such as family history and environmental factors including eye rubbing and nocturnal ocular compression.<sup>1,2</sup>

Population-based studies also reveal noteworthy discrepancies in keratoconus prevalence. KC seems to be slightly more common in men than women.<sup>6</sup> The reported rates span a spectrum, encompassing the previously cited 0.0002% (0.2/100.000) in Russia<sup>7</sup> and reaching a peak of 4% (4000/100.000) in an investigation conducted in Iran in 2018.<sup>8</sup> On the other hand, in the United States for people older than 65 years, a prevalence of only 0.0175% (17.5/100,000) has been published.<sup>9</sup> However, there remains a historical KC prevalence of 0.0545% (54.5/100,000) from a seminal United States study conducted 35 years ago.<sup>10</sup> The calculated global mean of 0.138% (138/100,000), drawn from studies in 15 countries encompassing diverse age groups and ethnicities, warrants careful consideration due to significant variations in findings among them.<sup>6</sup> It is entirely plausible that technological and diagnostic advances have facilitated the earlier detection of mild KC cases, contributing to its apparent increase in prevalence. However, this does not explain the notable geographical differences observed.<sup>1</sup>

The etiological origin of KC is varied and complex, leading researchers to believe that KC is often multifactorial, with various environmental and genetic factors contributing to its development.<sup>11</sup> Allergies, asthma, atopic disease, eye rubbing, and contact lens use are some environmental factors associated with KC, while smoking, UV exposure, and diabetes are considered questionable risk factors.<sup>12</sup> An emerging potential risk factor recently identified is nocturnal eye compression related to sleeping position.<sup>13,14</sup> While the etiology of KC remains unclear, numerous studies have indicated a genetic predisposition, with a positive family history observed in 6–8% and up to 25% of KC patients<sup>1</sup> and a higher concordance rate in monozygotic twins.<sup>15–17</sup> Despite these genetic associations, ongoing scientific discourse is fueled by findings such as the notable disparity among KC in some monozygotic twins,<sup>18</sup> the plausible mechanisms associating recurrent corneal trauma secondary to eye rub and nighttime ocular compression and KC,<sup>1</sup> the absence of corneal ectasia in Marfan syndrome,<sup>1</sup> and several reported cases of entirely unilateral KC related to unilateral eye rubbing.<sup>1,19</sup> This debate on the relative importance of genetic versus environmental factors in KC continues as new insights and complexities emerge.<sup>1,14,20</sup>

Accurate detection of KC in individuals seeking keratorefractive surgery is crucial to prevent complications. To assess the severity of KC, the Keratoconus Severity Score (KSS) and Randleman Ectasia Risk Score System (ERSS) scoring systems are utilized. The KSS is a scoring system that aids in KC risk assessment and considers clinical findings such as corrected distance visual acuity, keratometry, and topography features.<sup>21</sup> The ERSS helps determine postoperative ectasia risk in patients interested in refractive surgery based on topography findings, age, residual stromal bed thickness, preoperative corneal thickness, and preoperative spherical equivalent.<sup>22</sup> Although not specifically designed for KC risk evaluation, a higher ERSS score may suggest an increased chance of KC development postoperatively, as it is an ectatic corneal disorder.<sup>23</sup>

The genetic component of KC is evident in families with a history of the disease, displaying variable inheritance patterns.<sup>24</sup> The AvaGen (AG) Genetic Eye Test (Avellino, Seoul, Republic of Korea) offers a method to assess the inherited risk for KC, categorizing it as low, medium, or high.<sup>25</sup> It utilizes a polygenic keratoconus probability score based on various gene clusters that have demonstrated a high correlation with KC. This innovative approach may assist ophthalmologists in evaluating refractive surgery candidates suspected of KC or those with a genetic predisposition for the condition.<sup>26</sup> Despite advancements, early diagnosis of KC remains challenging, leading researchers to study KC family members to identify subtle or subclinical cases. This study aims to explore whether the AG test can provide additional clarity in determining KC risk in refractive surgery candidates.

#### **Materials and Methods**

In this retrospective study at Hoopes Vision Clinic in Draper, Utah, USA, all patients seeking keratorefractive procedures, who underwent voluntary AG genetic testing due to a family history of KC or positive KC indices between January 2022 and July 2023, were included. Thirty-six eyes of 18 patients were assessed. Informed consent was obtained from patients prior to obtaining genetic analysis and inclusion in this study. This study was approved by The Biomedical Research Alliance of New York (BRANY) Institutional Review Board (#A20-12-547-823). This study adhered to the tenets of the Declaration of Helsinki, and the Hoopes Vision Ethics Committee approved the consent procedure of this study.

Patient demographic information, medical history, and family history were collected. A complete ophthalmic examination, including uncorrected and corrected distance visual acuity, manifest refraction, slit lamp biomicroscopy, intraocular pressure, and fundus examination were performed for all patients. Extensive topographic indices were recorded through corneal tomography (Pentacam HR, OCULUS Optikgeräte GmbH, Wetzlar, Germany). Additionally, the Galilei G4 Dual Scheimpflug analyzer (Ziemer Ophthalmic Systems AG, Port, Switzerland) and Nidek Marco three-dimensional Wave wavefront analyzer (Marco Technologies, Jacksonville, FL) were used to assess the higher-order

KSS Criteria		ERSS Criteria	Combined Criteria	
Low	0 to 1 pts.	0 to 2 pts.	0 to 3 pts.	
Moderate	2 to 3 pts.	3 pts.	4 to 7 pts.	
High	4 to 5 pts.	4 to 10 pts.	8 to 15 pts.	

Table I KSS, ERSS, and Combined Criteria

aberration root mean square error (HOA-RMS) for a 6-mm pupil and average corneal power (ACP). From these clinical assessments, patients were categorized by the KSS criteria and ERSS criteria for each eye.

Collected measurements assessed corneal topography irregularities which aided in providing a tailored and personalized surgical approach. Clinicians analyzed Pentacam refractive indices in three parts. First, clinicians analyzed all indices (in the 8mm zone) of the Pentacam refractive measurements. After these measurements were examined, indices of the Pentacam Belin/Ambrósio enhanced ectasia display were independently evaluated. Subsequently, the six topographic maps derived from the front and back elevation were reviewed in conjunction with the five parameters allowing for anterior and posterior corneal elevation assessment. The following measurements were then exported into Microsoft Excel 2023 (Microsoft Corporation, Redmond, WA, USA), where subsequent statistical analyses were performed. Finally, the decision for refractive surgery took into account the patient's family history of KC, assessing the proximity of KC within the family and the associated risk level. This evaluation involved comparing the actual presence of KC in the family in addition to the presence of KC indicators such as cataracts, astigmatism, KC predisposition, and Fuchs' dystrophy among relatives.

The KSS criteria assess KC risk based on three categories: low (0-1), moderate (2-3), and high (4-5). Meanwhile, the ERSS criteria already have predetermined risk categories: low (0-2), moderate (3), and high (4-10). To create a unified set of risk criteria, we merged the results of KSS and ERSS scores. The combined categories were then established as low (0-3), moderate (4-7), and high (8-15) (Table 1). In cases where both eyes had different KC risk scores, the analysis utilized the category of the eye with the higher severity classification.

Patients with a family history of KC or KC indices, or both, were recommended to undergo an AG test by the ophthalmologist. For patients interested, a buccal swab was taken. AG conducted a sequence analysis of select exons from the patient against 75 pathogenic variants of KC risk genes giving patients a severity risk score. This scoring categorized patients into low, moderate, or high-risk groups. To enhance analysis, our study further subdivided the moderate risk group into low-moderate, moderate, and high-moderate categories, as depicted in Figure 1.

The study compared the AG genetic test against the combined risk criteria for KC risk scoring. Patients were categorized into three groups: genetic testing lower than screening (GLS), genetic testing equal to screening (GES), and



Figure I AG Risk Scoring Categorization.

genetic testing higher than screening (GHS). These groups represented cases where AG testing showed lower, equal, or higher KC risk than ocular screening, respectively.

### Results

Patient demographics, family history, respective KSS and ERSS criteria, and AG scoring and surgery recommendations are displayed in Table 2. The mean age and AG score for Categories GLS, GES, and GHS are reported in Table 3. The distribution of AG scores among the patient cohort is illustrated in Figure 2. The distribution of the values of the combined criteria was plotted against AG scores and is depicted in Figure 3 to determine a Pearson's correlation coefficient (r) of -0.15. Of the 19 patients, nine (47.4%) were female, and 10 (55.6%) were male. The three most commonly cited genes included ADAMTS18 in 13 (68.4%) patients, COL2A1 in 14 (73.6%) patients, and COL4A1 in 16 (84.2%) patients. Additionally, out of the 75 genes screened by AG, 16 unique genes were identified in our patient cohort as shown in Figure 3, the distribution of these genes across AG groups is depicted in Figure 4 and the comparison of KC risk genes across AG groups is shown in Figure 5.

No patient was recommended for laser in situ keratomileusis (LASIK) due to the high risk of keratectasia after surgery.<sup>27</sup> However, 16 (84.2%) patients were potential candidates for photorefractive keratectomy (PRK), with 11

Category	Patient No./ Sex/ Age	Indices/ Family Hx: Condition [Relative(s)]	Eye	KSS Criteria	Randleman Criteria	Combined Criteria	AvaGen	Recommendation
GLS	I/F/20	KC [U]	OD	Low (0)	High (5)	Moderate	Moderate Moderate (53)	Reevaluate for PRK in I year
			OS	Moderate (2)	High (8)	High		
	2/F/38	KC [F]	OD	Moderate (2)	High (6)	High	Moderate Moderate (45)	Reevaluate for PRK in I year
			OS	Moderate (2)	High (6)	High		
	3/F/31	Cataracts [GM, A]	OD	Moderate (2)	Moderate (3)	Moderate	Low Moderate (39)	Recommend PRK
			OS	Moderate (2)	Moderate (3)	Moderate		
GES	4/M/32	4/M/32 Astigmatism [F]	OD	Moderate (2)	Moderate (3)	Moderate	Moderate Moderate (45)	Received PRK
			OS	Moderate (2)	Moderate (3)	Moderate		
	5/M/30	KC [A]	OD	Moderate (2)	Moderate (3)	Moderate	Moderate Moderate (51)	Reevaluate for PRK in I year
			OS	Moderate (2)	Moderate (3)	Moderate		
	6/F/24	КС [В]	OD	Low (I)	High (6)	Moderate	Moderate	Reevaluate for PRK
			OS	Low (I)	High (6)	Moderate	Moderate (51)	in I year
GHS	7/M/37	7/M/37 KC [M]	OD	Low (0)	Low (2)	Low	High moderate (57)	No refractive surgery
			OS	Low (I)	Moderate (3)	Moderate		
	8/F/38	F/38 Cataracts [NOS]	OD	Moderate (3)	High (4)	Moderate	High moderate (63)	Reevaluate for PRK in I year
			OS	Moderate (3)	High (4)	Moderate		
	9/F/44	Astigmatism [F]	OD	Moderate (2)	Moderate (3)	Moderate	High moderate (58)	Recommend PRK
			OS	Moderate (2)	Moderate (3)	Moderate		
	10/M/25	5 KC predisposition [M]	OD	Low (0)	Low (2)	Low	Low	Reevaluate PRK/ LASIK/ SMILE in 5 years
			OS	Low (0)	Low (2)	Low	moderate (38)	

Table 2 Basic Demographic, Criteria Categorization, AvaGen Score, and Recommendations for Study Eyes

(Continued)

Category	Patient No./ Sex/ Age	Io./ Sex/ Condition Criteria		Randleman Criteria	Combined Criteria	AvaGen	Recommendation	
	I I/F/35	KC [NOS]	OD	Low (0)	Low (0)	Low	High (69)	Reevaluate for PRK in I year
			OS	Low (I)	Low (0)	Low		
	12/M/36	КС [U]	OD	Low (I)	Low (0)	Low	High (72)	Recommend PRK
			OS	Low (I)	Low (0)	Low	-	
	I 3/M/30	KC [F, A, U]	OD	Low (0)	Low (0)	Low	High	No refractive surgery
			OS	Low (0)	Low (2)	Low	Moderate (62)	
	14/F/46	кс [s]	OD	Low (0)	Moderate (3)	Low	Moderate Moderate (51)	Received PRK
			OS	Low (0)	Moderate (3)	Low		
	I 5/M/24	KC [F]	OD	Low (I)	Low (2)	Low	Low	No refractive surgery
			OS	Low (I)	Low (2)	Low	Moderate (42)	
	16/M/21	КС [М, В]	OD	Low (I)	Moderate (3)	Low	High (71)	Reevaluate PRK in 5 years
			OS	Low (I)	Moderate (3)	Low		
	17/M/23	KC [F, S]	OD	Low (0)	Low (2)	Low	Moderate Moderate (52)	Reevaluate PRK in I year
			OS	Low (0)	Low (2)	Low		
	18/F/45	Fuchs' dystrophy [M]	OD	Moderate (2)	Moderate (3)	Moderate	High (79)	Reevaluate PRK in 5 years
			OS	Moderate (2)	Moderate (3)	Moderate		
	19/M/44	KC predisposition	OD	Low (I)	Low (I)	Low	High (79)	Reevaluate PRK in 5
		[NOS]	OS	Moderate (2)	Moderate (3)	Moderate		years

#### Table 2 (Continued).

Abbreviations: Aunt [A], Brother [B], Father [F], Grandmother [GM], Mother [M], Not Otherwise Specified [NOS], Sister [S], Uncle [U].

Table 3 Average	Measurement	of Age	and AG	Scoring	Between	Categories
(n = 19 Eyes)						

Parameter (Mean ± SD)	GLS	GES	GHS	Total
	(n = 3)	(n = 3)	(n = 13)	(n = 19)
Age (years)	34.46 ± 9	28.67 ± 4.2		32.79 ± 8.48
AG Score	45.7 ± 7.0	49.0 ± 3.46		57.0 ± 13.1

(68.8%) patients advised to return later for reevaluation, whereas five (31.3%) patients were approved to undergo PRK without further assessment. Conversely, three (16.7%) patients were not recommended to undergo any refractive surgery.

There were three (15.8%) patients in Category GLS, three (15.8%) in Category GES, and 13 (68.4%) in Category GHS. Of these patients in Category GLS, one (33.3%) was a PRK candidate, while two (66.7%) were recommended to wait one year for a repeat evaluation. In Category GES, one (33.3%) patient received PRK, and the other two (66.7%) were recommended for future assessment in a year. For Category GHS, three (23.1%) patients were considered immediate candidates for PRK, seven (53.8%) patients were advised to return for another PRK evaluation, and three



AvaGen Distribution Amongst Patient Cohort

Figure 2 AvaGen Distribution Amongst Patient Cohort.



#### **Combined Criteria vs. AvaGen (AG)**

Figure 3 Depiction of Combined Criteria scoring against AvaGen scoring.

(23.1%) patients were advised against refractive surgery. The timeframe for patients recommended to return for further evaluation ranged from one year to five years.

Select values from Pentacam measurements and the Belin/Ambrósio enhanced ectasia display were cited to be most sensitive and specific in assessing for topographic abnormality and KC risk.<sup>28,29</sup> The distribution of these select values, including index of surface variance (ISV), index of vertical asymmetry (IVA), index of height decentration (IHD), maximum Ambrosio relational thickness (ARTmax), pachymetric progression index maximum



Figure 4 KC Risk Gene Distribution for Patient Cohort.



Figure 5 Comparison of KC Risk Genes Across Avagen Groups.

(PPI-max), and Belin/Ambrósio enhanced ectasia deviation (BAD-D) are depicted in Figure 6. Cut-off values were determined based on abnormal classifications from prior studies.<sup>30,31</sup> Combined assessment of parameters yielded better KC predictability compared to the separate evaluation of Corvis ST biomechanical measurements or tomographic values.



Figure 6 Depiction of Topographic Indices Between the Three Categories (GLS, GES, and GHS). Cut-off values for detecting KC were represented with a horizontal line for each measurement.

Abbreviations: GLS, genetic lower than screening; GES, genetic equal to screening; GHS, genetic higher than screening; ISV, index of surface variance; IVA, index of vertical asymmetry; IHD, index of height decentration; ARTmax, maximum Ambrosio relational thickness; PPI-max, pachymetric progression index maximum; BAD-D, Belin/ Ambrósio enhanced ectasia deviation.

# Discussion

The medical community has utilized AG as an instrumental tool to ascertain KC risk through polygenic risk scoring.<sup>25</sup> However, eyecare practitioners remain uncertain about the clinical validity and utility of the test, given its recent introduction.<sup>32</sup>

Among the three (15.8%) patients falling into Category GLS, AG scoring suggested that additional time could be taken to assess for corneal changes; however, any KC presentation was less likely to progress further. For patients with a low-moderate AG score but moderate KC risk, the AG score provided clarity and alleviated uncertainty regarding the appropriateness of PRK. Integrating the AG score with corneal measurements, including topography and tomography values, instilled confidence in the physician's decision to recommend PRK without needing further review for these patients. Conversely, for patients with a high combined criteria risk score, the ophthalmologist considered reevaluating for refractive surgery after one year. In these cases, the moderate AG score supported but did not alter the decision to reassess at a later time point. Younger age also contributed to this decision to allow more time to assess the possible manifestation of KC.

Of the three (15.8%) patients in Category GES, the AG scores supported the ophthalmologist's initial KC risk considerations and recommendation for PRK. However, it was observed that AG testing did not significantly impact the decision to undergo refractive surgery, as PRK was already indicated based on corneal screening alone.

Among the 13 (68.4%) patients in Category GHS, only three (23.1%) were considered suitable for refractive surgery at the time of evaluation. For the remaining patients, the ophthalmologist advised an extended reevaluation period. This cautious approach aimed to closely monitor corneal changes, considering the elevated AG score's indication of a high likelihood for these patients to develop KC, before considering PRK as a potential surgical option. This recommendation aligns with previous studies highlighting the contraindication of refractive surgery in cases of unstable refraction related to KC.<sup>23</sup> Studies, such as the one conducted by Abdolahian et al, emphasize the importance of regular follow-up visits to assess corneal topography and refractive stability before considering any refractive surgery.<sup>33</sup>

In patients older than the mean age of adult KC presentation of 27.4 years, it was presumed that corneal markers suggesting existing KC would have already developed.<sup>24</sup> For older patients in Category GHS, who did not exhibit these markers, as suggested by their low to moderate corneal screening results, the surgeon felt confident in directly recommending photorefractive keratectomy (PRK). Consequently, surgical recommendations in older individuals could be made without the need for genetic screening.

Our study implemented an individualized evaluation for each patient to determine the appropriate surgical direction. This personalized approach accounts for the variations in recommendations provided by different clinicians regarding refractive surgery. For instance, Patients 4 and 5 in Category GES shared similar age, criteria risk, and AG scores, but their recommendations differed. Patient 4 had no immediate family members with KC compared to Patient 5, who had an aunt with KC. Furthermore, Patient 4 exhibited only one abnormal Pentacam measurement, while Patient 5 exhibited six. These factors influenced the recommendation for Patient 5 to wait an additional year for reevaluation for KC. The extended period allowed the clinician to make a more informed decision. This recommendation aligns with the findings of Khakshoor et al, who reported enhanced safety in performing PRK on a stabilized cornea,<sup>34</sup> indicating a cessation of KC progression.

Although the ERSS and KSS diagnostic tools have revolutionized KC risk monitoring,<sup>35</sup> they still pose challenges in interpreting results for younger individuals.<sup>11</sup> Other tools, such as the corneal biomechanical index (CBI) and tomographic biomechanical index (TBI), utilizing Pentacam and Corvis ST parameters, integrate biomechanical and corneal tomographic measurements to predict KC risk.<sup>28</sup> The importance of the Pentacam Belin/Ambrósio enhanced ectasia display cannot be overstated, as the values obtained from that assessment were integral in evaluating for ocular abnormalities.<sup>29</sup> While these indexes are quite sensitive, further research is needed to validate their diagnostic efficacy.<sup>30</sup>

AG is transforming ocular healthcare with its first commercially available genetic test analyzing thousands of variants in 75 genes related to corneal structure.<sup>25</sup> Out of the 105 genes reported in our patient cohort, including overlapping genes between patients, ADAMTS18, COL2A1, and COL4A1 were identified as the three most common KC risk genes (Figure 4). Prior studies confirm these specific genes impact corneal structure and function.<sup>36–38</sup> Furthermore, specific genes were only reported in certain AG groups (Figure 5). For example, CRT3, KRT3, and TXDN were only found in patients of the high moderate and high risk AG group, whereas TBP2 was seen in low moderate and high risk patients, according to AG. While these findings provide clarity on the varied severity of KC risk, our analysis suggests that AG does not replace a comprehensive eye exam.<sup>30</sup>

In our study, AG testing significantly impacted the physician's refractive surgery recommendations for nine patients (47.3%) with a mean AG score of  $61.1 \pm 14.8$ , indicating that AG testing can enhance the ophthalmologists' confidence and decision-making in managing KC. However, our findings also revealed challenges in using AG as the sole indicator of KC risk.

As depicted in Figure 3, a Pearson's correlation coefficient (r) of -0.15 indicates a restricted correlation between KSS and ERSS scoring in comparison to AG. This lack of direct correlation between the combined scoring systems and AG may stem from the current ambiguity of the scoring ranges in AG. Specifically, some patients were categorized as having a moderate risk based on AG screening, but we observed great variability within this group. Among these patients, 13 (72.2%) were classified as moderate risk, while the remaining five (27.8%) were classified as high risk (Figure 2). This ambiguity highlights a limitation of AG in accurately distinguishing KC risk levels among patients, particularly in the moderate AG scoring range. Our research can help clinicians, who encounter conflicting situations concerning KC, better understand how to utilize the AG test. Despite these considerations, we maintain the belief that AG can still provide valuable guidance for physician decision-making in certain circumstances.

However, AG has also shown questionable effectiveness as a genetic screening tool due to its price point of \$300 and lack of insurance coverage. These factors make it very difficult for patients to access AG. Additionally, the absence of publicly available research on its sensitivity, specificity, accuracy, or precision makes it challenging for clinicians to assess KC risk and determine appropriate refractive surgery options. While AG serves as a valuable ancillary service, it falls short in fully guiding the decision-making process for qualifying refractive surgery patients. Clinical judgment and the use of diagnostic devices are deemed more crucial and effective than relying solely on AG.<sup>32</sup> In essence, AG is satisfactory but does not offer all the necessary components for a comprehensive diagnosis.

To improve the utility of AG as a genetic screening tool, future research endeavors should investigate diverse populations, including those with and without a family history of KC, while also assessing asymptomatic and suspected patients. Through the systematic analysis of data from these studies, a more comprehensive understanding of comparative values between patient groups, such as mean, median, and range of AG scores, can be obtained. This in-depth analysis has the potential to enhance AG-based KC risk determination, particularly in the low, moderate, and high scoring ranges.

Our current understanding of AG helps determine the appropriateness of PRK for individuals with different risk profiles. For patients with low-moderate AG scores and moderate keratoconus (KC) risk, the AG score provides clarity and confidence in recommending PRK without further review or in a short period of time. However, for patients with a high combined criteria risk score, the ophthalmologist may opt for an extended reevaluation period, closely monitoring corneal changes before considering PRK as a potential surgical option.

#### Conclusion

Prior parameters for KC risk, including corneal measurements, could serve to be secondary to AG screening if AG was proven to be highly effective. However, our study indicates that corneal and genetic tests possess limitations. We recommend that both tests be implemented to assess KC risk as their integrated use has proven to be greatly effective in the cases examined.

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# Disclosure

The authors report no conflicts of interest in this work.

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