## Corneal Imaging Abnormalities in Familial Keratoconus

**To the Editor:**

The etiology of keratoconus remains unknown, but several studies suggest that genetics plays a significant role in its pathogenesis.[1] Corneal topographic analysis in families with familial keratoconus has not been extensively studied before. In clinical settings, diagnosis and follow-up of patients relies on corneal topography.[1] Dual-Scheimpflug imaging provides topographic, pachymetric, and elevation maps of both the anterior and the posterior corneal surface, facilitating the diagnosis of subclinical keratoconus cases.[2]

Within this context, we attempted to analyze the corneal topographic findings of patients with familial keratoconus and their normal relatives, comparing them with a control group. There were 216 patients with keratoconus who were enrolled and screened for a family history of keratoconus. Of these patients, 21 families had a positive keratoconus family history; 51 patients with keratoconus were in the keratoconus group, 34 unaffected first-degree relatives were in the no keratoconus group, and 53 individuals with no disease were in the control group. All participants underwent corneal imaging with dual-Scheimpflug technology and analyses based on qualitative and quantitative data.

We encountered a 23.6% prevalence of familial keratoconus according to family history in this specific group of patients with keratoconus, which lies at the upper limits of relative reports regarding familial keratoconus.[1] This high prevalence could mean that the penetrance in those patients (cross-linking candidates) could be higher than in other patients with less progressive keratoconus. Moreover, the demographics of participants could play an important role because they were citizens of Crete, and therefore characterized by high exposure to sunlight.

Topographic corneal analysis of first-degree relatives who were diagnosed as having keratoconus seemed to be in conjunction with previous studies, using different imaging modalities.[3-5] Specifically, the majority of participants with keratoconus displayed inferior steepening, whereas superior keratoconus appeared to be rare. Unilateral keratoconus was present in 17.6%, whereas studies that analyzed sporadic cases of keratoconus reported 3% to 13%.[6]

According to the qualitative and quantitative analysis of first-degree relatives, we evaluated the diagnostic capacity of a series of keratoconus-specific indices, provided by the system's software, in discriminating subtle ectatic abnormalities from normal. Abnormal corneal patterns were present in at least one eye in 53% of clinically unaffected relatives. Two corneal patterns were overexpressed: asymmetric bow tie with inferior steepening without skewed axes and inferior steepening (**Figure 1**). The aforementioned patterns were significantly more common in relatives compared to controls and may indicate genetic predisposition and low penetrance of keratoconus. These findings complement the research findings of Levy et al., who supported the expression of two abnormal patterns in relatives of patients with keratoconus.[3] A series of Galilei keratoconus indices differed significantly between relatives and controls (inferior-superior index [IS], surface asymmetry index [SAI], oppsite sector index [OSI], keratoconus prediction index [KPI], keratoconus probability index [KProb], anterior elevation [AE], and posterior elevation [PE]). Moreover, according to receiver operating characteristic analysis, the IS index demonstrated the best overall predictive accuracy (area under the curve: 0.942) in distinguishing suspect corneal patterns from normal, with values greater than 0.82 probably suggesting suspect corneas, followed by SAI, OSI, KPI, and KProb indices. Moreover, the PE index differed statistically significantly between the abnormal patterns and the control group with a cut-off value of 12.5 mm, contributing to early detection of abnormal corneal patterns. This genealogical study was the first to further genetic analysis on these families. A possible match of gene mutations with specific corneal topographic profiles could yield valuable data concerning the pathogenesis of keratoconus.

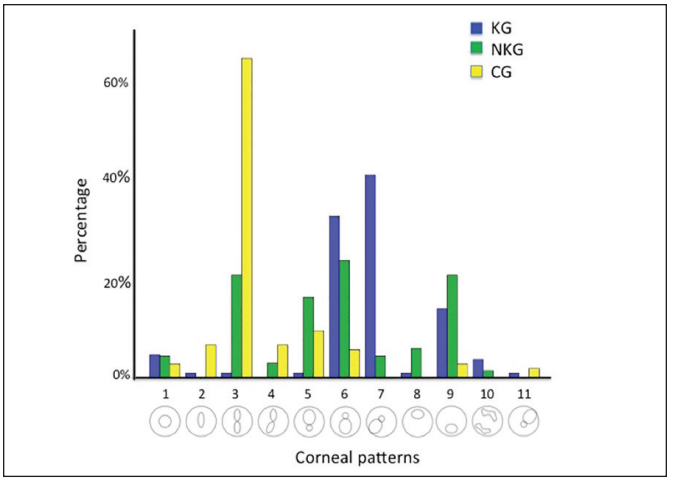


**Figure 1.** Distribution of corneal topographic patterns in the keratoconus (KG), no keratoconus (NKG), and control (CG) groups. The vertical axis represents the percentages of each pattern of each group.

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