



## Original research

# Corneal hysteresis and corneal resistance factor in pellucid marginal degeneration

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## Abstract

**Purpose:** To evaluate and compare corneal hysteresis (CH) and corneal resistance factor (CRF) in pellucid marginal degeneration (PMD), keratoconus (KCN), and normal eyes using the Ocular Response Analyzer (ORA).

**Methods:** In this retrospective study, corneal biomechanical parameters were measured in patients with PMD ( $n = 102$ ) and KCN ( $n = 202$ ) and normal subjects ( $n = 208$ ) using the ORA. Data, including full patient history as well as the results of refraction, slit-lamp biomicroscopy, Pentacam HR (Oculus), and ORA (Reichert; Buffalo, New York, USA), were collected from medical records. Also, the data of only one eye per individual were selected for the analysis. The inclusion criteria for PMD and KCN groups were a reliable diagnosis of these ectatic disorders based on the clinical and corneal tomographic findings. CH, CRF, CH–CRF, intraocular pressure (IOP) measurements were assessed for each subject. Data were analyzed with SPSS and MedCalc using the ANOVA, Pearson Correlation, and receiver operating characteristic (ROC) curve analysis.

**Results:** The mean CH was  $8.91 \text{ mmHg} \pm 1.05$  [standard deviation (SD)],  $8.43 \pm 0.78$ , and  $10.89 \pm 1.08$  in the PMD, KCN, and normal group, respectively. Also, the mean CRF was  $8.21 \pm 1.35$ ,  $7.19 \pm 1.11$ , and  $10.69 \pm 1.41$  in the PMD, KCN, and normal group, respectively. ANOVA showed differences in the mean CH, CRF, and CH–CRF between three groups ( $P < 0.001$ ). Also, ROC curve analysis showed the cut-off points  $\leq 9.5$ ,  $\leq 9.5$ , and  $> 1.3 \text{ mmHg}$  for CH, CRF, and CH–CRF in the PMD group, respectively. For biomechanical parameters in PMD eyes, CRF had the highest sensitivity (75.49%) while the greatest area under the ROC curve (AUC) was seen for CH (0.903). Moreover, central corneal thickness (CCT) showed no correlation with CH ( $P = 0.30$ ,  $r = -0.104$ ) or CRF ( $P = 0.75$ ,  $r = 0.033$ ) in the PMD group.

**Conclusions:** This study presented the values of corneal biomechanics for PMD using the ORA. The results of the ORA were markedly different between PMD, KCN, and normal eyes.

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**Keywords:** Pellucid marginal degeneration; Corneal biomechanics; Corneal hysteresis; Corneal resistance factor; Keratoconus

## Introduction

Pellucid marginal degeneration (PMD) is a non-inflammatory and progressive ectatic corneal disease involving the inferior cornea in a crescentic shape.<sup>1</sup> PMD is different from other ectatic corneal disorders by its location. The band of thinning usually extends between the 4 and 8

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o'clock positions and is apart from the limbus by 1–2 mm of the normal cornea. The area superior to the thinned part is ectatic, and the area between the limbus and thinned part is clear, without any scarring, lipid deposition, or vascularization.<sup>2</sup> Although PMD is localized as a bilateral inferior condition, its other features such as superior,<sup>3</sup> unilateral<sup>4</sup> or a combination of them<sup>5</sup> have also been reported. A typical topographic map in PMD shows flattening in the vertical meridian with marked against-the-rule astigmatism.<sup>6,7</sup> Moreover, corrected distance visual acuity usually decreases in the fourth to fifth decades of life.<sup>2,6</sup> Despite the similarities between PMD and keratoconus (KCN), differential diagnosis is based on clinical manifestations and diagnostic modalities.<sup>2,7–10</sup> On the other hand, it is very important to detect preoperative risk factors before corneal refractive surgery and to rule out corneal ectatic disorders. In eyes with KCN, significant alterations occur in corneal biomechanical properties which make it weaker than normal.<sup>11,12</sup> Considering the time of onset of PMD and KCN,<sup>4,13</sup> decreased corneal biomechanics in older patients probably suggests the onset or existence of PMD. Therefore, early detection of the changes of biomechanical characteristics can minimize the incidence of risk factors for refractive surgery in patients with PMD.<sup>14</sup>

The Ocular Response Analyzer (ORA), a device to determine corneal hysteresis (CH) and corneal resistance factors (CRF), can be used for evaluation of corneal biomechanics *in vivo*.<sup>15</sup>

To our knowledge, two studies have evaluated corneal biomechanical parameters in PMD using the ORA. The first study was conducted by Labiris et al. who evaluated the diagnostic capacity of ectasia specific indices,<sup>16</sup> and the second study was performed by Lenk et al. who investigated the diagnostic capacity of corneal biomechanical parameters in a small group of patients with PMD.<sup>17</sup> The above-mentioned studies focused on PMD diagnosis with specific software (version 3.01) and did not report the biomechanical outcomes of PMD in a large population.

Therefore, this study was designed to determine *in vivo* corneal biomechanics (CH and CRF) in PMD using the ORA and to estimate the diagnostic accuracy of these parameters. The secondary objective was to compare these parameters with the corresponding values in patients with KCN and subjects with normal cornea.

## Methods

This retrospective, observational case series study was performed at Sedaghat Eye Clinic, Mashhad, Iran, from February 2016 to October 2016. The Institutional Review Board/Ethics Committee of Mashhad University of Medical Sciences approved the study in 2016 (registration number: 940776), and its protocol was in accord with the tenets of the Declaration of Helsinki.

Data were collected from medical records (January 2012–January 2016), including a full patient history as well as the results of uncorrected and corrected distance visual acuity, manifest and cycloplegic refraction (Topcon KR-1, Tokyo,

Japan), regularity status of the retinoscopic reflex, non-contact computerized tonometry (Topcon CT-1/CT-1P, Tokyo, Japan), ophthalmoscopy, slit-lamp biomicroscopy, placido disc-based topography (TMS4, Tomey, Erlangen, Germany), Scheimpflug-based tomography (Pentacam HR, Oculus, Optikgerate GmbH, Wetzlar, Germany), and dynamic bidirectional applanation device (ORA; Reichert Ophthalmic Instruments, Buffalo, New York, USA).

Three study groups were PMD and KCN patients and normal subjects within the age range of 20–50 years.

The inclusion criterion for the PMD group was a reliable diagnosis of PMD made by an experienced corneal refractive surgeon (MR.S.) based on the results of slit-lamp biomicroscopy, corneal topography/tomography, with special attention to pachymetry maps.<sup>2,10</sup> On slit-lamp biomicroscopy and corneal tomography, we focused on a clear thinning band in the inferior corneal peripheral zone separated from the corresponding limbus by a 1–2 mm clear zone. Moreover, in corneal topography/tomography patterns, we considered the inferior corneal band of steepening above the band of thinning as well as against-the-rule or irregular astigmatism, while the corneal center is clear without considerable thinning or steepening. In addition to slit-lamp biomicroscopy and corneal tomography, we used clinical manifestations including visual acuity and refractive components of the cases for a diagnosis of PMD.

The patients in the KCN group were selected based on the topographic/tomographic patterns, KCN signs on slit-lamp examination, and an irregular retinoscopic reflex.<sup>9,18–21</sup> KCN cases were finally confirmed based on the results of corneal topography and tomography.

The normal group comprised individuals with healthy eyes, corrected distance visual acuity of 0.00 logarithm of the minimum angle of resolution (logMAR) or higher (Snellen Equivalent 20/20 or better), normal topography/tomography, and low refractive error (spherical equivalent between plano to –3.00 diopters and astigmatism <1.00 diopter to rule out the effect of high refractive error on corneal biomechanics).<sup>22</sup>

The exclusion criteria in all groups were previous eye surgery, corneal scarring, vascularization, inflammation, opacity, history of herpetic keratitis, severe dry eye, contact lens use 3 weeks before study, glaucoma or glaucoma suspect, intraocular pressure (IOP) lowering treatment, pregnancy, nursing, and underlying autoimmune or systemic diseases. Eyes diagnosed as KCN suspect were excluded from the study.

Since PMD is a rare condition, we recruited 102 patients with PMD in the study group. After excluding suspect or not true PMD eyes, we had 32 patients with bilateral clinical PMD and 70 patients with unilateral clinical PMD. In order to avoid experimental error, when both eyes were eligible in unilateral PMD cases, the data of only one eye were selected randomly for the study. Then, we selected and compared two participants from the control (normal and KCN) groups (with age matching) per PMD patient in the study group to avoid potential biases.

The number of right and left eyes in PMD group was 62 and 40, respectively. Considering the number of right and left eyes in the study group, we enrolled about the same number of

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