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**Research Article**

# Peculiarities of Biomechanical Properties of Ocular Tissue in Keratoconus

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**Abstract**
Considerable achievements having been recently made in modern diagnostics and treatment of keratoconus have not diminished the urgency of the given problem as the traditional views of the pathogenesis of keratoconus do not always allow to struggle effectively with this difficult and continuously progressing disease.
**The objective of the research** was to study the peculiarities of biomechanical properties of the cornea in keratoconus.
**Materials and methods.** The article presents the analysis of studying biomechanical properties of the cornea in keratoconus. 44 patients (88 eyes) with keratoconus and emmetropic refraction were examined. To calculate biomechanical indicators of the cornea there was carried out the comparative analysis between the measurements obtained with the use of several methods in the same patients, namely the Oculus Pentacam-Scheimpflug imaging device by a standard technique and the indicators calculated using the method proposed by us and the device for *in vivo* estimation of corneal rigidity.
**Results.** Considerable advantages of using the developed method and the device for estimation of corneal rigidity *in vivo* in comparison with keratotopography on the Oculus Pentacam-Scheimpflug camera were registered which allowed us not only to reveal the presence of biomechanical disorders of the cornea, but also to differentiate their character. To describe the degree of changes in biomechanical properties of the cornea *in vivo* the coefficient of corneal rigidity was developed.
**Conclusions.** Loading tests allow receiving more exact information on biomechanical properties of the cornea in comparison with standard researches on the Oculus Pentacam-Scheimpflug camera.

**Keywords**
keratoconus; biomechanical properties; rigidity; coefficient of corneal rigidity; fibrous tunic of eyeball

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## Problem statement and analysis of the recent research

Considerable achievements having been recently made in modern diagnostics and treatment of keratoconus have not diminished the urgency of the given problem as the traditional views of the pathogenesis of keratoconus do not always allow to struggle effectively with this difficult and continuously progressing disease. The lack of the methods for determining trigger, key pathogenetic links at an early subclinical stage of the disease do not allow to detect precisely the initial moment of their development, while well-known and available methods of treatment are mainly aimed at preventing and slowing the progression of the pathological process. Considering the rapid evolution of ophthalmic diagnostic equipment within the last decade, the study of the methods to solve the existing contradictions, the analysis and generalization of knowledge concerning the nature of biomechanical processes in the fibrous tunic of the eyeball as well as the development of the methods for *in vivo* clinical assessment of corneal biomechanical properties have received a strong impetus to the development in modern ophthalmology. According to recent clinical trials [17, 18, 21, 22, 27, 33], there are two predominant worldwide methods for assessing biomechanical properties of the cornea in keratoconus, namely, the Ocular Response Analyzer (ORA) and keratotopography performed using Orbscan II, Oculus Pentacam, Oculazer, etc. The ORA allows measuring corneal hysteresis (CH) which, according to the authors [17, 18, 20, 21, 22, 25, 33], is the most crucial component in the diagnosis of keratoconus. The second group of diagnostic devices allows detecting the difference in morphological features of normal cornea and the cornea of the eye with keratoconus which, according to the developers, is the main prognostic criterion for the diagnosis. However, despite the apparent advantages of both techniques there is still a wide range of controversial provisions, proved limitations and disadvantages of the aforementioned methods [17, 18, 27].

**The objective of the research** was to study the peculiarities of biomechanical properties of the cornea in keratoconus.

## 1. Materials and methods

44 patients (88 eyes) were examined. All the patients underwent complete ophthalmic examination at the Department of Ophthalmology of the P.L. Shupyk National Medical Academy of Postgraduate Education in the Kyiv City Clinical Ophthalmological Hospital “Center of Eye Microsurgery” and were

informed on the objectives of the study (protocol KE No 3 (71) of 14 March 2011 of the P.L. Shupyk National Medical Academy of Postgraduate Education Ethics Committee). All the patients were divided in two groups. The main group included 24 patients with keratoconus (48 eyes). The comparison group comprised 20 patients with emmetropic refraction and visual acuity above 0.5 (40 eyes). Both groups were comparable for age and sex distribution. When examining the patients of the main group in all cases (48 eyes - 100%) myopic refraction was observed. Visual acuity above 0.5 was detected in 33.3% of patients; in 50.0% of patients it ranged from 0.1 to 0.4; in 16.7% of cases visual acuity was less than 0.1. The initial level of the intraocular pressure (IOP) in the main group was equal to 10.31 ± 1.94 mm Hg, while the initial level of the IOP in patients of the comparison group corresponded to 13.46 ± 2.15 mm Hg. During primary examination, special attention was paid to the comorbidity. Retinal dystrophy was found in 8.3% of patients of the main group. Patients of the comparison group did not suffer from this ocular comorbidity.

According to biomicroscopic signs of the cornea [5, 14], all the eyes of patients of the main group were classified into stages (according to the Amsler classification updated by A.A. Kivaev et al.) [5, 12]. Thus, among 24 patients (48 eyes) there were 14 (29.17%) eyes with stage I keratoconus, 12 (25.0%) eyes with stage II keratoconus, 12 (25.0%) eyes with stage III keratoconus and 10 (20.83%) eyes with stage IV keratoconus.

Initially, patients of both groups underwent standard ophthalmic examination. To calculate biomechanical indicators of the cornea there was carried out the comparative analysis between the measurements obtained with the use of several methods in the same patients, namely the Oculus Pentacam-Scheimpflug imaging device by a standard technique and the indicators calculated using the method proposed by us and the device for *in vivo* estimation of corneal rigidity [8, 9]. Keratotopography on the Oculus Pentacam-Scheimpflug camera was performed using traditional methodology [2]. In vivo estimation of corneal rigidity [9] was carried out by means of the Oculus Pentacam-Scheimpflug camera using standard programs for working with the device under condition of high IOP being artificially elevated by means of the device for *in vivo* determination of corneal rigidity (Ukrainian patent UA 85810. 2009 Feb 25) [8, 9] which created a two-minute uniform compression of the eyeball under a pressure of 30 grams. Initially, keratotopografic characteristics were studied using the Oculus Pentacam-Scheimpflug camera without loading according to standard methods. Then, under conditions of artificially increased IPO the same indicators were repeatedly measured using standard programs of the Oculus Pentacam-Scheimpflug camera. The obtained results of the research were recorded in the statistical card of patient. The indicator ΔSE and the coefficient of corneal rigidity (KER) were calculated. To estimate changes in biomechanical properties of the cornea *in vivo* the formula describing the KER [10] was developed. The obtained results were statistically processed using Microsoft Office Excel 2010.

## 2. Results and discussion

The obtained results of the research are presented in Tables 1-2.

When analyzing the obtained results and studying keratotopograms of patients of the main group using the Oculus Pentacam-Scheimpflug camera according to standard methods the following facts attracted our attention: firstly, a perfectly uniform topographic pattern in the optical zone of a patient with keratoconus was not observed (Table 1); secondly, the degree of astigmatism very often exceeded 2.0 dioptres being on average 4.8 ± 0.03 dioptres (Table 1). The spherical equivalent of the cornea was relatively high (52.37 ± 0.83 dioptres) and correlated with the values of the anterior-posterior axis (APA) (26.41 ± 0.36 mm) (r = 0.71; $p<0.05$). Characteristic decrease in central corneal thickness (CCT) (432 ± 15.6 $\mu$m) and reduction in the IOP level (10.31 ± 1.94 mm Hg) in patients with keratoconus were observed. Mean coefficient Kmax (front) was equal to 63.91 ± 0.84 dioptres in the main group, and the maximum and minimum radii of the anterior corneal surface curvature were 6.62 ± 0.07 and 4.75 ± 0.04 mm, respectively (Table 1).

When applying the modified method of the research using the Oculus Pentacam-Scheimpflug camera and the device for *in vivo* determination of corneal rigidity [8] in patients with keratoconus of the main group under conditions of artificially raised IOP the following patterns were observed: under the influence of loading there was a statistically significant increase in the spherical equivalent of the anterior and posterior surfaces of the cornea (Δ = 3.45 and 2.2 dioptres, respectively), the increase in the coefficient Kmax (front) by 3.1 dioptres, the reduction in the maximum and minimum radii of the anterior corneal surface curvature (Δ = (-)1.2 and (-)1.4 mm, respectively), as well as the reduction in the maximum and minimum radii of the posterior corneal surface curvature (Δ = (-)0.98 and (-)1.33 mm) ($p<0.05$) (Table 1).

There were no changes in the depth of the anterior chamber of the cornea compared to reference value (Δ = (-)0.09 mm, $p <0.05$) (Table 1). During the research the KER [10] was equal to (+)6.59% in patients with keratoconus.

It should be noted that our research has revealed the fact of relative stability of the cornea in emmetropia. In patients with emmetropic refraction (the comparison group) under conditions of loading a slight flattening of the cornea was observed, as evidenced by the reduction in the spherical equivalent as well as the increase in the maximum and minimum radii of curvature of the anterior corneal surface and the reduction in the coefficient Kmax (front). In the comparison group, the indicator ΔSE decreased on average by 0.51 dioptres ($p<0.05$), and the KER was equal to (-)1.21% ($p<0.05$).

In addition, the performance of loading test under conditions of artificially increased IOP allowed us to reveal a significant decrease in the level of the supportive properties of the cornea (corneal rigidity) in patients with keratoconus

**Table 1.** Dynamics of changes in keratotopografic indicators under initial condition and under conditions of artificially raised IOP in patients of the main group, n = 48

| Indicators | M ± m | | M differences, Δ | Change in the indicator to reference value, % |
|---|---|---|---|---|
| | Reference values | Values during compression | | |
| Spherical equivalent, front, dioptres | 52.37 ± 0.83 | 55.82 ± 0.92[1]* | 3.45 | +6.59 |
| Spherical equivalent, back, dioptres | - 8.61 ± 0.03 | - 6.41 ± 0.03[1]* | 2.2 | -25.55 |
| Astigmatism degree | 4.8 ± 0.03 | 4.9 ± 0.02[1]* | 0.1 | +2.1 |
| Kmax. (Front), dioptres | 63.91 ± 0.84 | 67.01 ± 0.9[1]* | 3.1 | +4.85 |
| Pachy Pupil Center, μm | 432 ± 11.6 | 407 ± 21.4[1]* | 25.0 | -5.79 |
| Cornea front, Rm, mm | 6.62 ± 0.07 | 5.42 ± 0.05[1]* | 1.2 | -18.13 |
| Cornea front, Rmin, mm | 4.75 ± 0.04 | 3.35 ± 0.05[1]* | 1.4 | -29.47 |
| Cornea back, Rm, mm | 6.83 ± 0.09 | 5.85 ± 0.07[1]* | 0.98 | -14.35 |
| Cornea back, Rmin, mm | 4.27 ± 0.05 | 2.94 ± 0.02[1]* | 1.33 | -31.15 |
| Tangential curvature (front), dioptres | 53.13 ± 0.67 | 56.74 ± 0.81[1]* | 3.61 | +6.79 |
| A. C. Depth (int), mm | 3.25 ± 0.03 | 3.16 ± 0.02[1]* | 0.09 | -2.77 |
| APA, mm | 26.41 ± 0.37 | 26.83 ± 0.37[1]* | 0.42 | +1.59 |

Note.

[1] - parametric methods of estimating statistical significance of the results (the Student's t-test);

* - the difference in comparison with the initial level is statistically significant ($p<0.05$).

which was manifested as follows: corneal refraction amplified, and central corneal curvature became steeper (Table 1). Sufficient variability in the deformation as well as the correlation between keratoconus stage and the deformation level was found (the higher keratoconus stage - the more deformation) (the Pearson correlation coefficient r = 0.93, $p<0.05$) (Table 2).

The graph of liner regression of changes in the level of ΔSE depending on keratoconus stage in patients of the main group is presented in Fig. 1. Thus, in stages I, II, III and IV keratoconus, the increase in corneal refraction by 3.09 ± 0.03 dioptres, 3.33 ± 0.04 dioptres, 3.43 ± 0.02 dioptres and 4.14 ± 0.03 dioptres, respectively was found. The Pearson correlation coefficient was r = 0.77 ($p<0.05$) (Table 1, Fig. 1). This fact may be due to the weakness of the supportive properties of the cornea in keratoconus that is consisted with the data on corneal thickness.

In patients with stage IV keratoconus, biomechanical properties of the cornea were so weakened that ΔSE in some eyes reached 5.5-5.8 dioptres (Fig. 1). Such changes were observed in several patients with stage I keratoconus where ΔSE was within 3.3-3.9 dioptres (the Pearson correlation coefficient r = 0.73; ($p<0.05$). During the 5-year observation period, a persistent progression of keratoconus was detected. Studies have shown that the KER [10] in patients of the main group ranged from (+)6.27 to (+)7.53% and correlated with keratoconus stage (the Pearson correlation coefficient r = 0.85; $p<0.05$) (Table 2). The conditions of loading caused a slight thinning of CCT (Table 1-2). Thus, in the main group, the difference in ΔCCT was within 25.00 μm (Table 2) ($p<0.05$). There was no significant difference between changes in corneal thickness

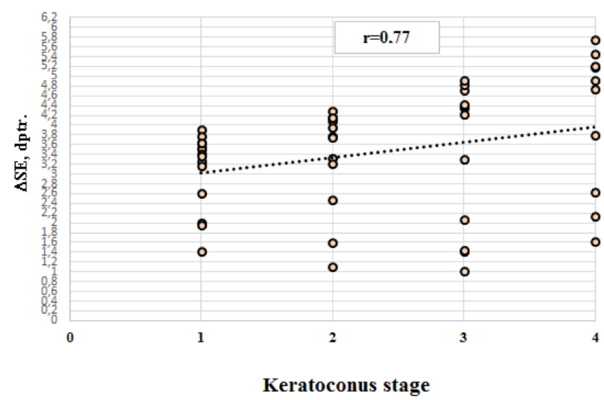


**Figure 1.** Graph of liner regression of changes in the level of ΔSE and keratoconus stage in patients of the main group.

under conditions of loading in patients with different stages of keratoconus (Table 2) ($p>0.05$). There was observed an inverse dependence of the weak force of changing CCT on keratoconus stage (the Pearson correlation coefficient r = (-)0.35; $p<0.05$). Under conditions of artificially raised IOP in all patients of the main group the depth of the anterior chamber did not change significantly (Δ = 0.07-0.09mm) in comparison with reference value ($p>0.05$) (Table 1).

The analysis of the research results revealed that the mechanical properties of the cornea in patients with keratoconus did not depend on CCT. The cornea could be thin, but resistant to deformations (Fig. 2). At the same time, in patients with thicker cornea, higher degrees of deformation under con-

**Table 2.** Dynamic of changes in biomechanical indicators of the cornea under initial condition and under conditions of artificially raised IOP in patients of the main group depending on the stage of the disease, n = 48

| Disease stage | M of a difference, change in ΔSE during compression | Coefficient of corneal rigidity, $K_{ER}$, % | ΔCCT, $\mu$m | Δ Cornea front, Rm, mm | IOP mm Hg |
|---|---|---|---|---|---|
| Stage I keratoconus, n = 14 | $3.09 \pm 0.03^{2.3}*$ | $+6.27^{2.3}*$ | $-23.41 \pm 5.13^{2.3}$ | $0.31 \pm 0.02^{2.3}*$ | $11.64 \pm 1.1^{2.3}*$ |
| Stage II keratoconus, n = 12 | $3.33 \pm 0.04^{2.3}*$ | $+6.34^{2.3}*$ | $-31.15 \pm 6.21^{2.3}$ | $0.42 \pm 0.03^{2.3}*$ | $10.25 \pm 1.2^{2.3}*$ |
| Stage III keratoconus, n = 12 | $3.43 \pm 0.02^{2.3}*$ | $+6.39^{2.3}*$ | $-28.04 \pm 5.43^{2.3}$ | $0.54 \pm 0.04^{2.3}*$ | $9.83 \pm 1.2^{2.3}*$ |
| Stage IV keratoconus, n = 10 | $4.14 \pm 0.03^{2.3}*$ | $+7.53^{2.3}*$ | $-32.23 \pm 7.22^{2.3}$ | $0.67 \pm 0.04^{2.3}*$ | $9.1 \pm 1.2^{2.3}*$ |

Note.

2 - parametric methods of estimating statistical significance of the results (the Fisher's exact test);

3 - nonparametric methods of estimating statistical significance of the results (the Wilcoxon signed-rank test);

* - the difference in comparison with the initial level is statistically significant (p<0.05).

ditions of artificially raised IOP (r = (-)0.36 were observed; p<0.05). In addition, the analysis showed that interpersonal

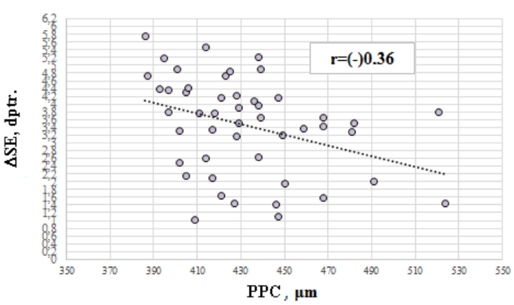


**Figure 2.** Graph of liner regression of changes in the level of SE and corneal thickness in patients of the main group.

variability in the initial level of the IOP correlated with keratoconus stage (the Pearson correlation coefficient r = (-)0.56; p<0.05). The initial level of the IOP in patients of the main group (n = 48 eyes) was equal to 10.31 ± 1.94 mm Hg. The mean value of the IOP level in patients with stage I keratoconus was 11.64 ± 1.1 mm Hg. The average value of the IOP level in patients with stage II keratoconus was 10.25 ± 1.2 mm Hg. In patients with stage III keratoconus the average value of the IOP level equaled to 9.83 ± 1.2 mm Hg, while in patients with stage IV keratoconus the mean value of IOP level was 9.1 ± 1.2 mm Hg (Table 2). The average values of ΔSE were 3.09 ± 0.03 dioptres, 3.33 ± 0.04 dioptres, 3.43 ± 0.02 dioptres and 4.14 ± 0.03 dioptres, respectively. The Pearson correlation coefficient was: r1 = (-)0.66; r2 = (-)0.62; r3 = (-)0.81; r4 = (-)0.82, respectively. The difference between the latter ones were statistically significant (p<0.05).

During the research, we have studied the correlation between changes in the level of DAPA and changes in the mean level of ΔCCT in all patients of the main group in general and depending on keratoconus stage. Under conditions of artificially raised IOP in patients with keratoconus there was observed the weakness of the supportive properties of the cornea alongside with the decrease in the supportive properties of the sclera being manifested as an increase in ΔAPA under conditions of loading which correlated with keratoconus stage (the Pearson correlation coefficient r = 0.59; p<0.05). Thus, in stage I keratoconus ΔAPA increased by 0.26 ± 0.02 mm, in stage II keratoconus ΔAPA increased by 0.27 ± 0.03 mm, in stage III keratoconus ΔAPA increased by 0.45 ± 0.04 mm and in stage IV keratoconus ΔAPA increased by 0.47 ± 0.03 mm.

The study of changes in ΔCCT in patients of the main group and depending on keratoconus stage revealed significantly greater enlargement (thinning) of the cornea under conditions of loading in patients with stage IV keratoconus in comparison with changes in CCT in patients with stage I keratoconus (the Pearson correlation coefficient was r = (-)0.35; p<0.05). The correlation analysis allowed us to establish a statistically significant inverse correlation between the level of ΔAPA and the level of ΔCCT in patients of the main group (the Pearson correlation coefficient r = (-)0.78; p<0.05) In particular, there was revealed that in all patients of the main group with increased values of ΔAPA the level of changes in the value of ΔCCT increased significantly towards the thinning of CCT. Moreover, it was observed in both patients with stage I keratoconus (r1 = (-)0.62; p<0.05) and patients with stages II, III, IV keratoconus (r2 = (-)0.61; r3 = (-)0.96; r4 = (-)0.83, respectively, $p<0.05$).

Thus, the conditions of loading and the use of the method for *in vivo* estimation of corneal rigidity [9] in patients with keratoconus proposed by us revealed the tendency of the eye to stretch in several directions.

We have studied the relationship between changes in the level of ΔSE and changes in the radius of the anterior corneal surface curvature in the steep meridian (Cornea front, Rm1) in patients of the main group in general and depending on keratoconus stage. Artificially raised IOP in patients with keratoconus revealed the following: the curvature of the cornea contributed to a decrease in the rigidity (stiffness) of the cornea. There was a strong direct correlation between the degree of deformation (ΔSE) in case of loading and the radius of the anterior corneal surface curvature in the steep meridian (the Pearson correlation coefficient r = 0.69; $p<0.05$).

In addition, it was observed that with the progression of keratoconus stages (from stage I to stage IV) under conditions of artificially raised IOP changes (an increase) in the indicator ΔSE from (+)3.09 to (+)4.14 dioptres correlated with fluctuations of Δ Rm1 level ranging from (-)0.98 mm to (-)1.42 mm (the Pearson correlation coefficient r = (-)0.89; $p<0.05$). With the progression of keratoconus, the cornea became steeper; the curvature of the cornea contributed to the decrease in its rigidity as well as the increase in its elasticity. According to the results, there was a strong correlation between the increase in the degree of corneal curvature of in the steep meridian in response to loading and the increase in the KER indicating greater degree of deformation of corneal tissue under the influence of artificially increased IOP. Thus, in stage I keratoconus the KER was equal to 6.27% (Table 2), the level of ΔRm1 changed on average by (-)0.98 mm (r = (-)0.79; $p<0.05$). In stage II keratoconus the KER was equal to 6.34%, and the mean level of the anterior corneal surface curvature (ΔRm1) changed by (-)1.13 mm (r = (-)0.86; $p<0.05$). In patients with stage III keratoconus, the KER increased to 6.39%, and the average radius of the anterior corneal surface curvature (ΔRm1) decreased by (-)1.35 mm (r = (-)0.94; $p<0.05$). In stage IV keratoconus, the KER increased to 7.53%, while the mean level of the anterior corneal surface curvature (ΔRm1) changed by (-)1.42 mm (r = 0.96; $p<0.05$). Under the influence of stressful increase in the IOP, the corneas having larger diameters stretched significantly more compared to those having standard diameter.

During the research, we made the analysis of the influence of the initial IOP level as well as biometric characteristics (CCT, corneal refraction, Rm1, APA and distance from the top of the cone to the corneal center) of patients' eyes (the main group) in case of keratoconus on biomechanical indicators calculated by us. The correlation analysis proved the absence of the dependence between the indicators of ΔSE, the KER and the IOP level in patients of the main group. The Pearson correlation coefficient for these indicators was r = 0.11 and r = 0.09, respectively ($p<0.05$). There was no dependence between the results of calculating the indicators of ΔSE, the KER and the APA. There was observed a direct correlation of low degree with the Pearson correlation coefficient being r = 0.22 and r = 0.25, respectively ($p<0.05$).

In addition, there was observed a weak inverse dependence between calculated biomechanical indicators of ΔSE and KER in patients with keratoconus and CCT (r = (-)0.36, r = (-)0.41, respectively ($p<0.05$). Slightly greater dependence was observed between the indicators of ΔSE and the KER (the minimum corneal thickness) (r = (-) 0.49 and r = (-)0.2; $p<0.05$) and the pachymetric progression index (r = (-)0.57 and r = (-) 0.59; $p<0.05$). There was a weak direct correlation between ΔSE and KER and corneal torricity (r = 0.43 and r = 0.44; $p<0.05$). It should be noted that according to the analysis, there was revealed a strong direct correlation between the indicators of ΔSE, the KER and the radius of corneal curvature in the steep meridian (Rm1) (r = 0.77 and r = 0.78; $p<0.05$). Moreover, there was a strong direct dependence between the values of ΔSE as well as the KER and the maximum refraction of the cornea; the Pearson correlation coefficient was r = 0.73 and r = 0.76 ($p<0.05$). Similar dependence was observed between the elevations of the anterior corneal surface and the indicators ΔSE as well as the KER (the Pearson correlation coefficient r = 0.77 and r = 0.78; $p<0{,}05$). A strong direct correlation between the KER, ΔSE and the distance from the top of the cone to corneal apex was noteworthy as well (r = 0.85 and r = 0.84; $p<0.05$).

The greatest correlation was found between biomechanical indicators of ΔSE, the KER and eccentricity, I-S asymmetry index, the elevation of the posterior corneal surface. The strength of Pearson correlation between the values of ΔSE and Asph Q was (r = 0.84 ($p<0.05$); between the KER and Asph Q it corresponded to r = 0.87 ($p<0.05$); between ΔSE and I-S asymmetry index it was equal to r = 0.86 ($p<0{,}05$); between the KER and I-S asymmetry index it was r = 0.89 ($p<0.05$). The Pearson correlation coefficients for the indicators of ΔSE, the KER and the elevation of the posterior corneal surface were equal to r = 0.91 and r = 0.93, respectively ($p<0.05$).

According to the latest global research [2, 17, 21, 26, 30], a number of factors and indicators which are considered in clinical practice as a mathematical expression of visual impairment due to anterior corneal surface irregularity have the most important diagnostic value when diagnosing keratoconus using standard set of programs for the Oculus Pentacam-Scheimpflug camera. The following indices are considered to be the most important ones: the variance of anterior corneal surface refraction along radii (the index of surface variance, the ISV); the degree of symmetry of corneal radii with respect to a horizontal axis (the index of vertical asymmetry, the IVA); the index of keratoconus over the cornea (the keratoconus index, the KI); the index of keratoconus in the center of the cornea (the central keratoconus index, the CKI); the degree of symmetry of the vertical meridian with respect to the horizontal one - the index of comparing the height of the upper andlower corneal segments (the index of height asymmetry, the IHA); the index of vertical decentration of keratoconus distribution (the index of height decentration, the IHD); minimal changes in pathological area of the cornea (Rmin); the classification of keratoconus according to Amsler (TKS); the Belin/Ambrósio enhanced ectasia module (the Belin/Ambrosio Enhanced Ectasia Display, the BAD).

When analyzing these factors, ophthalmologists try to connect the variability of actual indicators of the anterior corneal surface obtained using topography with optical properties and the best potential visual acuity which it is capable to provide.

In this research, under conditions of loading applying the device for *in vivo* estimation of corneal rigidity we have conducted a thorough correlation analysis between biomechanical indicators of ΔSE and the KER and the most important indices of diagnosing keratoconus [2, 17, 21, 26, 30]. The results are presented in Table 3.

It should be noted (Table 3) that there was a strong correlation between all factorial signs in patients of the main group. The greatest correlation dependence (the Pearson correlation coefficient equaled to $r = 0.921$ and $r = 0.943$ ($p<0.05$), was detected between the indicators of the BAD and biomechanical indicators: ΔSE and the KER.

Biomechanical properties of the cornea are known to affect the formation of refraction, the development of ophthalmopathology as well as the results of various diagnostic procedures, and knowledge of corneal peculiarities can be used in diagnosing the disease and when selecting the method of treating some ophthalmic diseases. However, nowadays the estimation of the supportive properties of eye capsule is not sufficiently developed, and the device for studying biomechanical properties of corneal tissue *in vivo* is not described in the available ophthalmology literature.

It should be noted that over the last decades the technology of an individual estimation of biomechanical properties of ocular tissue has been intensively developed. A lot of methods and approaches to the solution of this problem have been described, however each of them has some limitations.

Certainly, the most informative data on biomechanical state of the cornea can be received only under conditions of living eye. However, despite the undoubted urgency of such diagnostics, *in vivo* methods for assessing mechanical parameters of the cornea are still under development [19, 32]. As possible approaches to the indirect determination of the given parameters, scientists used optical and holographic interferometry [11, 13, 19], mechanical spectroscopy [15, 19], acoustic biometry [19] and the method of photoelasticity [4, 19]. The method of double-pulse holographic interferometry, being very complicated technically [13, 19], showed that the central zone of normal cornea under physiological conditions is characterized by practically linear dependence between $\delta$ ($\varepsilon$) and Young's modulus (elastic modulus) being approximately 10.3 MPa [19].

Other researchers tried to indirectly investigate *in vivo* pressure and deformations in the tissues including the cornea using the method of photoelasticity [19]. The study concerning the connection of corneal biomechanics with its optical characteristics (according to the data of aberrometry and keratotopography) [1, 24] deserves special attention as well. Nowadays there are many techniques which estimate the type and degree of optical aberrations; detailed classification of the available types of optical aberrations is given and the methods of their elimination are offered [1, 24]. However, in most scientific researches and in practice, ophthalmologists determine only such simple indicators as corneal hysteresis, corneal thickness and corneal topography [2, 3].

When studying the role of corneal biomechanical properties in the development of ophthalmopathology it is necessary to pay attention to the problem of keratoconus which is the disease being one of the most socially significant pathologies [6, 7, 16, 28] due to the increase in its incidence [6, 7, 16, 28], the extension of the age range [16, 28], the progressive nature of the disease resulting in visual impairment in young and working age [6, 16, 28]. Despite the rich scientific experience in studying the problems of the development and progression of keratoconus [7, 16, 28], the etiology, pathogenesis and, especially, early diagnostics of the given ophthalmic pathology are insufficiently studied which undoubtedly leads to a limited range of therapeutic actions.

Nowadays, genetic factors are known as those [16, 28] playing one of the leading roles in the development of keratoconus. The features of keratoconus clinical picture [5, 14, 16], possible surgical methods of its treatment [16], problems of rehabilitation [16], as well as the data on the attempts of conservative treatment of keratoconus [16, 34] are described. Nevertheless, the search for and the development of the methods of *in vivo* early diagnostics of keratoconus, the improvement of pathogenetically targeted therapy and the methods of the quantitative and qualitative analysis of treatment results remain to be relevant and unsolved. Considering the fact that the age range of the occurrence of the pathology over the past years has changed considerably and the average age of the disease onset shifted from 11-16 years [16] up to 21-37 years [7, 16], there is a need for an active search and further study of this problem.

To analyze the cornea and diagnose keratoconus, some scientists used the data of ultrasonic pachymetry and video keratography [16]. The estimation was made using morphological features of the pathogenesis of this disease [16]. However, many authors adhered to the same opinion that early diagnosis of keratoconus during its initial manifestations, as well as the prediction of disease progression is somewhat difficult [16].

For many years, the diagnostics of keratoconus has been based on the anamnestic data and the data of the complex of clinical examinations: visometry, biomicroscopy, retinoscopy, refractometry, ophthalmometry, pachymetry [16, 34]. However, each of these techniques has no independent prognostic value in the diagnosis of this disease.

For a long time, video keratography has remained the main technique for detecting keratoconus. Many models of auto

**Table 3.** Results of the correlation analysis between biomechanical indicators and indices of diagnosing keratoconus in patients of the main group, n = 48

| Factors between which the correlation analysis was carried out | Pearson correlation coefficient | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | SE, dioptres | $K_{ER}$, % | ISV | IVA | KI | CKI | IHA | IHD | Rmin | TKS | BAD |
| Δ SE, dioptres | - | 0.995 | 0.882 | 0.879 | 0.837 | 0.843 | 0.858 | 0.887 | 0.862 | 0.894 | 0.921 |
| $K_{ER}$, % | 0.995 | - | 0.895 | 0.883 | 0.841 | 0.848 | 0.867 | 0.896 | 0.874 | 0.908 | 0.943 |
| ISV | 0.882 | 0.895 | - | 0.866 | 0.846 | 0.857 | 0.844 | 0.869 | 0.849 | 0.855 | 0.842 |
| IVA | 0.879 | 0.883 | 0.866 | - | 0.842 | 0.846 | 0.856 | 0.871 | 0.853 | 0.847 | 0.854 |
| KI | 0.837 | 0.841 | 0.846 | 0.842 | - | 0.894 | 0.849 | 0.882 | 0.877 | 0.863 | 0.889 |
| CKI | 0.843 | 0.848 | 0.857 | 0.846 | 0.894 | - | 0.861 | 0.895 | 0.891 | 0.892 | 0.893 |
| IHA | 0.858 | 0.867 | 0.844 | 0.856 | 0.849 | 0.861 | - | 0.899 | 0.865 | 0.845 | 0.846 |
| IHD | 0.887 | 0.896 | 0.869 | 0.871 | 0.882 | 0.895 | 0.899 | - | 0.869 | 0.884 | 0.905 |
| Rmin | 0.862 | 0.874 | 0.849 | 0.853 | 0.877 | 0.891 | 0.865 | 0.869 | - | 0.898 | 0.897 |
| TKS | 0.894 | 0.908 | 0.855 | 0.847 | 0.863 | 0.892 | 0.845 | 0.884 | 0.898 | - | 0.913 |
| BAD | 0.921 | 0.943 | 0.842 | 0.854 | 0.889 | 0.893 | 0.846 | 0.905 | 0.897 | 0.913 | - |

keratotopographs (TMS-1, TMS-2, Orbscan, EyeSys, Keraton, Dicon CT2000 and others) were developed which using modern possibilities of science – laser devices, computer technologies and digital video equipment estimated topography of the anterior corneal surface [16]. These automatic keratotopographic systems allow you to measure the parameters of the anterior corneal surface accurately [16]. Many researches showed the advantage and the great diagnostic values of the given techniques in comparison with photokeratometry [16, 29].

Due to a high resolution of the described techniques and new possibilities in studying various abnormalities in corneal surface a promising direction studying the indicators of video keratography to identify the minimum diagnostic criteria for keratoconus began to develop. The scientists offered various algorithms facilitating the diagnostics of keratoconus - Smolek-Klyce, Klyce-Maeda, Rabinowitz-McDonnell [16, 29].

These indices detect keratoconus based on the data of topographic maps of corneal surface using the data of the central radius (K) as well as the difference between the lower (I) and upper (S) corneal radii [16]. Most scientists agree that video keratography increases possibilities of early diagnostics of keratoconus [16, 23], and the developed algorithms are effective in detecting keratoconus in 30-80% of cases [16, 35].

However, not everything concerning high efficiency of the offered diagnostic indices is so optimistically [16]. Some scientists [35] reported that video keratography is often incapable to obtain complete information in case of wrong or asymmetric topography of the cornea as the schemes in computer graphics are very simple and cannot display the detailed surface topography, which is observed in keratoconus [16]. In addition, when conducting the comparative analysis of the results of various video keratographic systems, the spread in values is observed that significantly reduces the reliability of repeated measurements and, accordingly, reduces the efficiency of the given method in dynamic observation of the course of the disease [16]. The author of one of the most effective diagnostic criteria for diagnosing keratoconus - the KISA% index and some other scientists [16] are doubtful of the absolute diagnostic value of video keratographic indicators as well. They consider that for the confirmation of the diagnosis of keratoconus the presence of one or several clinical signs of the disease is required.

In recent years, several techniques, namely the Oculus Pentacam-Scheimpflug imaging device and Oculazer (Alcon) which analyze the thickness and the shape of both corneal surfaces has remained the main techniques for diagnosing keratoconus. These methods being widely applied in ophthalmology quite reliably detect the difference in morphological features in keratoconus and normal cornea [17, 18, 21, 25, 26, 30, 33]. Many clinics where excimer laser surgeries are performed do not start excimer laser correction without the data obtained by means of the Oculus Pentacam-Scheimpflug camera concerning an exact estimation of morphological qualities of the cornea. The analyzer of corneal biochemical properties – the ORA and measured with its help corneal hysteresis and the factor of corneal resistance are widely used as well [3, 17, 18, 21, 22, 25, 26, 30, 33]. Nevertheless, several studies have demonstrated the disadvantages of these modern laser digital techniques which seemed unbeatable [17, 25, 27, 31]. A significant influence of the IOP level [27, 31], age [25], dystrophic changes [17], corneal edema [27], preliminary short-term (within 2 minutes) rubbing the eye before examination [20], ambient temperatures [25], biomechanical factors [25] on the results of CH measurements was observed when using the ORA.

Thus, the recognition of the primary role of the weakening of biomechanical properties of the cornea, as a key factor in the pathogenesis of the development and progression of keratoconus and other pathological conditions and diseases of the cornea have been widely reflected in modern literature. When analyzing modern ophthalmologic literature, attention is paid to the fact that the scientists have been searching for methods of studying biomechanical properties of ocular structures throughout the centuries. Nevertheless, the problem of clinical examination of ocular rigidity remains to be unsolved. The development of new methods of estimating biomechanical properties of ocular tissue *in vivo* as well as the systems of measures to combat the development and progression of this ophthalmologic pathology is relevant for ophthalmology.

Our improvement consists in a directed study of keratotopographic characteristics with the use of modern Scheimpflug camera under conditions of the eye capsule loading through the increase in the IOP. Due to the developed design of the device [8] there is a possibility to use modern Scheimpflug cameras to determine corneal rigidity which greatly increases the accuracy of the measurement. The device has the fixed weight and shape that greatly reduces the research time and allows us to study the results which do not depend on the executor and can be analyzed and compared among many patients.

It is worth mentioning that when using the same keratotopograph and standard programs under condition of high IOP being artificially elevated by means of a two-minute uniform compression of the eyeball under a pressure of 30 grams [8, 9] the distinct corneal deformations on the eyes with keratoconus were registered. The degree of corneal deformation was estimated using the factor of corneal rigidity [10] and depended on the stage of the pathological process. Moreover, our research has revealed the fact of relative stability of the cornea in emmetropia.

The results of the research have shown that under conditions of artificially elevated IOP the application of the method proposed by us as well as the device for estimating corneal rigidity [8, 9] allows detecting the presence of biomechanical disorders of the cornea in patients with keratoconus in comparison with control emmetropic patients as well as differentiating the character of these changes. The KER in all cases showed statistically significant results that were consistent with the clinical course of the process in these eyes.

## 3. Conclusions

The adequate technique for *in vivo* diagnosis of changes in biomechanical properties of the cornea was developed which became possible with the use of the device for estimating corneal rigidity through the measurement of ocular tissue deformation under conditions of loading. To describe the rate of change of biomechanical properties of cornea *in vivo* developed the coefficient of rigidity of the cornea. To describe the degree of changes in biomechanical properties of the cornea *in vivo* the coefficient of corneal rigidity was developed.

Loading tests allow receiving more exact information on biomechanical properties of the cornea in comparison with standard researches on the Oculus Pentacam-Scheimpflug camera.

The proposed method and the device for *in vivo* estimation of corneal rigidity allows us not only to reveal the presence of biomechanical disorders of the cornea, but also to differentiate their character.

## 4. Prospects for further research

The analysis of the literature indicates that diagnostics and monitoring of keratoconus are urgent problems of modern ophthalmology. Therefore, timely in-depth study of the role of biomechanical properties of the fibrous tunic of the eyeball in pathological conditions, the improvement of the existing methods and the development of new methods of diagnostics and prevention of keratoconus which will became the basis of a new model of the organization of ophthalmic care for patients with keratoconus while reforming the field of ophthalmology in Ukraine are relevant and promising.

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