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Evaluation of Corneal Endothelial Cell Loss Peak in Young Healthy Turkish Population

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Abstract

Clinical relevance: It is significant to determine main endothelial cell loss peak decades in order to decide surgical intervention time and be prepared for vital precautions in patients requiring ocular surgery.

Background: Although, endothelial cell loss during natural course of aging is an obvious clinical manifestation, remarkably in some ethnicities such as Turkish population, younger decades tend to have one of the main loss peaks. The knowledge of the endothelial cell structure database and main loss peaks between decades may help to predict the risk of ocular surgeries in clinical practice. The aim of this study is to investigate the endothelial cell loss peak in young Turkish volunteers.

Methods: Non-contact specular microscopy was performed on 300 eyes of 150 healthy volunteers aged between 21-40 years. The study population was divided into two groups (Group 1: Aged 21-30; Group 2: Aged 31-40) to compare the endothelial cell loss between these two decades. Cell Density (CD), coefficient of Variation in Cell density (CV), Hexagonal Cell percentage (HEX), Mean Cell Area (MCA), Central Corneal Thickness (CT) were the studied parameters.

Results: The mean CD of volunteers was 2659±283 (range 2116 to 3625) cell/mm^2 with 67% ±6 (range 37 to 79) HEX. The MCA was 376.3±48.1 (range 116 to 473) μm^2 and the mean CV was 28.3±4.4 (range 20 to 39). The mean CT was 550.3±34.6 (range 493 to 658) micrometers. CD, HEX and CT were decreased significantly while MCA was increased significantly by increasing age ($p<0.05$). The reduction of the CD was 0.4% per year. The cell loss rate at the 3rd decade was 9.2%.

Conclusion: The detected corneal endothelial cell loss rate at the 3rd decade is striking and should be taken into consideration before performing surgeries - especially refractive ones - that might trigger additional endothelial cell loss.

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Introduction

Endothelium, the most inner corneal layer, consists of a single coating of endothelial cells originated from neural crest beneath the Descemet's Membrane [1]. The cells of the endothelium layer of the cornea are tightly adherent and have a particular hexagonal shape. The key function of these cells is to maintain the corneal clarity with dedicated pumping systems such as Na+ K+-ATPase [2].

Regenerative capacity of the endothelial cells is limited; thus, the density and the topography of the cells change as enlarging and losing the hexagonality over the decades [3,4]. Beside the aging, ethnicity is one of the most important factors that affect endothelial Cell Density (CD). The mean CD tends to be higher in Japanese [5] and Chinese [6] populations while seems to be lower in American [5] and Iranian [7] eyes. There are two demographic studies about endothelial cell specialty in Turkish population and the mean CDs were reported to be 2732 ± 305 cell/mm^2 and 2671 ± 356 cell/mm^2 [8,9]. According to these reports, major endothelial cell loss tends to appear around third decade rather than elder ages in Turkish population. Although the total participants in these studies are wide, when divided into subgroups for decade comparison they seem to be insufficient for revealing the peak mainly in young individuals. The aim of the present study is to investigate the cell loss ratio in a larger sample size of young Turkish population.

Methods

This study was approved by the Institutional Review of Board and Ethics Committee and was performed in adherence to Helsinki Declaration. After revival of written informed consents, volunteers aged 21 to 40 who applied for routine ophthalmologic examination were included in the study. A detailed ophthalmological examination was performed. Presence of ocular diseases such as corneal scarring, dry eye disease, sign of infection, sign of corneal dystrophies, glaucoma or retinal diseases was exclusion criteria. Volunteers who had a previous ocular surgery or a history of contact lens wear were also excluded. Non-contact specular microscopy was performed to each volunteer with CEM-530 (Nidek, Japan). CD, coefficient of variation in Cell Density (CV), Hexagonal Cell percentage (HEX), Mean Cell Area (MCA), Central Corneal Thickness (CT) measurements were noted. To overcome diurnal variations all measurements were conducted between 10 to 11 am and were performed by same examiner for three times to each volunteer. The average of the measurements was used for statistical evaluation. Two volunteers were divided in two groups according to ages; Group 1: Aged 21 to 30, Group 2: Aged 31 to 40.

IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. was used for statistical analysis. The suitability of numerical variables to normal distribution was examined by Kolmogorov-Smirnov (n >= 50) test. Numerical variables are given as mean and standard deviation and median (minimum-maximum). To examine relationship between numeric variables Spearman correlation analysis was performed. The significance level was accepted as 0.05 for all hypotheses.

Results

Three hundred eyes of 150 participants were included in the study with a 0.92 male to female ratio. The average age of the participants was 30.5 ± 7 years. The mean CD was 2659 ± 283 (range, 2116 to 3625) cell/mm^2. The HEX was 67% ± 6 (range, 37 to 79), the MCA was 376.3 ± 48.1 (range, 116 to 473) μm^2 and the mean CV was 28.3 ± 4.4 (range, 20 to 39). The mean CT was 550.3 ± 34.6 (range, 493 to 658) micrometers (Table 1).

There was no statistical difference between the fellow eyes of the participants or between genders ($p > 0.05$) in terms of endothelial cellular features. CD, HEX and CT were decreased significantly while MCA was increased significantly by increasing age ($p < 0.05$). The reduction of the CD was 0.4% per year. The cell loss rate at the 3rd decade was 9.2%. (The comparison between other measurements from different studies may be seen on Table 2).

Table 1: The specular microscopy measurements of the participants.

	All volunteers	Group 1 (Aged 21-30)	Group 2 (Aged 31-40)
CD cell/mm^2	2659 ± 283	2840 ± 199	2578 ± 279
	(2116-3625)	(2477-3220)	(2116-36225)
HEX %	67 ± 6	66 ± 5	69 ± 5
	(37-79)	(54-77)	(37-79)
MCA μm^2	376.3 ± 48.1	353.7 ± 24.7	386.5 ± 52.7
	(116-473)	(311-404)	(116-473)
CV %	28.3 ± 4.4	27.9 ± 5	28.5 ± 4.1
	(20-39)	(20-39)	(22-38)
CT μm	550.3 ± 34.6	556.7 ± 32.6	547.4 ± 35.4
	(493-658)	(501-613)	(493-658)

CD: Cellular Density, HEX: The Percentage of the Hexagonal Cells, CV: Coefficient of Variation in Cell density, CT: Central Corneal Thickness.

Table 2: The comparison of specular microscopy measurements from different studies.

		CD (cell/mm^2)	HEX (%)	MCA (μm^2)	CV (%)	CT (μm)
Current study	All volunteers	2659 ± 283	67±6	376.3 ± 48.1	28.3 ± 4.4	550.3 ± 34.6
	Aged 21-30	2840 ± 199	66±5	353.7 ± 24.7	27.9 ± 5	556.7 ± 32.6
	Aged 31-40	2578 ± 279	69±5	386.5 ± 52.7	28.5 ± 4.1	547.4 ± 35.4
Egyptian [11]	Aged 20-30	2933 ± 345	60±9	345.3 ± 55.9	29.4 ± 3.5	525.9 ± 46.8
	Aged 31-40	2693 ± 287	54±7	416.7 ± 391.5	31.0 ± 4.2	518.6 ± 67.9
Iranian [7]	Aged 20-30	2407 ± 399	n/a	427.8 ± 74.9	20.4 ± 5.5	n/a
	Aged 31-40	2245 ± 349	n/a	458.9 ± 81.0	23.1 ± 7.2	n/a
American [5]	Aged 20-29	2977 ± 324	n/a	339.6 ± 36.8	28.5 ± 5.8	n/a
	Aged 30-39	2739 ± 208	n/a	367.1 ± 28.4	27.4 ± 3.7	n/a

Japanese [5]	Aged 20-29	3893 ± 259	n/a	258.0 ± 18.0	25.9 ± 4	n/a
	Aged 30-39	3688 ± 245	n/a	272.1 ± 17.6	25.7 ± 3.9	n/a
Turkish [9]	Aged 20-30	2910 ± 365	60.2±9.4	349.3 ± 46.5	30.5 ± 4.0	534.5 ± 32.6
	Aged 31-40	2738 ± 389	55.9±9.7	373.0 ± 56.7	34.9 ± 5.4	520.1 ± 31.4
Turkish [8]	Aged 20-29	2843 ± 285	46±8	355 ± 34	46 ± 7	516 ± 42
	Aged 30-39	2798 ± 247	46±7	360 ± 31	44 ± 7	513 ± 37

CD: Cellular Density, HEX: The Percentage of the Hexagonal Cells, CV: Coefficient of Variation in Cell Density, CT: Central Corneal Thickness, n/a: Not Applicable.

Discussion

The knowledge of the normative database of endothelial cell structure is important in order to predict the risk of various intraocular surgeries. The normative database varies between different nationalities. In the literature, CD in Turkish population was reported to be similar to Indian population [10]; lower than American [5] and Japanese [5] populations, and higher than Iranian population [7]. Even though the volunteers of the current study was younger, it was consistent with these results.

Different studies with different ethnicities reported that the main endothelial cell loss tends to appear at the 3rd and 5th decades. The endothelial cell loss rate of Chinese population was quite low (2.2%) at the 3rd decade when compared with other nationalities such as Egyptian, American, Iranian or Japanese (8.1%, 7.9%, 6.7%, 5.2%, respectively). The major cell loss in Chinese population was reported to occur at the 5th decade with a rate of 4.2%. The endothelial cell loss rates at the 5th decade were found to be 3% in Egypt, 6.3% in Iran and 9.6% in Japan populations. There was no significant endothelial cell loss in American population at the 5th decade. The loss rates in Iranian population were consistent between decades without a peak [5-7,11]. In the literature, there are only two demographic studies about endothelial cell properties in Turkish population. Endothelial cell loss peaks were reported to be different in those studies, one reporting two peaks in the 3rd and 5th decades with a significant rate in the 3rd decade and the other reporting the peak in between 3rd to 5th decades [8,9]. In order to assess the endothelial cell properties in young Turkish population, the present study aimed to demonstrate the 3rd decade endothelial cell loss rate in a larger sample size. The loss rate at the 3rd decade was found to be 9.2% in the present study, which was significantly higher than the other two studies in the same ethnicity.

Nowadays, with the advances in surgical techniques and the demand on spectacle-free lifespan, refractive surgical interventions are increasing. For this reason, patient age undergoing surgery decreases over the years. There are various conflicting studies indicating the effect of various refractive surgical techniques on the corneal endothelium [12,13]. Nevertheless, a healthy endothelium layer is essential for the success of the surgery and sparing corneal complications [14]. Likewise, as a part of refractive or combined surgeries phakic intraocular lens implantation is an option for young adults. Especially to correct high myopia and to prevent development of ectasia, this could be a preferable method [15]. There is also a special group of patients who require optic rehabilitation surgeries after corneal transplant. Cataract surgery as well as secondary intraocular lens implantation in patients with insufficient zonular support might be needed in these group of patients [16]. The iridocorneal angle or the iris itself might be used as a support tissue and endothelial damage may occur due to the close position of the intraocular lens [17,18]. Thus, anterior segment surgeons should consider the health and function of the corneal endothelium before and after the operations in an appropriate normative database to achieve better surgical outcomes.

Besides the endothelial cell loss, other parameters (CT, HEX, MCA, CV) are affected by ethnicity. The mean CT in Turkish and Egyptian volunteers in matched age groups were close to the current study data [8,9,11]. The current study showed a decrease in CT with increasing age in agreement with the literature [10,19]. The reduction of the CD in the study was 0.4% per year and it was in the range of the literature (0.3 to 1.1%) [20,21].

HEX in the current study was significantly higher from the previous studies in different ethnicities (49% to 62%) [6,8,9,11]. MCA and CV may reflect the cell size (polymegathism) and the cell shape (polymorphism) variations [19,22]. In the current study, MCA was close to Egyptian and American populations but higher than Japanese and Chinese populations. Mean CV percentage was reported to be similar to American and Egyptian populations, but the value was higher from Japanese and lower than Chinese populations [5,6,11].

Although the current study reported the data of young Turkish population, there are significant differences in some parameters compared to the previous two studies in the same ethnicity. HEX and MCA were found to be slightly higher and CV percentage was found to be lower than the previous Turkish studies for the age matched subgroups [8,9].

The main limitation of the study is the restricted decade involvement. To understand and verify the loss rate peak at the 3rd decade wider studies with larger subgroups are still needed. In the current study, non-contact specular microcopy was used for corneal endothelial evaluation. There are various specified measurement tools to assess endothelial features. More studies based on comparative measurements with other devices such as Scheimpflug cameras may eliminate the tool bias which may affect the normative database [23].

Conclusion

In conclusion, the endothelial cell loss rate at the 3rd decade was found to be different from previously reported Turkish studies, and the CD decrease diverged from the other ethnicities. The detection of a corneal endothelial cell loss peak in the 3rd decade among young population, should warn ophthalmologists for especially refractive surgeries that might trigger faster and higher endothelial cell loss.

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