Evaluation of Corneal Biomechanics in Primary Open Angle Glaucoma

Abd elraouf Omar Abd elghany, Hazem Effat Haroun , Safaa Awadalla Aboud,

Ophthalmology Department, Faculty of Medicine, Beni-Suef University. Egypt
raoufomar2013@gmail.com

ABSTRACT

Background: Elevated intraocular pressure (IOP) is one of the most important factors for diagnosis and monitoring of glaucoma. IOP is currently the only modifiable risk factor for glaucoma,cornea is the transparent tissue covering the front of the eye. It is a powerful refracting surface, providing 2/3 of the eye's focusing power. The adult cornea is only about 1/2 millimeter thick and is comprised of 6 layers: epithelium, Bowman's membrane, stroma, Dua's layer, Descemet's membrance and endothelium.

Objectives: Evaluation of the Corneal Biomechanics in eyes with primary open angle glaucoma.

Patients and Methods: This study is a prospective cross-sectional study, ocular response analyzer (ORA) parameters were measured in 40 patients with correlation to their Intraocular pressure (IOP), Perimetry (visual field) and ocular coherence tomography (OCT) retinal nerve fiber layer thickness (RNFL) on 80 eyes, Patients ages range between 40-65 years old. The study was prepared on patients seeking treatment in ophthalmology polyclinic in The Memorial Institute of Ophthalmic Researches in Giza in the period from May 2018 to October 2019, they were screened to identify those with primary open angle glaucoma.

Results: Our study was made to assess the correlation between corneal biomechanics Parameters (CH, CRF, IOPg and IOPcc) with visual field affection, OCT optic disc and IOPGAT in primary open angle glaucoma. Our study revealed that the corneal biomechanics Parameters are significantly lower in patients with advanced primary open angle glaucoma (POAG).

Conclusion: Studying corneal biomechanics is essential to enrich our ophthalmic knowledge and make better understanding of corneal pathologies, surgeries and glaucoma.

Keywords: Corneal Biomechanics, Primary Open Angle Glaucoma

Received: 22/11/2020	Accepted: 18/1/2021	Online publication: 1/4/2021

INTRODUCTION

Elevated intraocular pressure (IOP) is one of the most important factors for diagnosis and monitoring of glaucoma. IOP is currently the only modifiable risk factor for glaucoma, with a disease that is the second leading cause of blindness worldwide. As IOP reduction is the mainstay of treatment, accurate IOP assessment is important in monitoring the efficacy of therapy and for assessing the risk of glaucomatous progression. In addition, reduction of IOP in eyes with ocular hypertension has been proven to reduce the rate of conversion to glaucoma.[(1)]

Goldmann applanation tonometer (GAT), which is the most frequently used instrument to measure IOP, it didn't take into consideration

the corneal state like decreased corneal thickness post refractive surgeries. It operates on the basis of the Imbert-Fick law. This law assumes that the cornea is an infinitely thin, perfectly flexible membrane, however, this assumption is not true. The force required to a planate the cornea depends not only on IOP, but also on corneal rigidity, thickness, curvature, hydration, and viscoelastic properties.[2]

Recently, ocular response analyzer (ORA) is a new, noninvasive device that analyzes corneal biomechanical properties simply and rapidly, especially corneal hysteresis (CH), corneal resistance factor (CRF), ORA provides a measure of IOP that is corrected for these parameters, intraocular pressure by Goldmann (IOPg), and intraocular pressure after compensation of the cornea (IOPcc). [3]

CH represents 'viscous damping' in the corneal tissues; in addition, it is a direct measure of the corneal biomechanical properties, and therefore may more completely describe the contribution of corneal resistance to IOP measurements.[4]

Corneal Hysteresis is the difference in the inward and outward pressure values obtained during the dynamic bi-directional applanation process employed in the ocular response analyzer, as a result of viscous damping in the cornea. [1]

Corneal Biomechanics can be measured in vivo by ocular response analyzer, using an applied force-displacement relationship. An air jet similar to that used in traditional air-puff tonometers generates force or pressure on the cornea.[6].

Corneal hysteresis is an important indication of the biomechanical properties of the cornea. It is an indicator of viscous damping in the cornea during inward and outward applanation pressure events. That is the ability of the tissue to absorb and dissipate energy; a property that is determined by the visco-elastic properties of the corneoscleral shell.[5].

Other biomechanical properties such as viscoelastic properties may also influence corneal resistance to applanation[7].

Ocular response analyzer takes corneal biomechanical properties into consideration, providing a much more accurate intraocular pressure measurement other than other methods of tonometry[7].

Perhaps the most important future use of corneal hysteresis will be as a diagnostic tool for patients of glaucoma, glaucoma suspect and normal tension glaucoma, A lower corneal hysteresis value is recently found to be associated with progressive visual field loss in glaucomatous patients. That is the Era of Corneal biomechanics[8].

AIM OF THE WORK

- Evaluation of the Corneal Biomechanics in eyes with primary open angle glaucoma.
- Correlation of the corneal biomechanics in the eyes with primary open angle glaucoma With their IOP Measurements,

perimetry and OCT RNFL Thickness using corneal hysteresis (CH), corneal resistance factor (CRF), the intraocular pressure applanation Goldmann method (IOPg) and intraocular pressure after compensation of the cornea (IOPcc) using ocular response analyzer (ORA).

PATIENTS AND METHODS

Study design

This study is a prospective cross-sectional study, ocular response analyzer (ORA) parameters were measured in 40 patients with correlation to their Intraocular pressure (IOP), Perimetry (visual field) and ocular coherence tomography (OCT) retinal nerve fiber layer thickness (RNFL) on 80 eyes, Patients ages range between 40-65 years old.

The study was prepared on patients seeking treatment in ophthalmology polyclinic in The Memorial Institute of Ophthalmic Researches in Giza in the period from May 2018 to October 2019, they were screened to identify those with primary open angle glaucoma, all patients were subjected to: full careful history taking and full ophthalmic examination, the ORA was used to measure CH, CRF, IOPg and IOPcc, perimetry, OCT RNFL thickness measurement.

Criteria for Patient Selection:

Inclusion criteria:

- Patients of both sex male and female.
- Patients of age group ranges between 40- 65 years old.
- Patients known glaucomatous.
- Patients with primary open angle glaucoma.

Exclusion criteria:

- Corneal dystrophies.
- Corneal degenerations.
- Keratoconus.
- Post LASIK.
- Post cataract extraction.
- Post glaucoma surgery.

Methodology

Careful History Taking:

- Personal data: age, sex, occupation, residency.
- Ocular history: ocular surgeries and Refractive history
- Medical history: should exclude systemic conditions, prior surgeries, current and prior medication.
- A complete ocular examination was done using the following:
  - Visual Acuity Measurement
  - Slit-Lamp Examination
  - Intraocular Pressure Measurement
  - Fundus Examination
  - Measurement of ORA parameters
  - Visual Fields
  - Optical Coherence Tomography (OCT)

Statistical analysis:

Statistical analysis was done and Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Data was summarized using mean,

standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whitney tests. Correlations between quantitative variables were done using Spearman correlation coefficient. P-values less than 0.05 were considered as statistically significant.

RESULTS

Table 1: Demographic data:

		Count	Percentage %
Sex	**Males**	**18**	45.0%
	Females	**22**	55.0%
Side	**Right**	**40**	50.00%
	Left	**40**	50.00%

The patients included 22 females (55.0%) and 18 male (45.0%), whereas, each patient had assessment for visual field and OCT and ORA.

Table 2: Glaucoma severity was classified according to MD perimetry:

	Glaucoma stage single eye									P value
	Stage 1			Stage 2			Stage 3			
	Minimum	Maximum	Median	Minimum	Maximum	Median	Minimum	Maximum	Median	
IOP	10.00	19.00	14.00	11.00	22.00	17.00	15.00	27.00	19.50	<0.001
Perimetry MD eye	-5.75	4.80	-2.80	-11.97	-6.00	-8.70	-26.50	-12.10	-18.50	<0.001
OCT vertical CDR	0.30	0.90	0.61	0.43	0.90	0.70	0.80	1.00	0.90	<0.001
S Q	59.00	133.00	113.00	32.00	124.00	80.00	39.00	72.00	55.50	<0.001
I Q	60.00	148.00	119.00	33.00	131.00	87.00	47.00	90.00	61.00	<0.001
N Q	39.00	125.00	80.00	49.00	95.00	66.00	48.00	62.00	54.00	<0.001
T Q	12.00	127.00	70.00	25.00	98.00	64.00	35.00	95.00	56.50	0.235
IOPg	10.20	22.70	14.90	12.60	23.60	16.80	9.20	22.70	16.95	0.004
IOPcc	11.10	23.00	15.00	13.00	23.80	18.80	12.00	21.60	17.15	0.006
CH	7.00	12.60	9.70	6.70	12.20	9.40	7.10	12.50	10.50	0.337
CRF	7.20	12.20	9.80	7.20	13.00	9.40	6.30	12.90	10.35	0.964

The results in the comparative studies showing significantly results in the comparison between glaucoma stages and the following parameters, IOP, perimetry MD, CDR, (p value =< 0.001, respectively) while IOPg (p value =0.004) and IOPcc (p value=0.006), however no significantly results in comparison of glaucoma stages and CH and CRF (p value =0.337, 0.964 respectively).

Table 3: Correlations between Corneal Biomechanics and Other Parameters:

		IOPg	IOPcc	CH	CRF
IOP	**r**	0.151	0.121	0.455	0.443
	P value	**0.018**	0.286	**<0.001**	**<0.001**
	N	79	79	79	79
MD (perimetry)	**r**	-0.231-	-0.177-	-0.302-	-0.291-
	P value	**0.029**	**0.048**	**0.008**	**0.010**
	N	77	77	77	77
Vertical CDR (oct)	**r**	0.015	0.040	0.015	-0.090-
	P value	**0.049**	**0.037**	**0.003**	**0.011**
	N	79	79	79	79
S Q	**r**	-0.097-	-0.028-	-0.335-	-0.284-
	P value	**0.039**	**0.048**	**0.048**	**0.012**
	N	79	79	79	79
I Q	**r**	0.002	0.011	-0.232-	0.507
	P value	**0.045**	**0.026**	**0.039**	**<0.001**
	N	79	79	79	79
N Q	**r**	-0.013-	0.050	-0.176-	-0.085-
	P value	**0.011**	**0.016**	**<0.001**	**<0.001**
	N	79	79	79	79
T Q	**r**	-0.020-	-0.003-	-0.022-	-0.003-
	P value	0.053s	0.977	**<0.001**	**<0.001**
	N	79	79	79	79

The following results showed negatively significant correlation between perimetry MD and the ORA parameters, IOPg, CH, and CRF (p value =0.043 r=-0.231, p value=0.008 r=-0.302, p value =0.010 r=-0.291 respectively) also CH shows negatively significant with SQ of the OCT optic nerve, while no significant correlation between IOP, OCT " IQ, NQ and TQ" and vertical CDR with ORA parameters.

Table 4: Correlations between OCT and Other Parameters:

		Vertical CDR (oct)	S Q	I Q	N Q	T Q
IOP	**r**	0.589	-0.663-	-0.658-	-0.460-	-0.232-
	P value	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**0.038**
	N	80	80	80	80	80
MD (perimetry)	**r**	0.596	0.661	0.643	0.515	0.387
	P value	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**0.001**
	N	77	77	77	77	77

The following results showed positively significant correlation between perimetry MD and vertical CDR (p value <0.001 r=-0.596), positively significant correlation between IOP and vertical CDR (p value< 0.001 r=0.589).

Table 5: Correlations between IOP and Perimetry:

		MD (perimetry)
IOP	**r**	0.838
	P value	**< 0.001**
	N	77

The following results showed positively significant correlation between IOP and perimetry MD (p value <0.001 r=0.838).

DISCUSSION

The ocular surface health depends heavily on the preservation of the biomechanical properties of the cornea. Certain surgical procedures, and a series of corneal diseases, are associated with substantial changes in the corneal tissue structure, and prospectively with altered biomechanical properties[9]

Until recently the evaluation of corneal biomechanical properties was encountered, mainly, in research settings. The development of the Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, NY, USA), introduced a simple and reliable way for the assessment of a series of biomechanical factors of the cornea in clinical settings as well. These factors are CH, and CRF[10]

CH is known to represent the viscosity of the cornea, reflecting the collagen structure and hydration state of the cornea. CH is believed to have little association with CCT or IOP, although the degree of association varies among reports. CRF is thought to represent the elasticity of the cornea, with stronger correlations with IOP and CCT compared to those of CH.[11]

Glaucoma is the second leading cause of blindness worldwide. In the early 1800s, Sir William Bowman, an English ophthalmologist, recognized the relationship between the hardness of the eye and the structural optic nerve changes that we now identify as glaucomatous optic neuropathy. Since that discovery, a great emphasis is placed on obtaining accurate IOP measurement[12]

Glaucoma can be defined as a group of diseases that have in common a characteristic optic neuropathy with associated visual field loss, for which elevated IOP is one of the primary risk factors. GAT is currently the gold standard of IOP measuring.[13]

In a study to evaluate corneal biomechanical in primary open angle glaucoma patients using the ORA and to evaluate the relationship between Intraocular pressure, Visual field progression, OCT Optic Nerve changes and ORA parameters[14]

Our study was conducted on 80 eyes of 40 patients we found that the more the visual field affected, the thinnest the retinal nerve fiber layer thickness and the higher the vertical C/D ratio, is positively correlated with lower Corneal biomechanics. And these results showed agreement with the following studies.

Dana Dascalescu et al stated that CH is significantly lower in patients with advanced disease than in patients with mild disease.[1]

Also Ang, G. S. et al stated that there was statistically significant difference in the mean CH between POAG and NTG (CH was higher in

NTG). The highest recorded Goldmann applanation IOP was also statistically significantly correlated with lower CH and higher CRF, suggesting that alterations to the corneal biomechanical properties may occur as a result of chronic raised IOP in POAG[7]

Dr Mohamed A El-Malah stated that in his study, the selected parameters such as IOPg and IOPcc had higher readings and CH and CRF had lower readings in glaucomatous eyes and vice versa in normal eyes. The low readings of intraocular pressure in POAG eyes were most probably because of low readings of CH and CRF. more accurately evaluate the ORA machine and its role in early detection of glaucoma patients. [15]

Ghee Soon Ang. et al stated that the lower CH has been reported to be associated with glaucomatous visual field defect progression, Furthermore, patients with glaucoma have reduced CH in comparison to normal people.[7]

According to Vinciguerra, et al 2018 Corneal biomechanics might be a significant confounding factor for IOP measurement that should be considered in clinical decision-making. The abnormality of corneal biomechanics in NTG and the significant correlation with visual field parameters might suggest a new risk factor for the development or progression of NTG.[5]

Gaspar et al stated that the importance of corneal biomechanical properties in IOP interpretation and the influence of CH in glaucoma screening and diagnosis.[6]

Sayed Amal Hussnain stated that Corneal hysteresis (CH) is lower in glaucoma and has been shown in various studies to be strongly associated with structural and functional changes in glaucoma. In addition, CH has also been shown to predict glaucoma progression and response to glaucoma therapy, it is an important clinical measurement that can help risk stratify and set therapy goals for glaucoma patients.[17]

Nathan G.Congdon also stated that the lower corneal hysteresis were associated with progressive field worsening.[18]

Ming Chen et al stated that CH measurement is a valuable test to assist in early diagnosis of NTG, especially in the elderly population. With an established diagnosis, aggressive early treatments medically or surgically to further lower IOP can prevent irreversible blindness, which can severely impact the patient's family and socioeconomic status.[19]

Gaspar et al stated that there is a significant difference in CH and CCT between glaucoma patients and healthy controls.[5]

Christoph Hirneiß stated that IOPCC in his study is also significantly higher than GAT with a mean of 24.3 mmHg IOPCC in the affected eye compared to 15.6 mmHg GAT[20]

Grise-Dulac satated also that NTG was associated with significantly lower CRF than chronic POAG and N patients[21]

IOPcc may account for measurement error induced by corneal biomechanics. Compared to GAT, IOPcc may be a superior test in the evaluation of glaucoma.[22]

The Ocular Hypertension Treatment Study (OHTS), have brought to light the relevance of central corneal thickness (CCT) in glaucoma. Numerous studies utilizing the Ocular Response Analyzer have confirmed the importance of the cornea in glaucoma decision making and, in fact, demonstrated that Corneal Hysteresis is of far greater significance than CCT. [23]

CONCLUSION

Sometimes, it is difficult to diagnose glaucoma suspect patients and to detect progression in primary open angle glaucoma (POAG) patients and Normal tension glaucoma patients so we have to correlate IOPGAT, Perimetry, OCT Optic disc and ORA results.

Corneal biomechanical parameters (CH, CRF, IOPg and IOPcc) could be useful for early diagnosis glaucoma suspect and follow up primary open angle glaucoma patients. Our study revealed that the corneal biomechanics Parameters are significantly lower in patients with advanced primary open angle glaucoma (POAG).

REFERENCES

1. **Dascalescu, D., Corbu, C., Constantin, M., Cristea, M., Ionescu, C., Cioboata, M., & Voinea, L. (2015).** Correlations between Corneal Biomechanics and Glaucoma Severity in Patients with Primary Open Angle Glaucoma. Maedica, 10(4), 33.
2. **Gupta, D. (2005).** Glaucoma diagnosis and management. Lippincott Williams & Wilkins
3. **De Moraes, C. G. V., Prata, T. S., Liebmann, J., & Ritch, R. (2008).** Modalities of tonometry and their accuracy with respect to corneal thickness and irregularities. Journal of optometry, 1(2), 43-49.
4. **Girard, M. J., Dupps, W. J., Baskaran, M., Scarcelli, G., Yun, S. H., Quigley, H. A.,... & Strouthidis, N. G. (2015).** Translating ocular biomechanics into clinical practice: current state and future prospects. Current eye research, 40(1), 1-18.
5. **Vinciguerra, R., Rehman, S., Vallabh, N. A., Batterbury, M., Czanner, G., Choudhary, A.,... & Willoughby, C. E. (2019).** Corneal biomechanics and biomechanically corrected intraocular pressure in primary open-angle glaucoma, ocular hypertension and controls. British Journal of Ophthalmology, bjophthalmol-2018
6. **Gaspar, R., Pinto, L. A., & Sousa, D. C. (2017).** Corneal properties and glaucoma: a review of the literature and meta-analysis. Arquivos brasileiros de oftalmologia, 80(3), 202-206
7. **Ang, G. S., Bochmann, F., Townend, J., & Azuara-Blanco, A. (2008).** Corneal biomechanical properties in primary open angle glaucoma and normal tension glaucoma. Journal of glaucoma, 17(4), P259-262

8. **Chen, M., Kueny, L., & Schwartz, A. L. (2018).** The role of corneal hysteresis during the evaluation of patients with possible normal-tension glaucoma. Clinical ophthalmology (Auckland, NZ), 12, 555

9. **Ruberti, J. W., & Zieske, J. D. (2008).** Prelude to corneal tissue engineering–gaining control of collagen organization. Progress in retinal and eye research, 27(5), 549-577.

10. **Gkika, M., Labiris, G., Giarmoukakis, A., Koutsogianni, A., & Kozobolis, V. (2012).** Evaluation of corneal hysteresis and corneal resistance factor after corneal cross-linking for keratoconus. Graefe's Archive for Clinical and Experimental Ophthalmology, 250(4), 565-573.

11. **Shin, J. Y., Choi, J. S., Oh, J. Y., Kim, M. K., Lee, J. H., & Wee, W. R. (2010).** Evaluation of corneal biomechanical properties following penetrating keratoplasty using the ocular response analyzer. Korean Journal of Ophthalmology, 24(3), 139-142.

12. **Lawrence, W. (1854).** A Treatise on the Diseases of the Eye. Blanchard and Lea.

13. **Flammer, J., & Orgül, S. (1998).** Optic nerve blood-flow abnormalities in glaucoma. Progress in retinal and eye research, 17(2), 267-289.

14. **Mansouri, K., Leite, M. T., Weinreb, R. N., Tafreshi, A., Zangwill, L. M., & Medeiros, F.A. (2012).** Association between corneal biomechanical properties and glaucoma severity. American journal of ophthalmology, 153(3), 419-427.

15. **El-Malah, M. A. (2013).** Evaluation of corneal biomechanics using ocular response analyzer for normal and primary open angle glaucoma eyes. Journal of the Egyptian Ophthalmological Society, 106(4),P 249.

16. **Vinciguerra, R., Rehman, S., Vallabh, N. A., Batterbury, M., Czanner, G., Choudhary, A.,... & Willoughby, C. E. (2019).** Corneal biomechanics and biomechanically corrected intraocular pressure in primary open-angle glaucoma, ocular hypertension and controls. British Journal of Ophthalmology, bjophthalmol-2018.

17. **Hussnain, S. A., Kovacs, K. D., Warren, J. L., & Teng, C. C. (2018).** Corneal hysteresis and anterior segment optical coherence tomography anatomical parameters in primary angle closure suspects. Clinical & experimental ophthalmology, 46(5), 468-472

18. **Congdon, N. G., Broman, A.T., Bandeen-Roche, K., Grover, D., & Quigley, H.A. (2006).** Central corneal thickness and corneal hysteresis associated with glaucoma damage. American journal of ophthalmology, 141(5), 868-875.

19. **Chen, M., Kueny, L., & Schwartz, A. L. (2018).** The role of corneal hysteresis during the evaluation of patients with possible normal-tension glaucoma. Clinical ophthalmology (Auckland, NZ), 12, 555.

20. **Hirneiß, C., Neubauer, A. S., Yu, A., Kampik, A., & Kernt, M. (2011).** Corneal biomechanics measured with the ocular response analyser in patients with unilateral open-angle glaucoma. Acta ophthalmologica, 89(2), P189-192.

21. **Grise-Dulac, A., Saad, A., Abitbol, O., Febbraro, J. L., Azan, E., Moulin-Tyrode, C., & Gatinel, D. (2012).** Assessment of corneal biomechanical properties in normal tension glaucoma and comparison with open-angle glaucoma, ocular hypertension, and normal eyes. Journal of glaucoma, 21(7), P486-489.

22. **Board, D (2002).** IPCC Abstract deadline: May 1st 2002 Travel Awards available for IPCC: deadline May 15th 2002.

23. **Brandt, J. D., Beiser, J. A., Kass, M. A., Gordon, M. O., & Ocular Hypertension Treatment Study (OHTS) Group. (2001).** Central corneal thickness in the ocular hypertension treatment study (OHTS). Ophthalmology, 108(10), 1779-1788.