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Ranking of Zones of True IOP According to the Level of Rigidity of the Fibrous Membrane of the Eye in Healthy and Glaucoma Eyes

Olga V Svetlova[1,2]*, Ivan N Koshits[3], Roman M Pankratov[4], Oxana V Makarovskaya[4], Marina V Zaseeva[1], Maksat B Egemberdiev[5] and Marina G Guseva[6]

[1]*Department of Ophthalmology with Clinic Pavlov First Saint-Petersburg State Medical University of the Ministry of Health of Russia, Russia*

[2]*Department of Ophthalmology Mechnikov North-Western State Medical University of the Ministry of Health of Russia, Russia*

[3]*LLC Petercom-Networks / MS Consulting Group, Saint-Petersburg, Russian Federation, Russia*

[4]*LLC Ophthalmological laser clinic, Arkhangelsk, Russian Federation, Russia*

[5]*Department of Ophthalmology, Chuy Region United Hospital, Bishkek, Russia*

[6]*Department of Ophthalmology, Medical Diagnostic Center Vodokanal of Saint-Petersburg, Saint-Petersburg, Russia*

***Corresponding author:** Olga V Svetlova, 1Department of Ophthalmology with Clinic Pavlov First Saint-Petersburg State Medical University of the Ministry of Health of Russia, Leo Tolstoy str., 6-8, St. Petersburg, 197022, Russian Federation, Russia.

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Abstract

Purpose: To identify adequate ranges of true IOP in healthy and glaucoma eyes corresponding to the average ranges of rigidity and fluctuation in their fibrous membrane of the eye (FME), taking into account the age periods of aging according to the WHO classification.

Methods and Patients: Theoretical analysis of clinical values of rigidity and fluctuation of FME, the current level of true IOP and the calculated individual level of IOP in a patient in his youth, obtained using the ORA pneumoanalyzer using the Koshitz-Svetlova dynamic diagnostic method in 674 healthy and 518 glaucoma eyes aged 18 to 90 years, distributed according to the aging periods according to WHO.

Results: The following adequate ranges of IOP levels for healthy and glaucoma eyes were identified: low IOP zone (up to 13 mmHg); medium IOP zone (14-20 mmHg); high IOP zone (21-26 mmHgst); high IOP zone (27 - 32 mmHg); IOP sub compensation zone (33 - 39 mmHg) and IOP uncompensation zone (≥ 40 mmHg).

Conclusion: The fundamental criteria of rigidity and fluctuation do not depend on the central thickness of the cornea and objectively determine the current functional state of the FME. The ability to determine whether a healthy or glaucoma eye belongs to its adequate individual IOP zone is particularly important for the polyclinic network.

Keywords: Intraocular pressure; Pneumotonometry; Individual zones of IOP; Glaucoma; Age-related ophthalmic hypertension; Fibrous membrane of the eye; Rigidity; Fluctuation; biomechanics of the eye; Sclera

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Introduction

In 1998, the Russian scientist Academician of the Russian Academy of Sciences Arkady P Nesterov [1] made a truly revolutionary step in world ophthalmology - he proposed to assess the individual level of true IOP in the zones of low (9-12 mmHg), medium (13-16 mmHg) and upper (17-22 mmHg) norm [1]. This also meant that the traditional "average" IOP value should be determined separately for each zone of the IOP norm according to AP Nesterov.

Table 1 presents generalized results of measurements of the IOP level in healthy eyes performed by various authors using tonometers of different types and without taking into account age. Table 1 clearly shows large variations (2-3 times) in the range of extreme values of IOP levels in almost every study. This is especially true for studies performed by W Leydhecker in 18,800 patients [2]. Moreover, the average value of the IOP level in his numerous group of patients was 15.5 mmHg.

Table 1: The value of IOP in healthy eyes according to various authors.

Author	Year	Type of tonometer	Number of eyes	IOP, mmHg.	
				Average	Range
Goldmann	1957	Goldmann	400	15.4	8.9 - 22.0
Levene	1961		1686	15.6	7.0 - 24.2
Kolesnikova	1961	Dashevsky	1009	15	8.5 - 21.5
Melnik	1961	Maklakov (5 gr.)	3386	16.6	9.5 - 23.6
Nesterov	1963		427	16.6	9.8 - 23.5
Belorussov	1964		2400	16.4	9.7 - 22.9
Leydhecker [2]	1958	Shiots	18 800	15.5	8.8 - 22.2
Becker	1958	Shiots	909	16.1	8.8 - 23.4
Weekers	1959		487	17	9.9 - 24.1
Fronimopulos	1961		606	16.2	10.2 - 22.2
Katavisto	1964		11 520	16.1	9.1 - 23.2

It is obvious that in all this huge array of IOP measurements, eyes from different zones of the IOP norm are represented according to AP Nesterov and it is not only incorrect to evaluate them according to the average IOP level, but, often, it is also illegal. After all, eyes from different zones of the IOP norm according to AP Nesterov are, in their physiological essence, truly different eyes, the development in which the Age-related ophthalmohypertension (AROG) or pathological glaucoma process can radically differ. We tried to streamline the traditional criterion of "IOP level", making it more suitable for practice.

Theoretical and clinical results. It is worth noting that back in 2005-2007, we learned by our own methods, using double tonometry (weights of 5 and 10 or 10 and 15 grams), as well as on the ORA pneumoanalyzer, to determine the level of IOP in youth for a particular eye, even in an elderly patient with ophthalmic hypertension or glaucoma [3-6]. We have also introduced a new concept of fluctuation in ophthalmology. Fluctuation is the functional ability of the sclera to micro–volume fluctuations with the help of its viscoelastic structures. In fact, fluctuation is a measure of the current physiological ability of the fibrous membrane of the eye to perform its main functions: to maintain the turgor of the eye, to level the pulse of blood pressure, to push the intraocular fluid out along the outflow pathways, to maintain the necessary current volume of the eye, and also to pass through the internal volume of the eye the necessary daily volume of fresh watery moisture [7]. And the most important thing is that this key fundamental parameter of the eye can be reliably measured using express pneumo diagnostics on ORA using our simple in vivo technique.

The possibilities of the "fluctuation" parameter when using it in the fight against OAG are extremely large. This fundamental parameter does not depend on the thickness of the cornea and allows you to assess the level of preservation of the functions of FME, determine the effectiveness of hypotensive or surgical interventions, objectively separate the eyes with AROG from the eyes with OAG, as well as compare the functional state of the glaucoma and the second, not yet glaucoma eye of the patient. At the same time, the second – conditionally healthy eye of the patient - will allow to determine the individual rate of its fluctuation as another reference point for choosing an adequate method of treatment of OAG already on the affected eye. Both key physiological parameters of the eye: rigidity and fluctuation allow you to get a clear idea of the intensity of pathological processes occurring in the eye.

The volumetric rigidity of the FME can be correctly estimated only by the amount of work that the air jet of the ORA air analyzer needs to perform in order to achieve the first corneal applanation, when Intraocular fluid from under the cornea will be "thrown" (literally instantly displaced) into the eye, which will lead to a reciprocal expansion of both elastic and viscoelastic structures of the sclera. At the same time, the total volume of the eye will not change. I.e., the higher the current rigidity (mechanical rigidity) of the FME, the more time it will take for the sclera to expand its diameter and for the moment of the first corneal appplanation to

occur. Therefore, the time to achieve the first Corneal applanation, in fact, is an objective measure of the rigidity of the FME, which was used in our author's methodology.

After the end of the pneumatic action, the additionally stretched visco-elastic executive structures of the sclera begin to contract naturally and literally push the Intraocular fluid back under the cornea, i.e. they work to restore the original shape of the FME. Therefore, the time from the end of the pneumatic action to the moment of the second corneal applantation is, in fact, an objective measure of the current level of fluctuation of the sclera, i.e. the level of functional residual operability of its viscoelastic structures. This time of the "return" of the sclera to its initial state characterizes its ability to "breathe", i.e. to exercise its physiological functions. Such studies of fluctuations according to our author's methodology were carried out in this study.

One of the main physiological tasks of the eye is the need to pump a constant daily volume of explosives through its cavity to effectively maintain the metabolism of its structures [8]. As studies of morphologists have shown [9], there are no baroreceptors in the eye. However, there are mechanoreceptors and prostaglandin receptors in the sclera that allow the brain to constantly monitor the volume of the eye [9,10], the average volume of which remains constant during the day. I.e., the brain cannot control intraocular pressure, but controls the volume of the eye. And the key executive mechanism that allows this to be done is the sclera with its viscoelastic executive structures.

Fluctuation and rigidity of the sclera make it possible to maintain the constancy not only of the average volume of the eye during the day, but also the constancy of the average daily volume of intraocular fluid passing through its structures. And fluctuations in the level of the current IOP during the day are only a consequence of the joint work of these two key functional parameters of the eye [11].

Discussion

The purpose of our study was to use rapid diagnostics on the ORA pneumoanalyzer using the Koshits-Svetlova technique to identify in practice the zones of true IOP for healthy and glaucoma eyes that are adequate to the ranges of values of the functional criteria "rigidity" and "fluctuation" of the fibrous membrane of the eye, taking into account the age periods of human life according to World Health Organization (WHO) recommendations.

The following research methods were used: gonioscopy, ophthalmoscopy, keratometry, pachymetry and determination of the length optical axis of the eye, identification of individual visual acuity, assessment of functional and biomechanical parameters of the sclera according to the author's methodology, as well as Goldmann tonometry using the ORA pneumoanalyzer (USA), computer perimetry, optical examination of the optic nerve head and nerve fiber layer using computer of the analyzer OST.

Table 2 shows the distribution of the eyes of healthy and glaucoma patients by IOP zones and age periods of human life, including eyes with possible age-related ophthalmic hypertension. The observation period is 3 years, with a periodicity of six months. It should be noted a relatively high number of healthy eyes from the low zone with an IOP level of less than 13 mmHg (34%). And this is the second largest group among healthy eyes, and the first in number are eyes from the middle zone with an IOP level of 14-20 mmHg (47%). The breakdown in Table 2 of the IOP level by adequate ranges of FME rigidity was performed in the course of our study, a detailed description of which we will give below. It is also worth paying attention to the fact that 28 (4%) of perfectly healthy eyes among all age periods had a true pressure corresponding to the high IOP zone of 27-32 mm Hg. (see filling the cells of column 3 in Table 2). These eyes, with the consent of the patient, were examined with special care for 3 years 1 time every three months to reliably confirm the absence of pathological changes in them. And these eyes deservedly entered the general control group of comparison as "healthy eyes".

As a matter of fact, we went from the values of the average ranges of rigidity to the corresponding zones of the IOP level and managed, in the process of statistical processing of the entire array of our measurements, to identify those ranges of IOP that were adequate to the values of the independent parameters of the eye – rigidity and fluctuation. Ranges of IOP zones according to AP Nesterov [1] and the authors of the article are presented in Table 3. Apparently, this is a particularly important result of our research for practice, which expands and deepens the fundamental proposal of AP Nesterov on the need for mandatory accounting of the belonging of each eye to a certain IOP zone.

Table 2: Distribution of the eyes of healthy and glaucoma patients by IOP zones and age life periods according to WHO.

Age periods according to WHO, years	IOP zones, mm Hg	The number of eyes at the observation period of 3 years with a frequency of 6 months.		
		Healthy eyes	OAG I - II stage	OAG III - IV stage
1	2	3	4	5
Up to 18	Up to 13, low	3	-	-
	14 – 20, average	4	-	-
	21-26, increased	1	-	-
18-44	Up to 13, low	164	-	-
	14 – 20, average	177	2	-
	21-26, increased	31	4	-
	27- 32, high	10	-	-

45-59	Up to 13, low	19	5	-
	14 – 20, average	49	27	-
	21-26, increased	35	16	-
	27- 32, high	12	12	1
	33 – 39, subcompensations	-	6	2
	40 - … no-compensation	-	11	3
60-74	Up to 13, low	31	32	6
	14 – 20, average	64	79	14
	21-26, increased	30	37	9
	27- 32, high	3	27	5
	33 – 39, subcompensations	-	13	7
	40 - … no-compensation	-	18	19
75-89	Up to 13, low	11	5	9
	14 – 20, average	20	37	7
	21-26, increased	7	28	10
	27- 32, high	3	24	2
	33 – 39, subcompensations	-	9	3
	40 - … no-compensation	-	8	21
Total:		674	400	118

Table 3: Ranges of IOP zones according to AP Nesterov and the authors of the article.

Zones of the true norm IOP (P0), mm Hg (according to *AP Nesterov) [1]*		Zones of true IOP (P0) for healthy and glaucoma eyes, mm Hg (according to Olga V Svetlova, Ivan N Koshits et al., 2022)		
12-Sep	Low norm zone	up to 13	Low IOP zone	Healthy eyes. Eyes with OAG I - IV stage
13 -16	Average norm zone	14 - 20	Middle IOP zone	
17- 22	Upper norm zone	21 - 26	Increased IOP zone	
-		27- 32	High IOP zone	
		33 - 39	IOP subcompensation zone	Eyes with OAG III - IV stage
		40 - …	IOP no-compensation zone	

Figure 1 shows generalized ranges of values of parameters of healthy and glaucoma (I-IV stage) eyes aged 18-90 years, including eyes with possible age-related ophthalmic hypertension (AROG)Apparently, we managed to find a "stepwise" pattern of distribution of average values of rigidity and fluctuation in healthy and glaucoma eyes, which allowed us to rank the corresponding IOP zones. It is especially important that the "steps" of the extreme average values of rigidity and fluctuations in the IOP zones do not intersect. However, the values of the standard parameter of the ORA pneumonialike–corneal hysteresis (CH)- overlap in almost all neighboring zones of adequate IOP. This indicates a limited diagnostic reliability of the CH parameter.

Generalized ranges of average values of physiological parameters of healthy and glaucoma (I-IV st.) eyes in the age period of 18-90 years, including eyes with possible age-related ophthalmic hypertension are presented in Table 4. It is important to note that during the transition from the IOP zone with initially low pressure to the zones with higher IOP, the values of rigidity and IOP level in Table 4 significantly increase, and the values of fluctuation significantly fall ($p < 0.001$). The data in Table 4 also allow us to note that between each adequate zone IOP the average values of the ranges of rigidity, IOPGold. and the fluctuations don't overlap. The same cannot be said about the ranges of values for the CH parameter, which again indicates a relatively low diagnostic reliability of this standard criterion of the ORA pneumatic analyzer.

Table 5 shows the values of rigidity and fluctuation in healthy and glaucoma (I-II st.) eyes with hypotensive therapy from the zone of low IOP (≤ 13 mmHg). These clinical results allow us to note the

following. The data in Table 5 show that healthy and glaucoma (I-II st.) eyes from the low IOP zone (≤ 13 mm Hg) have low rigidity and high fluctuation in all age periods. And these values practically do not change with POAG, even after hypotensive therapy.

Table 4: Generalized ranges of values of physiological parameters of healthy and glaucoma (I-IV stage) eyes in the age period of 18-90 years, including eyes with possible age-related ophthalmic hypertension.

Age, according to WHO, years Eye type.	IOP zones, mm Hg	Number of eyes	Pneumatic analyzer ORA			
			IOP_{GOLD}, mm Hg	Rigidity, ms	Fluctuation, ms	Corneal hysteresis, mm Hg
1	2	3	4	5	6	7
18 – 90 Healthy eyes. Eyes with OAG I - IV stage	Up to 13 low	285	10,77-11,88	10,25-10,41	11,37-11,73	8,86 - 10,76
	14 - 20 average	480	16,39-18,31	11,02-11,19	10,58-10,83	9,21 - 12,33
	21-26 increased	208	22,10-23,62	11,68-11,88	9,88 -10,16	8,10 - 12,58
	27- 32 high	99	28,70-31,34	12,19-12,57	8,70 - 9,43	6,36 - 10,78
18 - 90 Eyes with OAG III - IV stage	33 - 39 subcompensations	40	34,18-35,59	12,72-12,85	7,98 - 8,38	5,38 - 6,97
	40 - ... no-compensation	80	50,03-61,68	14,12-15,53	2,83 - 5,55	1,50 - 2,61

Table 5: Low IOP zone (≤ 13 mm Hg). Rigidity and fluctuation in healthy and glaucoma (I-II st.) eyes with hypotensive therapy.

Age, according to WHO, years	Rigidity, ms		Fluctuation, ms	
	Healthy eyes	Glaucoma eyes with therapy	Healthy eyes	Glaucoma eyes with therapy
1	5	6	7	8
18-44	10,19 ± 0,31	-	11,66 ± 0,36	-
45-59	10,16 ± 0,21	10,54 ± 0,05	11,77 ± 0,31	11,51 ± 0,05
60-74	10,25 ± 0,21	10,30 ± 0,23	11,74 ± 0,32	11,67 ± 0,25
75-89	10,30 ± 0,14	10,27 ± 0,21	11,59 ± 0,14	11,62 ± 0,20
Average	10,22 ± 0,23	10,37 ± 0,19	11,65 ± 0,26	11,60 ± 0,18

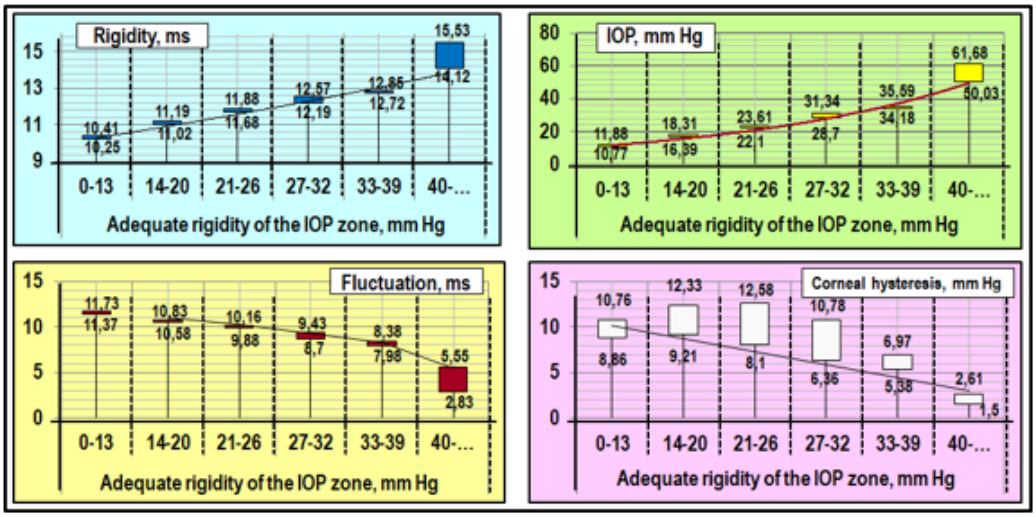

Figure 1: Generalized ranges of values of parameters of healthy and glaucoma (stage I-IV) eyes aged 18-90 years according to WHO for adequate IOP zones, including eyes with possible age-related ophthalmohypertension (AROG).

Therefore, it is important to note that in the eyes from the zone of low IOP (≤ 13 mmHg) with the initial stages of POAG, hypotensive therapy practically does not give the expected effect. It is possible that eyes with initial glaucoma from the low IOP zone (≤ 13 mmHg)

differ in etiology from glaucoma eyes from other IOP zones, which may be due to low values of systemic blood pressure. In such patients, respectively, intracranial cerebrospinal fluid pressure in the optic nerve is lowered, which can lead to an increased tendency to excavate the optic nerve disc [12-14].

Table 6 shows the values of rigidity and fluctuation in healthy and glaucoma (I-II st.) eyes with hypotensive therapy or without therapy from the zone of increased IOP (21-26 mmHg). These clinical results allow us to note the following. Data from Table 6 for healthy and glaucoma eyes of I-II st. from the zone of increased IOP (21-26 mm Hg) is shown that with the help of hypotensive therapy, it is possible to reduce the average rigidity of glaucoma eyes of I-II st. by no more than 1% compared with healthy eyes. At the same time, the fluctuation level (so, the current state level of the sclera functions) not only does it not increase, but, on the contrary, it decreases in all age groups, even in comparison with glaucoma eyes without therapy (see column 10 of Table 6 highlighted with fill).

Table 6: Zone of increased IOP (21-26 mm Hg). Rigidity and fluctuation in healthy and glaucoma (I-II st.) eyes with or without hypotensive therapy.

Age, according to WHO, years	Rigidity, ms			Fluctuation, ms		
	Healthy eyes	Glaucoma eyes		Healthy eyes	Glaucoma eyes	
		without therapy	with therapy		without therapy	with therapy
1	5	6	7	8	9	10
18-44	11,76±0,26	-	11,68±0,16	10,12±0,30	-	9,94±0,20
45-59	11,88±0,21	11,77 ± 0,35	11,78±0,18	10,14±0,26	9,97±0,33	9,94±0,51
60-74	11,82±0,22	11,82 ± 0,22	11,69±0,21	10,16±0,34	9,95±0,23	9,94±0,28
75-89	11,78±0,22	11,83 ± 0,22	11,70±0,19	9,88±0,51	9,99±0,21	9,86±0,25
Average	11,81±0,23	11,81±0,28	11,73±0,19	10,08±0,32	9,97±0,27	9,90±0,29

Since hypotensive therapy has the task of maintaining or restoring the functions of the sclera to stabilize or inhibit the glaucoma process, the clinical results obtained indicate a low effectiveness of hypotensive therapy in glaucoma eyes of I-II st., starting from the IOP level of 21-26 mmHg and higher. At the same time, the level of metabolism of intraocular structures will also fall due to a reduced level of fluctuation when using hypotensive therapy, which may not slow down, but accelerate the glaucoma process.

Conclusion

- The effectiveness and reliability of in vivo determination of FME rigidity and sclera fluctuations using express diagnostics on the ORA pneumonialike according to the author's method has been confirmed in various clinics and can be recommended for wide use in the polyclinic network.
- Adequate ranges of IOP levels have been identified, allowing healthy and glaucoma eyes to be ranked according to this indicator: the zone of low IOP (up to 13 mmHg); the zone of medium IOP (14-20 mmHg); the zone of increased IOP (21-26 mmHg); high IOP zone (27 - 32 mmHg); IOP sub compensation zone (33 - 39 mmHg) and IOP un-compensation zone (≥ 40 mmHg).
- The absence of noticeable changes in rigidity and fluctuation in healthy and glaucoma eyes with low (up to 13 mm Hg) and elevated (21-26 mm Hg) levels of IOP suggests that the processes of occurrence of low-pressure POAG or POAG in the group of patients with initially high IOP differ in their etiology or pathophysiology from other eyes.
- The possibility of monitoring the effectiveness of hypotensive therapy and the rate of development of the glaucoma process according to the criterion of "fluctuation", which determines the current state of the physiological functions of the sclera.

Transparency of Financial Activities

None of the authors has a financial interest in the submitted materials or methods.

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Conflict of Interest

There is no conflict of interest.

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