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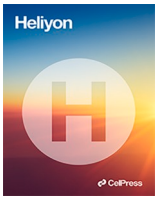

Research article

Intraocular pressure and its determinants in a very old population. The ural very old study

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A R T I C L E I N F O

Keywords:
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A B S T R A C T

Purpose: To explore intraocular pressure (IOP) and its associated parameters in an aged population.

Methods: The epidemiologic Ural Very Old Study (UVOS) conducted in Bashkortostan/Russia included 1526 participants with an age of ≥85 years. Besides a whole series of ocular and systemic examinations, IOP was determined applying non-contact tonometry. Body mass index, diastolic blood pressure and age were the factors used to estimate the cerebrospinal fluid pressure (CSFP).

Results: The study consisted of 904 participants (age: 88.6 ± 2.7 years) with available IOP readings and without anti-glaucomatous therapy. Mean IOP was 14.5 ± 5.1 mmHg (median: 14 mm Hg; Q1:11; Q3:16; 95%CI:8,25) and 14.8 ± 4.6 mmHg (median: 14 mm Hg; Q1:12; Q3:17; 95%CI:8,28) in the right and left eyes, respectively. Higher IOP correlated (multivariable analysis; correlation coefficient r^2:0.32) with female sex ($P < 0.001$), more sedentary lifestyle ($P = 0.006$), higher estimated CSFP ($P < 0.001$), higher total protein serum concentration ($P < 0.001$), stronger hand grip force ($P = 0.01$), thicker central cornea ($P < 0.001$), longer axial length ($P = 0.01$), absence of previous cataract surgery ($P = 0.001$), higher degree of pseudoexfoliation ($P = 0.02$, and thinner peripapillary retinal nerve fiber layer thickness ($P = 0.004$). Using this that model, IOP reading enlarged by 0.22 mmHg (95% CI: 0.09, 0.35) for each increase in estimated CSFP by 1 mm Hg, by 0.03 mm Hg (95% CI: 0.02,0.05) for each thickening in central corneal thickness by 1 μm, by 0.56 mm Hg (95%CI: 0.13,1.00) for each axial elongation by 1 mm, and by 0.40 mmHg (95% CI: 0.06,0.74) for each increase in the degree of pseudoexfoliation, and it decreased by 0.40 mmHg (95% CI: 0.06,0.74) by cataract surgery.

Conclusions: In this study population aged 85+years, IOP readings showed similar relationships as in younger study populations, including positive associations with higher estimated CSFP and longer axial length and a negative association with cataract surgery.

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1. Introduction

For ocular physiology and pathophysiology, the intraocular pressure (IOP) is of high importance [1–4]. A minimum of IOP is needed to stabilize the shape of the eye and to enable the centripetal axoplasmic flow in the retinal ganglion cells axons through the lamina cribrosa of the optic disc. An IOP higher than the pressure tolerability of the optic nerve fibers within the lamina cribrosa leads to glaucomatous damage of the optic nerve [1–4]. The IOP undergoes fluctuations in relationship to the daytime and depends on several other parameters including the body position. The IOP measurements are influenced by biometric parameters such as corneal anterior curvature and thickness [5,6]. Numerous previous investigations explored the IOP and its determining ocular and systemic factors [7–12]. In these studies, such as the South Indian Chennai Study and the Central India Eye and Medical Study, the mean IOP values were 14.3 ± 3.3 mm Hg, 13.6 ± 3.4 mm Hg, respectively. Differences in IOP measurements between the investigations were discussed to be due to various reasons, including ethnicity-related difference in factors influencing the IOP readings such as central corneal thickness. There has been a scarcity of information on the IOP and its relationships with other factors, including systemic disorders such as arterial hypertension and diabetes mellitus, in the very old group of the population and from the region of Central Asia and Russia. Existing literatures has shown however the impact of age and race/ethnicity on IOP, so that age- and race-/-ethnicity-specific IOP norms are needed to better understand the vision health in the oldest old population and in the population from Russia/Central Asia [7–12]. We therefore measured the IOP in a population-based group of individuals aged 85+ years. Such a group of elderly is clinically important since most non-communicable diseases are age-related and accumulate with older age.

2. Methods

The Ural Very Old Study (UVOS) is an epidemiologic investigation carried out in Bashkortostan/Russia in the Kirovskii region in the capital Ufa and in a rural region in the Karmaskalinsky area 65 km distant to Ufa [13]. Conditions to be included into the study were living in the study regions and an age of 85+ years. The study was approved by the Ethics Committee of the Academic Council of the Ufa Eye Research Institute. All participants gave an informed written consent. The study described in detail previously consisted of 1526 (81%) out of 1882 eligible inhabitants (390 (25.6%) men; 1136 (74,4%) women) [13]. The study cohort and the Russian population as assessed in the recent census of 2021 were comparable with respect to age and sex distribution [14,15]. The specific requirement for the present investigation were the availability of IOP readings and absence of any anti-glaucomatous therapy or previous anti-glaucomatous surgery.

Table 1
Demographic parameters of the study population.

Parameter	Mean ± standard deviation or prevalence or median and range
N	904
Age (years)	88.6 ± 2.7
Sex (male/female)	662 (73.2%) women
Rural/urban region of habitation	243 (26.9%)/661 (73.1%)
Ethnicity (non-Russian/Russian/undeclared)	588 (65.0%)/309 (34.2%)/7 (0.8%)
Body height (cm)	157.5 ± 9.2
Body weight (kg)	65.8 ± 11.4
Body mass index (kg/m^2)	26.5 ± 4.5
Waist circumference (cm)	91.9 ± 11.7
Hip circumference (cm)	98.4 ± 10.9
Waist/hip circumference ratio	0.94 ± 0.09
Smoking, currently (No/Yes/undeclared)	893 (98.8%)/10 (1.1%)/1 (0.1%)
Alcohol consumption, any (No/yes)	800 (88.5%)/104 (11.5%)
Blood pressure, systolic (mm Hg)	156.6 ± 26.7
Blood pressure, diastolic (mm Hg)	79.7 ± 14.1
Arterial hypertension (No/yes)	773 (85.5%)/113 (13.1%)
Arterial hypertension, stages	3 (0–4)
Cerebrospinal fluid pressure, estimated (mm Hg)	6.5 ± 3.1
Ankle-brachial index, right	1.10 ± 0.06
Ankle-brachial index, left	1.11 ± 0.06
Metabolic syndrome (No/yes)	488 (54.0%)/373 (41.3%)
Manual dynamometry, right hand (dekaNewton)	13.7 ± 7.6
Manual dynamometry, left hand (dekaNewton)	10.6 ± 7.0
Axial length (mm) right eyes	23.1 ± 1.0
Axial length (mm) left eyes	23.1 ± 1.1
Refractive error (diopters) right eyes	−0.28 ± 3.03
Refractive error (diopters) left eyes	−0.20 ± 3.00
Intraocular pressure (mmHg), right eyes	14.5 ± 5.3
Intraocular pressure (mmHg), left eyes	14.8 ± 4.6
Pseudoexfoliation, prevalence	67 (7.4%)
Pseudoexfoliation, degree	0 (0–5)

The reference values of the independent categorical variables are presented as the first value in brackets, and the reference values of continuous variables are given as measurement unit.

Social workers visited the study participants in their homes and conducted a standardized interview with more than 300 questions on a variety of topics (Tables 1 and 2). The list of physical examinations measurement of anthropomorphic parameters, arterial blood pressure and pulse rate, and dynamometric assessment of the handgrip strength. We determined the serum concentrations of various substances and molecules in blood samples obtained under fasting conditions. The Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER statement guidelines) were applied.

The series of ophthalmological examinations performed included automated refractometry and determination of best corrected visual acuity, static perimetry, Scheimflug camera-based and slit lamp-based imaging of the anterior segment, non-contact tonometry, exploration of lens pseudoexfoliation in medical mydriasis, photography of the cornea, lens, optic nerve head and macula, spectral-domain optical coherence tomography (RS-3000, NIDEK co., Ltd., Aichi Japan) of the optic disc and macula, and sonographic determination of the axial length. The amount of pseudoexfoliation was graded into stage 1 (darker island on the lens surface in the midperiphery), stage (clear central island on the lens surface), stage 3 (minor pupillary crest abnormalities), stage 4 (major minor pupillary crest abnormalities), and stage 5 (any more severe pseudoexfoliation associated signs such as subluxation of the lens or pseudophakos). Using non-contact tonometry, we determined the IOP (Tonometer Kowa KT-800, Kowa Company Ltd., Hamamatsu City, Japan). Tonometry was twice repeated, when the readings exceeded 21 mmHg. We took the mean value of the three measurements for further analysis. If the range of the three measurements was >4 mm Hg, two additional readings were performed, the extremes on both sides of the range were dropped, and the mean of the remaining three measurements was used for the analysis. We

Table 2
Associations (univariate analysis) between intraocular pressure (mmHg) and systemic parameters in the Ural Very Old Study.

	Standardized regression coefficient beta	Non-standardized regression coefficient B	95% confidence intervals of B	*P*-value
Age (years)	0.02	0.03	−0.09, 0.14	0.67
Sex (male/female)	0.16	1.73	1.04, 2.43	<0.001
Region of habitation (urban/rural)	0.18	1.90	1.21, 2.59	<0.001
Ethnicity (non-Russian/Russian)	0.01	0.11	−0.55, 0.77	0.75
Body height (cm)	0.01	0.01	−0.03, 0.04	0.76
Body weight (kg)	−0.01	−0.003	−0.03, 0.03	0.83
Body mass index (kg/m^2)	−0.02	−0.02	−0.09, 0.06	0.65
Waist circumference (cm)	−0.07	−0.03	−0.05, 0.001	0.06
Hip circumference (cm)	−0.03	−0.01	−0.04, 0.02	0.40
Waist/hip circumference ratio	−0.06	−3.27	−6.81, 0.26	0.07
Level of education (1 (illiterate)-8 (post graduation))	−0.10	−0.22	−0.37, −0.07	0.004
Smoking, currently (no/yes)	−0.03	−1.36	−4.43, 1.72	0.39
Alcohol consumption, any (no/yes)	−0.11	−1.57	−2.54, −0.59	0.002
Diet				
Number of daily meals (unit is every one more meal)	−0.05	−0.27	−0.66, 0.12	0.17
In a week how many days do you eat fruits? (number of days)	−0.09	−0.21	−0.36, −0.06	0.006
In a week how many days do you eat vegetables? (number of days)	−0.02	−0.06	−0.26, 0.14	0.56
Physical activity				
In your leisure time, do you do any moderate intensity activities like brisk walking, cycling or swimming for at least 10 min at a time? (no/yes)	−0.11	−1.01	−1.65, −0.38	0.002
Over the past 7 days, how much time did you spend sitting or reclining on a typical day? (hours)	0.17	0.03	0.02, 0.05	<0.001
Blood examinations				
Aspartate aminotransferase (IU/L)	0.15	0.07	0.04, 0.10	<0.001
High-density lipoproteins (mmol/L)	−0.16	−0.95	−1.35, −0.55	<0.001
Low-density lipoproteins (mmol/L)	0.19	0.84	0.54, 1.15	<0.001
Triglycerides (mmol/L)	0.08	0.49	0.08, 0.90	0.02
Glucose (mmol/L)	0.07	0.19	0.01, 0.36	0.04
Creatinine (μmol/L)	−0.06	−0.01	−0.03, 0.001	0.07
Total protein (g/L)	0.14	0.09	0.04, 0.13	<0.001
Prothrombin time (%)	−0.06	−0.03	−0.07, 0.003	0.08
Systemic parameters and disorders				
Prevalence of diabetes mellitus (no/yes)	0.06	0.82	−0.09, 1.72	0.08
Blood pressure, systolic (mm Hg)	0.29	0.05	0.04, 0.06	<0.001
Blood pressure, diastolic (mm Hg)	0.25	0.08	0.06, 0.11	<0.001
Blood pressure, mean (mm Hg)	0.31	0.09	0.07, 0.11	<0.001
Arterial hypertension (no/yes)	0.13	1.85	0.93, 2.77	<0.001
Arterial hypertension, stages (0–4)	0.25	1.09	0.80, 1.38	<0.001
Cerebrospinal fluid pressure, estimated (mm Hg)	0.19	0.28	0.18, 0.38	<0.001
Ankle-brachial index, right	−0.07	−4.99	−9.94, −0.04	0.048
Ankle-brachial index, left	−0.10	−7.27	−12.2, −2.33	0.004
Metabolic syndrome (no/yes)	0.12	1.12	0.51, 1.74	<0.001
Manual dynamometry, right hand (dekaNewton)	−0.12	−0.07	−0.11, −0.03	<0.001
Manual dynamometry, left hand (deka Newton)	−0.12	−0.08	−0.13, −0.04	<0.001

The reference values of the independent categorical variables are presented as the first value in brackets, and the reference values of continuous variables are given as measurement unit.

approximated the cerebrospinal fluid pressure (CSFP) by the equation of CSFP = 0.435 × body mass index + 0.162 × diastolic blood pressure - 0.181 × age −1.91 [16]. The Guidelines for Accurate and Transparent Health Estimates Reporting were applied [17].

While the interview was conducted in the homes for all study participants, the other examinations were scheduled to be undertaken in the hospital. Some of the individuals, who were interviewed but could not go the hospital for the other assessments, were examined in their homes by portable devices.

We used a statistical software package (IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY) for the statistical analysis. The data of only one randomly chosen eye per study participant were taken for the statistical analysis. After calculation of the mean values (given as mean ± standard deviation) and the 25th quantile and 75th quantile of the IOP, univariate analyses of the relationships between IOP and other ocular and systemic factors were carried out. The ensuing multivariable linear regression analysis had IOP as dependent factor and as independent factors all those variables which were related with IOP in the univariate assessments. Independent factors with a high collinearity or which were no longer significantly associated with IOP, were dropped from the analysis in a step-wise manner. The standardized regression coefficient beta and the non-standardized regression coefficient B and its 95% confidence intervals (CIs) were calculated. All *P*-values were two-sided and regarded to be statistically significant if < 0.05.

3. Results

The present investigation consisted of 1042 individuals (68.3% from 1526 individuals who initially took part in the UVOS) (770 (73.9%) women; 272 (26.1%) men) for whom IOP readings were obtained. The cohort comprised 366 (35.1%) persons of Russian ethnicity, 454 (43.6%) Tatars, 124 (11.9%) Bashkirs, 43 (4.1%) Chuvash, 7 (0.7%) Mari, and 48 (4.6%) others. The mean age was 88.1 ± 2.7 years (median: 88 years; range: 85–99 years). The persons with IOP readings were younger (88.1 ± 2.7 years versus 88.7 ± 3.2 years; $P < 0.001$) than those without IOP measurements, while both groups did not differ in sex ($P = 0.49$). After excluding individuals with anti-glaucomatous therapy (medical therapy: n = 131 (12.6%); previous anti-glaucomatous surgery (n = 22 (2.1%)), the study population consisted of 904 participants (662 (73.2%) women) with a mean age of 88.6 ± 2.7 years (range: 85–99.9 years) and a mean axial length of 23.1 ± 1.0 mm (range: 20.47 mm–28.89 mm) (Table 1) (Fig. 1).

The mean IOP was 14.5 ± 5.1 mmHg (median: 14 mmHg; Q1: 11; Q3: 16; 95% CI: 8, 25) and 14.8 ± 4.6 mmHg (median: 14 mmHg; Q1: 12; Q3: 17; 95% CI: 8, 28) in the right eyes and left eyes, respectively (Figs. 2 and 3). The IOP readings of the right eyes and left eyes were arranged in right-sided skewed distribution with a skewness of 2.83 (standard error (SE): 0.11) and 1.12 (SE: 0.22), respectively, and a kurtosis of 20.16 (SE: 0.21) and 2.42 (SE: 0.22), respectively.

In univariate analysis, higher IOP was associated ($P < 0.10$) with various systemic and ocular factors (Tables 2 and 3). In the multivariable regression analysis, we first dropped, due to collinearity (variance inflation factor >3.0), the parameters of waist circumference (VIF: 3.2), arterial hypertension stage (VIF: 13.9), diastolic blood pressure (VIF: 4.0), and mean blood pressure (VIF: 11.6). We then dropped due to the lack of statistical significance parameters such as alcohol consumption ($P = 0.44$), serum concentrations of high-density lipoproteins ($P = 0.99$), prothrombin time ($P = 0.96$), creatinine ($P = 0.33$), low-density lipoproteins ($P = 0.57$), triglycerides ($P = 0.59$), and glucose ($P = 0.25$), left ankle-brachial index ($P = 0.52$), waist/hip circumference ratio ($P = 0.77$), spherical refractive error ($P = 0.89$), level of education ($P = 0.64$), region of habitation ($P = 0.41$), prevalence of arterial hypertension ($P = 0.52$) and metabolic syndrome ($P = 0.37$), retinal foveal thickness ($P = 0.36$), pseudoexfoliation prevalence ($P = 0.99$), number of days with fruit intake ($P = 0.13$), moderate physical activity in leisure time ($P = 0.21$), prevalence of diabetes ($P = 0.16$), systolic blood pressure ($P = 0.24$), serum concentration of aspartate aminotransferase ($P = 0.08$), right ankle-brachial index ($P = 0.22$), corneal refractive power ($P = 0.98$), anterior chamber depth ($P = 0.14$)

In the final model, higher IOP was associated (correlation coefficient r^2: 0.32) with the systemic parameters of female sex ($P < 0.001$), more sedentary lifestyle ($P = 0.006$), higher CSFP ($P < 0.001$), higher total protein serum concentration ($P < 0.001$) and higher

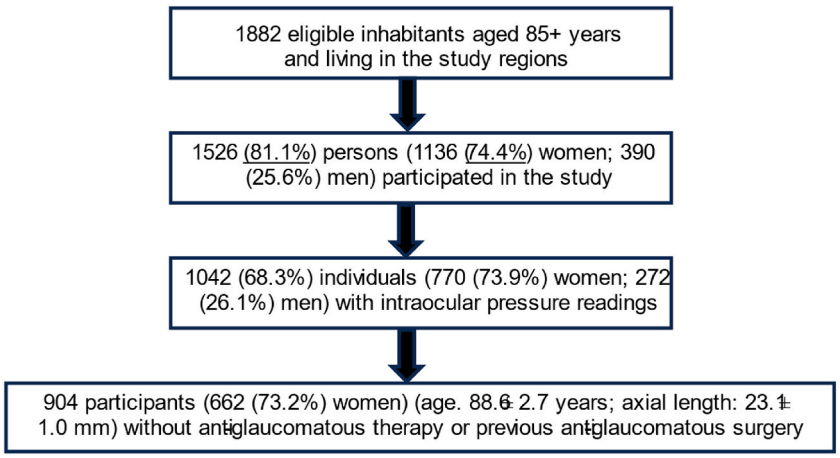

Fig. 1. Flowchart showing the selection and composition of the population of the Ural Very Old Study.

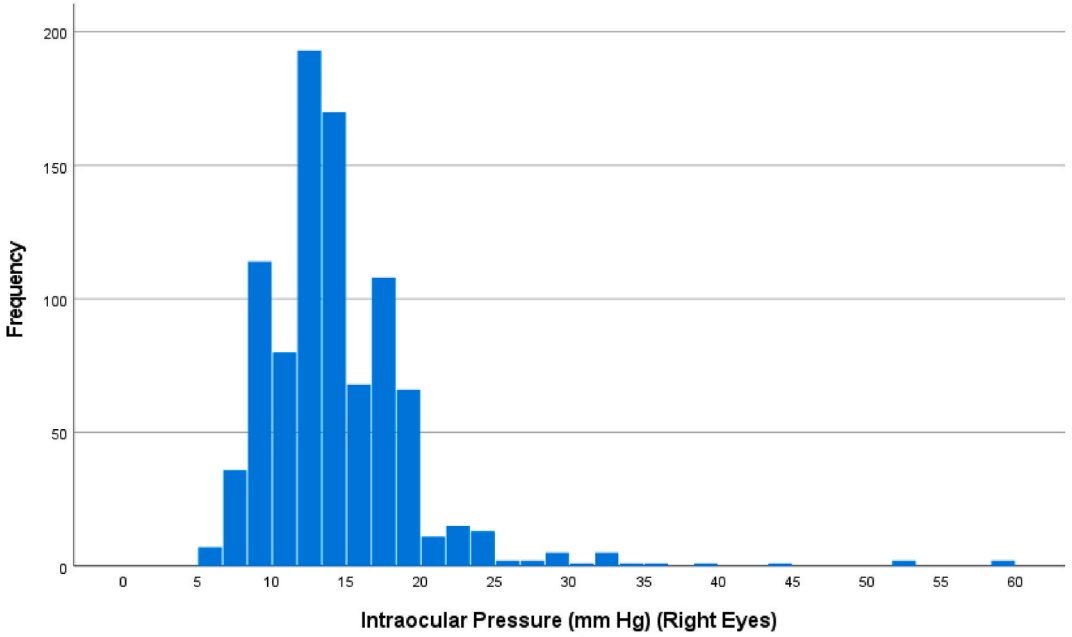

Fig. 2. Histogram showing the distribution of intraocular pressure in the right eyes in the Ural Very Old Study, after excluding eyes with anti-glaucomatous therapy.

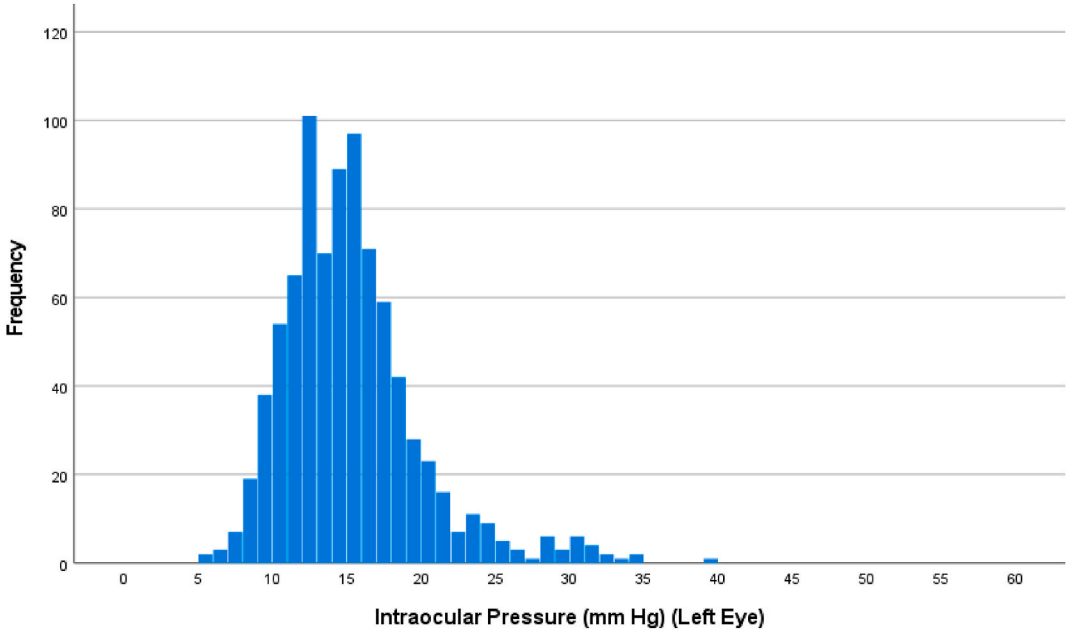

Fig. 3. Histogram showing the distribution of intraocular pressure in the left eyes in the Ural Very Old Study, after excluding eyes with anti-glaucomatous therapy.

dynamometric hand grip force ($P = 0.01$), and with the ocular parameters of thicker central cornea ($P < 0.001$), longer axial length ($P = 0.01$), absence of previous cataract surgery ($P = 0.001$), higher degree of pseudoexfoliation ($P = 0.02$), and thinner peripapillary retinal nerve fiber layer thickness ($P = 0.004$) (Table 4).

If the parameter of previous cataract surgery was replaced by anterior chamber depth, a deeper anterior chamber depth correlated with lower IOP (beta: 0.137 B: 0.69; 95%CI: 1.10, −0.28; $P = 0.001$). If the estimated CSFP was replaced by systolic blood pressure, the latter was associated with higher IOP (beta: 0.13; B: 0.02; 95%CI: 0.003, 0.04; $P = 0.02$).

In that model, the IOP measurements increased by 0.22 mmHg (95%CI: 0.09, 0.35) for each increase in estimated CSFP by 1 mmHg,

Table 3
Associations (univariate analysis) between intraocular pressure (mmHg) and ocular parameters in the Ural Very Old Study.

Parameter	Standardized regression coefficient beta	Non-standardized regression coefficient B	95% confidence intervals of B	*P*-value
Axial length (mm)	0.10	0.36	0.03, 0.69	0.03
Refractive error, spherical value (diopters)	−0.03	−0.05	−0.17, 0.08	0.46
Refractive error, spherical equivalent (Diopters)	−0.04	−0.07	−0.19, 0.05	0.26
Corneal refractive power (diopters)	−0.10	−0.24	−0.46, −0.02	0.04
Central corneal thickness (μm)	0.22	0.03	0.02, 0.04	<0.001
Anterior chamber depth (mm)	−0.15	−0.60	−0.97, −0.22	0.002
Lens thickness (mm)	0.03	0.17	−0.50, 0.84	0.63
Retinal thickness (total), fovea (μm)	−0.10	−0.005	−0.009, 0.000	0.04
Retinal Nerve Fiber Layer Thickness; peripapillary (μm)	−0.17	−0.02	−0.03, −0.01	0.002
Cataract surgery (no/yes)	−0.17	−1.62	−2.25, - 0.98	<0.001
Cataract stage (1–6)	−0.01	−0.06	−0.42, 0.30	0.74
Presence of pseudoexfoliation (no/yes)	0.14	2.22	1.14, 3.30	<0.001
Degree of pseudoexfoliation (0–5)	0.10	0.43	0.13, 0.73	0.005

The reference values of the independent categorical variables are presented as the first value in brackets, and the reference values of continuous variables are given as measurement unit.

Table 4
Associations (multivariable analysis) between intraocular pressure and systemic and ocular parameters.

	Standardized regression coefficient beta	Non-standardized regression coefficient B	95% confidence intervals of B	*P*-value	Variance inflation factor (VIF)
Sex (men/women)	0.27	2.27	1.18, 3.35	<0.001	1.77
Time spent sitting or reclining per day (hours)	0.15	0.02	0.01, 0.04	0.004	1.07
Estimated cerebrospinal fluid pressure (mm Hg)	0.17	0.22	0.09, 0.35	<0.001	1.08
Hand grip force (dekaNewton)	0.16	0.08	0.02, 0.15	0.01	1.62
Total protein serum concentration (g/L)	0.24	0.12	0.07, 0.17	<0.001	1.03
Axial length (mm)	0.13	0.56	0.13, 1.00	0.01	1.07
Central corneal thickness (μm)	0.29	0.03	0.02, 0.05	<0.001	1.01
Peripapillary retinal nerve fiber layer thickness (μm)	−0.15	−0.02	−0.03, −0.01	0.004	1.03
Pseudoexfoliation, degree (0–5)	0.12	0.40	0.06, 0.74	0.02	1.04
Status after cataract surgery (no/yes)	−0.17	−1.33	−2.12, −0.54	0.001	1.05

The reference values of the independent categorical variables are presented as the first value in brackets, and the reference values of continuous variables are given as measurement unit.

by 0.03 mmHg (95%CI: 0.02, 0.05) for each increase in central corneal thickness by 1 μm, by 0.56 mm Hg (95%CI: 0.13, 1.00) for each increase in axial length by 1 mm, and by 0.40 mm Hg (95%CI: 0.06, 0.74) for each increase in the degree of pseudoexfoliation, and it decreased by 0.40 mmHg (95%CI: 0.06, 0.74) by cataract surgery (Table 4).

4. Discussion

In this population-based study of elderly individuals, IOP showing a right-sided skew in its distribution, increased with female sex, higher estimated CSFP, thicker central cornea, longer axial length, higher prevalence and degree of pseudoexfoliation, and absence of previous cataract surgery. These observations obtained in our very old study population agree with findings made in younger populations in previous population-based investigations.

The mean IOP of 14.5 ± 5.1 mmHg found in our study population was comparable to the mean IOP reading of 14.3 ± 3.3 mm Hg found in the South Indian Chennai Study, and it was slightly higher than the values measured in other epidemiologic investigations, such as the Central India Eye and Medical Study (13.6 ± 3.4 mm Hg) and the Ural Eye and Medical Study (UEMS) (13.6 ± 3.8 mm Hg). The UEMS was performed in the same geographic area as the present investigation and included a younger cohort with an age of ≥40 years [10–13,18–20]. Differences in the mean IOP between various study populations may be related to differences between the study populations in the parameters influencing the IOP. To cite an example, the population-based mean central corneal thickness tends to decrease in direction to the equator, with higher values found in individuals of European descent, lower values in Chinese, and with the thinnest mean corneal thickness measurements obtained in South Indians and Sub-Saharan Africans [21]. In our cohort, mean central corneal thickness was 536 ± 37 μm, while it was 514 ± 33 μm in the cohort examined in rural Central India [22]. Also variations in other variables determining IOP may be effective such as variations in blood pressure, degree of obesity, age and corneal curvature.

Another potential reasons for differences in the mean IOP readings between various study populations may be differences in the measurement tool. To cite examples, in the UEMS as in the present UVOS, pneumo-tonometry was applied to record the IOP while in the Barbados Study, the Singaporean Tanjong Pagar Study and the Central India Eye and Medical Study applanation tonometry was used [8,10,21].

In our study population, higher IOP was related to a higher estimated CSFP, and if the parameter of estimated CSFP was replaced by the parameter of systolic blood parameter, the latter correlated with higher IOP (Table 4). The relationship between higher IOP and higher systolic blood pressure has been reported also for previously examined populations such as in the Tanjong Pagar Study, UK biobank study, Singapore Malay Eye Study, Blue Mountains Study, Beaver Dam Study, and Los Angeles Latino Eye Study [22–28]. In addition to systolic blood pressure, the IOP increased in our study with a higher estimated CSFP, the calculation of which was based on diastolic blood pressure, age and body mass index. A similar relationship was reported for the Central India Eye and Medical Study and the Beijing Eye Study [29,30]. With other studies having shown a positive relationship between blood pressure and CSFP, the association between IOP and (estimated) CSFP found in our study agrees with the hypothesis that arterial blood pressure, brain pressure and eye pressure are positively related to each other [29–31]. The observation of the relationship between IOP and CSFP made in our elderly study population agrees also with the result of a small-scaled interventional clinical study which showed a positive correlation between higher lumbar CSFP measurements and higher IOP [16,32]. The mechanism behind the relationship between IOP, CSFP and blood pressure has remained elusive so far. Samuels and colleagues found that stimulation of the dorsomedial and perifornical hypothalamus in rats was associated with an increase in pulse rate, arterial blood pressure, CSFP and IOP [33]. The authors considered the dorsomedial and perifornical hypothalamus as the main pathway for the regulation of the autonomic tone by the suprachiasmatic nucleus with respect to the central regulation of CSFP, blood pressure and IOP. Additionally, arterial blood pressure may play a role, influencing the CSFP and IOP in a parallel manner. An additional player may be the episcleral venous pressure, which may depend on the CSFP and which influences the IOP. In the interpretation of the findings, one should consider that the regression coefficient of the correlation IOP/estimated CSFP was relatively small (beta: 0.17 in the multivariable analysis) in our study. It shows that the IOP cannot give a clinical useful information on the CSFP. In addition, one has to consider that the results of the present study cannot be transferred to patients with a pathologically elevated CSFP or on patients with an increased IOP. In these situations, the physiological relationships between CSFP, IOP and blood pressure may no longer be valid. Interestingly, Saijadi and associates found in 50 patients with pathologically elevated CSFP that the lumbar CSFP measurements were strongly correlated with IOP [34]. Han and colleagues however did not find a significant association between CSFP and IOP in a retrospective clinical chart analysis [35].

Longer axial length was one of the determinants of IOP in our study population (Table 4). The association was statistically weak, with a beta value of 0.13. Similar results were obtained in previous epidemiological studies on younger study populations, like the Liwan Eye Study and the UK Biobank Study, in contrast to the Los Angeles Latino Eye Study which did not confirm such a relationship [23,24,36]. In experimental studies, longer axial elongation was associated with higher IOP in guinea pigs with lens-induced myopization [37].

The association between higher IOP readings and thicker central corneal thickness confirms multiple previous studies and can biomechanically be explained [38–40]. In our study population, the IOP readings decreased by 0.03 mm Hg for each increase in central corneal thickness by 1 μm (Table 4). In the UEMS, IOP decreased by 0.036 mm Hg for each increase in central corneal thickness by 1 μm [20]. In a clinical study with direct cannulation of the anterior chamber, the IOP changed by 0.4 mm Hg for a difference of 10 μm in central corneal thickness [40].

A status after cataract surgery reduced the IOP in our elderly population by 0.40 mm Hg (Table 4). It agrees with results of previous studies which revealed an IOP-reducing effect of cataract surgery. In a parallel manner, a shallower anterior chamber was associated with higher IOP in our study (if the parameter of previous cataract surgery was replaced by the anterior chamber depth in the statistical analysis). Similar results were obtained in the Singaporean Tanjong Pagar Study [41].

In contrast to previous epidemiologic investigations, age and IOP were not related with each other in our study cohort. Reason was likely the reduced range of age of the study population with a minimal age of 85 years. In the UEMS, IOP increased from an age of 40 years to an age of 70 years, and was reduced after that age [20]. In other studies, IOP increased with older age, while in studies form Japan and in the Beijing Eye Study IOP decreased with older age [9,12,22,42].

As in many clinical studies, higher IOP was associated with a higher prevalence and degree of pseudoexfoliation in our elderly study population. In a similar manner in the younger population of the UEMS, pseudoexfoliation was one of the determinants for a higher IOP [20]. That finding agreed also with many clinical studies [43]. In contrast in the Central India and Medical Study and in the Beijing Eye Study, IOP was not associated with pseudoexfoliation [44,45].

In addition to the results of the multivariable analysis, the IOP in the univariate analyses additionally associated with several other parameters such as the systemic parameters of sex, region of habitation, educational level, alcohol consumption, serum concentrations of blood lipids and glucose, blood pressure and ankle-brachial index; and with the ocular parameters of presence of pseudoexfoliation, foveal retinal thickness, anterior chamber depth, and corneal refractive error. In the multivariable analysis, these associations lost their statistical significance, either due to collinearity (such as presence of pseudoexfoliation in collinearity with the degree of pseudoexfoliation) or due to confounding effects.

Limitations of our study should be discussed. First, we used pneumo-tonometry instead of applanation tonometry for the determination of IOP. In previous studies, non-contact tonometric IOP readings differed from IOP readings obtained by applanation tonometry, in the sense of an underestimating the IOP measurements by pneumo-tonometry as compared to Goldmann applanation tonometry at lower IOP values and an overestimating of the IOP measurements by pneumo-tonometry at higher values [46]. If IOP values obtained in different population-based studies are compared with other, potential differences in the methods to measure IOP between the studies have to be taken into account. Second, the participation rate in our study was relatively low with IOP readings

from 1042 or 68.3% out of 1526 individuals of the UVOS available for the current investigation. It may be considered that the high minimal age of 85 years as inclusion criteria was associated with a high degree of multimorbidity in the eligible population, preventing them from participating in the clinical examination. In addition, the differences in age between the participants and the individuals not included into the present study, albeit being statistically significantly, might not have been clinically significant. Third, the strength of the statistical associations between IOP and its determinations was relatively low suggesting that only a part of the variability in IOP could be explained by the determinants. Fourth, the estimated CSFP values depended on the validity of the formula to calculate the CSFP. [16],[47] In a clinical study, the calculated CSFP values corresponded relatively well with CSFP values measured invasively by lumbar puncture [32]. Fifth, the present study was a cross-sectional investigation, which could explore parameters associated with the outcome parameter, i.e., the IOP; while, in contrast to ta longitudinal study, it could not explore a causal linkage between the exposures and the outcomes. Strengths of our investigations were that it is the first population-based study in ophthalmology on a population with an age of 85+ years, that the study sample size was relatively large in view of the high age of the participants, and that besides ophthalmological factors a large number of non-ocular parameters was assessed for associations with IOP.

In conclusion, in our elderly population-based study population with a minimal age of 85 years, IOP readings showed similar relationship as in younger study populations, including positive associations with higher estimated CSFP and longer axial length and a negative association with cataract surgery. The study extends the observations made in previous investigations on the age group of 85 years and older.

Data availability statement

Data will be made available on request.

Ethics statement

The study was reviewed and approved by the Ethics Committee of the Academic Council of the Ufa Eye Research Institute on 10th of August 2017 (protocol number 3). All participants (or their proxies/legal guardians) provided informed consent to participate in the study.

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Mukharram M. Bikbov: Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Gyulli M. Kazakbaeva:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ellina M. Rakhimova:** Writing – review & editing, Validation, Investigation, Formal analysis, Data curation. **Songhomitra Panda-Jonas:** Writing – review & editing, Writing – original draft, Validation, Investigation, Formal analysis, Data curation, Conceptualization. **Azaliia M. Tuliakova:** Writing – review & editing, Validation, Investigation, Formal analysis, Data curation. **Albina A. Fakhretdinova:** Writing – review & editing, Validation, Investigation, Formal analysis, Data curation. **Iulia A. Rusakova:** Writing – review & editing, Validation, Investigation, Formal analysis, Data curation. **Jost B. Jonas:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e25794.

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