

Original article

## Primary open-angle glaucoma combined with concomitant somatic pathology

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**Abstract:** The goal of the study was to assess the role of concomitant somatic pathology and calculate the total comorbidity index of primary open-angle glaucoma (POAG) in different age groups.

**Material and Methods** — The study included 624 patients (1199 eyes) with POAG aged 45 to 93 years. The control group included 161 people without glaucoma. Patients underwent a comprehensive ophthalmological examination. The Charlson comorbidity index (CI) was calculated, taking into account the concomitant somatic diseases and the age of the patients. Statistical processing of the obtained material was carried out using the IBM SPSS Statistics v.21 program with standard methods of descriptive statistics.

**Results** — with an increase in the age of POAG patients, significant growth in the number of patients with hypertension, coronary heart disease, cerebrovascular accident, atherosclerosis, degenerative diseases of the nervous system, diabetes mellitus, respiratory diseases, musculoskeletal system, and other pathologies were observed. CI was increased in POAG patients with age: 3.02 times for the old age patients, 4.2 times for very old age subjects, compared with middle-aged patients ( $p < 0.001$ ), as well as 1.42 and 1.97 times, respectively, compared with the control group ( $p < 0.001$ ).

**Conclusion** — In patients with POAG, the number of patients with hypertension, ischemic heart disease, cerebrovascular disorders, atherosclerosis, degenerative diseases of the nervous system, diabetes mellitus, respiratory diseases, musculoskeletal system disorders, and other pathologies increased significantly with age. The comorbidity index in POAG patients exhibited growth with age: 3.02 times in the old age group and 4.2 times in the group of very old age people vs. the group of middle-aged patients ( $p < 0.001$ ); and 1.42 and 1.97 times, respectively, vs. the control group ( $p < 0.001$ ).

**Keywords:** primary open-angle glaucoma, concomitant somatic pathology, Charlson comorbidity index, age groups.

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### Introduction

Currently, there is evidence that systemic factors play a specific role in the pathogenesis of primary open-angle glaucoma (POAG), exacerbating its course [1].

The main concomitant systemic diseases, primarily affecting POAG, include the pathology of the cardiovascular system: arterial hypertension, ischemic heart disease, discirculatory encephalopathy, as well as pathology of the endocrine system [2-4].

Epidemiological data indicate conflicting results of systemic hypertension's role in glaucoma development and progression [2]. Studies show that an increased prevalence of glaucoma is observed in patients with both extremes of the blood pressure range and differs in various age groups [5].

The issue of the correlation between POAG and atherosclerosis is debatable [6]. POAG and ischemic heart disease with atherosclerotic lesions of the coronary vessels from the point of view of hemodynamics may have common pathogenesis links. Several studies have revealed a significantly higher overall incidence of ischemic heart disease in the POAG group compared

with the group of people without glaucoma [7, 8]. A connection between the severity of POAG and decreased blood flow in the brain and eye vessels was found in patients with signs of cerebral insufficiency [9]. Along with this, it is believed that vascular dysregulation rather than a chronic decrease in blood flow due to atherosclerosis can lead to local vasospasm and systemic hypotension and, as a consequence, cause low perfusion pressure and insufficient blood supply to the optic nerve head [10].

The recent publications do not exhibit a clear correlation between POAG and concomitant endocrine pathology, primarily diabetes mellitus, and hypothyroidism, among patients of different age groups [3, 11].

There is evidence, though, that the presence of long-term hyperglycemia in diabetes, along with lipid metabolism disorders, may increase the risk of damage to retinal neurons as a result of metabolic stress, as well as impaired autoregulation [12, 13].

Thus, the concept of the correlation between concomitant somatic pathology and POAG can serve as a subject for further research. It is essential to study the relationship between the common POAG pathogenesis and many general somatic diseases.

It is also of interest to assess a total load of somatic pathology in POAG patients of different age groups.

Among the existing systems for assessing comorbidity in the scientific literature, the most common is the Charlson index proposed in 1987 by Professor M.E. Charlson [14]. This comorbidity index is a scoring system for assessing age and specific comorbidities. The total score includes points corresponding to comorbid diseases, and points are added for every ten years of life if the patient exceeds the age of forty.

The goal of our study was to assess the role of concomitant somatic pathology and calculate the total comorbidity index in POAG patients of different age groups.

## Material and Methods

### Study design

The study included 624 patients (1199 eyes) with POAG of various stages, aged 45 to 93 (average 64.59) years. The control group included 161 people (322 eyes) without glaucoma, comparable to patients with POAG by gender and age. The participants of the study submitted their written consent.

Each patient was considered as a separate clinical case while taking into account the data of the worst affected eye in the asymmetric course of the glaucomatous process.

All subjects were divided into three groups according to the current WHO age classification: the first with 215 (34.46%) middle-aged patients (45-59 years old), the second with 275 (44.07%) old aged patients (60-74), the third included 134 (21.47%) very old patients (75 years old and up).

All patients underwent a comprehensive ophthalmological examination, as well as had their medical documentation analyzed (outpatient records, medical history, etc.) to verify the somatic comorbidity.

### Inclusion criteria

- Primary open-angle glaucoma diagnosis (H40.1) established based on clinical, laboratory, and instrumental research methods by modern diagnostic criteria [1];
- age over 45;
- availability of physical examination results.

The participants of the study submitted their written informed consent.

### Exclusion criteria

- refractive errors (astigmatism above 2.0D, moderate and high myopia and hyperopia);
- pronounced opacity of the ocular media, pathology of the optic nerve and retina of non-glaucoma genesis;
- acute inflammatory and degenerative diseases of the organ of vision.
- acute infectious pathology, chronic diseases of internal organs in the acute stage.

### Study environment

The study was carried out at the Department of Ophthalmology with the Institute of Continuing Professional

Education course, Bashkir State Medical University, the Ministry of Healthcare of Russia, and the Laser Vision Center *Optimed*, Ufa.

The sample size was not pre-calculated. The Shapiro -Wilk test showed that the total sample of patients with POAG used in the study was distributed according to the normal distribution law.

### Basic features of patients

Among all patients with POAG, 333 were men, 444 were women. Of these, 448 (71.79%) were women, and 176 (28.21%) were men. Stage I glaucoma was diagnosed in 397 (31.81%) eyes, stage II in 624 (50%), III in 128 (10.26%), IV in 50 (4.01%).

Anamnestic and documentary evidence was collected to assess the somatic status, including the conclusion of a therapist and neurologist in the relevant medical documentation. We took into account the presence of the cardiovascular diseases: arterial hypertension (AH) (ICD-10 I11 code), ischemic heart disease (IHD) (ICD-10 I20 – I25 code), chronic cerebrovascular insufficiency (ICD-10 I65 – I68 code), atherosclerosis (ATS) (ICD-10 I70.9 code), arterial hypotension (ICD-10 I95.9 code); autonomic nervous system dysfunction (ICD-10 G90 code); degenerative diseases of the nervous system (ICD-10 G30-32 code), incl. Alzheimer's disease (ICD-10 G30 code), Parkinson's disease (ICD-10 G20 code); diabetes mellitus (DM) type I and II (ICD-10 E10-14 code); thyroid disorders (ICD-10 E00-07 code); chronic respiratory diseases (ICD-10 J00-J99 code), including bronchial asthma (ICD-10 J45 code), chronic non-specific lung diseases (ICD-10 J40-47 code), chronic bronchitis (ICD-10 J42 code); gastrointestinal tract diseases (ICD-10 K20-K31 code); musculoskeletal system disorders (ICD-10 M20-25, M30-35 code) and other pathologies.

The calculation of Charlson's comorbidity index (Charlson M.E., 1987, modified by Deyo R.A., 1992) was carried out considering concomitant somatic diseases and the age of the patients [14, 15].

### Statistical analysis

Statistical processing of the obtained material was carried out using the IBM SPSS Statistics v.21 program with standard methods of descriptive statistics calculating the reliability criterion and significance level. The sample size was not pre-calculated.

We used a t-test of means for independent samples in the absence of the assumption of dispersion equality. It was confirmed by Levene's criterion and a comparison of qualitative variables using the nonparametric chi-square criterion. The significance level in testing statistical hypotheses was assumed to be 0.05.

### Results

A comparative analysis of the concomitant somatic pathology prevalence in patients with POAG of different age groups and control groups is presented in *Table 1*.

An increase in concomitant somatic pathology was noted in the groups of patients with POAG increasing with age. This trend was most clearly observed among patients with various cardiovascular pathologies, degenerative diseases of the nervous system, and respiratory system disorders. Thus, the share of patients diagnosed with hypertension increased 1.84 times in the age group of 60-74 years and 2.09 times in the group of over 75 years compared with the middle age group of 45-59 years ( $p < 0.001$ ). The share of patients with ischemic heart disease in the old age group and the very old age group exceeded the share of

middle-aged patients by 2.76 times and 3.97 times, respectively ( $p < 0.001$ ).

The share of patients with chronic cerebrovascular diseases in the group of 60-74 years old increased 4.25 times, and 6.77 times in the group over 75 years old compared with the group of 45-59 years old ( $p < 0.001$ ). Respectively, the share of patients diagnosed with atherosclerosis increased 2.82 times in old age and 3.55 times in very old age compared with the middle-aged patients ( $p < 0.001$ ).

Among patients with cardiovascular diseases, the opposite tendency was observed in those who had arterial hypotension: the share of the old age patients and the very old age patients was lower than the share of middle-aged patients by 1.66 times and 3.42 times, respectively ( $p < 0.05$ ).

The share of patients with autonomic nervous system dysfunction in the group of 60-74 years old was 3.65 times lower than in the group of 45-59 years old ( $p < 0.05$ ). People over 75 years old did not have this diagnosis.

When assessing the prevalence of endocrine system pathology, it was noted that the share of people with diabetes exceeded the share of middle-aged patients in the old age group and very old age group ( $p < 0.001$ ) 2.18 times and 2.98 times ( $p < 0.05$ ), accordingly. A downward tendency in thyroid pathology was observed with increasing age: the share of this nosology vs.

the middle age group was 1.18 and 1.66 times less common in patients of 60-74 and over 75 years old, respectively.

We saw a significant 7.9-fold increase ( $p < 0.05$ ) in the share of degenerative diseases of the nervous system in the 60-74 years age group, and 19.48 times increase ( $p < 0.001$ ) in the group of 75 years and older, compared with the age group of 45 -59 years old.

The share of patients with respiratory system diseases in the group of 60-74 years old exhibited 1.62 ( $p < 0.05$ ) augmentation and 2.16 growth in the group over 75 years old ( $p < 0.001$ ), compared with the middle age group.

An upward tendency in digestive system diseases was observed in the old age group (1.12 times) and in the group of people over 75 years old (1.28 times), compared with the middle age group.

The share of patients with musculoskeletal system disorders exceeded the share of middle-aged patients among the old age group 3.32 times, as well as in the very old age group, and we observed a 3.51 times increase ( $p < 0.001$ ).

There was no significant difference between the indicators of concomitant somatic pathology of POAG patients in general compared with the control group.

**Table 1. Concomitant somatic pathology in the studied groups of patients with POAG depending on their age**

Somatic comorbidity	Age				Total POAG (n=624)	Control group (n=161)	Chi-square test P-level in comparison with the CG
	Middle age (n=215)	Old age (n=275)	Chi-square test P-level in comparison with the MAG	Very old age (n=134)			
Hypertension, n (%)	63 (29.3)	148 (53.82)	<0.001	82 (61.19)	293 (46.95)	72 (44.72)	0.613
Ischemic heart disease, n (%)	19 (8.83)	67 (24.36)	<0.001	47 (35.07)	133 (21.31)	30 (18.63)	0.455
Cerebrovas-cular disorders, n (%)	9 (4.19)	49 (17.82)	<0.001	38 (28.36)	96 (15.38)	19 (11.8)	0.252
Atheroscle-rosis, n (%)	28 (13.02)	101 (36.73)	<0.001	62 (46.27)	191 (30.61)	44 (27.33)	0.418
Arterial hypotension, n (%)	22 (10.23)	17 (6.18)	0.101	4 (2.99)	43 (6.89)	8 (4.99)	0.378
Autonomic nervous system disorders, n (%)	20 (9.3)	7 (2.55)	0.002	-	27 (4.33)	3 (1.86)	0.147
Diabetes mellitus, n (%)	15 (7.0)	42 (15.27)	0.005	28 (20.89)	85 (13.62)	20 (12.42)	0.691
Thyroid disorders, n (%)	24 (11.16)	26 (9.45)	0.536	9 (6.72)	59 (9.46)	12 (7.45)	0.430
Degenerative diseases of the nervous system, n (%)	1 (0.46)	10 (3.64)	0.019	12 (8.96)	23 (3.69)	3 (1.86)	0.250
Respiratory diseases, n (%)	25 (12.09)	54 (19.64)	0.017	35 (26.12)	114 (18.26)	27 (16.77)	0.659
Digestive diseases, n (%)	30 (13.95)	43 (15.64)	0.604	24 (17.91)	97 (15.54)	28 (17.39)	0.569
Musculoskeletal system disorders, n (%)	16 (7.44)	68 (24.73)	<0.001	35 (26.12)	119 (19.07)	27 (17.39)	0.504
Other disorders, n (%)	14 (6.51)	21 (7.63)	0.632	15 (11.19)	50 (8.01)	16 (9.94)	0.433

Qualitative data presented as frequencies and percentages – n (%). MAG, middle age group; CG, control group.

**Table 2. Combinations of concomitant somatic pathology in study groups**

Somatic comorbidity	Age				Total POAG (n=624)	Control group (n=161)	Chi-square test P-level in comparison with the CG	
	Middle age (n=215)	Old age (n=275)	Chi-square test P-level in comparison with the MAG	Very old age (n=134)				Chi-square test P-level in comparison with the MAG
Comorbidity not diagnosed, n (%)	71 (33)	42 (15.27)	<0.001	-	113 (18.27)	47 (29.19)	0.002	
1 comorbidity, n (%)	64 (29.76)	59 (21.45)	0.036	27 (20.15)	150 (24.04)	37 (22.98)	0.779	
2 comorbidities n (%)	51 (23.72)	60 (21.81)	0.618	29 (21.64)	140 (22.43)	27 (16.77)	0.118	
3 comorbidities n (%)	19 (8.83)	54 (19.63)	<0.001	34 (25.37)	107 (17.15)	24 (14.9)	0.497	
4 comorbidities n (%)	8 (3.72)	44 (16.0)	<0.001	27 (20.15)	79 (12.66)	16 (9.94)	0.346	
5 comorbidities n (%)	2 (0.93)	16 (5.81)	<0.001	15 (9.31)	33 (5.29)	9 (5.59)	0.880	
6 and more comorbidities n (%)	-	-	-	2 (1.49)	2 (0.32)	1 (0.62)	0.581	
Parameter	Middle age (n=215)	Old age (n=275)	t-criterion P-level in comparison with the MAG	Very old age (n=134)	t-criterion P-level in comparison with the MAG	Total POAG (n=624)	Control group (n=161)	t-criterion P-level in comparison with the CG
Comorbidity Index, M±SD	0.97±0.054	2.93±0.058	<0.001	4.07±0.068	<0.001	2.5±0.060	2.07±0.096	<0.001

Qualitative data presented as frequencies and percentages – n (%); quantitative data presented as means with its standard deviations – M±SD. MAG, middle-aged group; CG, control group.

A comparative analysis of the frequency of concomitant somatic pathology in different age groups in patients with POAG and the control group is presented in *Table 2*.

When comparing the frequency of concomitant pathology in patients with POAG by age groups, a decreasing tendency in the share of people with one and two concomitant pathologies from middle age to old age and very old age was detected. The share of patients with three concomitant pathologies increased 2.22 times in the age group of 60-74 years and 2.87 times in the group of over 75 years, compared with the age group of 45-59 years ( $p < 0.001$ ). The share of patients with four concomitant pathologies was 4.3 times and 5.42 times higher in the old age group and in the very old age group ( $p < 0.001$ ), respectively, than the share of middle-aged POAG patients with the same number of pathologies.

The share of people with POAG and five concomitant diseases increased 6.25 times in the group of 60-74 years old, 10.01 times in the group over 75 years old compared with the middle age group ( $p < 0.001$ ). Patients with POAG and six concomitant somatic diseases were found only in the age group of 75 years and older.

An increase in the comorbidity index with age was noted: 3.02 times in the old age group and 4.2 times in the very old age group, compared with the group of middle age patients ( $p < 0.001$ ); while considered against the control group, it was higher 1.42 and 1.97 times, respectively ( $p < 0.001$ ).

### Discussion

The study established a difference in the prevalence of concomitant somatic pathology among various age groups. On the one hand, as the age of POAG patients increased, the number of patients with hypertension, ischemic heart disease, cerebrovascular accident, atherosclerosis, degenerative diseases of the nervous system, diabetes mellitus, diseases of the respiratory system, musculoskeletal system, and other pathologies (from middle-aged to old and very old patients) grew statistically. On the other hand, a significant decrease in the diagnosis of arterial hypotension, thyroid pathology, and gastrointestinal tract disorder was observed in very old patients with POAG.

Several authors noted the prevalence of cardiovascular pathologies, such as A.H., IHD, DEP, ATS, among concomitant somatic diseases, autonomic and endothelial dysfunction in patients with POAG [2, 3, 7, 8].

H.C. Lin et al., when comparing the prevalence of somatic diseases in groups of patients with POAG and without glaucoma, established the following prevalence of diseases: diabetes 30.2% versus 19.5%, hypertension 50.5% versus 40.3%, congestive heart failure 6.5 % versus 5.0%, hyperlipidemia 30.5% versus 19.3%, and IHD 2.4% versus 1.9% [16].

Many studies demonstrated that changes in systemic and cerebral hemodynamics play a significant role in the ischemia progression in the tissues of the brain and eye, as well as glaucoma development and progression [9, 10]. A connection between the POAG severity and a decrease in blood flow was found in the vessels of the brain and eye [17].

The endocrine system pathology has been noted as a significant risk factor for POAG development, along with cardiovascular diseases [11, 18]. We revealed an increase in the share of diabetic patients and a decrease in the share of patients with thyroid pathology in the old age and very old age groups.

Our study identified a statistically significant increase in the comorbidity index with age when comparing the groups with each other and with the control group. Significant growth in the comorbidity index for somatic pathology in patients with POAG in different age groups was observed in the study by S.I. Makogon et al., who identified M. Charlson's comorbidity index values of 1.5 in the middle age group, 2.3 in the elderly group, and 3.4 in the very old age group [19]. Thus, the emergence of clinically associated conditions, manifested by an increase in the comorbidity index, is associated with POAG and is a natural manifestation of age-related changes.

### Conclusion

In patients with POAG, the number of patients with hypertension, ischemic heart disease, cerebrovascular disorders, atherosclerosis, degenerative diseases of the nervous system, diabetes mellitus, respiratory diseases, musculoskeletal system disorders, and other pathologies increased significantly with age.

The comorbidity index in POAG patients exhibited an upward tendency with age: 3.02 times in the old age group and 4.2 times in the group of very old age people vs. the group of middle-aged patients ( $p < 0.001$ ); and 1.42 and 1.97 times, respectively, vs. the control group ( $p < 0.001$ ).

### Limitations

The main limitation of our study is a relatively small sample size and the lack of a follow-up in POAG patients and the control group for some time. The somatic status of patients was assessed using anamnestic and documentary data, including the medical report by the therapist and other specialists within the last six months, as per medical documentation provided without using the laboratory and additional instrumental research methods to identify, confirm, or refute the established somatic pathology. This study focuses more on analyzing concomitant somatic diseases in POAG patients rather than examining some aspects of their mutual influences. However, the necessity to identify such interaction patterns in further studies is beyond any doubt.

### Conflict of Interest

Conflict of interest is not stated.

### Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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