

Table 2

Harris Hip Score (HHS) evaluation after 12 and 24 m post-OP (M \pm m, points)

	Study group, n=24		Control group, n=23	
	12m	24m	12m	24m
HHS (total)	90,6 \pm 4,67	96,47 \pm 2,8	89,38 \pm 5,97	95,09 \pm 3,22
HHS (pain)	39,13 \pm 4,58	42,43 \pm 1,99	38,95 \pm 5,42	42 \pm 2,34
HHS (static-dynamic function of the operated limb)	42,86 \pm 3,01	44,69 \pm 2,97	41,52 \pm 4,13	44,28 \pm 3,71

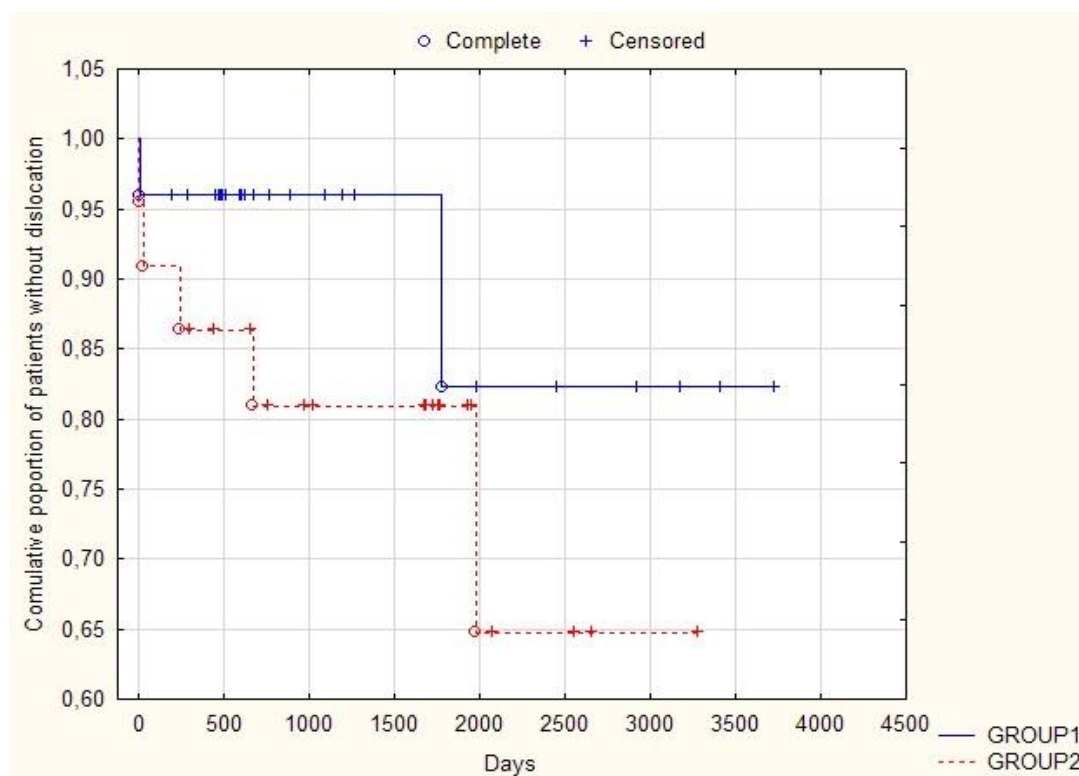


Fig.3 Graph of the cumulative proportion of patients by Kaplan-Meier survival analysis

Zakharevych G.Ye.

Assistant of the Department of Ophthalmology

Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

INFLUENCE OF VEGFA GENE POLYMORPHISMS RS2010963 AND RS699947 ON CLINICAL AND LABORATORY INDICATORS IN DIABETIC RETINOPATHY AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

Abstract. A key factor in the development of neoangiogenesis in diabetic retinopathy (DR) in patients with type 2 diabetes mellitus (DM2) is Vascular Endothelial Growth Factor (VEGF). The important role of VEGFA gene polymorphisms is highlighted by numerous studies and meta-analyses showing their association with DR, particularly with its proliferative form (PDR), which varies in different populations.

Objective. To investigate the relationship between polymorphic genotypes rs2010963 and rs699947 of the VEGFA gene and clinical signs and laboratory parameters of DR in patients with DM2 in the Ukrainian population.

The study involved 302 patients with DM2 and DR. The diagnosis was determined according to the International Clinical Classification adopted by the American Academy of Ophthalmology (2003). The control group included 98 people without DM2, DR or other ophthalmic diseases. All patients underwent cataract surgery. The level of VEGFA in intraocular fluid (IOF) collected during the surgery was measured using the enzyme-linked immunosorbent assay (ELISA) method. Analysis of polymorphic DNA loci of the VEGFA gene – rs2010963 and rs699947 – was performed by real-time polymerase chain reaction using unified TaqMan Mutation Detection Assays Thermo Fisher Scientific test systems (USA).

Analysis of the results of the study showed that the rs2010963 polymorphism influenced the level of VEGFA in IOF (maximum – in the C/C risk genotype). This polymorphism was associated with gender (C/C genotype was more common in males than females – 3:1), presence of PDR (most comm. only determined in the presence of C/C genotype – 45.4%) and neovascularization of the optic disc (most commonly determined in the presence

of G/C heterozygotes – 21.4%). The rs699947 polymorphism had an influence on visual acuity (minimum acuity – in C/C genotype), retinal thickness (maximum value – in C/C genotype), level of VEGFA in IOF (maximum level - in C/C genotype), as well as the presence of PDR and hemophthalmia (most commonly determined in the presence of C/C genotype – 44.7% and 27.7%, respectively).

The pathogenic influence of C/C risk genotype of rs2010963 polymorphism was more commonly detected in males, was realized due to the high level of VEGFA in IOF and was manifested by the maximum frequency of PDR. The pathogenic influence of C/C risk genotype of rs699947 polymorphism was also realized due to the high level of VEGFA in IOF, caused decreased visual acuity, retinal thickening and was manifested by the maximum frequency of PDR and vitreous hemorrhage.

Key words: *diabetic retinopathy, VEGFA gene polymorphisms; rs2010963; rs699947*

INTRODUCTION. In Ukraine, as elsewhere in the world, the number of patients with diabetes mellitus (DM) is increasing every year [1, 2]. Every year, screening tests for DM identify 3–4 patients with DM diagnosed for the first time for every previously identified patient with DM [2, 3]. The main complications of DM include retinopathy, lesions of renal vessels and lower extremities [4, 5].

As there is currently an epidemic of DM, the problem of diabetic retinopathy (DR) is one of the priorities in ophthalmology [4, 6–8]. During the first ten years of DM, the incidence of DR increased from 20 to almost 50% [2]. The risk factors for the development of DR include hyperglycemia, hypertension, hyperlipidemia [5–7].

Recent studies have shown that the development of DR depends not only on the level and duration of hyperglycemia, but also on genetic factors, since even with severe glycemic control, retinal lesions are observed in a certain proportion of patients with type 2 DM [9, 11, 12]. A key factor in the development of neoangiogenesis in patients with DR is Vascular Endothelial Growth Factor (VEGF). The importance of VEGFA and the defining role of genetic polymorphisms affecting its gene expression have been highlighted by numerous studies, meta-analyses [11–14] and advanced overview by P. Priscakova et al. [15]. A meta-analysis undertaken by Lu Yan et al. indicates the presence of the association of two VEGFA gene polymorphisms, rs2010963 and rs699947, varying in different populations [16].

The objective of this study was to investigate the influence of polymorphic genotypes rs2010963 and rs699947 of the VEGFA gene on clinical and laboratory parameters of DR in patients with DM2.

MATERIALS AND METHODS. The study was conducted at the Department of Ophthalmology of Danylo Halytsky Lviv National Medical University. All studies were conducted in compliance with the principal provisions of the Convention of the Council of Europe on Human Rights and Biomedicine, the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (1964, as subsequently amended, including 2000 version) and the Order of the Ministry of Healthcare of Ukraine No. 690 as of September 23, 2009.

A total of 302 people were involved in this study. The diagnosis was determined according to the International Clinical Classification adopted by the American Academy of Ophthalmology (2003). The

control group included 98 people without DM2, DR or other ophthalmic diseases. All patients underwent cataract surgery.

The ophthalmological examination included visometry, Goldmann tonometry, static perimetry with the Humphrey Field, Carl Zeiss (Germany), biomicroscopy with Haag-Streit BQ 900 slit lamp (Switzerland), gonioscopy, ophthalmoscopy with contact and noncontact lenses (Volk Optical, USA), seven-field fundus photography according to ETDRS protocols, and fluorescence angiography with the Topcon TRC NW7 SF RTVue (Optovue, USA). The best corrected visual acuity (BCVA, units) and intraocular pressure (IOP, mm Hg) were determined. Beside, the optical coherence tomography (OCT) was used to measure the central retinal thickness (CRT, μm) and central retinal volume (CRV, mm^3). fundus camera (Japan), spectral domain optical coherence tomography with Optovue A sample of intraocular fluid (IOF) was collected by anterior chamber paracentesis before phacoemulsification cataract surgery by aspiration of 0.05–0.1 ml of fluid with a 1.0 ml disposable syringe (Hemoplast, Etalon+, Ukraine). The level of VEGFA in IOF was measured by ELISA (enzyme-linked immunosorbent assay) technique using commercial eBioscience Thermo Fisher Sci (USA) test systems. All samples were two-fold diluted and the results were expressed in pg/ml.

Analysis of polymorphic DNA loci of the VEGFA gene - rs2010963 and rs699947 - was performed by real-time polymerase chain reaction (PCR) using unified TaqMan Mutation Detection Assays Thermo Fisher Scientific test systems (USA).

The clinical results were statistically processed with the SPSS 11.0, MedStat (Yu.Ye. Liakh, V.H. Guryanov, 20042012), MedCalc (MedCalc Software bvba, 1993–2013) software package. In all cases, the significance level was set at 0.05.

The influence of polymorphic genotypes rs2010963 and rs699947 of the VEGFA gene, taking into account the nonnormal data distribution, was assessed using the ANOVA on ranks test (Kruskal – Wallis ANOVA by ranks). This method tests the null hypothesis for equality of median values across the comparable groups using ranks of original scores. Cross-tabulation tables and the Pearson Chi-square criterion with Yates correction were used for similar evaluation of qualitative variables. The influence of each of the polymorphisms on the quantitative and qualitative variables of patients with DR was analyzed separately.

RESULTS. As evidenced by data in Table 1, the age of patients did not differ between the group of different genotypes of the VEGFA gene polymorphism rs2010963 ($p = 0.83$). The duration of DM in minor homozygote C/C carriers was longer than that of ancestral homozygote G/G and heterozygote G/C carriers (5 and 4 years, respectively), but this trend was not statistically significant ($p = 0.14$). The blood glucose level in C/C risk genotype carriers was statistically

significantly higher ($p = 0.04$) 1.8 times than in G/G genotype carriers and 1.6 times than in G/C genotype carriers. The level of glycated hemoglobin (HbA1c) in C/C risk genotype carriers was also higher, but this discrepancy was not statistically significant ($p = 0.19$). Considering the indicators of the best corrected visual acuity, IOP, CRT and CRV, no statistically significant differences between carriers of different genotypes were detected ($p > 0.05$ for all indicators).

Table 1

Influence of polymorphic genotypes rs2010963 of the VEGFA gene on quantitative indicators

Indicators	Me (QI-QIII)			H	P
	G/G, n = 92	G/C, n = 89	C/C, n = 22		
Age, years	66.0 (62.0-73.0)	66.0 (60.0-72.0)	65.0 (61.0-75.0)	0.38	0.83
Duration of diabetes, years	6.0 (4.0-11.0)	7.0 (3.0-12.0)	11.0 (6.0-14.0)	3.87	0.14
Blood glucose, mmol / L	7.9 (6.7-9.7)	8.1 (6.5-10.0)	9.6 (8.1-10.5)	6.40	0.04
HbA1c, %	7.7 (6.9-8.90)	7.8 (7.1-9.1)	8.3 (7.7-9.0)	3.33	0.19
BCVA, units	0.6 (0.3-0.8)	0.7 (0.2-0.9)	0.7 (0.1-0.9)	0.84	0.66
IOP, mm Hg	18.0 (16.0-19.0)	16.0 (15.0-19.0)	16.0 (14.0-19.0)	5.79	0.06
CRT, μ m	275.0 (230.0-352.0)	265.0 (245.0-350.0)	256.5 (222.0-317.0)	1.85	0.39
CRV, mm3	7.1 (5.9-7.7)	6.9 (6.3-7.9)	6.8 (5.9-8.0)	0.41	0.81
VEGFA, pg/ml	643.5 (545.5-824.0)	1003.0 (825.0-1432.0)	1712.0 (1520.0-1950.0)	102.9	< 0.001

Remarks: n – number of observations; Me – median value; QI and QIII – 1st and 3rd quartiles of data samples, respectively; H – Kruskal - Wallis test ANOVA by ranks; p – statistical significance of differences compared to the null hypothesis (accepted at $p < 0.05$).

The level of VEGFA in IOF ($x_2 = 102.9$; $p < 0.001$) had the highest degree of genotype dependence and was highest in C/C risk genotype carriers. It was 2.7 times higher than in ancestral G/G genotype carriers and 1.6 times higher than in heterozygous G/C genotype carriers.

Table 2 presents the analysis of the influence of VEGFA gene polymorphism rs2010963 on qualitative parameters. It was found that the ancestral G/G genotype and the heterozygous G/C genotype were

more frequent among females (76.1 and 68.5%, respectively) than males (23.9 and 31.5%, respectively), while the homozygous C/C genotype was more frequent among males (72.7%) than females (27.3%). These differences were highly significant ($x_2 = 19.4$; $p = 6.2e-05$). Therefore, it has been established that C/C risk genotype was predominantly common to males.

This study has not revealed any dependence of macular edema development on VEGFA gene polymorphism rs2010963 ($p = 0.26$).

Table 2

Influence of polymorphic genotypes rs2010963 of the VEGFA gene on qualitative indicators

Indicators		n (f, %)			X ²	P
		G/G, n = 92	G/C, n = 89	C/C, n = 22		
Sex	M	22 (23.9)	28 (31.5)	16 (72.7)	19.36	6.2e-05
	F	70 (76.1)	61 (68.5)	6 (27.3)		
Macular edema	No (0)	42 (45.6)	40 (44.9)	14 (63.6)	2.65	0.26
	Yes (1)	50 (54.3)	49 (55.1)	8 (36.4)		
Presence of PDR	No (0)	73 (79.3)	54 (60.7)	12 (54.5)	9.52	0.01
	Yes (1)	19 (20.6)	35 (39.3)	10 (45.4)		
Optic disc neovascularization	No (0)	84 (91.3)	63 (70.8)	20 (90.9)	14.32	7.8e-04
	Yes (1)	8 (8.7)	26 (29.2)	2 (9.1)		
Neovascularization elsewhere	No (0)	75 (81.5)	64 (71.9)	14 (63.6)	4.08	0.13
	Yes (1)	17 (18.5)	25 (28.1)	8 (36.4)		
Vitreous hemorrhage	No (0)	84 (91.3)	70 (78.6)	16 (72.7)	7.52	0.02

	Yes (1)	8 (8.7)	19 (21.4)	6 (27.3)		
Vitreous neovascularization	No (0)	88 (95.6)	79 (88.8)	18 (81.8)	5.30	0.07
	Yes (1)	4 (4.4)	10 (11.2)	4 (18.2)		

Remarks: *n* – number of observations; *f* – frequency in% corresponding to *n*; χ^2 – Pearson Chi-square criterion with Yates correction; *p* – statistical significance of differences (accepted at $p < 0.05$).

The proliferative diabetic retinopathy (PDR) was more common in C/C risk genotype carriers (45.4%) as compared to G/G genotype carriers (20.6%) and G/C genotype carriers (39.3%), which had statistical significance ($\chi^2 = 9.52$; $p = 0.01$). The optic disc neovascularization (ODN) hardly differed between homozygous genotypes and was more common in heterozygous genotype carriers - 29.2%, versus 8.7 and 9.1% for G/G and C/C genotypes, respectively ($\chi^2 = 14.32$; $p = 7.8e-04$). Vitreous hemorrhage was more common in G/C (21.4%) and C/C (27.3%) genotypes as compared to G/G genotype (8.7%), which was statistically significant ($\chi^2 = 7.52$; $p = 0.02$). Neovascularization elsewhere and vitreous neovascularization did not depend significantly on the presence of one or the other genotype ($p = 0.13$ and $p = 0.07$, respectively).

Thus, polymorphic genotype rs2010963 of the VEGFA gene influenced the glycemic level and the VEGFA level in IOF, which were maximal in the presence of C/C risk genotype. In addition, this genotype was more common in males and caused the development of PDR and vitreous hemorrhage. The heterozygous G/C genotype occurred more often in the presence of optic disc neovascularization. As shown in Table 3, the age of patients and duration of DM in the presence of different polymorphic genotypes rs699947

of the VEGFA gene did not differ ($p = 0.31$ and $p = 0.07$, respectively).

It is important to point out that duration of DM in minor homozygote A/A carriers was the shortest – up to one year in both cases. Indirectly, this could confirm the presence of a protective effect in this genotype, which was revealed earlier.

Indicators of carbohydrate metabolism, blood glucose and HbA1c level, did not differ significantly between the carriers of different polymorphic genotypes rs699947 of the VEGFA gene ($p = 0.54$ and $p = 0.33$, respectively). When considering the ophthalmic indicators, the BCVA was higher in carriers of the projective A/A genotype ($\chi^2 = 6.27$; $p = 0.04$), whereas the CRV was lower than in other genotypes ($\chi^2 = 5.83$; $p = 0.005$). It has to be taken into account that there were only two such patients, and the CRV did not differ significantly in the C/C and C/A genotypes: 6.9 mm³ (QI-QIII - 6.4-8.2) and 7.0 mm³ (QI-QIII — 6.1-7.8), respectively.

The strongest influence of VEGFA gene polymorphism rs699947 was observed in the level of VEGFA in IOF ($\chi^2 = 33.0$; $p = 3.5E-13$), which was highest in ancestral C/C risk genotype carriers. It was 3.4 times higher than in minor A/A genotype carriers and 1.8 times higher than in heterozygous C/A genotype carriers.

Table 3

Influence of polymorphic genotypes rs699947 of the VEGFA gene on quantitative indicators

Indicators	Me (QI—QIII)			H	p
	C/C, n = 47	C/A, n = 154	A/A, n = 2		
Age, years	65.0 (60.0-69.0)	66.0 (61.0-74.0)	68.5 (68.0-69.0)	2.34	0.31
Duration of DM, years	8.0 (3.0-13.0)	7.0 (4.0-11.0)	1.0 (1.0-1.0)	5.33	0.07
Blood glucose, mmol / L	8.1 (7.0-9.6)	8.2 (6.5-10.2)	6.8 (6.7-6.8)	1.21	0.54
HbA1c, %	8.3 (7.4-9.0)	7.7 (6.8-8.8)	8.9 (8.9-9.0)	2.15	0.33
BCVA, units	0.5 (0.1-0.8)	0.6 (0.3-0.9)	0.9 (0.9-0.9)	6.27	0.04
IOP, mm Hg	17.0 (15.0-19.0)	17.0 (15.0-19.0)	17.0 (16.0-18.0)	0.37	0.83
CRT, μ m	275.0 (249.0-363.0)	267.5 (234.0-350.0)	223.0 (221.0-225.0)	2.97	0.22
CRV, mm ³	6.9 (6.4-8.2)	7.0 (6.1-7.8)	5.2 (5.1-5.2)	5.83	0.05
VEGFA, pg/ml	1524.0 (820.0-1809.0)	824.5 (627.0-984.0)	445.5 (440.0-451.0)	32.98	3.5E-13

Remarks: *n* – number of observations; *Me* – median value; *Q_I* and *Q_{III}* – 1st and 3rd quartiles of data samples, respectively; *H* – Kruskal - Wallis test ANOVA by ranks; *p* – statistical significance of differences compared to the null hypothesis (accepted at $p < 0.05$).

Table 4 presents the analysis of the influence of VEGFA gene polymorphism rs699947 on qualitative parameters. It was found that genotype had no significant influence on sex, macular edema and PDR ($p = 0.16$, $p = 0.26$ and $p = 0.06$, respectively).

When considering ophthalmic indicators, significant differences in disposition of patients were

detected only in respect to vitreous hemorrhage, which was more often detected in the presence of ancestral C/C risk genotype (27.7%) than in the presence of heterozygous C/A genotype (13.0%; $\chi^2 = 6.07$; $g = 0.04$). As to the other neovascularization indicators, no significant difference in genotype distribution was found ($p > 0.05$).

Table 4

Influence of polymorphic genotypes rs699947 of the VEGFA gene on qualitative indicators						
Indicators		n (f, %)			X2	p
		C/C, n = 47	C/A, n = 154	A/A, n = 2		
Sex	M	20 (42.5)	46 (29.9)	0 (0.0)	3.61	0.16
	F	27 (57.5)	108 (71.1)	2 (100.0)		
Macular edema	No (0)	20 (42.6)	74 (48.0)	2 (100.0)	2.69	0.26
	Yes (1)	27 (57.4)	80 (52.0)	0 (0.0)		
Presence of PDR	No (0)	26 (55.3)	111 (72.1)	2 (100.0)	5.61	0.06
	Yes (1)	21 (44.7)	43 (27.9)	0 (0.0)		
Optic disc neovascularization	No (0)	35 (74.5)	130 (84.4)	2 (100.0)	2.88	0.24
	Yes (1)	12 (25.5)	24 (15.6)	0 (0.0)		
Neovascularization elsewhere	No (0)	34 (72.3)	117 (76.0)	2 (100.0)	0.92	0.63
	Yes (1)	13 (27.7)	37 (24.0)	0 (0.0)		
Vitreous hemorrhage	No (0)	34 (72.3)	134 (87.0)	2 (100.0)	6.07	0.04
	Yes (1)	13 (27.7)	20 (13.0)	0 (0.0)		
Vitreous neovascularization	No (0)	43 (91.5)	140 (90.9)	2 (100.0)	0.21	0.90
	Yes (1)	4 (8.5)	14 (9.1)	0 (0.0)		

Remarks: n – number of observations; f – frequency in% corresponding to n; x² – Pearson Chi-square criterion with Yates correction; p – statistical significance of differences (accepted at p < 0.05).

In order to increase the reliability of the assessment of influence of genotypes rs2010963 and rs699947 of VEGFA gene on quantitative and qualitative indicators of patients with DR in conditions of abnormal data distribution, regression models belonging to the class of generalized linear models were applied.

The analysis based on their use is less critical to the parameters of the normality and homogeneity of

variance in variation series. Qualitative and quantitative data of patients with DR were used as dependent variables in the analysis. The corresponding indicator values of VEGFA genotypes after over-parameter transformations were used as independent variables. The results of this analysis are presented in Table 5.

Table 5

Influence of the polymorphic genotypes rs2010963 and rs699947 of the VEGFA gene on quantitative and qualitative indicators (based on the results of regression analysis)

Indicators	rs2010963		rs699947	
	W	p	W	p
Age, years	0.40	0.84	1.32	0.25
Duration of diabetes, years	3.76	0.15	0.33	0.57
Blood glucose, mmol / L	1.14	0.56	0.19	0.66
HbA1c, %	1.17	0.56	1.59	0.21
BCVA, units	0.44	0.80	6.01	0.01
IOP, mm Hg	2.63	0.27	0.37	0.54
CRT, μ m	1.73	0.42	7.39	0.01
CRV, mm ³	1.61	0.45	1.38	0.74
VEGFA, pg/ml	216.04	< 0.001	73.24	1,1E-16
Gender	21.01	2.3E-05	3.42	0.06
Macular edema	1.88	0.39	1.02	0.31
Presence of PDR	7.61	0.02	6.04	0.01
Optic disc neovascularization	8.39	0.01	3.08	0.08
Neovascularization elsewhere	3.96	0.14	0.47	0.49
Vitreous hemorrhage	4.97	0.08	6.52	0.04
Vitreous neovascularization	3.91	0.14	2.5e-05	0.99

Remarks: W – Wald criterion; p – statistical significance of differences compared to the null hypothesis (accepted at p < 0.05).

Discussion. The results obtained correspond to those found by F.B. Vailati et al. demonstrating the increased incidence of ophthalmic and retinal diseases

and increased VEGFA gene expression in genotype containing the C-allele (C/C or G/C) of polymorphism rs2010963 in patients who did not have DM [17]. That

is, these genotypes caused the increased VEGFA gene expression, whereas, in our studies, they caused increased levels of VEGFA in IOF. Research by C.F. Chen et al. revealed a higher frequency of G/C and C/C risk genotypes of polymorphism rs2010963 in patients with DR as compared to patients with DM2 without retinopathy ($p = 0.0205$). In addition, it revealed 1.6-2 times higher VEGFA gene expression and probably higher VEGFA level in the presence of the C-allele [18].

The regression analysis showed statistically significant influence of VEGFA gene polymorphism rs2010963 on the level of VEGFA in IOF ($x_2 = 216.0$; $p = < 0.001$), sex ($x_2 = 21.0$; $p = 2.3E-05$), PDR ($x_2 = 7.6$; $p = 0.02$) and optic disc neovascularization ($x_2 = 8.39$; $p = 0.01$). The remaining indicators had no significant influence that is fundamentally in line with the results presented in Table 1 and 2. The exceptions are indicators of blood glucose level and genotype distribution of patients with vitreous hemorrhage; the regression analysis did not confirm the association of these indicators with polymorphic genotypes rs2010963 of the VEGFA gene.

With regard to polymorphism rs699947, the regression analysis showed a statistically significant influence on the following indicators: BCVA ($x_2 = 33.0$; $p = 3.5E-13$), CRT ($x_2 = 7.4$; $p = 0.01$), VEGFA level in IOF ($x_2 = 73.2$; $p = 1.1E-16$), as well as the presence of PDR ($x_2 = 6.0$; $p = 0.01$) and vitreous hemorrhage ($x_2 = 6.5$; $p = 0.04$). At the same time, the figures given in Table 3 show that differences in CRT values among genotypes were not statistically significant ($p = 0.22$), while the results of regression analysis confirmed the genotype influence on this indicator. The data presented in Table 4 also did not confirm the statistical significance of differences in the number of patients with PDR ($p = 0.06$) among genotypes, while the regression analysis showed the influence of genotypes on this indicator.

Similar results were achieved by researchers [19] who found an increased level of VEGFA in blood serum of patients with DR as compared to the control group and it was more expressed in carriers of C/C genotype of rs2010963.

The strongest influence of VEGFA gene polymorphism rs699947 was observed in the level of VEGFA in IOF ($x_2 = 33.0$; $p = 3.5E-13$), which was highest in ancestral C/C risk genotype carriers. It was 3.4 times higher than in minor A/A genotype carriers and 1.8 times higher than in heterozygous C/A genotype carriers.

Similar results were obtained in a study by X. Fan et al. (2014) that showed an increase in serum VEGFA level in patients with DR, which was more expressed in carriers of C/C genotype than in carriers of C/A genotype of polymorphism rs699947 [19].

CONCLUSIONS. The study has proven the influence of rs2010963 polymorphism on the level of VEGFA in IOF (C/C risk genotype had the maximum level) and its association with gender (C/C risk was more common in males than females - 3: 1), presence of PDR (most frequently determined with the presence

of the C/C risk genotype: 45.4%) and optic disc neovascularization (most frequently determined in the presence of the G/C risk genotype: 21.4%). Thus, the pathogenic influence of C/C risk genotype of this polymorphism was more commonly detected in males, was realized due to the high level of VEGFA in IOF and was manifested by the maximum frequency of PDR.

With regard to polymorphism rs699947, the study has proven the influence of genotype on the BCVA (minimum visual acuity was in C/C genotype), CRT (maximum value was in C/C genotype), level of VEGFA in IOF (maximum level was in C/C genotype), as well as the presence of PDR and (most frequently vitreous hemorrhage determined in the presence of C/C genotype – 44.7% and 27.7%, respectively). Thus, the pathogenic influence of C/C risk genotype of this polymorphism was also realized due to the high level of VEGFA in IOF, caused decreased visual acuity, retinal thickening and was manifested by the maximum frequency of PDR and vitreous hemorrhage.

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Bahtiyar .N. Aliev

*Scientific-Research Cardiology Institute named after J.Abdullayev
Main Clinical Hospital of the Armed Forces of Azerbaijan Republic*

THE RELATIONSHIP BETWEEN THYROID GLAND FUNCTION AND THE RESULTS OF CORONARY ANGIOGRAPHY

Abstract. The aim of this study was the investigation of the relationship between functional changes of heart undergoing coronary angiography and functional condition of thyroid gland in patients with ischemic heart disease. 101 patients with ischemic heart disease were undergone coronary angiography. The plasma levels of low density lipoproteins, triglycerids and thyroid stimulating hormone and alternations in echocardiography were included to the trial. In addition, all patients were divided into two subgroups dependent on sex and TSH level, in which LDL and TG levels were compared. According to the results of coronary angiography the levels TSH, LDL and TG were different and its relationship with constricted coronary arteries were established.

Keywords: *thyroid gland function, hypotireosis, hipertireosis, coronary angiography, thyroid stimulating hormone, low density lipoproteins, triglycerids.*

Thyroidal gland diseases is the second most commonly endocrine disease in the world after diabetes mellitus[1]. Hormones secreted by the gland are considered to be important modifiers of metabolism. Thyroid hormones have the ability to affect the synthesis, mobilization and fragmentation of lipids, and the effects of the fragmentation are far superior to the synthesis effects [2]. As a result, thyroid dysfunction, in particular hypothyroidism, is associated with dyslipidemia, which increases the risk of endothelial dysfunction, arterial hypertension, and cardiovascular disease. Thyroidal hormones have numerous effects on the cardiovascular system, including effects on the ability of heart contraction, electrophysiological functions and cardiac structure [3, 4, 5]. In addition, vascular tone, lipid levels and oxygen administration are also dependent on thyroid status. Due to heart contraction, thyroid hormones stimulate the systolic contraction frequency and strength and the frequency of diastolic emptying [5].

Electrophysiological effects can be demonstrated by increased tachycardia in hyperthyroid patients and the occurrence of tachycardia in calmness. Continuous activation of elevated thyroid hormones also accelerates heart protein synthesis and leads to the development of concentric hypertrophy [6, 7]. When the hyperthyroid status passes to the euthyroid status, the heart's hypertrophy also reverts to normal heart configuration. Increased thyroid hormone activity also leads to decreased tone of the muscle tissue in arterial vessels and, ultimately, a reduction in heart afterload [8]. Thyroid hormones are also not ineffective in the lipid spectrum. Hypothyroidism leads to an increase in cholesterol levels, as the LDLP (**Low-density lipoprotein**) is due to a decrease in its excretion and increased levels [9, 10].

Taking into consideration all these statements, the evaluation of the thyroid status in patients with ischemic cardio disease is of great importance. Given that Azerbaijan is an endemic zone for iodine