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Analysis of the risk factors impact on the life quality of patients with arterial hypertension

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Objective. Recently, multicomponent quality-of-life indicators have become increasingly important in monitoring the health status of patients with hypertension and evaluating the effectiveness of treatment. Improving patient quality of life is considered one of the key objectives of the medical intervention.

Methods. To assess the quality of life of patients with, we used the standardized SF-36 (Short Form-36 Health Survey) questionnaire, which allows to explicitly examine the respondent physical and psycho-emotional status.

Results. We analyzed the association between polymorphisms of endothelial nitric oxide (NO) synthase (eNOS) (NOS3, T786C) and angiotensin II receptor type 1 (AGTR1, A1166C) genes and quality of life. Patients with polymorphisms associated with lower intravascular pressure had lower baseline QoL scores, particularly on the "physical functioning" and "general health" scales ($p<0.05$). Patients with heterozygous or homozygous "unfavorable" genotypes (AGTR1_CC, NOS3_CC) have significantly lower total indicators of both physical and psycho-emotional health compared to patients with "better" genotypes (AA, TT) and the control group.

Conclusion. Patients with polymorphisms that cause reduced bioavailability of NO or excessive activation of AGRT1 show a significant deterioration in quality of life on all key SF-36 scales. This indicates the significant role of genetic factors in shaping the subjective perception of health in patients with arterial hypertension.

Keywords: life quality, arterial hypertension, genetic polymorphism, endothelial nitric oxide synthase, angiotensin II receptor type 1

Arterial hypertension is a serious global problem for healthcare systems around the world. According to the World Health Organization (WHO), more than 1.28 billion people suffer from high blood pressure with nearly 46% of them unaware of their condition. The highest incidence of hypertension is found in low- and middle-income countries where public awareness and access to treatment remain inadequate (Alifer 2019; Pidruchna et al. 2024a,b).

In Europe, according to the latest guidelines from the European Society of Cardiology (ESC),

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hypertension occurs in 30–45% of adults and in 60–70% of people over 60.

Ukrainian indicators are largely consistent with European trends; according to the Ministry of Health, up to one-third of the adult population has high blood pressure, but only about 50% receive treatment and only one-third of them achieve the desired results. In rural areas, the situation is complicated by low access to medical services and irregular medication intake, which reduces the effectiveness of hypertension control (Trevisol et al. 2011; Kandasamy et al. 2023).

Recently, multicomponent quality-of-life indicators have become increasingly important in monitoring the health status of patients with hypertension and evaluating the effectiveness of treatment (Pezzilli et al. 2007; Oparil et al. 2018; Mills et al. 2020).

The aim of this study was to investigate the association between the quality of life and clinical manifestations of arterial hypertension.

Material and Methods

Study population. We examined 86 patients with arterial hypertension who were undergoing treatment and examination in the therapeutic department of the Kozova Central District Hospital (Ternopil, Ukraine). Written informed consent to participate in the study was obtained from all patients. During the experiment, measures were taken to ensure patient safety, respect for their rights, human dignity, and the moral and ethical standards set forth in the World Medical Association's Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects (1964–2000), the Council of Europe Convention on Human Rights and Biomedicine (dated 04.04.1997), Order No. 281 of the Ministry of Health of Ukraine dated 01.11.2000, Declaration of Helsinki "World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects" (2001), and the Code of Ethics for Scientists of Ukraine (2009).

A total of 86 people aged 45 to 76 (47 women and 39 men) participated in the study. The average age of participants was 61.35±13.3 years. Depending on the prescribed complex drug treatment, patients were randomly divided into two groups. The first group included 43 people who took a fixed combination of valsartan and amlodipine. The second group included 43 patients whose complex treatment regimen included a drug based on a fixed combination of olmesartan and amlodipine. Thirty individuals without signs of hypertension formed the control group including 17 women and 13 men.

The effectiveness of antihypertensive therapy was assessed according to domestic and European criteria of cardiology and hypertension societies after 6 months of treatment. The endpoints of treatment were: achieving target blood pressure levels, reducing left ventricular myocardial hypertrophy, and improving patient quality of life.

Inclusion and exclusion criteria. The criterion for inclusion in the study was the presence of essential hypertension stage II, grade 1–3. The diagnosis of hypertension was established in accordance with orders No. 54 and 384 of the Ministry of Health of Ukraine, the recommendations of the Ukrainian Association of Cardiologists for the prevention and treatment of arterial hypertension, and the recommendations of the European Society of Cardiology (ESC), based on anamnestic data, complaints, and physical and clinical-instrumental examination data.

The exclusion criteria were stage III hypertension (history of myocardial infarction and/or stroke), secondary hypertension, any heart defects, rhythm and conduction disorders, NYHA functional class III–IV heart failure, as well as severe comorbidities (chronic obstructive pulmonary disease, diabetes mellitus, chronic kidney disease, oncological and mental disorders).

Quality-of-life indicators. To assess the quality of life in patients with arterial hypertension, we used the standardized SF-36 (Short Form-36 Health Survey) questionnaire, which allows for a comprehensive examination of the respondent physical and psycho-emotional status (Ware et al. 1992). The questionnaire includes 36 questions grouped into eight domains: 1) physical functioning (PF); 2) role physical functioning (RP); 3) pain intensity (BP); 4) general health (GH); 5) vitality (VT); 6) social functioning (SF); 7) role emotional functioning (RE); 8) mental health (MH).

Each scale is scored from 0 to 100 with higher scores indicating a better quality of life. To simplify interpretation, two additional summary scales were calculated: a) PCS (Physical Component Summary) – physical component of quality of life and b) MCS (Mental Component Summary) – psycho-emotional component of quality of life. The summary scales were calculated as the arithmetic means of the corresponding four domains (PCS: PF, RP, BP, GH; MCS: VT, SF, RE, MH).

Life quality was assessed twice: 1) before the start of antihypertensive therapy and 2) after completion of treatment with fixed combinations: valsartan with amlodipine and olmesartan with amlodipine.

Results

The clinical and anamnestic characteristics of the study participants are shown in Table 1. A family history of early development of cardiovascular disease (CVD) (for men <55 years, for women <65 years) was found in 47 patients (54.7%). At the time of inclusion in the study, 27 people (31.4%) were active smokers and 11 subjects (12.8%) abused alcohol. Thirty patients (34.9%) were obese. Among the patients examined, 19 (22.1%) had stage I hypertension and 67 (77.9%) had stage II hypertension.

According to the WHO classification, all patients were divided into three age groups: middle age (45–59 years), elderly (60–74 years), and senile (over 75 years) ones. The distribution of patients by age groups is shown in Table 2. Overall, 54.7% of women and 45.3% of men participated in the study.

Most patients had stage 2 hypertension (55%) with an almost equal distribution of patients with stage 1 and stage 3 hypertension, 24% and 21%, respectively.

Among patients with A1166C polymorphism of angiotensin II receptor type 1 (AT1R) gene (AGTR1), the number of individuals with AA, AC, and CC genotypes was 18, 38, and 30, respectively, and for the T786C polymorphism of the endothelial nitric oxide synthase (eNOS) gene (*NOS3*), the distribution of patients was as follows: 24 with the TT genotype, 31 with the TC genotype, and 31 with the CC genotype. Systolic and diastolic blood pressure (SBP and DBP, respectively) levels in patients depending on the detected gene polymorphism of the studied genes are presented in Table 3. At the time of inclusion in the study, 63 patients (73%) were receiving regular antihypertensive therapy. The target blood pressure level was achieved in 43% of patients who were continuously taking antihypertensive drugs.

In order to comprehensively assess the clinical course of arterial hypertension and study the influence of genetic polymorphisms on the subjective perception of health, a study of the quality of life of patients was conducted using the SF-36 questionnaire. We analyzed the relationship between the NOS3 T786C and AGTR1 A1166C polymorphisms and quality of life. Patients with polymorphisms associated with poorer vascular tone had lower baseline QoL scores, particularly on the "physical functioning" and "general health" scales ($p<0.05$) (Tables 4 and 5).

Next, we analyzed the physical and mental components of health and formed summary indicators (Table 6). These data clearly illustrate that patients with heterozygous or homozygous "unfavorable" genotypes (**AGTR1_CC**, **NOS3_CC**) have significantly lower total indicators of both physical and psycho-emotional health compared to patients with "better" genotypes **(AA**, **TT**) and the control group ($p<0.05$). The lowest physical functioning (PF) scores were recorded in carriers of the AGTR1 CC genotype (47.1±2.3 points) and NOS3 CC genotype (51.4±2.6 points). Patients with CC genotypes also had the worst results in terms of mental health: vitality (VT) in the AGTR1 CC group was 35.9±2.5 points and in the NOS3 CC group 41.2±1.9 points. The total physical

Table 1
Characteristics of the patients examined (n=86)

Variable	Value
Average age (years)	61.35±13.3*
Men [n (%)]	39 (45.3)
Women [n (%)]	47 (54.7)
Duration of illness (years)	12.6
Average BMI (kg/m^2)	32.6±1.1*
Obesity (BMI > 30 kg/m^2) [n (%)]	30 (34.9)
Smoking [n (%)]	27 (31.4)
Alcohol abuse [n (%)]	11 (12.8)
Family history of early development of CVD (for men <55 years, for women <65 years), [n (%)]	47 (54.7)

*Data are presented as mean±SD. Abbreviations: BMI – body mass index; CVD – cardiovascular disease.

Table 2
Distribution of patients by age in the study groups

Age	Years	Group 1 (n=43) VAL+AML		Group 2 (n=43) OLM+AML		Total (n=86)	
		n	%	n	%	n	%
Middle	45–59	24	55.8	27	62.8	51	59.3
Elderly	60–74	14	32.6	10	23.2	24	26.7
Senile	>75	5	11.6	6	14.0	11	14.0

Abbreviations: AML – amlodipine; OLM – olmesartan; VAL – valsartan.

(PCS) and mental (MCS) health indices were significantly lower in carriers of unfavorable genotypes (CC) than in carriers of "favorable" genotypes (AA, TT): for AGTR1_CC, PCS was 54.5±1.9 points and MCS was 47.1±2.2 points; for NOS3_CC, PCS was 57.6±1.7 points and MCS was 50.9±1.4 points ($p<0.05$).

Patients with polymorphisms associated with reduced NO bioavailability or hyperactivation of the AT1R have a poorer quality of life on all major SF-36 scales. This indicates that genetic background significantly influences the subjective perception of health in patients with arterial hypertension.

Table 3
Distribution of patients by blood pressure level and detected polymorphism

Group	Genotype	n	SBP (mmHg)	DBP (mmHg)
Control	–	30	122.63±2.36	75.90±1.53
AGTR1 A1166C	AA	18	138.00±2.73	85.00±1.96
	AC	38	148.50±2.66	89.75±1.69
	CC	30	159.00±1.52	109.96±1.39
NOS3 T786C	TT	24	141.00±1.90	90.00±1.72
	TC	31	147.30±2.10	93.28±2.30
	CC	31	162.50±1.90	107.25±2.80

Data are presented as mean±SD; n – number of participants. Abbreviations: AGTR1 – angiotensin II receptor type 1 gene; NOS3 – endothelial nitric oxide synthase gene; DBP – diastolic blood pressure; SBP – systolic blood pressure.

Discussion

In order to comprehensively assess the clinical course of arterial hypertension and study the influence of genetic variations on the subjective perception of one's own health, a study of the quality of life of patients was conducted using the standardized SF-36 questionnaire. This validated tool allows characterizing the physical and psycho-emotional state of the patient on eight scales: physical functioning, role physical functioning, pain, general health, vitality, social functioning, role emotional functioning, and mental health. The total score ranges from 0 to 100 points, with higher scores indicating a better quality of life.

The study analyzed the relationship between NOS3 T786C and AGTR1 A1166C polymorphisms and quality-of-life indicators. Patients with genetic variants associated with impaired vascular tone had lower baseline scores on the physical functioning and general health scales ($p<0.05$). In particular, individuals with heterozygous or homozygous "unfavorable" variants of the genotypes (AGTR1_CC, NOS3_CC) showed significantly worse overall indicators of both physical and psycho-emotional health compared to patients with "favorable" genotypes (AA, TT) and the control group ($p<0.05$). The lowest physical functioning scores were recorded in carriers of CC genotypes of AGTR1 and NOS3:

Table 4
Physical health component scores on the SF-36 questionnaire in patients (n=86) with arterial hypertension depending on gene polymorphism

Group	Genotype	n	Indicators (points)			
			PF	RP	BP	GH
Control		30	87.3±0.9	95.1±1.3	88.4±3.8	71.2±2.1
AGTR1 A1166C	AA	18	65.2±2.8 p<0.05	74.7±1.5 p<0.05	72.5±2.6 p<0.05	65.4±2.1 p<0.05
	AC	38	54.3±2.3 p<0.05	69.2±2.1 p<0.05	64.5±1.7 p<0.05	59.8±1.3 p<0.05
	CC	30	47.1±2.3 p<0.05 p_1<0.05	62.3±1.9 p<0.05 p_1<0.05	59.2±2.2 p<0.05 p_1<0.05	49.5±2.1 p<0.05 p_1<0.05
NOS3 T786C	TT	24	68.2±2.5 p<0.05	77.4±1.4 p<0.05	74.1±1.7 p<0.05	66.3±2.4 p<0.05
	TC	31	61.4±2.9 p<0.05	70.2±1.2 p<0.05	66.6±2.7 p<0.05	57.2±2.2 p<0.05
	CC	31	51.4±2.6 p<0.05 p_1<0.05	65.3±2.2 p<0.05 p_1<0.05	62.4±2.5 p<0.05 p_1<0.05	51.4±2.9 p<0.05 p_1<0.05

Data are presented as mean±SD; n – number of participants; p – a statistical significance compared to the control group; p_1 – a statistical significance compared to homozygotes for a particular gene (AA, TT). Abbreviations: AGTR1 – angiotensin II receptor type 1 gene; NOS3 – endothelial nitric oxide synthase gene; BP – pain intensity; GH – general health; PF – physical functioning; RP – role physical functioning.

Table 5
Mental health scale scores according to the SF-36 questionnaire in patients (n=86) with arterial hypertension depending on gene polymorphism

Gene	Genotype	n	Indicators (points)			
			VT	SF	RE	MH
Control	–	30	64.2	75.8±2.2	77.7±2.1	58.5±2.1
AGTR1 A1166C	AA	18	51.4±3.1 p<0.05	69.4±2.5 p<0.05	65.4±3.2 p<0.05	51.4±1.7 p<0.05
	AC	38	42.5±1.8 p<0.05	63.8±2.4 p<0.05	61.5±2.7 p<0.05	44.2±2.3 p<0.05
	CC	30	35.9±2.5 p<0.05 p_1 <0.05	57.7±2.1 p<0.05 p_1<0.05	55.2±2.2 p<0.05 p_1<0.05	39.5±1.8 p<0.05 p_1<0.05
NOS3 T786C	TT	24	54.5±2.7 p<0.05	71.5±1.9 p<0.05	69.8±2.7 p<0.05	56.1±2.1 p<0.05
	TC	31	44.4±2.3 p<0.05	66.8±2.2 p<0.05	67.4±2.2 p<0.05	51.1±3.2 p<0.05
	CC	31	41.2±1.9 p<0.05 p_1<0.05	59.3±3.2 p<0.05 p_1<0.05	60.5±1.5 p<0.05 p_1<0.05	42.7±2.3 p<0.05 p_1<0.05

Data are presented as mean±SD; n – number of participants; p – a statistical significance compared to the control group; p_1 – a statistical significance compared to homozygotes for a particular gene (AA, TT). Abbreviations: AGTR1 – angiotensin II receptor type 1 gene; NOS3 – endothelial nitric oxide synthase gene; MH – mental health; RE – role emotional functioning; SF – social functioning; VT – vitality.

47.1±2.3 points and 51.4±2.6 points, respectively. In terms of mental health, the lowest vitality scores were also observed among patients with CC genotypes of AGTR1 and NOS3: 35.9±2.5 and 41.2±1.9 points, respectively. The overall physical and mental health indices were statistically significantly lower in the group of carriers of unfavorable variants (CC) compared to carriers of favorable alleles for AGTR1_CC: PCS 54.5±1.9; MCS 47.1±2.2; for NOS3_CC: PCS 57.6±1.7 points; MCS 50.9±1.4 points (p<0.05).

Thus, patients with polymorphisms that cause reduced bioavailability of NO or excessive activation of the AT1R show a significant deterioration in quality of life on all key SF-36 scales. This indicates the significant role of genetic factors in shaping the subjective perception of health among patients with arterial hypertension.

Summary. The use of the SF-36 questionnaire allowed for a comprehensive assessment of the quality of life of patients with hypertension in terms of physical and psycho-emotional components. A reliable relationship was established between the presence of unfavorable genetic polymorphisms (AGTR1 A1166C and NOS3 T786C) and reduced quality-of-life indicators, in particular on the scales of physical functioning, general health, vitality, and mental health. Patients with homozygous CC genotypes (AGTR1_CC and NOS3_CC) have significantly lower total physical (PCS) and mental (MCS) health indices compared to carriers of favorable genotypes (AA, TT) and members of the control group. Genetic variations associated with reduced NO bioavailability or increased AT1R activity negatively affect the subjective perception of health status in patients with arterial hypertension. The results confirm the important role of genetic background in individualizing approaches to assessing and correcting the quality of life of patients with hypertension.

Table 6
Summary indicators of physical (PCS) and mental (MCS) health components on the SF-36 scale

Group	Genotype	n	PCS (points)	MCS (points)
Control	–	30	85.5	69.0±2.1
AGTR1 A1166C	AA	18	69.4±2.3	59.4±2.4*
	AC	38	62.0±1.7*	53.0±1.8*
	CC	30	54.5±1.9**	47.1±2.2**
NOS3 T786C	TT	24	71.5±2.2	63.0±2.5*
	TC	31	63.8±2.4	57.4±2.0*
	CC	31	57.6±1.7**	50.9±1.4**

Data are presented as mean±SD; n – number of participants; *p<0.05 compared to the control group; **p<0.05 compared to homozygotes for a single gene (AA, TT). Abbreviations: AGTR1 – angiotensin II receptor type 1 gene; NOS3 – endothelial nitric oxide synthase gene.

Conclusion. This study demonstrated a significant association between genetic polymorphisms of the AGTR1 (A1166C) and NOS3 (T786C) genes and quality-of-life indicators in patients with arterial hypertension. Carriers of unfavorable homozygous CC genotypes exhibited significantly lower scores across key SF-36 domains, particularly physical functioning, general health, vitality, and mental health, compared to individuals with favorable genotypes (AA, TT) and the control group ($p<0.05$).

The presence of genetic variants associated with reduced nitric oxide bioavailability or enhanced angiotensin II receptor activity was linked to poorer physical and psycho-emotional health status. Patients with AGTR1_CC and NOS3_CC genotypes had significantly decreased Physical Component Summary (PCS) and Mental Component Summary (MCS) indices, indicating a substantial negative impact of genetic background on subjective health perception.

These findings confirm the important role of genetic factors in modulating the clinical course and patient-reported outcomes in arterial hypertension. Assessment of AGTR1 and NOS3 polymorphisms may contribute to a more personalized approach to risk stratification, therapeutic decision-making, and quality-of-life optimization in hypertensive patients.

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