UDC 575.174.015.3+616.1-008.4-092-05-053.7+577.121
DOI: 10.56871/RBR.2025.20.71.004

THE ROLE OF THE *SIRT1* GENE POLYMORPHISM IN THE DEVELOPMENT OF VASCULAR TONE DISORDERS AND OVERWEIGHT IN YOUNG PEOPLE

© Elizaveta V. Razumova, Anastasia S. Vorozheikina, Lyubov A. Avtaikina, Kira Yu. Pankina, Artyom V. Ryzhov, Tatiana I. Vlasova

Ogarev National Research Mordovian State University. 68 Bolshevistskaya str., Saransk Republic of Mordovia 430005 Russian Federation

Contact information: Tatiana I. Vlasova — Doctor of Medical Sciences, Professor, Head of the Department of Normal and Pathological Physiology, Chief Researcher of the Department of Faculty Surgery with courses in Topographic Anatomy and Operative Surgery, Urology and Pediatric Surgery. E-mail: vlasova-t.i@mrsu.ru ORCID: https://orcid.org/0000-0002-2624-6450 SPIN: 5314-3771

For citation: Razumova EV, Vorozheikina AS, Avtaikina LA, Pankina KYu, Ryzhov AV, Vlasova TI. The role of the *SIRT1* gene polymorphism in the development of vascular tone disorders and overweight in young people. Russian Biomedical Research. 2025;10(2):30–40. DOI: https://doi.org/10.56871/RBR.2025.20.71.004

Received: 08.04.2025 **Revised: 22.05.2025** **Accepted: 24.06.2025**

Abstract. ***Introduction.*** Cardiovascular and metabolic diseases are the most common diseases in the world, and their association with genetic factors such as polymorphisms of the *SOD2* (superoxide dismutase), *SIRT* (sirtuins) and *eNOS* (endothelial nitric oxide synthase) genes is becoming increasingly apparent. ***Objectives to study*** the relationship between the frequency of alleles of the *SIRT1* (C/G polymorphism, rs7069102), *eNOS* (C/G polymorphism, rs7069102) and *SOD2* (T/C polymorphism, rs4880) genes and the formation of vascular tone disorders, as well as the functional state of the cardiovascular system in young people, depending on the gene polymorphism. Materials and methods. Assessment of the functional state of the cardiovascular system in young people. Sampling and genetic examination of venous blood for polymorphisms of the *SIRT1*, *eNOS*, and *SOD2* genes. Statistical data processing using the StatTech software version 4.7.2. ***Results.*** The study showed that in young people in the Republic of Mordovia, the carriage of the G allele of the *SIRT1* C/G gene, rs7069102 is associated with increased average daily blood pressure and stress index. Polymorphism of the *SOD2* gene (TT (T/C, rs4880)) is significantly more common in the carriage of *SIRT1* (GG, (C/G, rs7069102)). ***Conclusion.*** We established relationship between the polymorphisms of the *SOD2* (TT) and *SIRT1* (GG) genes, which is associated with changes in the functional state of the cardiovascular system in young people. Further studies with larger samples are needed to clarify the role of the *SIRT1* mutation as a risk factor for vascular tone disorders.

Keywords: gene polymorphism, oxidative stress, metabolic disorders, cardiovascular risk

DOI: 10.56871/RBR.2025.20.71.004

РОЛЬ ПОЛИМОРФИЗМА ГЕНА *SIRT1* В РАЗВИТИИ НАРУШЕНИЙ СОСУДИСТОГО ТОНУСА И ИЗБЫТОЧНОЙ МАССЫ ТЕЛА У МОЛОДЕЖИ

© Елизавета Валерьевна Разумова, Анастасия Сергеевна Ворожейкина, Любовь Алексеевна Автайкина, Кира Юрьевна Панькина, Артем Владимирович Рыжов, Татьяна Ивановна Власова

Национальный исследовательский Мордовский государственный университет имени Н.П. Огарёва. 430005, г. Саранск, ул. Большевистская, д. 68, Республика Мордовия, Российская Федерация

Контактная информация: Татьяна Ивановна Власова — д.м.н., профессор, заведующая кафедрой нормальной и патологической физиологии, главный научный сотрудник кафедры факультетской хирургии с курсами топографической анатомии и оперативной хирургии, урологии и детской хирургии. E-mail: vlasova-t.i@mrsu.ru ORCID: https://orcid.org/0000-0002-2624-6450 SPIN: 5314-3771

Для цитирования: Разумова Е.В., Ворожейкина А.С., Автайкина Л.А., Панькина К.Ю., Рыжов А.В., Власова Т.И. Роль полиморфизма гена *SIRT1* в развитии нарушений сосудистого тонуса и избыточной массы тела у молодежи. Российские биомедицинские исследования. 2025;10(2):30–40. DOI: https://doi.org/10.56871/RBR.2025.20.71.004

Поступила: 08.04.2025 **Одобрена: 22.05.2025** **Принята к печати: 24.06.2025**

Резюме. ***Введение.*** Сердечно-сосудистые и метаболические заболевания представляют собой наиболее распространенные заболевания в мире, и их связь с генетическими факторами, такими как полиморфизмы генов *SOD2* (супероксиддисмутаза), *SIRT* (сиртуины) и *eNOS* (эндотелиальная синтаза оксида азота), становится все более очевидной. ***Цель*** — изучение связи между частотой встречаемости аллелей генов *SIRT1* (полиморфизм C/G, rs7069102), *eNOS* (полиморфизм C/G, rs7069102) и *SOD2* (полиморфизм T/C, rs4880) и формированием нарушений сосудистого тонуса, а также функционального состояния сердечно-сосудистой системы у молодых людей в зависимости от полиморфизма генов. ***Материалы и методы.*** Оценка функционального состояния сердечно-сосудистой системы у молодых лиц. Забор и генетическое исследование венозной крови на полиморфизм генов *SIRT1*, *eNOS*, *SOD2*. Статистическая обработка данных с использованием программы StatTech версии 4.7.2. ***Результаты.*** Исследование показало, что у молодых людей в Республике Мордовия носительство аллеля G гена *SIRT1* C/G, rs7069102 ассоциировано с повышенным среднесуточным уровнем артериального давления и индекса стресса. Полиморфизм гена *SOD2* (TT (полиморфизм T/C, rs4880)) достоверно чаще встречается при носительстве *SIRT1* (GG (C/G, rs7069102). ***Вывод.*** Установлена связь между полиморфизмами генов *SOD2* (TT) и *SIRT1* (GG), что сопряжено с изменением функционального состояния сердечно-сосудистой системы у молодых людей. Необходимы дальнейшие исследования с более крупными выборками для уточнения роли мутации *SIRT1* как фактора риска нарушений сосудистого тонуса.

Ключевые слова: полиморфизм генов, оксидативный стресс, метаболические нарушения, сердечно-сосудистый риск

INTRODUCTION

Human sirtuins (SIRT) are NAD+-dependent deacetylating enzymes characterized by their similarity to the yeast precursor Sir2 (silent information regulator) [1]. Seven sirtuins (SIRT1–SIRT7) have been identified in humans and other mammals. Sirtuins belong to class III histone deacetylases, which are characterized by the presence of a highly conserved NAD+-dependent catalytic core domain consisting of 250–270 amino acid residues. According to research, sirtuins play a role in a large number of physiological processes, from gluconeogenesis to cell cycle regulation. The scientific community's interest in these enzymes has been growing recently, as they may become potential targets for the treatment of many diseases [2, 3].

FEATURES OF SIRTUINS AND THEIR BIOLOGICAL ROLE

Sirtuin 1 (SIRT1) is currently the most studied human sirtuin. It most closely resembles yeast SIR2 in terms of amino acid sequence and enzymatic activity. It is localized in the nucleus but can move to the cytoplasm to act on specific targets. Initially described as a histone deacetylase, it was soon discovered that SIRT1 can also deacetylate other proteins [3, 4]. SIRT1 is involved in the control of reactive oxygen species generation, ketogenesis, and cell death.

SIRT2 is located in the cytoplasm. It deacetylates tubulin microtubules and transcription factors that move from the cytoplasm to the nucleus, and mainly functions during mitosis. When DNA damage occurs, SIRT2 can stop cell division, effectively protecting the cell from incorrect replication. In addition, there is evidence that SIRT2 also has anti-inflammatory effects.

SIRT3, SIRT4, and SIRT5 are mitochondrial enzymes. SIRT3 regulates various mitochondrial functions, such as the production of adenosine triphosphate (ATP). The metabolic effects of SIRT3 on carbohydrate and lipid metabolism are similar to those of SIRT1 (e.g., stimulation of gluconeogenesis, inhibition of lipogenesis, activation of fatty acid oxidation, and some neuroprotective effects) [5, 6].

Table 1

Localization and enzymatic activity of sirtuins [7]

Таблица 1

Локализация и ферментативная активность сиртуинов [7]

Сиртуин / Sirtuin	Класс / Class	Локализация / Localization	Ферментативная активность / Enzymatic activity	Функции / Functions
SIRT1	I	Ядро, цитозоль / Nucleus, cytosol	Деацетилирование / Deacetylation	Обмен веществ, защита от свободных радикалов и стресса, регуляция воспаления / Metabolism, protection from free radicals and stress, regulation of inflammation
SIRT2	I	Цитозоль / Cytosol	Деацетилирование / Deacetylation	Регуляция митоза (защита от ошибочной репликации), противовоспалительное действие / Regulation of mitosis (protection against erroneous replication), anti-inflammatory effect
SIRT3	I	Митохондрии / Mitochondria	Деацетилирование / Deacetylation	Выработка АТФ, регуляция активных форм кислорода, кетогенез, апоптоз / ATP production, regulation of reactive oxygen species, ketogenesis, apoptosis
SIRT4	II	Митохондрии / Mitochondria	АДФ-рибозилирование / ADP-ribosylation	Обмен веществ, в частности регуляция секреции инсулина / Metabolism, in particular regulation of insulin secretion
SIRT5	III	Митохондрии / mitochondria	Деацетилирование, демалонилирование, десукцилинирование/ Deacetylation, demalonylation, desuccination	Метаболизм глутамина и жирных кислот регулирует гомеостаз АТФ / the metabolism of glutamine and fatty acids regulates ATP homeostasis
SIRT6	IV	Ядро / Nucleus	Деацетилирование, АДФ-рибозилирование / Ddeacetylation, ADP-ribosylation	Репарация ДНК, метаболизм, секреция TNF / DNA repair, metabolism, TNF secretion
SIRT7	IV	Ядрышко / Nucleolus	Деацетилирование / Deacetylation	рРНК транскрипция / rRNA transcription

Unlike other sirtuins, SIRT4 is a mitochondrial sirtuin that does not possess deacetylase activity *in vitro.* SIRT4 is believed to be involved in many important processes, particularly in the metabolism of glutamine and fatty acids, and also regulates ATP homeostasis.

In addition to its deacetylase activity, recent studies have shown that SIRT5 can mediate the desuccinylation, demalonylation, and deglutarylization of proteins.

SIRT6 is a nuclear protein, although it is also present in the endoplasmic reticulum, where it deacetylates TNFα. Recent studies have shown that SIRT6 also interacts with other non-histone proteins.

SIRT7 is the only sirtuin localized in the nucleolus. It is a component of the RNA polymerase I transcription mechanism. Presumably, SIRT7 regulates DNA transcription in mammalian cells by interacting with RNA polymerase I and histones. In addition, SIRT7 may mediate histone desuccinylation [2].

Sirtuins are divided into classes (I–IV) depending on the structure of their amino acid sequence, similarity in functional properties and localization in cells, as well as their common evolutionary origin (Table 1).

Sirtuins have attracted considerable attention from researchers over the past decade due to their potential to control fat and carbohydrate metabolism. Sirtuins modulate a number of cellular processes involved in maintaining glucose homeostasis in tissues such as muscle, liver, and pancreas. Sirtuins influence glucose and lipid metabolism in several tissues. SIRT1 inhibits adipogenesis in adipocytes. SIRT1 increases insulin secretion in the pancreas. SIRT1 attenuates glycolysis and enhances lipid utilization in skeletal muscle and liver.

Obesity is a known risk factor for cardiovascular disease and is often associated with impaired fat and carbohydrate metabolism. An Asian-Pacific cohort study of the adult population found a 9% increase in the incidence of coronary heart disease for each unit of body mass index (BMI) [8].

Excess weight and obesity are a global problem not only for patients but also for doctors of all specialties. According to Rosstat statistics for 2022, more than 419,000 new cases of obesity were identified in the Russian Federation, which is 10% more than in 2021 [9].

Currently, the search for genetic risk factors for various diseases is actively continuing, which is also relevant for obesity. In particular, researchers have identified a link between a tendency to dyslipidemia and the G allele of the rs7069102 polymorphism of the *SIRT1* gene. It has been proven that the GG genotype had higher levels of low-density lipoproteins (LDL) and cholesterol than CG and CC [10].

Interestingly, SIRT1 plays a dual and contradictory role in gluconeogenesis. On the one hand, SIRT1 can suppress glucose production for liver by deacetylating one of the transcription factors, which leads to a subsequent decrease in the transcription of gluconeogenic genes. On the other hand, SIRT1 can also stimulate the gluconeogenic transcriptional program [11].

It is believed that, unlike SIRT1, SIRT2–4 support gluconeogenesis, for example during energy deficiency. In particular, SIRT2 deacetylates and increases the stability of one of the gluconeogenic enzymes. In addition, SIRT3 and SIRT4 can regulate gluconeogenesis from amino acids. Further research is obviously needed to fully understand the role of sirtuins in regulating gluconeogenesis.

Mice studies have demonstrated that when energy is restricted, SIRT3 suppresses glycolysis, promotes fatty acid oxidation, protects against ROS, and increases ketone body formation. Based on *in vitro* studies, SIRT3 stimulates cellular respiration in brown adipocytes [10].

Recent studies have provided insight into the role of various sirtuins in glycolysis. It has been established that SIRT1 is involved in controlling glycolysis by activating an enzyme that weakens the transcription of glycolytic genes. In addition, SIRT1, SIRT3, and SIRT6 suppress a transcription factor that inhibits glucose oxidation [12].

When these observations are combined, SIRT1, SIRT3, and SIRT6 inhibit glycolysis and stimulate mitochondrial fatty acid oxidation. This discovery is particularly interesting because tumor cells are highly dependent on glycolysis, known as the Warburg effect. Consequently, this transition from glycolysis to oxidative metabolism, induced by sirtuin activators, may contribute to their antitumor activity [13, 14].

CInsulin secretion is closely linked to blood glucose levels through a complex signaling pathway. SIRT1 has been shown to induce glucose-stimulated insulin secretion by increasing the yield of ATP produced by glucose oxidation. This is achieved by suppressing the transcription of uncoupling protein 2 (UCP2), which uncouples mitochondrial ATP production during oxidative phosphorylation. Thus, SIRT1 deficiency leads to high levels of UCP2 and decreased insulin secretion [10].

SIRT4 appears to inhibit insulin secretion, as SIRT4 deficiency increases amino acid-stimulated insulin secretion.

Thus, SIRT1 and SIRT4 control insulin secretion in opposite directions in response to feeding and calorie restriction. Although elucidation of the underlying mechanisms is ongoing, current results suggest the existence

of a network of sirtuins to maintain proper insulin secretion.

Insulin is known to promote triglyceride synthesis in the liver and triglyceride accumulation in the gastrointestinal tract (GIT) during feeding, whereas glucagon and adrenaline stimulate lipolysis in the GIT and fatty acid oxidation in other tissues during nutrient restriction.

Fatty acid synthesis occurs in the cytosol, where acetyl-CoA, produced as a result of catabolic processes, and malonyl-CoA are used as substrates for the production of fatty acids, catalyzed by fatty acid synthase. A key transcription factor controlling the expression of genes involved in lipid synthesis is the liver X receptor (LXR). SIRT1 increases the transcriptional activity of LXR126. Therefore, activation of SIRT1 could theoretically increase fatty acid synthesis. However, SIRT1 also deacetylates the lower target of LXR, destabilizing it, which leads to the suppression of fatty acid synthesis. Consequently, SIRT1-mediated activation of LXR appears to target cholesterol metabolism rather than triglyceride synthesis. SIRT6 is also involved in the control of fatty acid synthesis [15, 16].

SIRT1 stimulates fatty acid oxidation and oxidative phosphorylation in response to fasting. An experiment showed that activation of SIRT1 protects mice from diet-induced obesity by increasing the rate of fatty acid oxidation. SIRT3, SIRT4, and SIRT6 have also been shown to regulate fatty acid oxidation in the liver. As discussed above, SIRT3 deacetylates and activates a key enzyme involved in the oxidation of long-chain fatty acids. In contrast, SIRT4 appears to be a negative regulator of fatty acid oxidation, while SIRT6 has been reported to stimulate the expression of genes involved in fatty acid oxidation, although the exact mechanism is unclear [12].

THE ROLE OF SIRTUINS IN THE DEVELOPMENT OF CARDIOVASCULAR DISEASE

The impact of sirtuins on cardiovascular disease is a big focus of research, and SIRT1 keeps getting special attention. There's a bunch of evidence showing it plays a role in aging and oxidative stress, which makes it a potential link in the pathogenesis of many diseases [16].

Ageing is associated with an increasing level of free radicals, which contributes to inflammatory processes and damage of the endothelial lining of blood vessels. Endothelial cell aging is the result of several mechanisms, such as DNA damage, telomere shortening below a critical length, and mitochondrial dysfunction accompanied by accumulation of reactive oxygen species. Although aging cells are quiescent from a replicative point of view, they are metabolically active and have a specific secretory profile consisting of secreted cytokines, chemokines, growth factors, and proteases, which have a pro-inflammatory effect. SIRT1, SIRT3, and SIRT6 can suppress inflammation and oxidative stress, thereby slowing the progression of atherosclerosis and ischemic heart disease [2, 17].

SIRT1 has a direct activating effect on eNOS through deacetylation at Lys496 and Lys506. The *eNOS* gene, its product, and nitric oxide play an important role in maintaining normal endothelial function. In addition, SIRT1 inhibits the transcription of the adapter protein p66Shc through deacetylation of histone H3 in the promoter region. p66Shc promotes the formation of reactive oxygen species in mitochondria and inhibits the transcription of the antioxidant enzyme superoxide dismutase 2 (SOD2), i.e., SIRT1 leads to an overall antioxidant effect through negative regulation of transcription [13].

However, its function is not limited to the above-mentioned. SIRT1 also plays an important role in cardiomyocytes, where it performs anti-apoptotic functions, counteracts endoplasmic reticulum stress, increases myocardial contractility, and resistance to ischemic damage [18, 19].

Sirtuins can influence blood clotting and thrombus formation. Some studies show that SIRT1 can suppress platelet activity and reduce the risk of thrombus formation [7, 20].

Polymorphisms in the *SIRT1* gene may be associated with pathological processes in the vascular endothelium. Studies show that certain *SIRT1* alleles can influence its activity and, consequently, the predisposition to cardiovascular disease. Carriers of the mutant allele G rs7069102 had a 2.4-fold increase in the risk of developing cardiovascular disease, and carriers of rs2273773 had a 1.9-fold increase compared to carriers of the wild-type allele. This indicates the protective role of the C allele for both single nucleotide polymorphisms [21]. Taking into account the analyzed information, we tried to figure out the role of polymorphic variants of the *SIRT1* gene in the development of early vascular tone disorders and predisposition to hypertension in young people in the Republic of Mordovia.

AIM

The aim of the study was to explore the relationship between the frequency of *SIRT1* (*C/G* polymorphism, rs7069102), *eNOS* (*C/G* polymorphism, rs7069102), and *SOD2* (T/C polymorphism, rs4880) and the development of vascular tone disorders; to assess the functional state of the cardiovascular system in young people depending on the *SIRT1* polymorphism.

MATERIALS AND METHODS

The study was conducted at the Medical Institute in collaboration with the Faculty of Biotechnology and Biology of the N.P. Ogarev Moscow State University. The study included 48 people, with an average age of 20.3±0.1 years, including 25 women and 23 men. Cardiovascular risk was assessed in accordance with the recommendations of the Ministry of Health of the Russian Federation for the diagnosis and treatment of arterial hypertension (AH) in adults (2022). The research complies with the requirements of the Helsinki Declaration and was conducted in strict accordance with international standards of good clinical practice. Each participant provided written informed consent to participate. The study protocol was reviewed and approved by the local ethics committee of the N.P. Ogarev Moscow State University.

Participants were divided into groups: the first (control) group consisted of relatively healthy individuals (n=31) with normal average daily blood pressure (BP) (mean systolic BP from 101 to 130 mmHg, mean diastolic BP from 61 to 85 mmHg). The second (main) (n=17) group included conditionally healthy individuals with normal elevated average daily BP (mean systolic BP from 130 to 139 mmHg, mean diastolic BP from 86 to 89 mmHg), confirmed by data from daily blood pressure monitoring (DBPM).

Systolic and diastolic blood pressure (SBP and DBP) and heart rate (HR) were measured in the morning, three times on each upper limb, using an Omron M2 Basic automatic blood pressure monitor. Anthropometric data were also recorded. Body mass index (BMI) and body surface area (BSA) were calculated based on these data. Waist circumference (WC) and hip circumference (HC) were measured, followed by calculation of the waist-to-hip ratio (WHR).

To assess the condition of the vascular wall, photoplethysmography (PPG) was performed by means of Angio-Code-301 equipment.

The main characteristics of the vascular system were analyzed, including vascular wall stiffness, pulse filling index, augmentation index, and pulse wave velocity. All measurements were taken in the morning (from 9:00 to 11:00) on an empty stomach in a laboratory setting with constant microclimate parameters (temperature +23±1 °C, humidity 40–60%).

Blood samples were collected in accordance with the Protocol for the collection, transportation, and storage of venous blood [22]. Lipid metabolism indicators and glucose levels were measured (Mindray-BS-480 automatic analyzer). DNA was extracted by L.L. Boodram method with modifications. DNA concentration and purity were assessed by spectrophotometry using Nanodrop2000 (Thermo Scientific, USA). Real-time PCR was performed with a set of reagents for determining gene polymorphism: *SIRT1* (C/G polymorphism, rs7069102), *eNOS* (T/C polymorphism, rs20700744), *SOD2* (T/C polymorphism, rs4880) (Syntol, Russia). *CFX96* (Bio-Rad, USA) was used as an amplifier [1].

StatTech version 4.7.2 software was used for statistical data processing. Confidence intervals for percentage shares were calculated using the Klopper–Pearson method. Percentage shares in four-field contingency tables were

Table 2

Descriptive statistics of quantitative variables depending on systolic blood pressure (SBP)

Таблица 2

Описательная статистика количественных переменных в зависимости от систолического артериального давления (САД)

Показатели / Indicators	САД / SBP		P
	первая группа / first group	вторая группа / second group	
Возраст / Age	20,00 [19,00; 20,00]	20,00 [20,00; 22,00]	0,006*
Масса тела / Body weight	66,00 [55,50; 72,80]	85,00 [63,00; 92,00]	0,031*
Рост / Height	168,00 [161,00; 175,00]	175,00 [170,00; 178,00]	0,025*
Индекс массы тела / Body mass index	21,78 [20,04; 25,38]	26,30 [21,87; 29,41]	0,079
САД / SBP	122,00 [113,50; 126,00]	136,00 [124,00; 139,00]	<0,001*
Площадь поверхности тела, м^2 / Body surface area, m^2	1,75 [1,61; 1,89]	2,04 [1,77; 2,14]	0,007*
Окружность талии, см / Waist circumference, cm	77,00 [71,00; 84,50]	89,00 [82,00; 96,00]	0,013*
Окружность бедер, см / Hip circumference, cm	96,00 [92,50; 106,00]	103,00 [96,00; 115,00]	0,075
Индекс талия–бедра / Waist–hip index	0,78 [0,76; 0,80]	0,82 [0,78; 0,86]	0,065

compared using Fisher's exact test. The Mann–Whitney U test was also calculated. Pearson's χ^2 test was used to analyze multi-field contingency tables. Differences were considered statistically significant at a level of $p < 0.05$.

RESULTS

Anthropometric parameters were analyzed depending on the level of systolic blood pressure (Table 2).

The second group had lower body weight and height compared to the control group with normal blood pressure, but BMI did not show statistically significant differences. Respondents in the main group had significantly higher waist circumference and body surface area values ($p < 0.05$). Lipid and carbohydrate metabolism indicators did not show significant differences between the groups. The data confirm that an increase in abdominal fat mass is a significant risk factor contributing to the early development of hypertension. An increase in waist circumference is associated with metabolic disorders and changes in the vascular wall, which can lead to an increase in blood pressure [23, 24].

When assessing the prevalence of homozygous and heterozygous variants of the SIRT1 gene in the first group, the following genotype distribution was determined: CC — 19.4% (6 people), CG — 51.6% (16 people), GG — 29% (9 people). In the second group: CG — 41.2% (7 people), GG — 58.8% (10 people), the CC genotype was not detected (Fig. 1).

When analyzing the data using Pearson's χ^2 criterion, a statistically significant difference was found in the frequency of homozygous and heterozygous variants of the *SIRT1* gene ($p < 0.05$). These results indicate a link between predisposition to cardiovascular disease and the GG genotype in the study sample.

The next step was to analyze the main indicators of the functional state of the cardiovascular system and blood pressure (SBP and DBP) in young people in the context of *SIRT1* gene polymorphism. All participants were divided into groups based on their genotype: the CC group (CC genotype), the CG group (CG genotype), and the GG group (GG genotype). The GG group had an average SBP of 138.79 mmHg, while the first group with the CC genotype had an average SBP of 116.67 mmHg ($p < 0.05$). Normal-high blood pressure, ranging from 130 to 139 mmHg, was also more common in the second group with the CG genotype. Diastolic blood pressure did not show statistically significant differences between the groups.

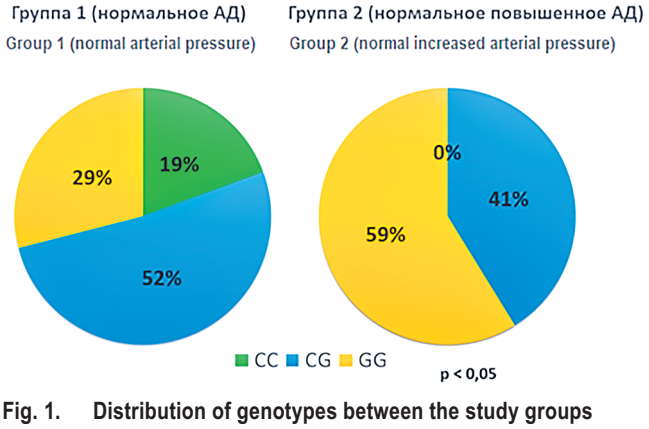

Fig. 1. Distribution of genotypes between the study groups

Рис. 1. Распределение генотипов между исследуемыми группами

The calculated stress index (c.u.) was distributed as follows. It was 83 for the GG genotype, 145 for the CG genotype, and 220 for the CC genotype ($p < 0.05$), which may be associated with higher heart rate (HR) in participants with the CC genotype as a compensatory mechanism for low blood pressure. Anthropometric, lipid metabolism, and photoplethysmography indicators did not show statistically significant differences between the groups (Table 3).

When analyzing the association between polymorphic variants of the genes, a relationship was found between the T/C polymorphism, rs4880 of the *SOD2* gene, and the *SIRT1* polymorphism (Table 4).

Thus, a higher frequency of *SOD2* TT polymorphism was observed in the third group with the GG genotype, amounting to 10 cases (52.6%), while the first group with the CC genotype showed this polymorphism in 1 case (20.0%). The activity of the enzyme containing valine (allele T) is known to be 23% lower than that of the enzyme with the Ala allele (allele C). This means that *SOD2* shows higher activity in carriers of the CC and CT genotypes compared to carriers of the TT genotype. Thus, a mutation associated with the T allele can be hypothetically linked with the development of cardiovascular and metabolic diseases [25, 26].

This interrelationship is particularly interesting considering the analysis of cardiovascular disease risk factors. It is known that *SIRT1* can influence the expression of *SOD2*. These effects are mediated by *SIRT1* deacetylation of *FOXO3a,* which induces an antioxidant response through the activation of SOD2 and catalase, thereby improving cellular protection against oxidative stress [27].

The study of *eNOS* gene polymorphism did not reveal any significant statistical differences between the groups.

CONCLUSION

Sirtuins differ from each other in their activity in various chemical reactions, localization in the cell, points of application, and targets. Human sirtuins are divided into four

Table 3

Anthropometry and photoplethysmography data depending on *SIRT1* polymorphism

Таблица 3

Данные антропометрии и фотоплетизмографии в зависимости от полиморфизма *SIRT1*

Показатели / Indicators	*SIRT1*			P
	GG	GC	CC	
Индекс массы тела, Me [IQR] / Body mass index, Me [IQR]	24,19 [20,04; 28,25]	22,60 [20,48; 28,15]	21,29 [19,82; 22,70]	0,598
Площадь поверхности тела, м^2, M (SD) / Body surface area, m^2, M (SD)	1,88 (0,23)	1,85 (0,24)	1,70 (0,29)	0,283
Окружность талии см, M (SD) / Waist circumference, cm, M (SD)	81,37 (12,00)	83,48 (13,09)	75,17 (14,18)	0,372
Окружность бедер, см, Me [IQR] / Hip circumference, cm, Me [IQR]	102,00 [95,50; 109,00]	99,00 [93,00; 110,00]	92,50 [86,50; 99,25]	0,411
Индекс талия–бедра, Me [IQR] / Waist–hip index, Me [IQR]	0,78 [0,76; 0,82]	0,79 [0,77; 0,85]	0,79 [0,78; 0,79]	0,758
Жесткость сосудистой стенки, %, Me [IQR] / Stiffness of the vascular wall, %, Me [IQR]	–16,80 [–19,90; –8,60]	–14,30 [–19,25; –7,40]	–10,75 [–16,23; –7,97]	0,727
Индекс стресса, у.е., Me [IQR] / Stress Index, c.u., Me [IQR]	83,00 [58,00; 107,00]	145,00 [74,50; 276,00]	220,00 [142,00; 328,75]	0,039*
Холестерин, M (SD) / Cholesterol, M (SD)	3,99 (0,52)	4,16 (0,82)	3,83 (0,60)	0,536
Глюкоза, Me [IQR] / Glucose, Me [IQR]	3,67 [3,51; 3,94]	3,80 [3,59; 3,92]	3,91 [3,74; 4,18]	0,365
Липопротеины высокой плотности, Me [IQR] / High density lipoproteins, Me [IQR]	1,00 [0,94; 1,12]	1,01 [0,95; 1,15]	0,96 [0,93; 1,04]	0,625
Липопротеины низкой плотности, M (SD) / Low density lipoprotein, M (SD)	2,53 (0,67)	2,62 (0,74)	2,62 (0,83)	0,921

Table 4

Descriptive statistics of categorical variables SOD2 depending on SIRT1

Таблица 4

Описательная статистика категориальных переменных SOD2 в зависимости от SIRT1

SOD2 / SOD2	*SIRT1*		
	группа CC / group CC	группа CG / group CG	группа GG / group GG
(TT) абс. (%) / abs (%)	1 (20,0%)	14 (63,6%)	10 (52,6%)
(CT) абс. (%) / abs (%)	0 (0,0%)	5 (22,7%)	5 (26,3%)
(CC) абс. (%) / abs (%)	4 (80,0%)	4 (13,6%)	4 (21,1%)
p=0,035 $p_{GC–CC}$=0,027			

classes (I–IV). Sirtuins play a significant role in cells: they maintain normal mitochondrial function, protect cells from free radicals and peroxidation, and have anti-inflammatory and neuroprotective effects.

Sirtuins influence various aspects of lipid, carbohydrate, and protein homeostasis in many tissues. This determines their role in controlling the development and progression of metabolic diseases such as obesity and diabetes mellitus. The antitumor activity of sirtuins is determined by their ability to inhibit glycolysis, which is the main pathway for energy production by cancer cells.

The study allows us to draw the following conclusions.

1. Young individuals from the Republic of Mordovia, who are carriers of the G allele of the *SIRT1* C/G gene, rs7069102, demonstrate changes in the functional state of the cardiovascular system; no correlations between

the studied polymorphism and lipid metabolism disorders or BMI were identified.

2. The *SOD2* gene polymorphism (TT (T/C polymorphism, rs4880)) is significantly more common in *SIRT1* carriers (GG (C/G polymorphism, rs7069102); no association between polymorphic variants of the *eNOS* gene and the *SIRT1* gene was found within the groups.

Thus, the identified differences in the functional state of the cardiovascular system in various polymorphic variants of the *SIRT1* gene, as well as the interaction between the *SIRT1* and *SOD2* genes in the context of antioxidant protection, require further research with larger samples and a variety of analytical methods to clarify the role of this mutation as a risk factor for vascular tone disorders.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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