



Evaluation of the Effect of Semaglutide on Certain Cardiovascular Risk Factors in Overweight or Obese Healthcare Workers. The “Start with Yourself” Program: A Post-registration, Single-center, Prospective Study of Routine Clinical Practice

L.A. Balykova¹, V.V. Stolyarova¹, D.A. Orlova¹, S.V. Shokina¹, M.V. Esina¹, E.I. Yamashkina¹,
T.A. Surina¹, L.A. Zorina², V.S. Shcherbakova³, K.Ya. Zaslavskaya¹, P.A. Bely⁴

¹ National Research Ogarev Mordovia State University,
68, Bolshhevistskaya Str., Saransk, Russia, 430005

² Federal Scientific and Clinical Center for Specialized Types of Medical Care and Medical Technologies,
28 Orekhovy Blvd, Moscow, Russia, 115682

³ Tver State Medical University,
4 Sovetskaya Str., Tver, Russia, 170100

⁴ Russian University of Medicine,
4 Dolgorukovskaya Str., Moscow, Russia, 127006

E-mail: larisabalykova@yandex.ru

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The aim. To evaluate the effect of semaglutide on certain cardiovascular risk factors in patients with obesity.

Materials and methods. The study included 50 individuals: men and women aged 18 to 65 years, patients with overweight (BMI ≥ 27 and < 30) and obesity (BMI ≥ 30), combined with at least one comorbidity (prediabetes or type 2 diabetes mellitus), arterial hypertension, dyslipidemia, obstructive sleep apnea syndrome, or cardiovascular disease. Patients received subcutaneous semaglutide (Velgia®) once a week. Clinical examination was performed, including: interview, blood pressure measurement, anthropometric data assessment (height, weight, BMI, waist circumference, and hip circumference), cardiovascular risk assessment using the SCORE scale, biochemical blood analysis (including lipid profile), and adverse event registration.

Results. A significant decrease in body weight, BMI, waist circumference, and hip circumference was observed after 12 weeks of semaglutide therapy. By 24 weeks, a sustained reduction in these indicators continued. After 6 months of semaglutide use, positive changes in the lipid profile were identified: a decrease in total cholesterol by 8.27 % due to a decrease in non-HDL cholesterol, LDL cholesterol by 12.73 %, triglycerides by 13.09 %, and the atherogenic index by 1.83 %. Velgia® therapy for 6 months led to a reduction in the calculated 10-year cardiovascular risk according to the SCORE2 scale by 18.6 %. Analysis of anthropometric and biochemical blood data showed a significant decrease in indicators, indicating a reduced risk of cardiovascular events in patients with obesity.

Conclusion. During semaglutide therapy, no clinically significant changes were observed in liver function parameters (ALT, AST, ALP, bilirubin), pancreas (amylase), kidneys (creatinine, urea, GFR), and systemic inflammation markers (CRP). However, a significant decrease in transaminase activity (ALT, AST) and blood uric acid concentration was noted. The registered adverse events (primarily gastrointestinal: nausea, epigastric discomfort) were temporary and moderate in nature. No cardiovascular events were observed during the use of semaglutide.

Keywords: semaglutide; diabetes mellitus; obesity; glucagon-like peptide-1 receptor agonist; atherosclerosis; prediabetes

Abbreviations: BMI — body mass index; TC — total cholesterol; HDLs — high-density lipoproteins; LDLs — low-density lipoproteins; ALT — alanine aminotransferase; AST — aspartate aminotransferase; ALP — alkaline phosphatase; GFR — glomerular filtration rate; CRP — C-reactive protein; T2DM — type 2 diabetes mellitus; GLP-1 RAs — glucagon-like peptide-1 receptor agonists; MACE — major adverse cardiovascular events; CVD — cardiovascular disease; SBP — systolic blood pressure; DBP — diastolic blood pressure; FPG — fasting plasma glucose; MI — myocardial infarction.

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Т.А. Сурина, Л.А. Зорина, В.С. Щербакова, К.Я. Заславская, П.А. Белый, 2026

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Оценка влияния препарата семаглутид на некоторые факторы сердечно-сосудистого риска у медицинских работников с избыточной массой тела или ожирением. Программа «Начни с себя»: пострегистрационное одноцентровое проспективное исследование рутинной клинической практики

Л.А. Балыкова¹, В.В. Столярова¹, Д.А. Орлова¹, С.В. Шокина¹, М.В. Есина¹, Е.И. Ямашкина¹, Т.А. Сурина¹, Л.А. Зорина², В.С. Щербакова³, К.Я. Заславская¹, П.А. Белый⁴

¹ Федеральное государственное бюджетное образовательное учреждение высшего образования «Национальный исследовательский Мордовский государственный университет им. Н.П. Огарева» Министерства науки и высшего образования Российской Федерации, Россия, 430005, Республика Мордовия, г. Саранск, ул. Большевикская, д.68

² Федеральное государственное бюджетное учреждение «Федеральный научно-клинический центр специализированных видов медицинской помощи и медицинских технологий Федерального медико-биологического агентства России» Россия, 115682, г. Москва, Ореховый бульвар, д.28

³ Федеральное государственное бюджетное образовательное учреждение высшего образования «Тверской государственный медицинский университет Министерства здравоохранения Российской Федерации», Россия, 170100, г. Тверь, ул. Советская, д.4

⁴ Федеральное государственное бюджетное образовательное учреждение высшего образования «Российский университет медицины» Министерства здравоохранения Российской Федерации, Россия, 127006, г. Москва, ул. Долгоруковская, д.4

E-mail: larisabalykova@yandex.ru

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Цель. Провести оценку влияния препарата семаглутид на некоторые факторы сердечно-сосудистого риска у пациентов с ожирением.

Материал и методы. В исследование включено 50 человек: мужчины и женщины в возрасте от 18 до 65 лет, пациенты с избыточной массой тела (ИМТ $\geq$ 27 и <30) и ожирением (ИМТ $\geq$ 30), в сочетании с хотя бы одним сопутствующим заболеванием (предиабет или сахарный диабет 2 типа), артериальная гипертензия, дислипидемия, синдром обструктивного апноэ во сне или сердечно-сосудистые заболевания. Пациентам вводился препарат семаглутид (Велгия®) подкожно 1 раз в неделю, проводилось клиническое обследование, включающее: опрос, измерение артериального давления, оценку антропометрических данных (рост, масса тела, ИМТ, окружности талии и окружности бёдер), оценка сердечно-сосудистого риска по шкале SCORE, проведение биохимического анализа крови (в т.ч. липидограммы), регистрация нежелательных явлений.

Результаты. Отмечено достоверное снижение массы тела, ИМТ, окружности талии и бёдер через 12 нед терапии препаратом семаглутид. К 24 нед продолжилось устойчивое снижение данных показателей. Через 6 месяцев применения препарата семаглутид выявлены позитивные изменения в липидном спектре: снижение общего холестерина на 8,27% за счёт снижения холестерина не-ЛПВП, холестерина ЛПНП — на 12,73%, тиреоглобулина — на 13,09%, индекса атерогенности — на 1,83%. Терапия препаратом Велгия® в течение 6 мес привела к снижению расчётного 10-летнего сердечно-сосудистого риска по шкале SCORE2 на 18,6%. При анализе данных антропометрии, биохимического анализа крови отмечено достоверное снижение показателей, что свидетельствует о снижении риска сердечно-сосудистых событий у пациентов с ожирением.

Заключение. На фоне терапии препаратом семаглутид не наблюдалось клинически значимых изменений в показателях функции печени (АЛТ, АСТ, ЩФ, билирубин), поджелудочной железы (амилаза), почек (креатинин, мочевины, СКФ) и маркеров системного воспаления (СРБ). При этом отмечено достоверное снижение активности трансаминаз (АЛТ, АСТ) и концентрации мочевой кислоты в крови. Зарегистрированные нежелательные явления (преимущественно со стороны ЖКТ: тошнота, дискомфорт в эпигастрии) носили временный и умеренный характер. Сердечно-сосудистых событий в период применения препарата семаглутид не отмечено.

Ключевые слова: семаглутид; сахарный диабет; ожирение; агонист рецепторов глюкагоноподобного пептида-1; атеросклероз; предиабет

Список сокращений: ИМТ — индекс массы тела; ОХС — общий холестерин; ХС — холестерин; ЛПВП — липопротеины высокой плотности; ЛПНП — липопротеины низкой плотности; АЛТ — аланинаминотрансфераза; АСТ — аспартатаминотрансфераза; ЩФ — щелочная фосфатаза; СКФ — скорость клубочковой фильтрации; СРБ — С-реактивный белок; СД2 — сахарный диабет 2 типа; арГПП-1 — агонисты рецепторов глюкагоноподобного пептида-1; MACE — риск серьезных сердечно-сосудистых событий; ССЗ — сердечно-сосудистые заболевания; САД — систолическое артериальное давление; ДАД — диастолическое артериальное давление; ГПН — глюкоза плазмы натощак; ОИМ — острый инфаркт миокарда

INTRODUCTION

Obesity is a chronic disease characterized by the excessive accumulation and dysfunction of adipose tissue [1]. Obesity is a significant risk factor for many comorbid conditions, primarily type 2 diabetes mellitus (T2DM), cardiovascular diseases, as well as a range of oncological, gastrointestinal, and musculoskeletal diseases, and psychological problems [2]. An increased risk of cardiovascular disease (CVD) is the most common cause of mortality in patients with obesity [3].

In the Russian Federation, as of 2016, the proportion of individuals with overweight was 62.0%, and with obesity, it was 26.2% [4]. Based on a survey of a representative sample of the population aged 35–74 years residing in 15 regions of the Russian Federation within the framework of the “ESSE-RF” study, 3 phases of prospective studies have been conducted [5]. The third survey (“ESSE-RF3”) showed the prevalence of overweight (BMI) at 44.0% and 33.7%, obesity at 30.0% and 39.5%, and abdominal obesity at 30.9% and 55.1% among men and women, respectively [6].

In patients with existing obesity, comorbid pathology progresses: cardiometabolic disorders (T2DM, hypercholesterolemia, ischemic heart disease, stroke, hypertensive disease) and non-metabolic diseases (gastroesophageal reflux disease, non-alcoholic fatty liver disease, malignant neoplasms, musculoskeletal damage, sleep-wake disorders, depressive disorders), which significantly leads to a reduction in average life expectancy [7].

The low efficacy of obesity treatment, despite financial costs, necessitates a review of existing approaches and the development of new treatment methods and medications based on a deeper understanding of the pathogenetic basis of obesity [8].

Traditional therapeutic approaches demonstrate limited effectiveness in terms of weight loss and cardiovascular outcomes in the long term. The emergence and implementation of incretin-based drugs in clinical practice have ushered in a new era in the treatment of metabolic diseases. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and, subsequently, dual and multi-agonists, exert a complex effect on key pathophysiological links of T2DM and obesity [9–11].

Semaglutide is the latest GLP-1 RA, approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the long-term treatment of obesity in 2021. The approval of semaglutide at a dose of 2.4 mg per week for weight loss is based on the results of the STEP (1–8) research program [12]. Furthermore, the STEP 4

study demonstrated the positive effect of long-term semaglutide treatment for weight loss [13].

In the treatment of obesity, it is crucial to define individual goals for each patient, going beyond simple weight reduction [14]. The SELECT trial proved that the drug at a dose of 2.4 mg reduces the risk of major adverse cardiovascular events (MACE) by 20% in patients with obesity and established cardiovascular disease, but without diabetes [15]. These results allowed for the registration of a new indication for semaglutide is the reduction of cardiovascular event risk in patients with obesity.

Thus, studying the effect of semaglutide on key cardiovascular risk factors in patients with obesity is relevant.

PROMED Group (Russia) has developed the “Start with Yourself” program to support doctors and care for their own health and well-being, which is directly related to patient health. This study was conducted within the framework of this program.

THE AIM is to evaluate the effect of semaglutide (Velgia®) on certain cardiovascular risk factors in patients with obesity.

MATERIALS AND METHODS

Study Design

A post-registration, single-center, prospective study with minimal intervention in routine clinical practice was conducted.

Study Conduct and Duration

The study was conducted from May 5, 2025, to January 31, 2026, at the National Research Ogarev Mordovia State University and the Republican Clinical Hospital No. 4 (Saransk, Republic of Mordovia, Russia). The total duration of the study for each volunteer was no more than 171 days (including the screening period). All patients completed the study fully in accordance with the approved Study Protocol.

Study Subjects and Eligibility Criteria

The study “Efficacy and Safety of the Russian Analog of Long-Acting Human GLP-1 Drug Velgia® (Semaglutide) in Routine Clinical Practice in the Republic of Mordovia: “Republican Program for Prevention of Risks of Atherosclerosis-Mediated Cardiovascular Diseases and Diabetes Mellitus in Healthcare Workers with Overweight (BMI 27–30) or Obesity (BMI ≥ 30)” included 50 individuals.

Inclusion Criteria: Men and women aged 18 to 65 years, patients with overweight (BMI ≥ 27 and < 30) and obesity (BMI ≥ 30), combined with at least one

concomitant disease (prediabetes or T2DM, arterial hypertension, dyslipidemia, obstructive sleep apnea syndrome, or cardiovascular diseases), voluntary informed consent to participate in the study.

Exclusion Criteria: Age younger than 18 years and older than 65 years, oncological diseases, severe decompensated pulmonary, hepatic, or renal pathology.

Methodology

Investigator physicians screened patients in accordance with the inclusion / exclusion criteria. Anthropometry was performed (measurement of height, body weight, waist circumference, hip circumference), BMI was calculated; complaints and medical history were collected; a physical examination was conducted (including measurement of BP, HR); cardiovascular risk was calculated (SCORE2-Diabetes / SCORE / SCOREII index) using the MDCalc calculator; quality of life was assessed according to EQ 5D-3L questionnaires; biochemical blood analysis results were assessed (fasting plasma glucose, insulin, HOMA-IR index, Hb_{A1c} , creatinine with eGFR calculation, bilirubin, urea, C-reactive protein, uric acid, ALT, AST, ALP, total cholesterol, LDL, HDL, triglycerides), performed using an AU480 automated biochemical analyzer (Beckman Coulter, USA).

Patients received semaglutide (Velgia®) subcutaneously once a week, regardless of the time of day, in the abdomen, thigh, or upper arm, irrespective of food intake. The initial dose was 0.25 mg once a week, and the dose was increased over 16 weeks, starting from 0.25 mg up to a maintenance therapeutic dose of 2.4 mg once a week. Participation in the study lasted 24 weeks from Visit 1. In total, there were 6 visits in the study, including screening, dose titration, treatment, and follow-up. During each visit, the investigator completed the patient case report form and paper-based patient questionnaire forms. Any adverse events detected during the study were documented by the investigator in an adverse event report.

Ethics Approval

The study protocol was approved at a meeting of the Local Ethics Committee of the Medical Institute, National Research Ogarev Mordovia State University (Protocol No. 137 dated February 28, 2025).

Statistical Analysis

Statistical analysis was performed using Jamovi 2.6.44 Software. Normality of distribution was assessed using the Shapiro-Wilk test. For normal distribution,

means (M) and standard error of the mean (m) were evaluated. For non-normal distribution, median (Me) and interquartile range [Q1; Q3] were evaluated. The significance of differences was determined by the paired Student's t-test for normal distribution, and by the Wilcoxon test for non-normal distribution. Comparison of groups for qualitative characteristics was performed using the chi-square test. The critical level of statistical significance was taken as $p < 0.05$.

RESULTS

Population

The study group included 50 patients: 4 men (8%) and 46 women (92%) aged 22–65 years (mean age 46.06 ± 1.42 years) at the time of signing informed consent, with confirmed overweight and obesity. The duration of obesity or overweight ranged from 5 to 35 years, with an average of 15.36 ± 1.08 years at the time of inclusion in the study (Table 1).

Only 8 (16%) patients had no concomitant pathology. 24 (48%) had more than two concomitant diseases. The structure of concomitant pathology was as follows: arterial hypertension—23 (46%) patients, T2DM—8 (16%), prediabetes—8 (16%), musculoskeletal diseases—6 (12%), hypothyroidism—5 (10%), 2 (4%) each—iron deficiency anemia, chronic pancreatitis, varicose veins of the lower extremities, chronic heart failure, urolithiasis, chronic pyelonephritis—1 (2%) (see Table 1).

Smoking as an additional cardiovascular risk factor was noted in 5 patients (10%). At Visit 1, cardiovascular risk was assessed as low in 11 (22%) patients, moderate—in 7 (14%), high—in 20 (40%), and very high—in 12 (24%) subjects. The 10-year CVD risk (SCORE) was $4.85 [2.00; 9.13]\%$.

The mean systolic blood pressure (SBP) at the time of inclusion in the study was 127.74 ± 1.82 mmHg, and diastolic blood pressure (DBP) was 80.34 ± 1.28 mmHg.

Fasting plasma glucose (FPG) was 5.80 ± 0.22 mmol/L, and glycated hemoglobin (Hb_{A1c}) was $5.30 \pm 0.18\%$.

Alanine aminotransferase (ALT) activity was 32.90 ± 2.57 U/L, and aspartate aminotransferase (AST) was 24.09 ± 1.35 U/L. In 80% of cases, ALT activity exceeded reference values, and in 8% of cases, AST elevation was detected.

In 18% of cases, hyperuricemia was detected, and in 2% of cases, elevated urea was found (mean levels were 315.02 ± 11.38 mmol/L and 5.53 ± 0.17 mmol/L, respectively). Bilirubin and amylase levels did not exceed reference values. The mean bilirubin level was 9.95 ± 0.44 μ mol/L, and amylase was 38.57 ± 1.79 U/L.

Elevated C-reactive protein (CRP) was noted in

14% of patients. The median CRP in the study group was 1.65 [0.20; 3.35].

The mean glomerular filtration rate (GFR), calculated using the CKD-EPI formula, was 82.39 ± 1.91 mL/min/1.73 m². GFR less than 90 mL/min/1.73 m² was observed in 64% of subjects, and less than 60 mL/min/1.73 m² in 8%.

Lipid profile abnormalities were recorded in the majority of the examined patients. The most common deviations were hypercholesterolemia and elevated low-density lipoprotein cholesterol (LDL-C) levels.

Hypercholesterolemia was detected in 32 (64%) patients with a mean total cholesterol (TC) level of 5.57 ± 0.15 mmol/L. Elevated LDL-C was observed in 34 (68%), with a mean value reaching 3.85 ± 0.14 mmol/L. Hypertriglyceridemia was diagnosed in 16 (32%), with a mean triglyceride level of 1.91 ± 0.17 mmol/L. Hypo-alpha-lipoproteinemia (decreased HDL-C) was noted in 17 (34%) patients with a mean value of 1.19 ± 0.03 mmol/L. The atherogenic index was elevated in more than half of the patients (56%, $n = 28$) and averaged 3.82 ± 0.40 .

Dynamics of anthropometric parameters in patients

A significant decrease in body weight, BMI, waist circumference, and hip circumference was observed after 12 weeks of semaglutide therapy. By 24 weeks, a sustained reduction in these parameters continued.

After 12 weeks of therapy, body weight decreased by an average of 6.65 kg, and after 24 weeks, by 12.0 kg, which corresponded to 6.71% and 11.3% respectively. BMI decreased by 2.50 kg/m² and 4.33 kg/m² respectively. The average reduction in waist circumference was 4 cm by 12 weeks and 7.65 cm by 24 weeks, and hip circumference decreased by 4 cm and 9 cm respectively (Table 2).

As early as 12 weeks of semaglutide therapy, amidst significant changes in body weight, a redistribution of patients towards less severe obesity categories was recorded: the number of patients with overweight increased to 5 (10.2%), while the number of subjects with class III obesity decreased by half compared to baseline, amounting to 20.4% ($n = 10$) (Figure 1).

By 24 weeks of semaglutide use, the total proportion of patients with any degree of obesity was 75% ($n = 36$). Further improvement in anthropometric parameters was observed: normalization of body weight (BMI < 25 kg/m²) was achieved in 2 (4.2%) patients, and another 9 (18.8%) who initially had obesity moved into the overweight group. The most pronounced reduction was noted in the severe obesity groups: the proportion of patients with class II obesity

decreased by 7%, and with class III obesity by 23.2% relative to baseline values (see Figure 1). The obtained data indicate a dose-dependent and time-dependent effect of the drug, most pronounced in patients with severe forms of obesity. The use of semaglutide for 24 weeks allowed for body weight reduction sufficient to move out of the obesity category in every fourth patient ($n = 12$).

Dynamics of blood pressure

Initially and throughout 6 months of semaglutide therapy, patients maintained stable and well-controlled blood pressure levels. Systolic blood pressure (SBP) from the Visit 4 and diastolic blood pressure (DBP) by the Visit 6 showed a significant decrease and corresponded to target values, including patients with arterial hypertension (Figure 2).

Dynamics of blood biochemical parameters

Initially, transaminase activity exceeded reference values but did not exceed a 3-fold increase from normal: ALT in 10 patients (20.8%) and AST in 4 (8.3%). After 6 months of semaglutide use, ALT activity exceeded normal levels in only 2 (4%, $p < 0.05$), and AST activity was within normal limits in all patients ($p < 0.05$). Transaminase levels significantly decreased: ALT from 32.65 ± 2.63 U/L to 22.09 ± 1.36 U/L—a 32.4% reduction, and AST from 24.10 ± 1.39 U/L to 18.40 ± 0.72 U/L—a 23.7% reduction (Table 3).

The levels of alkaline phosphatase, bilirubin, amylase, urea, and creatinine after 6 months of semaglutide use did not differ from baseline values and remained within their respective reference ranges. The mean levels were: alkaline phosphatase 157.68 ± 6.44 U/L, bilirubin 10.75 ± 0.69 μmol/L, amylase 42.60 ± 2.98 U/L, urea 5.07 ± 0.19 mmol/L (see Table 3).

Initially, elevated CRP was detected in 6 patients, and by the end of the study, in 5 patients.

Uric acid levels significantly decreased from 314.23 ± 11.66 μmol/L to 281.58 ± 11.23 μmol/L (an 11.4% reduction, $p < 0.05$), and the number of patients with hyperuricemia decreased from 9 (18.7%) to 5 (10.4%) (see Table 3).

The mean glomerular filtration rate (GFR), calculated using the CKD-EPI formula, did not change compared to baseline and was 82.87 ± 1.73 mL/min/1.73 m² (99.9% of baseline, $p = 0.9$). GFR between 60–89 mL/min/1.73 m² was observed in 68.8% (baseline 66.6%, $p = 0.8$), and less than 60 mL/min/1.73 m² in 2.1% (baseline 8.3%, $p = 0.16$) (Table 3).

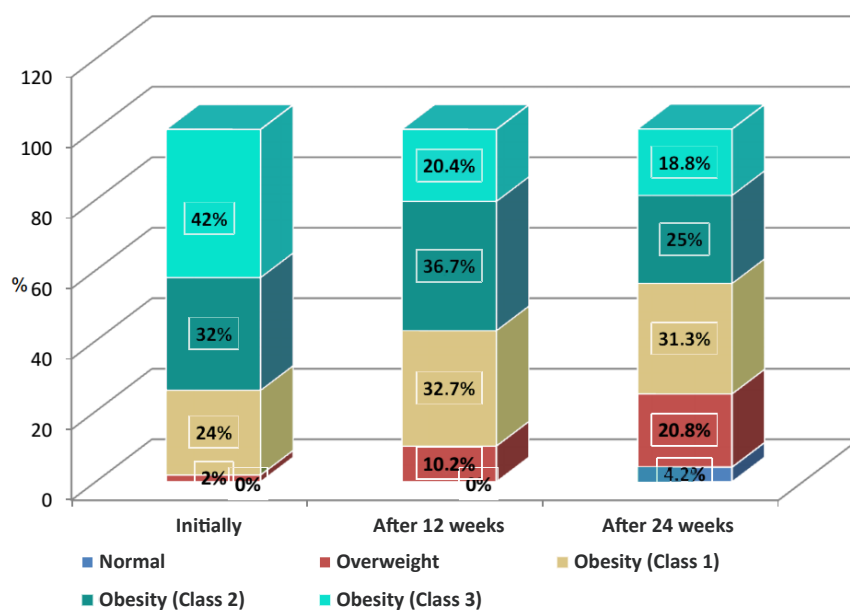


Figure 1 — Dynamics of obesity by body mass index during treatment with semaglutide.

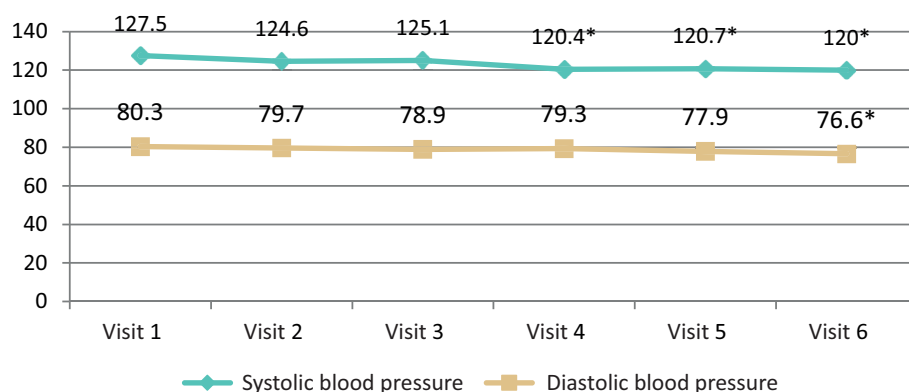


Figure 2 — Dynamics of systolic and diastolic blood pressure during treatment with semaglutide.

Note: * is differences are statistically significant at $p < 0.05$.

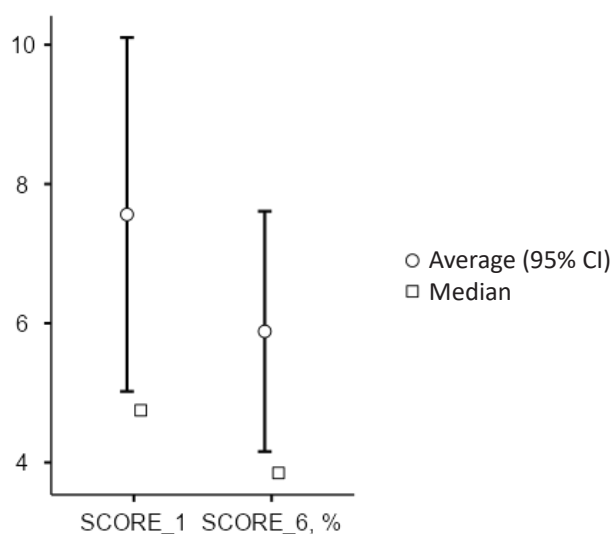


Figure 3 — Cardiovascular risk by SCORE after 6 months of therapy with semaglutide ($n = 48$).

Note: missing values were excluded pairwise.

Table 1 — Clinical characteristics of the study group

Characteristic	Total (n = 50)
Age, (M ± m), years	46.06 ± 1.42
Sex	
Female, n (%)	46 (92%)
Male, n (%)	4 (8%)
Duration of obesity, (M ± m), years	15.36 ± 1.08
Body weight, (M ± m), kg	108.59 ± 2.99
Body mass index, (M ± m), kg/m ²	39.06 ± 0.84
Waist circumference, (M ± m), cm	113.32 ± 1.95
Hip circumference, (M ± m), cm	124.89 ± 1.63
Overweight, n (%)	1 (2%)
Obesity, n (%)	49 (98%)
	Grade I 12 (24%)
	Grade II 16 (32%)
	Grade III 21 (42%)
Comorbidities, n (%):	
Type 2 Diabetes Mellitus	8 (16%)
Prediabetes	8 (16%)
Arterial Hypertension	23 (46%)
Musculoskeletal disorders	6 (12%)
Hypothyroidism	5 (10%)
Iron deficiency anemia	2 (4%)
Chronic pancreatitis	2 (4%)
Varicose veins of the lower extremities	2 (4%)
Chronic heart failure	2 (4%)
Urolithiasis	2 (4%)
Chronic pyelonephritis	1 (2%)

Table 2 – Dynamics of anthropometric parameters in patients receiving semaglutide at 12 and 24 weeks of therapy

Characteristic	At 12 weeks (n = 49)	At 24 weeks (n = 48)
Body weight, kg	6.65 [5.15 ; 9.30]	6.71 ± 0.500
Body mass index, kg/m ²	2.50 [1.80 ; 3.20]	4.33 ± 0.268*
Waist circumference, cm	4.00 [1.00 ; 7.00]	7.65 ± 0.927*
Hip circumference, cm	4.00 [1.00 ; 7.00]	9.00 [6.50 ; 12.0]*

Note: * is differences are statistically significant at $p < 0.05$.

Table 3 — Blood parameters after 6 months of semaglutide treatment (n = 48)

Characteristic	Visit 1	Visit 6	% of baseline value	p (t-test)
ALT, U/L	32.65 ± 2.63	22.09 ± 1.36	67.6	0.0005*
AST, U/L	24.10 ± 1.39	18.40 ± 0.72	76.3	0.0004*
Alkaline phosphatase, U/L	148.6 ± 6.10	157.68 ± 6.44	106	0.3
Bilirubin, μmol/L	9.88 ± 0.44	10.75 ± 0.69	108.8	0.3
Amylase, U/L	38.18 ± 1.84	42.60 ± 2.98	111.5	0.2
Creatinine, μmol/L	78.03 ± 1.61	79.10 ± 1.21	101.3	0.6
Urea, mmol/L	5.48 ± 0.17	5.07 ± 0.19	95.5	0.12
Uric acid, μmol/L	314.23 ± 11.66	281.58 ± 11.23	89.6	0.04*
C-reactive protein, mg/L	1.65 [0.20 ; 3.35]	0.10 [0.057 ; 0.575]	6	0.002*
GFR, mL/min/1.73 m ² :	82.97 ± 1.91	82.87 ± 1.73	99.9	0.9
GFR ≥ 90, n (%)	12 (25%)	14 (29.1%)	3.9	0.8
GFR 60–89, n (%)	32 (66.6%)	33 (68.8%)	1.8	0.8
GFR < 60, n (%)	4 (8.3%)	1 (2.1%)	6.2	0.16

Note: missing values were excluded pairwise, * is differences are statistically significant at $p < 0.05$.

Cardiovascular Risk Assessment

Initially, cardiovascular risk in the study group was assessed as low in 11 (22%) patients, moderate in 7 (14%), high in 20 (40%), and very high in 12 (24%).

When calculated using SCORE, the 10-year cardiovascular disease risk in the baseline group was 4.85 [2.00; 9.13]%. After 6 months of semaglutide therapy, it decreased by 20.6% to 3.85 [1.00; 7.45]% ($p < 0.001$) (Figure 3).

No cardiovascular events were registered during the study period.

After 6 months of semaglutide use, a number of positive changes in the lipid profile were noted. A significant decrease in TC by 8.27% ($p < 0.05$) was observed, attributed to a reduction in non-HDL cholesterol ($p < 0.05$). LDL-C decreased by 12.73% ($p < 0.05$), and thyroglobulin by 13.09% ($p < 0.05$). Additionally, a decrease in the atherogenic index by 1.83% was noted. HDL-C data were statistically insignificant, with no negative trend observed.

Safety Assessment

Adverse events that could be associated with the use of the investigational drug at a dose of 0.25 mg of semaglutide were reported by 18 patients (36%). The majority of patients, 9 (18%), reported nausea, predominantly when consuming fatty foods. Heartburn, diarrhea, feeling of fullness, and joint pain were reported by 4% of patients for each symptom. In 2% of cases, upper abdominal pain, constipation, diarrhea, leg weakness, and lower back pain were observed.

No cardiovascular events (acute myocardial infarction, unstable angina, acute cerebrovascular accident, hypertensive crises requiring hospitalization) were registered among patients who completed the 6-month study.

DISCUSSION

The conducted study showed that 6-month therapy with Velgia® in patients with obesity (mean BMI 39.06 kg/m²) and high comorbidity (84% had concomitant diseases) led to a significant reduction in body weight, improvement in metabolic profile, and reduction in cardiovascular risk. After 24 weeks, body weight decreased by 12.0 kg (11.3%), BMI decreased by 4.33 kg/m², and waist circumference by 7.65 cm. The proportion of patients with class III obesity halved (from 42% to 19.5%), and 4.2% achieved normal body weight. These data are consistent with the

STEP 1 study [12], where body weight reduction over 68 weeks was 14.9%, however, our study demonstrates the achievement of a pronounced effect already in the medium term.

A significant decrease in TC by 8.27% ($p < 0.001$), LDL-C by 12.73% ($p < 0.001$), and triglycerides by 13.09% ($p < 0.05$) was recorded. The atherogenic index decreased by 1.83% with no negative trend in HDL-C. The calculated 10-year cardiovascular risk using the SCORE2 scale decreased by 18.6% (from 7.01% to 5.9%), and the proportion of patients with very high risk decreased from 25% to 16.7%. Over 6 months of observation, not a single cardiovascular event was registered, which, considering the initially high (42%) and very high (25%) risk, confirms the cardioprotective potential of the therapy. These results correlate well with the data from the SELECT study [15] in patients with obesity without diabetes.

Semaglutide is widely used for the treatment of T2DM and is gaining attention due to its cardioprotective properties [16]. As shown in the clinical study by M.N. Kosiborod et al. [17], semaglutide can reduce the risk of cardiovascular death and worsening of condition in patients with heart failure. Specific mechanisms may be related to semaglutide's ability to attenuate inflammatory responses, preserve mitochondrial function, reduce oxidative stress, and inhibit cellular apoptosis [18–22]. The NOD-like receptor protein 3 (NLRP3) inflammasome is associated with cardiac damage, such as myocardial ischemia and fibrosis [23–25]. The study by W. He et al. [26] demonstrated that semaglutide can improve impaired mitophagy caused by transverse aortic constriction (TAC) and suppress NLRP3 inflammasome activation, thereby reducing cardiac hypertrophy. This finding reveals a link between semaglutide and the NLRP3 pathway, highlighting its pronounced anti-inflammatory effect. Further verification in a diabetic model showed that semaglutide treatment attenuates inflammation-induced cardiac damage by increasing RKIP expression and suppressing the TBK1 / NF- κ B signaling pathway. These effects are confirmed by improved cardiac function and reduced biomarkers of myocardial injury [19], providing a theoretical basis for expanding the clinical application of semaglutide.

A recent clinical study showed that semaglutide improves cardiovascular outcomes by enhancing vascular endothelial function and reducing

inflammation, independent of weight loss [27]. In a model of obesity-related cardiac damage, its anti-inflammatory effect was confirmed. Semaglutide significantly reduced body weight in obese mice while suppressing the expression of genes associated with inflammation and oxidative stress (such as S100A8, S100A9, and Cxcl2) in neutrophils, thereby reducing cardiac damage [18, 28]. Clinical studies show that the anti-inflammatory properties of semaglutide may prevent atrial fibrosis and alleviate symptoms of atrial fibrillation in individuals with obesity [29]. When used with antihypertensive and lipid-lowering drugs, semaglutide reduced high-sensitivity CRP levels by 37.8% [30]. These data support the potential application of semaglutide in treating inflammation-induced heart damage.

Furthermore, semaglutide has demonstrated a protective effect against myocardial damage caused by acute myocardial infarction (AMI), coronary artery perfusion impairment, and ischemia-reperfusion injury [31, 32]. Key mechanisms include, but are not limited to, mitigating cellular damage, modulating metabolism and vascular function, and inhibiting apoptosis. For instance, in experimental animal models of AMI, semaglutide not only significantly reduced myocardial edema, necrosis, and fibrous tissue hyperplasia but also effectively lowered residual post-infarction risks by modulating energy metabolism, reducing blood glucose, lipids, and body weight [31, 33]. In Yorkshire pigs with myocardial ischemia, semaglutide treatment significantly enhanced AMPK, AKT, and eNOS activation and expression, improved vascular diastolic function, and increased coronary perfusion in ischemic areas [41]. Previous studies have confirmed that the AMPK / AKT / eNOS signaling pathway plays a critical role in regulating vasodilation and stimulating angiogenesis [18, 34], which may be one of the key mechanisms by which semaglutide alleviates myocardial ischemia. Additionally, semaglutide exerted cardioprotective effects by inhibiting ferroptosis [32] and activating the PKG/PKC ϵ /ERK1/2 signaling pathway [22], thereby reducing cellular apoptosis and infarct size. Meanwhile, subsequent clinical studies have further confirmed that the combined use of GLP-1RAs (such as semaglutide) and SGLT-2 inhibitors after percutaneous coronary intervention can increase myocardial salvage in the peri-infarct period, highlighting its potential value for clinical application. Clinical studies show that semaglutide

significantly reduces the risk of myocardial infarction and heart failure compared to tirzepatide and has a numerical advantage over it in reducing MACE [35]. Another important mechanism by which semaglutide improves cardiovascular health is by enhancing cardiac metabolic function. Myocardial damage is primarily associated with mitochondrial dysfunction and impaired glucose and lipid metabolism, leading to the accumulation of toxic lipids [36–38]. For example, semaglutide can improve mitochondrial function through the PI3K / AKT / CREB5 / NR4A1 axis, thereby mitigating myocardial damage caused by TAC [39]. Recent studies suggest that semaglutide can reduce Slc27a2 expression and decrease cardiac damage by enhancing lipid metabolism and reducing lipid accumulation in cardiac cells. Although Slc27a2 levels are higher in the blood of obese individuals [40], confirmation in human cardiac tissues is lacking due to ethical limitations. Despite this, studies strongly support the cardioprotective effects of semaglutide in obesity. The work by H. Yan et al. [31] and C. Stone et al. [41] further demonstrated in models of AMI and chronic cardiac injury, respectively, that semaglutide modulates glucose and lipid metabolism to optimize myocardial energy utilization. Thus, the mitochondrial protective and metabolic regulatory effects of semaglutide underscore its potential therapeutic value in both acute and chronic cardiac injury, opening promising prospects for future CVD treatment.

As research progresses, opportunities arise for developing personalized treatment plans tailored to individual patient characteristics. Creating algorithms that consider biomarkers, genetic variations, and metabolic profiles can help clinicians optimize drug selection, dosage, and combination therapy. This approach aims to enhance treatment efficacy while minimizing side effects and reducing the financial burden on patients. Furthermore, dynamic monitoring of cardiac and renal function, as well as metabolic changes, will allow for treatment adjustments—such as altering dosage and combination therapy regimens—based on the evolving pathophysiological state throughout the disease course [16]. This strategy is particularly promising for optimizing the management of patients with multiple comorbidities.

For the production of the medicine Velgia®, Promomed Group uses the solid-phase peptide synthesis (SPPS) method. This allows for process automation and precise reproduction of the desired

peptide structure, which negates the risks of changes in the resulting substance and, consequently, adverse immune reactions during drug administration.

In 2025, the unique semaglutide in the Russian Federation, Velgia® Eco, was introduced, which does not contain preservatives, including phenol and benzyl alcohol. The drug is supplied in single-use devices, eliminating the need for protection of the solution from microbial contamination. A simpler composition is particularly important for sensitive patients, as it reduces the additional component load during multi-month use and lowers the likelihood of adverse reactions associated with excipients. Such a composition is of fundamental importance in patients with concomitant liver and kidney diseases, where the accumulation of certain preservatives is associated with additional risks. Velgia® Eco is available in single-use autoinjectors. This delivery form does not require needle attachment, manual dose setting, or assessment of injection completion. The simplicity of the procedure reduces the risk of user errors and helps to more accurately reproduce the prescribed treatment regimen [42].

Study Limitations

Although semaglutide may have therapeutic effects in patients with obesity and concomitant cardiovascular risk, future research should focus on understanding the mechanisms of semaglutide action depending on the subtype of cardiovascular disease. A thorough evaluation of the efficacy and safety of semaglutide in real-world patient populations with cardiovascular

risk is necessary through multicenter and long-term studies. In clinical practice, improved monitoring and personalized risk management are crucial for the effective use of semaglutide, which will help integrate semaglutide into precision CVD therapy.

CONCLUSION

A significant reduction in anthropometric parameters (body weight, body mass index, waist and hip circumference) was observed after 24 weeks of semaglutide therapy. During therapy, no clinically significant changes were observed in liver function parameters (ALT, AST, ALP, bilirubin), pancreatic function (amylase), renal function (creatinine, urea, GFR), and systemic inflammation markers (CRP). However, a significant decrease in transaminase activity (ALT, AST) and serum uric acid concentration was noted.

After 6 months of semaglutide use, positive changes in the lipid profile were identified: a decrease in total cholesterol by 8.27% due to a reduction in non-HDL cholesterol, LDL cholesterol by 12.73%, triacylglycerols by 13.09%, and the atherogenic index by 1.83%. During the 6-month follow-up, patients maintained stable target blood pressure levels. Semaglutide therapy for 6 months led to a 18.6% reduction in the calculated 10-year cardiovascular risk according to the SCORE2 scale. The registered adverse events, predominantly gastrointestinal, were moderate and short-term. No cardiovascular events were recorded during the period of semaglutide use. Thus, the use of Velgia® is promising in the pharmacotherapy of obesity.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTION

Larisa A. Balykova — conceptualization, data analysis, writing—review & editing; Vera V. Stolyarova, Darya A. Orlova — data analysis, investigation, visualization, writing—original draft; Svetlana V. Shokina, Ekaterina I. Yamashkina — data analysis, visualization, writing—original draft; Marina V. Esina, Tatiana A. Surina — investigation, data analysis; Larina A. Zorina, Victoria S. Scherbakova — data analysis, writing—review & editing; Kira Ya. Zaslavskaya, Petr A. Bely — conceptualization, writing—review & editing. All the authors confirm their authorship compliance with the ICMJE international criteria (all the authors made a significant contribution to the conceptualization, conduct of the study and preparation of the article, read and approved the final version before publication).

REFERENCES

- Blüher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol*. 2019;15(5):288–98. DOI: 10.1038/s41574-019-0176-8
- Berkovskaya MA, Gurova OYu, Surkova EV, Fadeev VV. The history of the pharmacotherapy of obesity. *Problems of Endocrinology*. 2025;71(2):82–92. DOI: 10.14341/probl13469. EDN: AUKOVL
- Matheus AS, Tannus LR, Cobas RA, Palma CC, Negrato CA, Gomes MB. Impact of diabetes on cardiovascular disease: an update. *Int J Hypertens*. 2013;2013:653789. DOI: 10.1155/2013/653789
- Dedov II, Mokrysheva NG, Mel'nichenko GA, Troshina EA, Mazurina NV, Ershova EV, Komshilova KA, Andreeva EN, Antsiferov MB, Biriukova EV, Bordan NS, Vagapova GR, Volkova AR, Volkova NI, Volynkina AP, Dzgoeva FK, Kiseleva TP, Neimark AE, Romantsova TI, Ruiatkina LA, Suplotova LA, Khalimov YS, Yashkov YI. Obesity. *Consilium Medicum*. 2021;23(4):311–25. DOI: 10.26442/20751753.2021.4.200832. EDN: GYUULJ
- Boytsov SA, Drapkina OM, Shlyakhto EV, Konradi AO, Balanova YuA, Zhernakova YuV, Metelskaya VA, Oshchepkova EV, Rotar OP, Shalnova SA. Epidemiology of Cardiovascular Diseases and their Risk Factors in Regions of Russian Federation (ESSE-RF) study. Ten years later. *Cardiovascular Therapy and Prevention*. 2021;20(5):3007. DOI: 10.15829/1728-8800-2021-3007. EDN: ZPGROP
- Drapkina OM, Shalnova SA, Imaeva AE, Balanova YuA, Maksimov SA, Muromtseva GA, Kutsenko VA, Karamnova NS, Evstifeeva SE, Kapustina AV, Yarovaya EB, Litinskaya OA, Pokrovskaya MS, Efimova IA, Borisova AL, Doludin YuV, Kontsevaya AV. Epidemiology of Cardiovascular Diseases in Regions of Russian Federation. Third survey (ESSE-RF-3). Rationale and study design. *Cardiovascular Therapy and Prevention*. 2022;21(5):3246. DOI: 10.15829/1728-8800-2022-3246. EDN: EZUGUW
- Timasheva YaR, Balkhiyarova ZhR, Kochetova OV. Current state of the obesity research: genetic aspects, the role of microbiome, and susceptibility to COVID-19. *Problems of Endocrinology*. 2021;67(4):20–35. DOI: 10.14341/probl12775 EDN: LNCEYT
- Shishkina VV, Glukhov AA, Andreev AA, Kovalenko NS, Iseev MV, Laptiyova AYU, Ostroushko AP, Frolov AYU. Adipocytes and the role of their hormonal activity in the development of obesity. *Obesity and metabolism*. 2025;22(3):245–54. DOI: 10.14341/omet13149. EDN: GMGSU
- Troshina EA, Antsiferov MB, Ametov AS, Galstyan GR, Markova TN, Romantsova TI, Mazurina NV, Koteshkova OM. A personalized, evidence-based approach to obesity therapy using clinical algorithms: semaglutide or tirzepatide. *Problems of Endocrinology*. 2025;71(5):19–30. DOI: 10.14341/probl13677. EDN: TXGMRM
- Kurkin DV, Bakulin DA, Morkovin EI, Petrov VI, Strygin AV, Koryanova KN, Gorbunova YuV, Kolosov YuA, Ivanova OV, Pavlova EV, Dzhavakhyan MA, Zaborovsky AV, Saparova VB, Makarenko IE, Drai RI, Chumachenko AN. Physiology and pharmacology of glucagon-like peptide-1 receptor. *Pharmacy & Pharmacology*. 2023;11(4):347–80. DOI: 10.19163/2307-9266-2023-11-4-347-380. EDN: XFDHKA
- Ametov AS, Shokhin IE, Rogozhina EA, Bodrova TG, Nevretdinova ME, Bely PA, Zaslavskaya KYa, Scherbakova VS, Kurkin DV, Koryanova KN, Mishchenko ES, Kesova EYu, Kozlov ED, Samoshkina ES, Andreev DN, Kazaishvili YuG, Noskov SM, Balykova LA. Comparative analysis of physicochemical properties, bioequivalence, safety and tolerability of the first domestic semaglutide. *Pharmacy & Pharmacology*. 2023;11(4):324–46. DOI: 10.19163/2307-9266-2023-11-4-324-346. EDN: PABLBC
- Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, McGowan BM, Rosenstock J, Tran MTD, Wadden TA, Wharton S, Yokote K, Zeuthen N, Kushner RF; STEP 1 Study Group. Once-Weekly Semaglutide in Adults with Overweight or Obesity. *N Engl J Med*. 2021;384(11):989–1002. DOI: 10.1056/NEJMoa2032183
- Rubino D, Abrahamsson N, Davies M, Hesse D, Greenway FL, Jensen C, Lingvay I, Mosenzon O, Rosenstock J, Rubio MA, Rudofsky G, Tadayan S, Wadden TA, Dicker D; STEP 4 Investigators. Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity: The STEP 4 Randomized Clinical Trial. *JAMA*. 2021;325(14):1414–25. DOI: 10.1001/jama.2021.3224
- Garvey WT, Mechanick JL, Brett EM, Garber AJ, Hurley DL, Jastreboff AM, Nadolsky K, Pessah-Pollack R, Plodkowski R; Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines for Medical Care of Patients with Obesity. *Endocr Pract*. 2016;22 Suppl.3:1–203. DOI: 10.4158/EP161365.GL
- Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH; SELECT Trial Investigators. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *N Engl J Med*. 2023;389(24):2221–2232. DOI: 10.1056/NEJMoa2307563
- Ye L, Tang P, Wan H, Zhong X, Chen X, Liu C, Huang R. A Comprehensive Review on the Cardioprotective and Nephroprotective Effects of Semaglutide, and Its Therapeutic Efficacy and Mechanisms in Cardiorenal Syndrome. *Drug Des Devel Ther*. 2026;20:581491. DOI: 10.2147/DDDT.S581491
- Kosiborod MN, Deanfield J, Pratley R, Borlaug BA, Butler J, Davies MJ, Emerson SS, Kahn SE, Kitzman DW, Lingvay I, Mahaffey KW, Petrie MC, Plutzky J, Rasmussen S, Rönnbäck C, Shah SJ, Verma S, Weekes PE, Lincoff AM; SELECT, FLOW, STEP-HFpEF, and STEP-HFpEF DM Trial Committees and Investigators. Semaglutide versus placebo in patients with heart failure and mildly reduced or preserved ejection fraction: a pooled analysis of the SELECT, FLOW, STEP-HFpEF, and STEP-HFpEF DM randomised trials. *Lancet*. 2024;404(10456):949–61. DOI: 10.1016/S0140-6736(24)01643-X
- Pan X, Yang L, Wang S, Liu Y, Yue L, Chen S. Semaglutide ameliorates obesity-induced cardiac inflammation and oxidative stress mediated via reduction of neutrophil Cxcl2, S100a8, and S100a9 expression. *Mol Cell Biochem*. 2024;479(5):1133–47. DOI: 10.1007/s11010-023-04784-2
- Lin K, Wang A, Zhai C, Zhao Y, Hu H, Huang D, Zhai Q, Yan Y, Ge J. Semaglutide protects against diabetes-associated cardiac inflammation via Sirt3-dependent RAMP pathway. *Br J Pharmacol*. 2025;182(7):1561–81. DOI: 10.1111/bph.17327
- Li Q, Tuo X, Li B, Deng Z, Qiu Y, Xie H. Semaglutide attenuates excessive exercise-induced myocardial injury through inhibiting oxidative stress and inflammation in rats. *Life Sci*. 2020;250:117531. DOI: 10.1016/j.lfs.2020.117531

21. Zhu Q, Luo Y, Wen Y, Wang D, Li J, Fan Z. Semaglutide inhibits ischemia/reperfusion-induced cardiomyocyte apoptosis through activating PKG/PKCe/ERK1/2 pathway. *Biochem Biophys Res Commun.* 2023;647:1–8. DOI: 10.1016/j.bbrc.2023.01.049
22. Butler J, Shah SJ, Petrie MC, Borlaug BA, Abildstrøm SZ, Davies MJ, Hovingh GK, Kitzman DW, Møller DV, Verma S, Einfeldt MN, Lindegaard ML, Rasmussen S, Abhayaratna W, Ahmed FZ, Ben-Gal T, Chopra V, Ezekowitz JA, Fu M, Ito H, Lelonek M, Melenovský V, Merkely B, Núñez J, Perna E, Schou M, Senni M, Sharma K, van der Meer P, Von Lewinski D, Wolf D, Kosiborod MN; STEP-HFpEF Trial Committees and Investigators. Semaglutide versus placebo in people with obesity-related heart failure with preserved ejection fraction: a pooled analysis of the STEP-HFpEF and STEP-HFpEF DM randomised trials. *Lancet.* 2024;403(10437):1635–48. DOI: 10.1016/S0140-6736(24)00469-0
23. Duan Y, Li Q, Wu J, Zhou C, Liu X, Yue J, Chen X, Liu J, Zhang Q, Zhang Y, Zhang L. A detrimental role of endothelial S1PR2 in cardiac ischemia-reperfusion injury via modulating mitochondrial dysfunction, NLRP3 inflammasome activation, and pyroptosis. *Redox Biol.* 2024;75:103244. DOI: 10.1016/j.redox.2024.103244
24. Lv SL, Zeng ZF, Gan WQ, Wang WQ, Li TG, Hou YF, Yan Z, Zhang RX, Yang M. Lp-PLA2 inhibition prevents Ang II-induced cardiac inflammation and fibrosis by blocking macrophage NLRP3 inflammasome activation. *Acta Pharmacol Sin.* 2021;42(12):2016–32. DOI: 10.1038/s41401-021-00703-7
25. Zhang J, Huang L, Shi X, Yang L, Hua F, Ma J, Zhu W, Liu X, Xuan R, Shen Y, Liu J, Lai X, Yu P. Metformin protects against myocardial ischemia-reperfusion injury and cell pyroptosis via AMPK/NLRP3 inflammasome pathway. *Aging (Albany NY).* 2020;12(23):24270–87. DOI: 10.18632/aging.202143
26. He W, Wei J, Liu X, Zhang Z, Huang R, Jiang Z. Semaglutide ameliorates pressure overload-induced cardiac hypertrophy by improving cardiac mitophagy to suppress the activation of NLRP3 inflammasome. *Sci Rep.* 2024;14(1):11824. DOI: 10.1038/s41598-024-62465-6
27. Deanfield J, Lincoff AM, Kahn SE, Emerson SS, Lingvay I, Scirica BM, Plutzky J, Kushner RF, Colhoun HM, Hovingh GK, Stensen S, Weekes PE, Jeppesen OK, Bravo R, Wu CC, Komuro I, Santini F, Hjelmæsæth J, Urina-Triana M, Buscemi S, Ryan DH. Semaglutide and cardiovascular outcomes by baseline and changes in adiposity measurements: a prespecified analysis of the SELECT trial. *Lancet.* 2025;406(10516):2257–68. DOI: 10.1016/S0140-6736(25)01375-3
28. Gavini MP, Mahmood A, Belenchia AM, Beauparlant P, Kumar SA, Ardhanari S, DeMarco VG, Pulakat L. Suppression of Inflammatory Cardiac Cytokine Network in Rats with Untreated Obesity and Pre-Diabetes by AT2 Receptor Agonist NP-6A4. *Front Pharmacol.* 2021;12:693167. DOI: 10.3389/fphar.2021.693167
29. Wu R, Xing B, Zhou Z, Yu L, Wang H. Effect of semaglutide on arrhythmic, major cardiovascular, and renal outcomes in patients with overweight or obesity: a systematic review and meta-analysis. *Eur J Med Res.* 2025;30(1):835. DOI: 10.1186/s40001-025-03124-y
30. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH; SELECT Trial Investigators. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *N Engl J Med.* 2023;389(24):2221–32. DOI: 10.1056/NEJMoa2307563
31. Yan H, Yao W, Li Y, Li T, Song K, Yan P, Dang Y. Cardiometabolic Modulation by Semaglutide Contributes to Cardioprotection in Rats with Myocardial Infarction. *Drug Des Devel Ther.* 2024;18:5485–500. DOI: 10.2147/DDDT.S491970
32. Liu Y, Li Z, Xu X, Zou Y, Zhang M, Chen Y, Zhu W, Han B. Semaglutide attenuates myocardial ischemia-reperfusion injury by inhibiting ferroptosis of cardiomyocytes via activation of PKC-S100A9 axis. *Front Pharmacol.* 2025;16:1529652. DOI: 10.3389/fphar.2025.1529652
33. Ajmera R, Karim H, Fegan PG, Dwivedi G, Lan NSR. Eligibility for Semaglutide 2.4 mg in Patients With Acute Myocardial Infarction and Overweight or Obesity Without Diabetes: A Real-World Analysis. *Heart Lung Circ.* 2025;34(9):977–9. DOI: 10.1016/j.hlc.2025.01.011
34. Wang S, Miao J, Qu M, Yang GY, Shen L. Adiponectin modulates the function of endothelial progenitor cells via AMPK/eNOS signaling pathway. *Biochem Biophys Res Commun.* 2017;493(1):64–70. DOI: 10.1016/j.bbrc.2017.09.073
35. Krüger N, Schneeweiss S, Desai RJ, Sreedhara SK, Kehoe AR, Fuse K, Hahn G, Schunkert H, Wang SV. Cardiovascular outcomes of semaglutide and tirzepatide for patients with type 2 diabetes in clinical practice. *Nat Med.* 2026;32(1):342–52. DOI: 10.1038/s41591-025-04102-x
36. Ritterhoff J, Tian R. Metabolic mechanisms in physiological and pathological cardiac hypertrophy: new paradigms and challenges. *Nat Rev Cardiol.* 2023;20(12):812–29. DOI: 10.1038/s41569-023-00887-x
37. Da Dalt L, Cabodevilla AG, Goldberg IJ, Norata GD. Cardiac lipid metabolism, mitochondrial function, and heart failure. *Cardiovasc Res.* 2023;119(10):1905–14. DOI: 10.1093/cvr/cvad100
38. Lopaschuk GD, Karwi QG, Tian R, Wende AR, Abel ED. Cardiac Energy Metabolism in Heart Failure. *Circ Res.* 2021;128(10):1487–513. DOI: 10.1161/CIRCRESAHA.121.318241
39. Chakraborty P, Niewiadomska M, Farhat K, Morris L, Whyte S, Humphries KM, Stavrakis S. Effect of Low-Level Tragus Stimulation on Cardiac Metabolism in Heart Failure with Preserved Ejection Fraction: A Transcriptomics-Based Analysis. *Int J Mol Sci.* 2024;25(8):4312. DOI: 10.3390/ijms25084312
40. Pan X, Wang S, Yang X, Jia B, Chen S. Semaglutide attenuates lipotoxicity-induced cardiac injury by inhibiting Slc27a2 expression. *Chem Biol Interact.* 2025;418:111583. DOI: 10.1016/j.cbi.2025.111583
41. Stone C, Harris DD, Broadwin M, Kanuparth M, Nho JW, Yalamanchili K, Hamze J, Abid MR, Sellke FW. Semaglutide Improves Myocardial Perfusion and Performance in a Large Animal Model of Coronary Artery Disease. *Arterioscler Thromb Vasc Biol.* 2025;45(2):285–97. DOI: 10.1161/ATVBAHA.124.321850
42. Truong TH, Nguyen TT, Armor BL, Farley JR. Errors in the Administration Technique of Insulin Pen Devices: A Result of Insufficient Education. *Diabetes Ther.* 2017;8(2):221–6. DOI: 10.1007/s13300-017-0242-y

AUTHORS

Larisa A. Balykova — Doctor of Sciences (Medicine), Professor, Corresponding Member of the Russian Academy of Sciences, Acting Rector, National Research Ogarev Mordovia State University. ORCID ID: 0000-0002-2290-0013. E-mail: larisabalykova@yandex.ru

Vera V. Stolyarova — Doctor of Sciences (Medicine), Professor, Head of the Department of Outpatient Therapy, National Research Ogarev Mordovia State University. ORCID ID: 0000-0002-6164-4737. E-mail: vera_s00@mail.ru

Darya A. Orlova — Assistant of the Department of Outpatient Therapy, National Research Ogarev Mordovia State University. ORCID ID: 0000-0001-6398-9993. E-mail: karpova-dasha1996@mail.ru

Svetlana V. Shokina — Candidate of Sciences (Medicine), Assistant Professor, Assistant Professor of the Department of Outpatient Therapy, National Research Ogarev Mordovia State University. ORCID ID: 0000-0001-8650-1778. E-mail: sveti-kh@mail.ru

Ekaterina I. Yamashkina — Candidate of Sciences (Medicine), Assistant Professor, Assistant Professor of the Department of Outpatient Therapy, National Research Ogarev Mordovia State University. ORCID ID: 0009-0004-5092-7872. E-mail: yamashkinamzrm@inbox.ru

Marina V. Esina — Candidate of Sciences (Medicine), Assistant Professor, Assistant Professor of the Department of Outpatient Therapy, National Research Ogarev Mordovia State University. ORCID

ID: 0000-0002-5318-2966. E-mail: esina.marina.val@yandex.ru

Tatiana A. Surina — Candidate of Sciences (Medicine), Assistant Professor, Assistant Professor of the Department of Outpatient Therapy, National Research Ogarev Mordovia State University. ORCID ID: 0009-0000-4460-2220. E-mail: surinata13@yandex.ru

Larina A. Zorina — Candidate of Sciences (Medicine), clinical pharmacologist, obstetrician-gynecologist, dietitian, lecturer of the Department of Therapy, Geriatrics, and Anti-Aging Medicine, Federal Scientific and Clinical Center for Specialized Types of Medical Care and Medical Technologies. ORCID ID: 0009-0006-4544-5486. E-mail: slarisa@bk.ru

Victoria S. Scherbakova — Candidate of Sciences (Biology), Assistant Professor of the Department of Pharmacology, Tver State Medical University. ORCID: 0000-0002-7251-8744. E-mail: victoria_kaptar@mail.ru

Kira Ya. Zaslavskaya — Assistant of the Department of Biological and Pharmaceutical Chemistry with the course of organization and management of pharmacy, National Research Ogarev Mordovia State University. ORCID ID: 0000-0002-7348-9412. E-mail: kiryonok@yandex.ru

Petr A. Bely — Doctor of Sciences (Medicine), Professor of the Department of Internal Medicine and Gastroenterology, Russian University of Medicine. ORCID ID: 0000-0001-5998-4874. E-mail: pbely@ncpharm.ru