УДК 616-008.9-021.6-02:616.12/.13]-092.9
https://doi.org/10.20538/1682-0363-2022-3-13-21

Morphological changes in the heart and aorta of rats with diet-induced metabolic syndrome

Birulina J.G., Ivanov V.V., Buyko E.E., Bykov V.V., Dzyuman A.N., Nosarev A.V., Grigoreva A.V., Gusakova S.V.

Siberian State Medical University
2, Moscow Trakt, Tomsk, 634050, Russian Federation

ABSTRACT

Aim. To identify early morphological changes in the heart and aorta of rats with experimental metabolic syndrome induced by a high-fat and high-carbohydrate diet (HFHCD).

Materials and methods. The study was carried out on male Wistar rats. The animals were divided into two groups: a control group (n = 10) and an experimental group (n = 10). The rats from the control group were fed with a standard laboratory diet. The rats from the experimental group received HFHCD for 12 weeks. Body weight, blood pressure (BP), and individual parameters of carbohydrate and lipid metabolism were assessed in the rats. A histologic examination of the heart and aorta in the animals was performed.

Results. Feeding rats with HFHCD led to an increase in body weight, elevation of BP, obesity, hyperglycemia, and triglyceridemia. The histologic examination of the heart in the rats of the experimental group showed signs of vascular disease, lipomatosis, and focal myocardial degeneration. Lipid accumulation in the cells of the media, hyperplasia of adipocytes in the adventitia, and depletion and fragmentation of the elastic lamina were revealed in the aortic wall of the rats receiving HFHCD.

Conclusion. The study indicated that HFHCD is an effective way to model metabolic syndrome. Structural disorders in the heart and aorta may be the mainstay for the development of cardiomyopathy and arterial hypertension in diet-induced metabolic syndrome.

Keywords: high-fat, high-carbohydrate diet, metabolic syndrome, myocardium, aorta, obesity

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The study was carried out within the research project No. 21-22-07-03-05 and supported by the Council for Grants Awarded by the President of the Russian Federation (MK-3302.2022.1.4).

Conformity with the principles of ethics. The study was approved by the Commission for Control over Care and Use of Laboratory Animals at Siberian State Medical University (Protocol No. 1 of 07.12.2021).

For citation: Birulina J.G., Ivanov V.V., Buyko E.E., Bykov V.V., Dzyuman A.N., Nosarev A.V., Grigoreva A.V., Gusakova S.V. Morphological changes in the heart and aorta of rats with diet-induced metabolic syndrome. *Bulletin of Siberian Medicine.* 2022;21(3):13–21. https://doi.org/10.20538/1682-0363-2022-3-13-21.

✉ *Birulina Julia G.,* birulina20@yandex.ru

Морфологические изменения в сердце и аорте крыс при диет-индуцированном метаболическом синдроме

Бирулина Ю.Г., Иванов В.В., Буйко Е.Е., Быков В.В., Дзюман А.Н., Носарев А.В., Григорьева А.В., Гусакова С.В.

Сибирский государственный медицинский университет (СибГМУ)
Россия, 634050, г. Томск, Московский тракт, 2

РЕЗЮМЕ

Цель – выявить ранние морфологические изменения в сердце и аорте крыс при экспериментальном метаболическом синдроме, вызванном высокожировой и высокоуглеводной диетой (ВЖВУД).

Материалы и методы. Исследование выполнено на самцах крыс линии Wistar, которые были распределены на контрольную (n = 10) и экспериментальную (n = 10) группы. Крысы контрольной группы получали стандартный корм. Крысы экспериментальной группы в течение 12 нед находились на ВЖВУД. У животных определяли массу тела, артериальное давление (АД) и отдельные параметры углеводного и липидного обмена. Выполняли гистологическое исследование тканей сердца и аорты животных.

Результаты. Установлено, что ВЖВУД вызывает у крыс увеличение массы тела, ожирение, повышение АД, гипергликемию, триглицеридемию. При гистологическом исследовании сердца крыс экспериментальной группы выявлены признаки сосудистого поражения, липоматоза, очаговой дистрофии миокарда. В стенке аорте крыс, получавших высокожировой и высокоуглеводный рацион, выявлено накопление липидов в клетках медии, гиперплазия жировых клеток в адвентиции, истончение и разволокнение эластических мембран.

Заключение. Исследование показало, что ВЖВУД является эффективным способом моделирования метаболического синдрома. Обнаруженные структурные изменения в тканях сердца и аорты могут лежать в основе развития кардиомиопатии и артериальной гипертензии при диет-индуцированном метаболическом синдроме.

Ключевые слова: высокожировая и высокоуглеводная диета, метаболический синдром, миокард, аорта, ожирение

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

Источник финансирования. Исследование выполнено в рамках научного проекта № 21-22-07-03-05 и при финансовой поддержке Совета по грантам Президента Российской Федерации (МК-3302.2022.1.4).

Соответствие принципам этики. Исследование одобрено комиссией по контролю содержания и использования лабораторных животных СибГМУ (протокол № 1 от 07.12.2021).

Для цитирования: Бирулина Ю.Г., Иванов В.В., Буйко Е.Е., Быков В.В., Дзюман А.Н., Носарев А.В., Григорьева А.В., Гусакова С.В. Морфологические изменения в сердце и аорте крыс при диет-индуцированном метаболическом синдроме. *Бюллетень сибирской медицины.* 2022;21(3):13–21. https://doi.org/10.20538/1682-0363-2022-3-13-21.

INTRODUCTION

Over the past decades, the prevalence of cardiovascular diseases (CVDs) has increased dramatically around the world. According to experts, CVDs would be the cause of more than 23 million deaths around the world by 2030 [1]. Recent epidemiologic studies have shown a relationship between the nature of nutrition and an increase in the prevalence of CVDs [2, 3]. The studies have shown that dietary fats play an important role in the development of cardiovascular disease [4]. Currently, 49% of patients with CVDs are overweight and obese. These components are crucial in metabolic syndrome (MS) along with hyperglycemia, insulin resistance, arterial hypertension, and atherogenic dyslipidemia [5, 6].

Recent studies have proven the possibility and mechanisms of myocardial lipotoxic injury in obesity, which alters both the structure and the functional state of the myocardium [7, 8]. Systemic inflammation and oxidative stress that occur in MS result in myocardial fibrosis and are associated with damage to the endothelial and smooth muscle cells of the vascular wall [9]. In addition, obesity and vascular dysfunction accelerate the development of arterial hypertension, which increases the risk of heart failure [10].

Experimental diet-induced MS models are the most accessible way to study the morphofunctional features of the impact of metabolic disorders on the cardiovascular system [11, 12]. In recent years, a combined high-fat and high-carbohydrate diet has become widespread, since it most closely resembles a diet of a modern person and is considered appropriate for reproducing the pathogenetic factors and phenomenology of MS [13, 14]. A detailed description of the histologic changes that occur in the myocardium and blood vessels at early stages of MS may contribute to the development of potential approaches to CVD treatment in metabolic disorders.

The aim of the study was to identify early morphological changes in the heart and aorta of rats with experimental MS induced by HFHCD.

MATERIALS AND METHODS

The studies were carried out in compliance with the principles of humanity set out in the directives of the European Community (86 / 609 / EEC) and the Declaration of Helsinki. The rats were kept at a constant room temperature (23º C) and exposed to 12 h : 12 h light : dark cycles with free access to food and water. Male Wistar rats (20 rats, average weight 270.6 ± 30.1 g, 6 weeks old) were randomly divided into a control group (n = 10) and an experimental group (n = 10). The rats of the control group (CG) were fed with a standard diet (Chara, Assortiment-Agro, Russian Federation, the ratio of proteins, fats, and carbohydrates was 26%, 5%, and 45%, respectively). The rats of the experimental group (EG) received a specially designed HFHCD (the ratio of proteins, fats, and carbohydrates was 16%, 22%, and 54%, respectively) containing a standard food with the addition of animal fat (lard, 17%), fructose (17%), and cholesterol (0,25%). Drinking water was replaced with a 20% fructose solution. The duration of the experiment was 12 weeks, after which the animals were euthanized via CO_2 inhalation.

To confirm MS in the rats fed with HFHCD, body weight and blood pressure (BP) were measured at the end of the experiment (Systola, Neurobotics, Russian Federation). In the euthanized animals, whole blood was taken from the heart; visceral adipose tissue, the heart, and the thoracic aorta were removed. Serum for biochemical studies was obtained by centrifugation of the whole blood (3,000 rpm, 10 min) and stored at −20° C for further analysis. The levels of glucose, triacylglycerols (TAG), and cholesterol (CHOL) in the blood serum were determined by enzymatic colorimetric methods (Chronolab Systems SL., Spain). The concentrations of TAG and CHOL in the aorta (in mg / g of tissue) were measured photometrically using test kits (Chronolab, Spain) after extraction of the lipid fraction from the tissue samples with a chloroform – methanol mixture. Before the analysis, a 20% solution of Thesit (Sigma-Aldrich, USA) dissolved in chloroform was added to the organic phase. Chloroform was removed with a stream of nitrogen, and emulsified lipids were dissolved in distilled water. Working reagents from the TAG and CHOL assay kits were added to the resulting aqueous emulsion.

To study structural changes, the heart and thoracic aorta were fixed in 10% neutral buffered formalin (BioVitrum, Russian Federation) for 24 h, washed from the fixative, and then dehydrated in an isopropanol-based solution IsoPrep (BioVitrum, Russian Federation). The prepared objects were embedded in the Histomix paraffin medium (BioVitrum, Russian Federation), and thin (5–6 μm) sections were made on the HM355 S automatic microtome (Thermo Fisher Scientific, USA). The sections were stained with hematoxylin (BioVitrum, Russian Federation), eosin (BioVitrum, Russian Federation), and orcein (Bio Vitrum, Russian Federation) to identify elastic units of the aorta. To detect lipids, the aortic samples were frozen at –80° C. Then, they were poured into a cryogel, and 20 μm thick sections were made on the HM525 NX cryostat (Thermo Fisher Scientific, USA) at –25° C. The sections were mounted on poly-L-lysine-coated slides and stained with Sudan III according to Herxheimer (BioVitrum, Russian Federation). Micropreparations were examined using the AxioSkop 40 microscope (Carl Zeiss, Germany). Digital images of the sections were obtained using the AxioVision 4.6 software. In histology specimens of the aorta, the thickness of the intima, media, and adventitia (in μm) was measured.

The data were analyzed using the SPSS Statistics 23 software. Normally distributed data were presented

as the mean and standard deviation ($M \pm SD$). Non-normally distributed variables were presented as the median and the interquartile range Me (Q_1; Q_3). The Student's t-test or the Mann – Whitney U-test were used to identify differences between the samples. The differences were considered statistically significant at $p < 0.05$.

RESULTS

Feeding rats with HFHCD for 12 weeks resulted in an increase in body weight, systolic and diastolic BP, specific gravity of abdominal fat, including mesenteric, epididymal, and retroperitoneal adipose tissue in the EG rats. HFHCD led to hyperglycemia, an increase in TAG in the blood serum, as well as an increase in the levels of TAG and CHOL in the aortic wall (Table 1).

Table 1

Physiological and biochemical indicators in rats, $M \pm SD$

Indicator	Group	
	control (n = 10)	experimental (n = 10)
Body weight, g	415.3 ± 35.6	466.1 ± 32.1 (p = 0.002)
Systolic BP, mm Hg	129.1 ± 8.4	138.2 ±8.1 (p = 0.005)
Diastolic BP, mm Hg	92.3 ± 8.2	110.4 ± 12.6 (p = 0.04)
Adipose tissue weight / body weight ratio, g	2.2 ± 0.3	4.8 ± 1.3 (p = 0.001)
Glucose (serum), mmol / l	4.1 ± 0.5	5.6 ± 0.7 (p = 0.002)
TAG (serum), mmol / l	1.2 ± 0.8	3.2 ± 0.9 (p = 0.001)
CHOL (serum), mmol / l	2.2 ± 0.3	2.9 ± 0.4 (p = 0.055)
TAG (aorta), mg / g	4.2 ± 1.2	6.8 ± 1.4 (p = 0.001)
CHOL (aorta), mg / g	1.1 ± 0.4	2.6 ± 0.6 (p = 0.03)

Note: here and in Table 2: p – significance of differences compared with the control group.

The heart wall in the CG rats had normal structure. Ventricular cardiomyocytes had an elongated cylindrical shape, with distinguishable longitudinal and transverse striations; they lacked pathological tortuosity. The interstitium was represented by a few vessels, which were single arteries in the right ventricle (Fig. 1, *A*). The interstitium of the left ventricular myocardium was more pronounced due to plethora of capillaries, dilatation and emptying of venules, and the presence of optically empty slit-like spaces between the cardiomyocytes of the middle and inner layers of the myocardium (Fig. 1, *B*).

Compared with the CG, the micropreparations of the right ventricle obtained from the experimental rats showed local aggregates of adipocytes in the epicardium of the right ventricle (Fig. 1, *C*). In the wall of the left ventricle, foci of fragmented cardiomyocytes and cardiomyocytes with intense cytoplasm staining and loss of longitudinal and transverse striations were identified. Areas of myocardial disarray were found (Fig. 1, *D*). The changes in the vessels described for the CG persisted, but they were more pronounced: increased number of erythrocytes and vascular dilatation were more common; they were present in all small vessels and in larger arteries and veins, in some of the latter, blood separation was noted and the lumen of such veins was filled with plasma (Fig. 1, *D*).

The aortic wall in the CG rats had normal architecture in all three layers (Fig. 2, *A*). In the EG, the structure of the aortic wall was preserved, but aggregates of adipocytes appeared in the adventitia. Besides, in the cytoplasm of many interstitial cells (fibroblasts, smooth muscle cells), multiple small, irregularly shaped, optically empty inclusions were noted, and the interstitial cells took the form of foam cells (Fig. 2, *B*). The arrangement of the foam cells varied according to the depth of the wall: they were almost always localized in the media closer to the adventitia, less often – in the middle and outer parts of the media. The morphometric study revealed an increase in the thickness of the middle and outer layer of the aortic wall (Table 2).

Table 2

Thickness of aortic wall layers, μm, Me (Q_1; Q_3)

Group	Intima	Media	Adventitia
Control, n = 10	5.2 (4.6; 6.9)	63.4 (60.7; 0.4)	10.5 (9.5; 13.1)
Experimental, n = 10	6.1 (5.1; 7.3)	71.6 (67.1; 78.5) (p = 0.01)	14.8 (13.3; 16.5) (p = 0.001)

In the frozen sections of the CG rat aorta, stained with Sudan III according to Herxheimer, Sudan III-stained components were detected exclusively in lipocytes of the adventitia (Fig. 3, *A*) and were not numerous. In the EG, adipocytes in the adventitia of the aorta were characterized by abundant Sudan III-stained inclusions, which were also detected in small amounts in the cells of the outer part of the media (Fig. 3, *B*).

The aortic wall of the CG rats stained with orcein revealed elastic units, such as membranes and fibers, with a normal structure (Fig. 4, *A*). In the EG, signs of elastolysis were observed, such as a decrease in staining, thinning, and defibrated fenestrated elastic laminae. The tortuosity of the elastic components of the media also increased, and their mutual parallel arrangement was disturbed (Fig. 4, *B*).

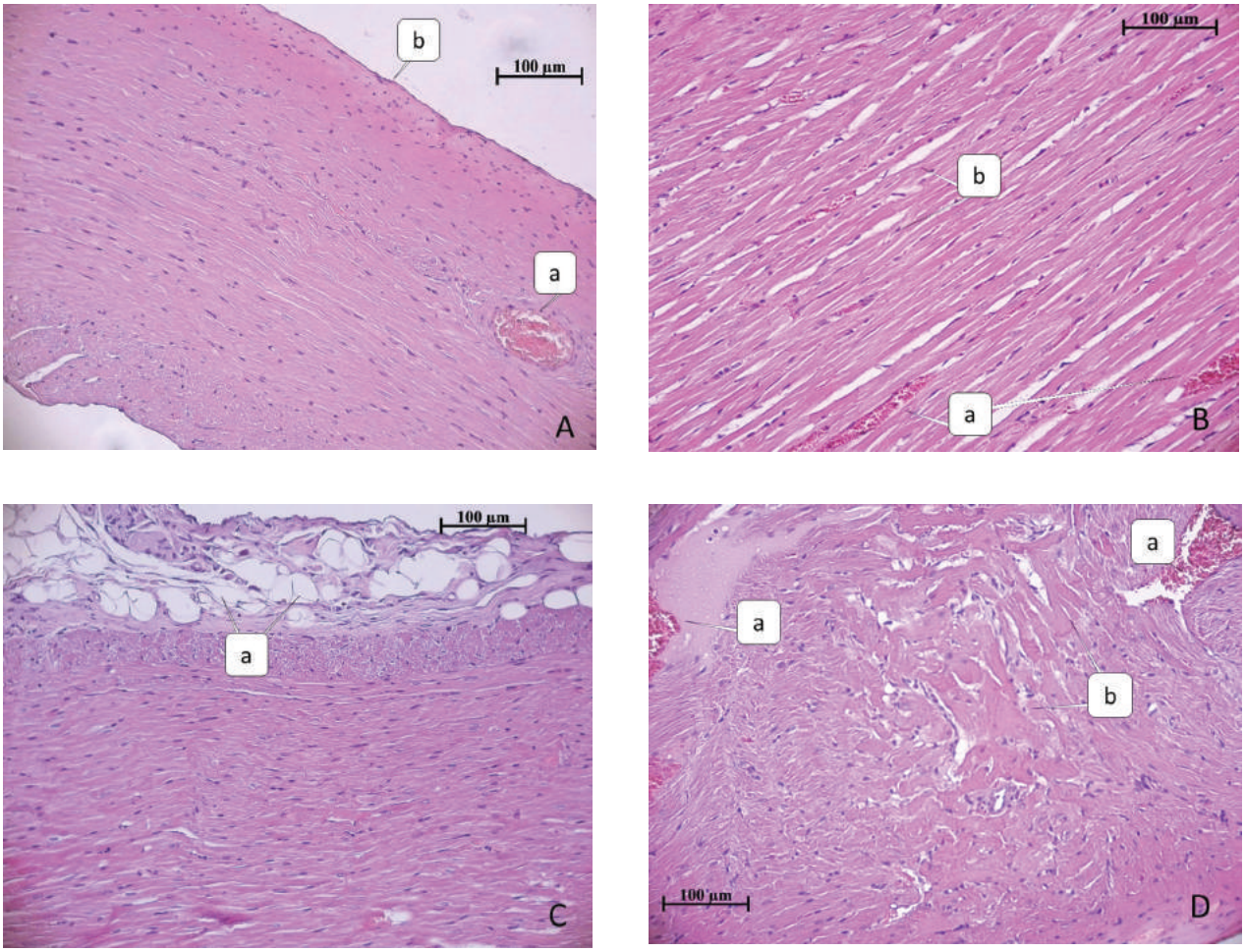

Fig. 1. Effect of HFHCD on the morphological structure of rat myocardium. *A* – fragment of the right ventricular wall of the rat in the CG: plethora of the artery (*a*), absence of epicardial lipomatosis (*b*). *B* – fragment of the left ventricular wall of the rat in the CG: plethora of the capillaries (*a*), interstitial edema (*b*). *C* – fragment of the right ventricular wall of the rat in the EG: epicardial lipomatosis (*a*). *D* – fragment of the left ventricular wall of the rat in the EG: plethora and plasma stasis in the vessels (*a*), myocardial disarray and striations in cardiomyocytes (*b*) ×200. Here and in Fig. 2, staining with hematoxylin and eosin

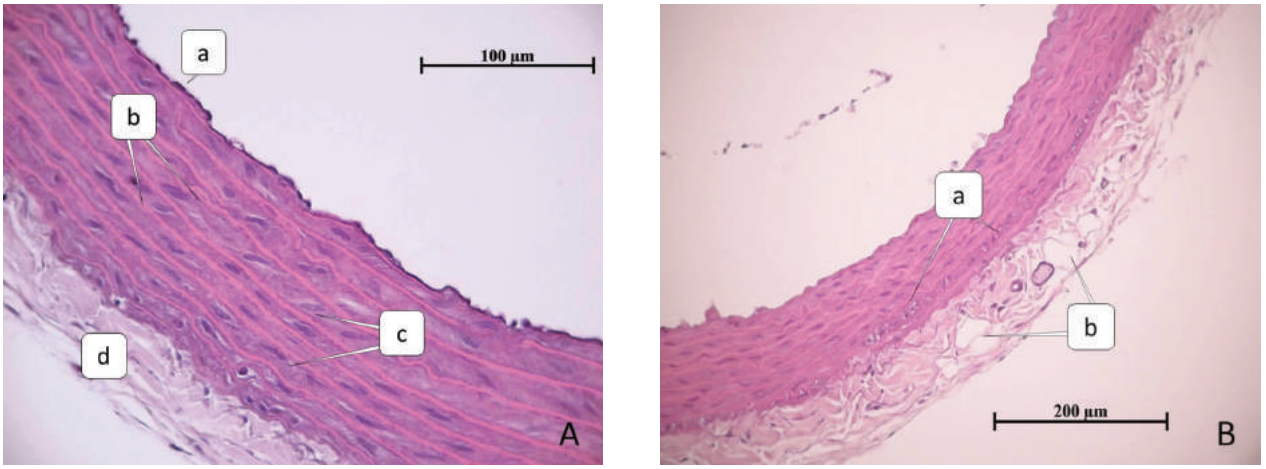

Fig. 2. Effect of HFHCD on the morphological structure of the aortic wall. *A* – transverse section of the CG rat aorta: endothelium (*a*), fenestrated elastic laminae (*b*), interstitial cells (*c*), adventitia (*d*) have a normal structure. ×200. *B* – transverse section of EG rat aorta: xanthomatous cells in the media (*a*), adipocytes in the adventitia (*b*). ×100

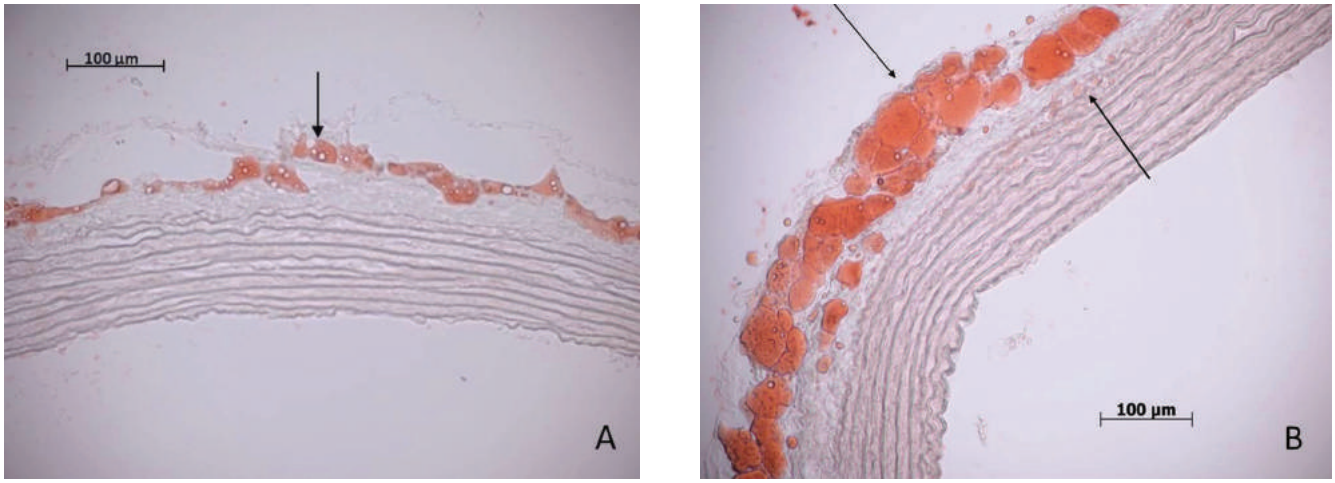

Fig. 3. Accumulation of lipids in the aortic wall of the rats fed with HFHCD. *A* – transverse section of the CG rat aorta. Localization of Sudan III-stained components (lipids) in the adypocytes of the adventitia (black arrow). *B* – transverse section of the EG rat aorta. Accumulation of Sudan III-stained components (lipids) in the adipocytes of the adventitia and cells of the media (black arrow). *A, B* – Sudan III staining according to Herxheimer. ×200

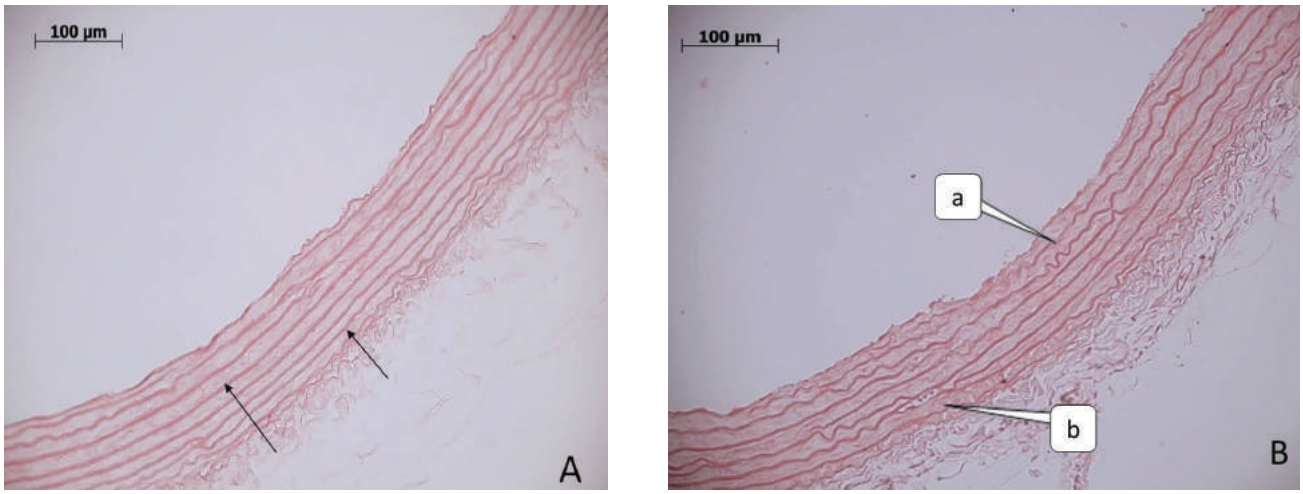

Fig. 4. Changes in the elastic lamina in the aortic wall of the rats fed with HFHCD. *A* – transverse section of the CG rat aorta. Normal structure of fenestrated elastic laminae (black arrow). *B* – transverse section of the EG rat aorta. Increase in tortuosity (*a*), disturbed parallel arrangement of fenestrated elastic laminae (*b*). *A, B* – orcein staining. 200x

DISCUSSION

Animal models represent some of the most effective and available tools for understanding the pathophysiological mechanisms underlying MS. One way to model MS is to use specially designed diets [3, 11]. Diets containing both high-fat and high-carbohydrate components have been reported to be more clinically representative than single-component diets alone [12, 15].

In the present study, MS in the rats was induced with HFHCD. Feeding the animals with HFHCD for 12 weeks resulted in an increase in animals' body weight, obesity, increased BP, development of hyperglycemia, and a rise in the concentration of TAG in the blood serum. The data obtained indicate that feeding the rats with a HFHCD contributes to the formation of MS [4, 13].

Disorders of carbohydrate and lipid metabolism that occur in MS, in combination with chronic inflammation and oxidative stress, lead to the development of pathomorphological changes in the cardiovascular system [16, 17]. It is known that dysregulation of energy homeostasis in the heart in MS is associated with various adaptations and changes in the structure and function of the myocardium, which occur with abnormal lipid accumulation and adipose tissue hyperpla-

sia [18]. Studies on rats receiving high-fat and (or) high-carbohydrate diet also showed that oxidative stress is a potential mechanism for obesity-induced cardiotoxicity [8, 19]. In the cardiac muscle of the animals fed with such a diet, the absence of myofilaments and / or their disorganization, dilatation of the sarcoplasmic reticulum vesicles, a decrease in the diameter of myofibrils, intracellular vacuolization, the presence of lipid inclusions, hypertrophy, and signs of fibrotic changes are morphologically determined [10, 14, 20], the latter being most pronounced with an increased content of saturated fatty acids in food.

At the same time, it has been noted that HFHCD-induced vascular endothelial dysfunction in MS [16] provokes stasis of formed elements and dilatation of the vascular lumen in the myocardium. Our findings, namely focal lesions of cardiomyocytes in the left ventricle in the form of striations and fragmentation, lipomatosis in the epicardium, and microcirculatory disorders (hyperemia) in the hearts of the EG rats are consistent with the known data. However, the revealed changes were not pronounced.

The histologic study of the micropreparations of the EG rat aorta showed the beginning of atherosclerotic vascular wall remodeling, which to a greater extent affected the media and adventitia. A decrease in orcein staining, discontinuity of fenestrated elastic laminae, the presence of foam cells, the emergence of Sudan III-stained inclusions in the interstitial cells of the media, and hyperplasia of adipocytes in the adventitia may be the cause of the increase in the aortic wall thickness in the animals receiving HFHCD, which is also characteristic of experimental MS [9, 21, 22]. Similar morphological changes in the aorta are manifested by changes in its mechanical properties, including a decrease in elasticity and an increase in wall stiffness [23]. This is due to elastolysis and a decrease in production of elastic components with a simultaneous rise in collagen production, resulting in an increase in the collagen / elastin ratio. Thickening of the aortic wall and its stiffness due to an increase in the collagen level, as well as degeneration of smooth muscle cells can be a structural basis that contributes to arterial hypertension. At the same time, accumulation of TAG in the aorta can be considered as an additional prognostic criterion for vascular wall stiffness [24].

CONCLUSION

The study showed that HFHCD is an effective way to simulate MS in rats, causing obesity, increased BP, hyperglycemia, and triglyceridemia. Morphological changes in the heart wall that occur in MS are characterized by damage to the vascular bed, lipomatosis, and focal myocardial degeneration. In the aorta, signs of media remodeling, lipid infiltration of interstitial cells of the media, hyperplasia of adipocytes, and defibrated elastic membranes were revealed. The detected structural disorders may underlie the development of cardiomyopathy and hypertension in diet-induced MS. The resulting experimental model can be used to study the mechanisms of development of metabolic and hemodynamic disorders in MS, as well as to test potential cardioprotective and angioprotective pharmacological agents.

REFERENCES

1. Michos E.D., Khan S.S. Further understanding of ideal cardiovascular health score metrics and cardiovascular disease. *Expert. Rev. Cardiovasc. Ther.* 2021;19(7):607–617. DOI: 10.1080/14779072.2021.1937127.
2. Rider O.J., Lewis A.J., Neubauer S. Structural and metabolic effects of obesity on the myocardium and the aorta. *Obesity Facts*. 2014;7(5):329–338. DOI: 10.1159/000368429.
3. Rodríguez-Correa E., González-Pérez I., Clavel-Pérez P.I., Contreras-Vargas Y., Carvajal K. Biochemical and nutritional overview of diet-induced metabolic syndrome models in rats: what is the best choice? *Nutr. Diabetes*. 2020;10(1):24. DOI: 10.1038/s41387-020-0127-4.
4. Poudyal H., Panchal S.K., Ward L.C., Waanders J., Brown L. Chronic high-carbohydrate, high-fat feeding in rats induces reversible metabolic, cardiovascular, and liver changes. *Am. J. Physiol. Endocrinol. Metab.* 2012;302(12):E1472–E1482. DOI: 10.1152/ajpendo.00102.2012.
5. Aydin S., Aksoy A., Aydin S., Kalayci M, Yilmaz M., Kuloglu T. et al. Today's and yesterday's of pathophysiology: Biochemistry of metabolic syndrome and animal models. *Nutrition*. 2014;30(1):1–9. DOI: 10.1016/j.nut.2013.05.013.
6. Saklayen M.G. The global epidemic of the metabolic syndrome. *Curr. Hypertens. Rep.* 2018;20(2):12. DOI: 10.1007/s11906-018-0812-z.
7. Chumakova G.A., Veselovskaya N.G., Kozarenko A.A., Vorobyeva Yu.V. Morphology, structure, and function of the heart in obesity. *Russ. J. Cardiol*. 2012;(4):93–99 (in Russ.). DOI: 10.15829/1560-4071-2012-4-93-99.
8. Jiménez-González S., Marín-Royo G., Jurado-López R., Bartolomé M.V., Romero-Miranda A., Luaces M. et al. The crosstalk between cardiac lipotoxicity and mitochondrial oxidative stress in the cardiac alterations in diet-induced obesity in rats. *Cells*. 2020;9(2):451. DOI: 10.3390/cells9020451.
9. Saraf R., Huang T., Mahmood F., Owais K., Bardia A., Khabbaz K.R. et al. Early cellular changes in the ascending aorta and myocardium in a swine model of metabolic syndrome. *PLoS One*. 2016;11(1):e0146481. DOI: 10.1371/journal.pone.0146481.
10. Leopoldo A.S., Sugizaki M.M., Lima-Leopoldo A.P., do Nascimento A.F., Luvizotto R., de Campos D.H. et al. Car-

diac remodeling in a rat model of diet-induced obesity. *Can. J. Cardiol.* 2010;26(8):423–429. DOI: 10.1016/s0828-282x(10)70440-2.
11. Leonardi, B.F., Gosmann, G., Zimmer, A.R. Modeling diet-induced metabolic syndrome in rodents. *Mol. Nutr. Food Res.* 2020;64(22):2000249. DOI: 10.1002/mnfr.202000249.
12. Panchal S.K., Brown L. Rodent Models for Metabolic Syndrome Research. *J. Biomed. Biotechnol*. 2011;2011:351982. DOI: 10.1155/2011/351982.
13. Wong S.K., Chin K.Y., Suhaimi F.H., Ahmad F., Ima-Nirwana S. The effects of a modified high-carbohydrate high-fat diet on metabolic syndrome parameters in male rats. *Exp. Clin. Endocrinol. Diabetes.* 2018;126(4):205–212. DOI: 10.1055/s-0043-119352.
14. Okatan E.N., Kizil S., Gokturk H., Can B., Turan B. High-carbohydrate diet-induced myocardial remodelling in rats. *Curr. Res. Cardiol.* 2015;2(1):5–10. DOI: 10.4172/2368-0512.1000020.
15. Artinano A.A., Castro M.M. Experimental rat models to study the metabolic syndrome. *Br. J. Nutr.* 2009;102(9):1246–1253. DOI: 10.1017/S0007114509990729.
16. Tran V., De Silva T.M., Sobey C.G., Lim K., Drummond G.R., Vinh A. et al. The vascular consequences of metabolic syndrome: rodent models, endothelial dysfunction, and current therapies. *Front. Pharmacol.* 2020;11:148. DOI: 10.3389/fphar.2020.00148.
17. Ruan X.-H., Ma T., Fan Y., Ablation of TMEM126B protects against heart injury via improving mitochondrial function in high fat diet (HFD)-induced mice. *Biochem. Biophys. Res. Commun.* 2019;515(4):636–643. DOI: 10.1016/j.bbrc.2019.05.084.
18. Sahraoui A., Dewachter C., Vegh G., Mc Entee K., Naeije R., Bouguerra S.A. et al. High fat diet altered cardiac metabolic gene profile in Psammomys obesus gerbils. *Lipids Health Dis*. 2020;19(1):123. DOI: 10.1186/s12944-020-01301-y.
19. Feriani A., Bizzarri M., Tir M., Aldawood N., Alobaid H., Allagui M.S. et al. High-fat diet-induced aggravation of cardiovascular impairment in permethrin-treated Wistar rats. *Ecotoxicol. Environ. Saf.* 2021;222:112461. DOI: 10.1016/j.ecoenv.2021.112461.
20. Lepczyński A., Ożgo M., Michałek K., Dratwa-Chałupnik A., Grabowska M., Herosimczyk A. et al. Effects of three-month feeding high fat diets with different fatty acid composition on myocardial proteome in mice. *Nutrients*. 2021;13(2):330. DOI: 10.3390/nu13020330.
21. Logvinov S.V., Naryzhnaya N.V., Kurbatov B.K., Gorbunov A.S., Birulina Y.G., Maslov L.L. et al. High carbohydrate high fat diet causes arterial hypertension and histological changes in the aortic wall in aged rats: The involvement of connective tissue growth factors and fibronectin. *Exp Gerontol.* 2021;154:111543. DOI: 10.1016/j.exger.2021.111543.
22. Tarimov K.O., Subbotkin M.V., Kulanova A.A., Petrenko V.I., Kubyshkin A.V., Fomochkina I.I. et al. Comparative analysis of correction of morphofunctional disorders in the cardiovascular system in simulated metabolic syndrome. *Obesity and Metabolism.* 2020;17(2):208–219 (in Russ.). DOI: 10.14341/omet12296.
23. Martinez-Quinones P., McCarthy C.G., Watts S.W., Klee N.S., Komic A., Calmasini F.B. et al. Hypertension induced morphological and physiological changes in cells of the arterial wall. *Am. J. Hypertens.* 2018;31(10):1067–1078. DOI: 10.1093/ajh/hpy083.
24. Wang X., Ye P., Cao R., Yang X., Xiao W., Zhang Y. et al. Triglycerides are a predictive factor for arterial stiffness: a community-based 4.8-year prospective study. *Lipids Health Dis.* 2016;15:97. DOI: 10.1186/s12944-016-0266-8.

Authors contribution

Birulina J. G., Ivanov V.V. – conception and design, drafting of the manuscript. Dzyuman A.N., Bykov V.V. – carrying out of the histologic examination, analysis and interpretation of the data. Nosarev A.V., Gusakova S.V. – approval of the manuscript. Buyko V.V., Grigoreva A.V. – simulation of the metabolic syndrome, carrying out of the biochemical studies.

Authors information

Birulina Julia G. – Cand. Sci. (Biology), Associate Professor, Biophysics and Functional Diagnostics Division, Siberian State Medical University, Tomsk, birulina20@yandex.ru, https://orcid.org/0000-0003-1237-9786

Ivanov Vladimir V. – Cand. Sci. (Biology), Head of the Center for Preclinical Research, Central Research Laboratory, Siberian State Medical University, Tomsk, ivanovvv1953@gmail.com, https://orcid.org/0000-0001-9348-4945

Buyko Evgeny E. – Laboratory Assistant, Center for Preclinical Research, Central Research Laboratory, Siberian State Medical University, Tomsk, buykoevgen@yandex.ru, https://orcid.org/0000-0002-6714-1938

Bykov Vladimir V. – Cand. Sci. (Med.), Teaching Assistant, Pharmacology Division, Siberian State Medical University, Tomsk, vladimir.b.1989@gmail.com, https://orcid.org/0000-0002-5145-2184

Dzyuman Anna N. – Cand. Sci. (Med.), Associate Professor, Morphology and General Pathology Division, Siberian State Medical University, Tomsk, dzyman@mail.ru, https://orcid.org/0000-0002-0795-0987

Nosarev Alexey V. – Dr. Sci. (Med.), Professor, Biophysics and Functional Diagnostics Division, Siberian State Medical University, Tomsk, avnosarev@yandex.ru, https://orcid.org/0000-0002-0119-9707

Grigoreva Anna V. – Teaching Assistant, Biology and Genetics Division, Siberian State Medical University, Tomsk, Russian Federation, anna-grigoreva-87@mail.ru, https://orcid.org/0000-0002-1962-9584

Gusakova Svetlana V. – Dr. Sci. (Med.), Head of the Biophysics and Functional Diagnostics Division, Siberian State Medical University, Tomsk, gusacova@yandex.ru, https://orcid.org/0000-0001-5047-8668

(✉) **Birulina Julia G.,** birulina20@yandex.ru

Received 21.01.2022;
approved after peer review 21.02.2022;
accepted 17.03.2022