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Gut microbiota and vascular biomarkers in patients without clinical cardiovascular diseases

Daria Kashtanova [a,c,*,1], Olga Tkacheva [c,2], Anna Popenko [b,4], Lilit Egshatyan [d,3], Alexander Tyakht [b,5], Dmitry Alexeev [f], Yulia Kotovskaya [c,e,6], Ekaterina Plokhova [c,7], Sergey Boytsov [a,8]

[a] National Research Centre for Preventive Medicine, Moscow, Russian Federation
[b] Institute for Physical-Chemical Medicine, Moscow, Russian Federation
[c] Pirogov Russian National Research Medical University, Russian Clinical Research Center for Gerontology, Moscow, Russian Federation
[d] Federal State Budgetary Establishment Endocrinology Research Centre, Russian Federation
[e] RUDN-University, Moscow, Russian Federation
[f] Complex Biological Systems Lab, Moscow Institute of Physics and Technology (State University), 9 Institutskiy per., Dolgoprudny, Moscow Region, 141700, Russian Federation

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* Corresponding author. "Research of Age and Age-associated Conditions" Department, National Research Centre for Preventive Medicine, bld. 10, Petroverigskiy Lane, Moscow, 101000, Russian Federation.
E-mail addresses: dr.kashtanova@gmail.com (D. Kashtanova), Tkacheva@rambler.ru (O. Tkacheva), a.s.popenko@niifhm.ru (A. Popenko), lilit.egshatyan@yandex.ru (L. Egshatyan), at@niifhm.ru (A. Tyakht), exappeal@gmail.com (D. Alexeev), kotovskaya@bk.ru (Y. Kotovskaya), evplokhova@gmail.com (E. Plokhova), prof-boytsov@mail.ru (S. Boytsov).
[1] Russian Clinical Research Center for Gerontology, Pirogov Russian National Research Medical University, bld. 16, 1st Leonova Street, Moscow, 129226, Russian Federation.
[2] Russian Clinical Research Center for Gerontology, bld. 16, 1st 15 Leonova Street, Moscow, 129226, Russian Federation.
[3] Federal State Budgetary Establishment Endocrinology Research Centre, Moscow.
[4] Laboratory of Bioinformatics, Scientific Research Institute for Physical-Chemical Medicine, bld. 1a, Malaya Pirogovskaya St, Moscow, 119435, Russian Federation.
[5] Laboratory of Bioinformatics, Scientific Research Institute for Physical-Chemical Medicine, bld. 1a, Malaya Pirogovskaya St, 119435, Moscow, Russian Federation.
[6] Department of Cardiology and Personified Medicine, RUDN-University, 6 Miklukho-Maklaya St., Moscow, Russian Federation, Laboratory of Cardiovascular Ageing, Russian Clinical Research Center for Gerontology, Pirogov Russian National Research Medical University, bld. 16, 1st Leonova Street, Moscow, 129226, Russian Federation.
[7] "Research of Age and Age-associated Conditions" Department, National Research Centre for Preventive Medicine, bld. 10, Petroverigskiy Lane, Moscow, 101000, Russian Federation.
[8] Department of Cardiology and Molecular Genetics, National Research Centre for Preventive Medicine, bld. 10, Petroverigskiy Lane, Moscow, 101000, Russian Federation.

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Abstract The aim of this research was to study the association between the gut microbiota composition and arterial wall properties. The study included 92 participants, men and women aged 25—76 years old without clinical manifestation of chronic diseases but with the possible presence of cardiovascular risk factors. Carbohydrate metabolism examination, duplex scanning of the carotid arteries with the measurement of the intima-media thickness (IMT), the carotid-femoral pulse wave velocity (PWV) measurement, and 16S rRNA (V3—V4 regions) sequencing of the gut microbiota were performed in all participants. Higher *Serratia* abundance was associated with the increased IMT and CRP levels. *Blautia* representation was associated with IMT. Higher *Bacteroides* representation was associated with higher pulse wave velocity in non-diabetic subjects. Although this study had some limitations, we have demonstrated that the composition of the gut microbiota was associated both with atherosclerotic and arterial stiffness markers.

Introduction

Cardiovascular diseases (CVD) are the leading cause of mortality and morbidity globally. The principal underlying mechanisms of CVD are the arterial wall stiffness and atherosclerosis.[1] The key markers of these processes are the increased pulse wave velocity (PWV), the intima-media thickening, vascular stenosis and the presence of atherosclerotic plaques. Despite the obvious relevance of this issue and a huge amount of funding and research, the cause of the vascular wall damage is still the subject of debate. To date the gut microbiota is considered to be a new player in the pathophysiology of vascular wall changes. Microorganisms that inhabit us have a huge metabolic potential, the number of genes in metagenome exceeds the number of genes in the human genome. Microbiota affects the immune system, inflammatory processes and may either suppress or aggravate low-grade inflammation[2] underlying the atherogenesis and other disorders.

Karlsson et al. in 2012 published a study that showed the differences of the gut microbiota in healthy people and in patients with symptomatic atherosclerosis. Greater abundance of Collinsella genus was more typical to the clinical group and *Eubacterium*, *Roseburia* and *Bacteroides* — for healthy subjects. Metagenome of patients with clinical atherosclerosis contained many genes involved in the peptidoglycan synthesis regulation which may be one of the causes of low-grade inflammation, while metagenome of healthy subjects contained more genes responsible for the anti-inflammatory agents and antioxidants production.[3]

In 2014 Jill Gregory et al. conducted an interesting experiment, they transplanted the gut microbiota from donor mice with atherosclerosis and without atherosclerosis to the recipient mice with the apolipoprotein E deficiency (predisposed to atherosclerosis) and with the gut microbiota suppressed by antimicrobial drug therapy. In mice, which were transplanted with feces from atherosclerotic mice, atherogenesis was much more pronounced than in the second group. Thus, during the transplantation mice were "infected" with atheroclerosis.[4]

Almost all studies that investigated the relationship between the blood vessels and gut microbiota were devoted to the atherosclerotic changes and occasionally to the arterial stiffness. Rossi et al. found that some of bacteria metabolites were associated with the PWV increase and were the "cardiovascular toxins",[5] afterward these data have been confirmed by Gulhan et al.[6] However, there were no sequencing of the gut microbiota and metabolites were measured precisely (not as part of metabolome) in these studies.

In the present study, we have first examined the relationship between the gut microbiota composition and the markers of both athero- and arteriosclerosis.

Aim

To study the association between the gut microbiota composition and arterial wall properties in patients without clinical manifestation of cardiovascular disease.

Materials and methods

Patients from Moscow and Moscow Region (the Caucasian race) aged from 25 to 76 years old who had passed the preventive outpatient examination in the FGBI National Research Center for Preventive Medicine (Moscow) were included in the cross-sectional study.

The inclusion criteria were as follows:

Men and women over 25 without clinical manifestations of cardiovascular diseases (but with the possible presence of cardiovascular risk factors) and other noncommunicable diseases were included in the study. Participants were not treated with any medicine and signed informed consent to participate in the study.

The exclusion criteria were as follows:

Clinically evident atherosclerosis (coronary artery disease including history of myocardial infarction, stable or unstable angina, cerebrovascular disease including stroke, intermittent claudication, etc.) or any cardiovascular diseases (e.g valvular heart disease). Regular intake of any