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The best practices of the Russian Federation in the organization of anticoagulant therapy in patients with high risk of thromboembolic events

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Organization of anticoagulant therapy control plays a key role in ensuring the effectiveness and safety of anticoagulant use. Currently, several models of organization are successfully used in the Russian Federation, which cover more than 23,000 patients at high risk for thromboembolic events. There are following common features of the models used: the maximum reduction in the time from the moment of international normalized ratio (INR) testing with a quick communication with a patient for the need to adjust the dose, the ability to sort patients depending on the degree of hypocoagulation and the risks of events with the creation of a personalized approach to treatment, the organization of a shared information space and maintaining a register of patients.

Key words: anticoagulant therapy, anticoagulant offices, vitamin K antagonists, time of the therapeutic margin.

Relationships and Activities: none.

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Many cardiovascular complications are associated with thromboembolic events (TEE): cardioembolic stroke and systemic embolism in atrial fibrillation (AF) and deep vein thrombosis and pulmonary embolism in patients with mechanical valves. The basis of these complications are blood coagulation disorders. Risk of TEE is significantly reduced with anticoagulant therapy, which is prescribed for short and long term [1]. For more than 50 years, vitamin K antagonists (VKA) have been used to reduce the activity of vitamin K-dependent clotting factors. A meta-analysis of controlled studies showed that the use of such agents in patients with nonvalvular AF reduces the relative risk of all strokes by 64%, which corresponds to an absolute risk reduction of 2,7% per year [2]. In the last 10 years, novel inhibitors of clotting factors began to be used — direct oral anticoagulants (DOAC), which are not less effective than VKA but require careful monitoring of a patient [3]. One danger in using anticoagulants is the risk of bleeding events. A risk-benefit ratio is determined in each patient and specifies the drug selection.

Laboratory assessment and organization of outpatient monitoring is a key factor for the successful prevention of TEE using VKA. In world practice, various organizational models for monitoring patients receiving VKA and DOAC are used [4]. This study presents the Russian experience in monitoring patients with a high risk of TEE receiving anticoagulants.

The aim was to study the best practices of providing anticoagulant therapy in patients with high risk of TEE in different subjects of Russia.

Material and methods

The study descripts the experience of 5 Russian regions in the organization of anticoagulant therapy monitoring in outpatients with high risk of TEE: St. Petersburg, Arkhangelsk, Kursk, Chelyabinsk and Tatarstan. More than 23,000 patients took part in the implemented projects.

Results

One of the first projects to structure work with patients receiving warfarin was the organization of offices for anticoagulant therapy control in **St. Petersburg**. It started in 2013 at the City Consultative and Diagnostic Center № 1. From the very beginning, the following principles were laid down: the shortest time from the moment of blood sampling for assessing the international normalized ratio (INR) to the doctor's consultation on test results, thorough identifying the risks TEE and bleeding events, work with modifiable risk factors, increasing patient motivation to improve medication adherence, a multidisciplinary team approach to solving individual problems. Since 2015, successful practices have been extended to city healthcare facilities and a network of eight offices was organized in St. Petersburg within the outpatient care system based on large hospitals and one federal institution — Almazov National Medical Research Center. In laboratory monitoring, the emphasis was on the use of portable INR analyzers, which significantly increased the efficiency and ensured the implementation of single window mode. INR measurement is carried out during a doctor's appointment in mentioned or another special office. A patient receives the result of a laboratory test and a doctor's consultation in one visit with the adjustment, if necessary, of the drug dose. Since 2018, a tariff for the study of INR using portable coagulation analyzer was provided, which, together with the tariff for a doctor's appointment, made it possible to fully ensure monitoring in anticoagulant office at the expense of the compulsory health insurance fund. Patient capacity of one such office is up to 2 thousand visits per year. During the implementation of the project, over 8 thousand patients were observed through network of offices. With the accumulation of experience and an increase in using DOAC, such patients also began to be referred to offices and amounted to 30% in 2019. The positive effect of anticoagulant offices is primarily to increase the INR time in therapeutic range to 75% (above the therapeutic range — 8,5%; below — 16,5%, mainly due to first-time visits). There were 0,6% of TEE events, 7% — minor bleeding events. No fatal bleedings or TEE were recorded. The work of multidisciplinary team, coordination of work with the Stroke Prevention Center allowed to monitor the most complex patients — with hereditary thrombophilia and antiphospholipid syndrome (2%), intracardiac thrombosis (2%), those requiring adjustment of antiplatelet therapy after stent implantation but having bleedings (5%).

Active and successful work on organizing monitoring of patients receiving long-term anticoagulation therapy is carried out in **Arkhangelsk**, which began in 2007. By 2016, it was implemented within a regional project to centralize monitoring of VKA therapy based on 28 medical organizations of the Arkhangelsk Oblast. In 2019, the number of offices increased to 38. A total of 6763 patients is monitored. An IT organizational structure based on a WEB server and network, coordinated by the Regional Center for Antithrombotic Therapy of the Arkhangelsk Oblast was created and implemented. This allowed to create a register of patients receiving long-term anticoagulation with a personalized approach to each patient.

The strategic goal of organizing a network of offices in the Arkhangelsk Oblast is to increase the availability, quality, safety and effectiveness of long-

term anticoagulation with VKA, and since 2020 — DOAC. There are following main tasks: determining indications for anticoagulant therapy; laboratory tests of INR; adjustment of VKA and DOAC therapy individually for each patient; patient-centered approach. Much attention is paid to education activity with the creation of programs for patients (1st level), the general medical community (doctors, nurses, pharmacists) (2nd level) and anticoagulation specialists, offices' staff (3rd level). 'Patient schools' for those receiving VKA and DOAC were organized, videos and audio presentations were prepared for nursing staff to help educate patients, a training manual on patient education based on questions and answers, and handouts were created. On the website of the Department of Clinical Pharmacology and Pharmacotherapy of the Northern State Medical University and the Regional Center for Antithrombotic Therapy, a section has been created for doctors and patients on the work of anticoagulant offices.

According to the analysis of anticoagulant office work in the Arkhangelsk Oblast for 2019, the INR time in therapeutic range amounted to 73% (Me 73 (65-82)). The advantages of WEB support were revealed and tested in actual clinical practice: accessibility for a larger number of patients in remote areas; implementation of a quality management system for medical workers; integration of various medical specialists and medical organizations into a single system; maintaining a register of patients receiving VKA therapy. In 2017, the project was awarded the M.V. Lomonosov prize as the best innovation and research work.

The original centralized VKA monitoring system was created in **Kursk**, which has been implemented since 2012. The model is based on the following principles: providing a qualitative and reliable determination of INR, creating conditions for the patient to quickly receive information and adjust therapy on the day of blood sampling, developing a software package that allows, under the under medical supervision, to monitor and interpret the INR value in real time with memorization of all results, test dates, and drug doses on the server in the electronic patient record. For the implementation of the project, conditions were created for the collection, transportation and analysis of INR in one centralized laboratory — a single center for determining INR. For emergency determination of INR and/or analysis on unplanned days, portable coagulation analyzers were additionally delivered to each medical institution. The software package "Warfarin manager" and "Warfarin manager 0.1.0" was developed as the central element of the centralized monitoring system. The patient monitoring system reduced the number of ischemic strokes from 8,06% at to 0,73% without fatal outcomes ($p<0,001$), major bleedings requiring hospitalization from 3,0% to 0,9% without statistical significance, minor bleedings from 16,13% to 5,15% ($p<0,05$). The INR time in therapeutic range was increased from 40,1% to 73,2% ($p<0,01$). Thus, the clinical and laboratory model of monitoring of VKA therapy in the Kursk Oblast is a novel form of interaction between the doctor and cardiovascular patients, based on personalized medicine and innovative technologies. The authors proved the economic efficiency of model by preventing TEE and bleeding events, which are expensive in the treatment and further disability of patients.

The centralized system of anticoagulant offices was organized in **Chelyabinsk**. It includes 10 local offices based on medical organizations with a single coordinating center. The main aim at the organization phase was to improve control of VKA therapy. All offices were equipped with portable coagulation analyzers, consumables and software at the expense of the regional budget. This allowed to develop a single electronic database for patients taking VKA. The offices include 8 cardiologists and 2 therapists, nurses who have undergone special training. The work is carried out under the supervision of coordinating center. There are following functions of coordinating center: consultation of patients with difficulties in selecting a dose in the office; formation of a single city register; development and implementation of training programs for patients and medical staff; preparation of regular single reports on the operation results. Currently, 1830 people are in the general register. Indications for VKA therapy in 74,9% of patients were nonvalvular AF, in 17,4% — mechanical valves and valvular AF; in 6,4% — secondary prevention of venous thromboembolism (VTE); in 1,3% — other causes (intracardiac thrombosis, arterial thrombosis). Over 8 months, an increase in the average INR time in therapeutic range from 49% to 62%. There were 40% of patients with INR time in therapeutic range $\geqslant$65%. During the year, among the patients included in the register, 7 people died (0,38%), 6 (0,32%) had major bleeding, 3 — hemorrhagic strokes, 12 (0,7%) — thrombotic events, including ischemic strokes, myocardial infarction and VTE. High medication adherence within the implementation of this model is noted.

In the **Republic of Tatarstan**, the decision to introduce a centralized monitoring system for patients receiving anticoagulant therapy was made in 2018. To implement this project and solve a number of tasks, the Portavita Anticoagulation application was chosen as the most optimal and modern, evidence-based medical software. Extensive experience in its use has been gained in the Netherlands; the software was adapted for Russia together with the Almazov National

Medical Research Center in St. Petersburg and tested in actual clinical practice. The Anticoagulation module not only forms a register for dynamic monitoring of included patients, but also is the basis for selecting VKA dosage. Centralized monitoring system is based on anticoagulant offices, where patients are registered and monitored, with a staff of 1 therapist and 1 nurse. The expertise center coordinates with a staff of 2 cardiologists and 1 nurse, created on the basis of Interregional Clinical and Diagnostic Center. To date, 27 offices operate in the Republic of Tajikistan, where 4500 patients receiving VKA are monitored. There are 2207 patients (51,6%) with AF, 1692 (39,5%) — mechanical valves, 228 (5,3%) — VTE, 17(0,4%) — pulmonary hypertension. In the module, patients are divided into 3 dosing lists based on the algorithm taking into account ~40 parameters. The program prompts the recommended dose and the date of next visit. The recommendations are validated by the medical specialist. According to reports, 46% of patients belonged to the 3rd list, that is, they needed care of a highly qualified specialist due to bleeding vents, a planned surgery, which had out-of-range INR in last 3 tests. In general, INR time in therapeutic range, which is easily monitored by the program, increased in the region from 45% to 60%. During operation offices deaths were not recorded, and none of the patients needed hospitalization. During the pandemic, personal accounts were created for all interested patients for remote interaction.

Conclusion

The system for anticoagulant therapy monitoring through the creation of specialized organizational models and software systems can significantly increase the effectiveness and safety of treatment in patients at high risk for TEE, reduce cardiovascular mortality and disability of the population from and is cost-effective.

Such a model provides support to primary care physicians and reduces the risk of bleeding; the doctor is "not afraid" to prescribe anticoagulants, delegating the authority to monitor the patient to specially trained medical workers. A patient-centered care is implemented as part of "patient schools". The use of software systems makes it possible to maintain registers with full and operational monitoring of results. The implementation of the models gained particular importance during the COVID-19 epidemic, making it possible not to reduce the number of monitored patients.

Promising is the adaptation of DOAC programs. This program is a part of the Portavita Anticoagulation application, and can also become an additional solution in the Warfarin manager and Warfarin manager 0.1.0, which will fully cover this category of patients. The implementation of mobile applications is also a modern and effective addition to the centralized and remote monitoring system.

Relationships and Activities: none.

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The prevalence of wide QRS complex (⩾110 ms) among the population, depending on sex, age and place of residence

Muromtseva G. A.[1], Vilkov V. G.[1], Shalnova S. A.[1], Konstantinov V. V.[1], Deev A. D.[1], Evstifeeva S. E.[1], Balanova Yu. A.[1], Imaeva A. E.[1], Kapustina A. V.[1], Karamnova N. S.[1], Shlyakhto E. V.[2], Boytsov S. A.[3], Nedogoda S. V.[4], Shabunova A. A.[5], Chernych T. M.[6], Belova O. A.[7], Indukaeva E. V.[8], Grinstein Yu. I.[9], Trubacheva I. A.[10], Efanov A. Yu.[11], Astachova Z. T.[12], Kulakova N. V.[13], on behalf of ESSE-RF study participants

Aim. To assess the prevalence of wide QRS complex (≥110 ms) among the population, depending on sex, age, place of residence (urban or rural area), the presence of obesity and cardiovascular disease.

Material and methods. The analysis was based on the ESSE-RF study (n=17364, men — 38%). Twelve-lead resting electrocardiography (ECG) data from the regions participating in the study were analyzed according to the Minnesota code manual. Patients were divided into groups of QRS <110 ms and ≥110 ms (wide QRS).

Results. QRS groups did not differ in heart rate and age. The prevalence of wide QRS complex in the population amounted to 17,2%. Men were likely to have wide QRS than women (18,5% and 16,2%, respectively, p<0,0005) due to the increased frequency of "preblock" QRS duration (110-119 ms; 12,3% vs 10,9%, respectively, p<0,025). The prevalence of QRS ≥120 ms in the sex groups was the same, almost 7%. The prevalence of widened QRS in the population significantly exceeded other unfavorable prognostic ECG indicators, such as major ECG abnormalities, conduction disorders, abnormal Q wave (QS). The prevalence of wide QRS complex increased with age from 11,1% to 19,2, (p<0,001). The highest increase in prevalence of wide QRS complex was observed after 55 years; nondynamic periods were recorded in men from 25, and in women from 35 to 54 years. In contrast to women, the prevalence of wide QRS in men did not depend on the place of residence (18,6% in urban and 18,3% in rural areas); in rural women this parameter was observed as often as in men. This may indicate a more severe epidemiological situation of cardiovascular disease in rural residents. Obesity, high blood pressure, and a history of coronary artery disease were more common in the group of wide QRS complex.

Conclusion. For wide QRS complex, the same age and sex relationships are characteristic as for the basic routine ECG indicators. The prevalence of wide QRS in the population exceeds major ECG abnormalities, conduction disorders, abnormal Q wave (QS). In rural residents, the increased prevalence of wide QRS is probably due to the greater prevalence of obesity and hypertension.

Key words: QRS ≥110 ms, prevalence of wide QRS complex, age and sex characteristics.

Relationships and Activities. The data of this paper was presented at the International Congress of Electrocardiology. Joint meeting of ISHNE and ISE, Belgrad, 2019 (ICE 2019) and the X International Conference "Arterial hypertension and cardiovascular disease prevention", Vitebsk, 2019.

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Electrocardiographic (ECG) predictors of fatal and nonfatal cardiovascular events are still of great interest. The search for new significant prognostic parameters continues. In recent years, wide QRS complex (⩾110 ms) considers as one of these parameters.

It is known that diseases leading to changes in cardiac size and structure, such as hypertension (HTN), myocarditis, heart defects, coronary artery disease (CAD) and myocardial infarction, heart failure, are often accompanied by impaired conduction and decreased ventricular depolarization [1, 2]. The latter, in turn, are associated with left ventricular dysfunction, morbidity and mortality. For example, people with left bundle branch block are 10 times more likely to have death as the first manifestation of cardiovascular disease (CVD) than without it [3]. "Preblock" QRS duration (100-120 or 90-120 ms) is also associated with an increased cardiovascular risk. Thus, the QRS duration of 102±25 vs 97±20 ms in the Oregon Sudden Unexpected Death Study was independently associated with sudden cardiac death [4], and in patients with aortic stenosis, but without complete bundle branch blocks, QRS ⩾100 ms vs QRS <85 ms — with an increase in the risk of sudden death by 5 times, cardiovascular death by 2,5 times [5]. An increased risk of death and hospitalization was also found in patients with atrial fibrillation with QRS within 90-119 ms [6]. The closest associations were revealed for the "preblock" QRS duration ⩾110 ms. Patients with QRS duration ⩾110 ms have a 2,5 times higher risk of sudden cardiac death even after adjustment for demographic and clinical risk factors. According to authors from Thomas Jefferson University, QRS duration ⩾110 ms without bundle branch blocks is an independent predictor of death from non-ST elevation myocardial infarction, as well as the ventricular arrhythmias within 30 days or 1 year after the event [7].

Despite the great deal of clinical data on the prognostic value of different QRS duration (>90, 100, 110, 120 ms, etc.), the epidemiological characteristics of this ECG indicator, including "preblock" QRS, have not been studied enough.

The aim was to assess the prevalence of wide QRS complex (⩾110 ms) among the population, depending on sex, age, place of residence (urban or rural area), the presence of obesity and CVD.

Material and methods

The analysis included the ECG of 17364 men and women aged 25-64 years as part of random samples of the population in regions participating in the ESSE-RF study (2012-2014). The study was approved by the ethics committees of three research centers: National Medical Research Center for Preventive Medicine; Almazov National Medical Research Center; National Medical Research Center of Cardiology. All participants signed an informed consent.

In all regions participating in the study, ECG was recorded on a PadSy ECG management system (MedSet, Germany), followed by the transfer of digitized ECG information to the Federal Database located in the National Medical Research Center for Preventive Medicine (Moscow). Twelve-lead ECG was recorded in the supine position, at rest, according to standard methodological requirements. ECG analysis and coding according to the Minnesota code manual was carried out by two specialists of National Medical Research Center for Preventive Medicine. The third specialist was involved in disputed cases. ECGs were classified into two groups (QRS <110 ms, QRS ⩾110 ms), and for a more detailed analysis, into 3 groups (QRS <110 ms, 110-119 ms and ⩾120 ms). Heart rate (HR) was calculated by the RR interval.

The prevalence of QRS ⩾110 ms was estimated in sex and age groups, depending on place of residence (urban or rural area), as well as among people with general or abdominal obesity, with high BP ⩾140/90 mm Hg at the examination time or history of CAD, as well as among people with major ECG abnormalities (Table 1).

History of diseases was assessed by interviewing subjects. People with a history of disease included those who answered in the affirmative the question: "*Have you ever been told by a doctor or other medical professional that you have myocardial infarction or coronary artery disease?*". BP was measured on the right hand three times with a 5-minute interval in the sitting position using an OMRON M3 Expert monitor (Japan). In individuals with a body mass index >30 kg/m^2, obesity was recorded; in men with a waist circumference ⩾102 cm (for women ⩾88 cm) — abdominal obesity.

Results

The characteristics of the subjects are presented in Table 2. The mean age in groups with different QRS duration did not statistically differ. Men were slightly younger than women in all categories studied. The prevalence of obesity and history of CAD prevailed in women, and elevated BP — in men.

Before the analysis start, the groups with normal and wide QRS complex (QRS <110 ms vs QRS ⩾110 ms) were compared by HR (Table 3). The compared groups with QRS <110 ms and QRS ⩾110 ms did not differ in HR, either in the population as a whole or in sex groups. Although in women, compared with men, HR was 2-3 bpm higher, regardless of the QRS duration. At the same time, women were on average 2,6 years older than men, but these differences were not significant (Table 2).

Prevalence, age and sex differences. The prevalence of wide QRS ⩾110 ms among all subjects was 17,2%. In men, this ECG sign was more common than in women (18,5% vs 16,2%, respectively; p<0,0005) (Figure 1). These differences were characteristic of all age groups.

An increase in the prevalence of wide QRS complex with age was observed regardless of sex (from 11,1% to 19,2%, p<0,001); the greatest increase (by 5%) was recorded after 55 years. At the same time, an increase in the prevalence of QRS ⩾110 ms in men began only after 45 years, while in women — from 25-34 years, remaining on a plateau for the next 20 years (35-54 years). In addition, the proportion of women with wide QRS ⩾110 ms in the last age group was more than 2 times higher than the youngest group (18,6% in 55-64 vs 8,9% in 25-34 years old) (Figure 1).

Table 1

Major ECG abnormalities

ECG abnormalities	2009 Minnesota code
Major Q/QS waves	Minnesota codes 1-1-1 through 1-2-7
Major ischemia	Minnesota codes 4-1 or 4-2, (ST abnormalities), 5-1 or 5-2 (T wave abnormalities), no 3-1 and 3-3 (LVH)
Major arrhythmias and conduction defects	
Atrial fibrillation or flutter	any of group of Minnesota codes 8-3
A-V conduction defect	Minnesota codes 6-1 or 6-2 (third and second degree A-V block), 6-8 (artificial pacemaker)
Ventricular conduction defect	Minnesota codes 7-1 or 7-2 (Complete left or right bundle branch block), 7-4 (intraventricular block), 7-8 (bifascicular block)

Abbreviations: A-V — atrioventricular, ECG — electrocardiographic.

Table 2

Characteristics of the subjects

Parameters	Number of subjects, n:		
	Men	Women	Total in population
Total of subjects aged 25-64 years:	6656	10708	17364
25-34 years	1661	1861	3518
35-44 years	1423	2062	3478
45-54 years	1728	3158	4898
55-64 years	1844	3627	5470
Mean age, years	45,0±11,8	47,6±11,3	46,3±11,5
Mean age (years) in the group with QRS <110 ms	44,6±11,8	47,1±11,3	45,1±11,6
Mean age (years) in the group with QRS ⩾110 ms	47,2±12,0	50,1±10,7	48,6±11,3
Place of residence: Urban area	5439	8566	14005
Rural area	1265	2233	3498
Obesity, % (n)	27,8	32,0*	30,7 (5890)
Abdominal obesity, % (n)	26,0	38,6*	34,0 (6613)
Increased blood pressure, % (n)	45,0	37,0*	40,1 (8858)
History of coronary artery disease, % (n)	23,2	33,2*	29,3 (2649)
Major ECG abnormalities, % (n)			6,8 (1176)

Note: * — differences between men and women at p<0,0005.
Abbreviations: ECG — electrocardiogram.

Table 3

Mean heart rate in groups with QRS <110 ms and QRS ⩾110 ms in men, women and in the population

Parameter — Groups:	Men		Women		P men vs women	Total in population	
	n	M±m.	n	M±m.		n	M±m.
1. QRS <110	5387	67,15±0,15	8830	69,33±0,11	<0,001	14217	68,50±0,09
2. QRS ⩾110	1272	66,56±0,37	1879	69,79±0,27	<0,001	3151	68,49±0,22
Significance of differences, p in groups 1 vs 2		>0,05		>0,05			>0,05
Total	6659	67,03±0,14	10709	69,41±0,10	<0,001	17368	68,50±0,08

The analysis of age dynamics among three groups with QRS duration <110 ms, 110-119 ms and ⩾120 ms showed that wide QRS occurred with age not so much due to intraventricular block (QRS ⩾120 ms), but due to an increase in the prevalence of "preblock" QRS duration (110-119 ms) (Figure 2). It should be noted that "preblock" QRS was more common in men than women (12,3% vs 10,9%, p<0,025). QRS duration ⩾120 ms in the sex groups was almost the same (6,7% in women and 6,8% in men). Thus, the revealed higher prevalence of QRS ⩾110 ms in men was due to an increase of "preblock" QRS duration (110-119 ms).

Urban-rural residence. In men living in urban and rural areas, QRS ⩾110 ms was found with the same frequency (18,6% and 18,3%, respectively; p>0,05), while in women, this indicator was less common for urban residents and compared to men, regardless of place of residence (Figure 3).

QRS duration and diseases. To determine the cause of revealed differences in wide QRS prevalence in various categories of subjects and taking into account the higher prevalence of some CVDs and metabolic disorders in rural residents [8, 9], the relationship of wide QRS with obesity, high BP and CAD was analyzed.

The results showed that the prevalence of obesity, regardless of type (general or abdominal), increased BP, history of CAD in groups with wide QRS complex is higher both in the population (Figure 4) and in sex groups. Among people with QRS ⩾120 ms, the number of patients with these diseases was about

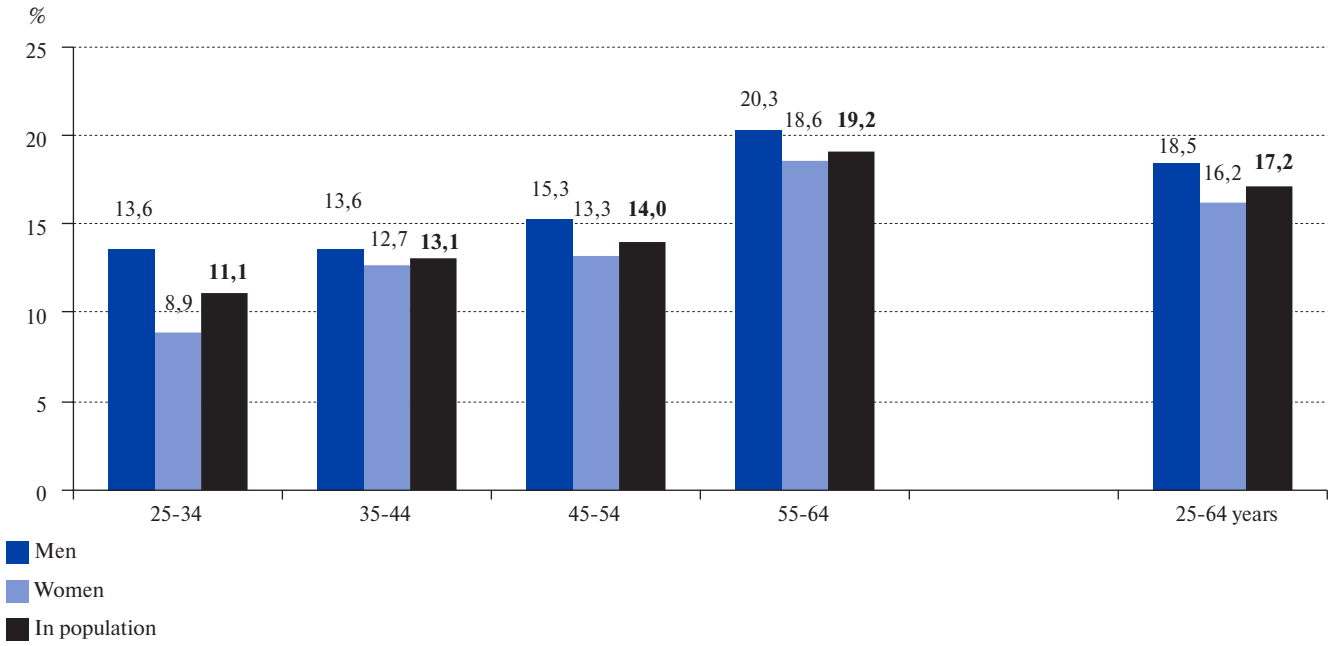

Figure 1. Prevalence of QRS ⩾110 ms in the population and sex groups depending on age (%).

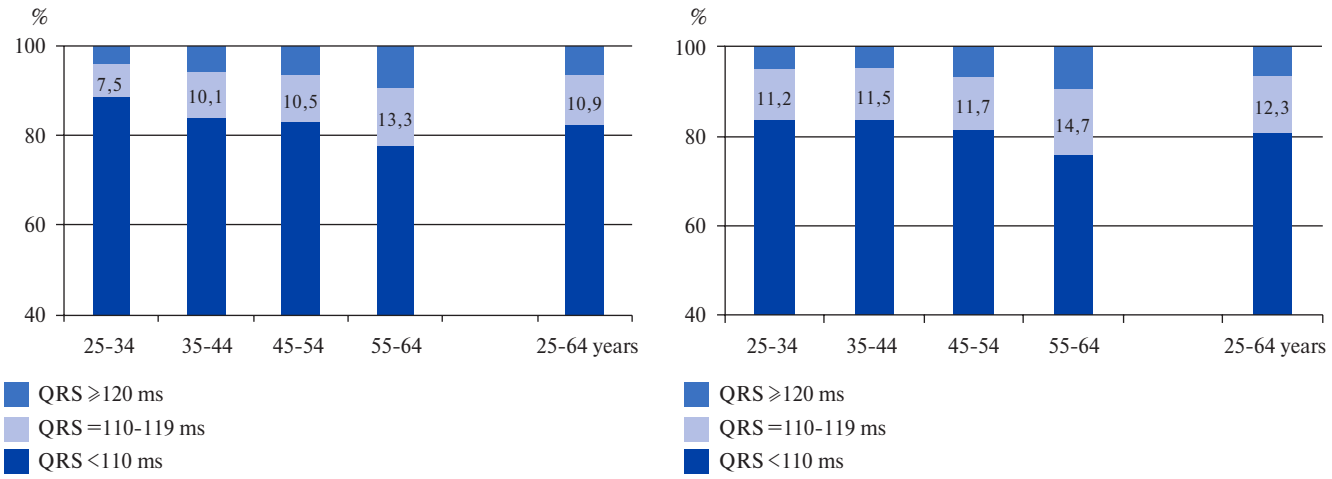

Figure 2. Distribution of QRS duration among women (left diagram) and men (right diagram) depending on age (%).

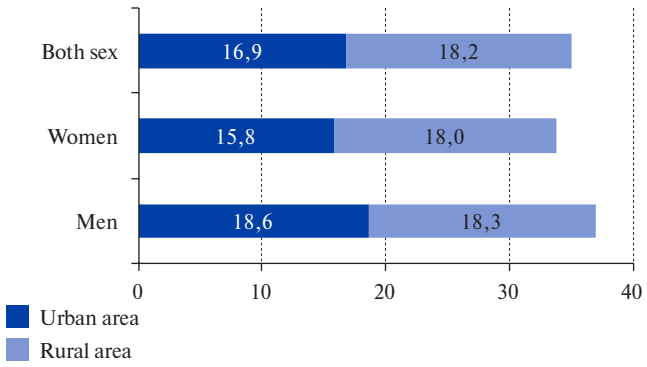

Figure 3. Prevalence of QRS ⩾110 ms in men and women depending on the place of residence (%).

10-12% higher than among people with normal QRS duration. These differences were significant, while between groups with "preblock" and "block" QRS, the proportions of obese and CAD patients differ only as a trend (p<0,1). This may indicate that people with these diseases already have a "preblock" duration of ventricular depolarization (110-119 ms), indicating the presence of myocardial changes.

QRS duration and ECG abnormalities. Wide QRS was often combined with other ECG abnormalities. Among people with QRS ⩾110 ms, major ECG abnormalities characteristic of people with CAD were more common, accounting for 14,3% vs 4,7% in people with normal QRS duration (p<0,001).

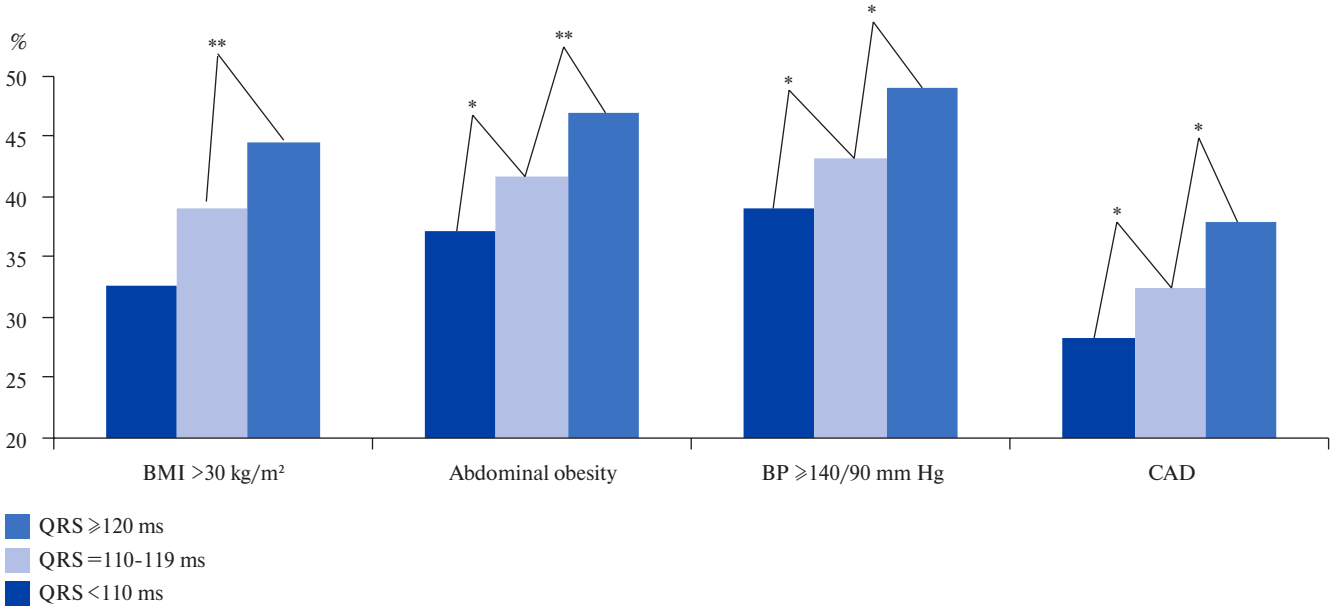

Figure 4. The proportion of individuals with general (BMI >30 kg/m^2) and abdominal obesity, high blood pressure (⩾140/90 mm Hg) and CAD in groups with different QRS duration (%).
Note: * — p<0,05, ** — p<0,1, other differences — p<0,0005.
Abbreviations: CAD — coronary artery disease, BMI — body mass index.

At the same time, sex differences in the prevalence of ECG with abnormalities were noted only among individuals with wide QRS: 16,6% in men vs 12,9% in women (p<0,01). The prevalence of major ECG abnormalities in men and women with normal QRS duration did not differ (4,6% and 4,9%, respectively; p>0,05). After excluding subjects with complete intraventricular block, similar proportions between the prevalence of major ECG abnormalities in groups with different QRS durations remained, but sex differences were not observed in the wide QRS group: prevalence of major ECG abnormalities was 9,9% in men and 9,6% in women with QRS ⩾110 ms (p>0,05). Taking into account the same prevalence of complete bundle branch blocks in the analyzed sex groups, the latter seems natural.

Despite the rather high prevalence of elevated BP in individuals with "preblock" and "block" QRS (Figure 4), left ventricular hypertrophy (LVH) in groups with different QRS duration did not differ significantly (1,7% in normal QRS group vs 2,2% in QRS ⩾110 ms group; p>0,05). Although in men, the prevalence of LVH was expectedly higher compared with women (3,0% vs 0,9%, p<0,0005). No significant difference was found in groups with different QRS duration either in the population or in the sex groups.

Discussion

For the first time, the prevalence of wide QRS (⩾110 ms) in the population of Russian men and women was presented, which was 18,5% and 16,2%, respectively, and in the sample in general — 17,2%. In the analyzed literature, we did not find data on the prevalence of QRS ⩾110 ms in populations of other regions The prevalence of such unfavorable prognostic ECG indicators, such as major ECG abnormalities, is more often estimated. Comparison of the prevalence of the analyzed parameter with other unfavorable prognostic ECG criteria showed that the prevalence of wide QRS (⩾110 ms) obtained in this analysis is higher than the prevalence of conduction disorders and major ECG abnormalities detected in the population (6,5% in the population, 7,0% in men and 6,3% in women). The higher frequency of wide QRS (⩾110 ms) obtained in our study allows to expect a slightly larger number of adverse cardiovascular events in the population than is predicted by routine ECG analysis.

The sex relations and age dynamics of wide QRS obtained in the study are consistent with the results of other studies [2]. It has been shown that the association of QRS duration with morbidity and mortality depends on age [6]. Although almost all researchers recognize an increase in cases of wide QRS with age. Observation of 25-year-old men and women of white and black race with normal QRS duration (n=2537) at baseline after 20 years did not reveal modifiable risk factors leading to QRS >100 ms [10]. Researchers noted that in middle age there is an increased risk of QRS lengthening in white men with increased left ventricular mass index and QRS dura-

tion at a young age. The significant increase in the prevalence of wide QRS after 55 years in our study also corresponds to previous data on the frequency of conduction disorders, including intraventricular block [11, 12].

It can be assumed that the revealed differences in the prevalence of wide QRS depending on sex and place of residence are associated with special distribution of CVD and metabolic disorders in different population groups. Thus, the predominance of increased BP in the male population relative to the female has been shown in different countries [13], including in Russia according to the ESSE-RF study [8]. The differences can also be enhanced by the fact that the number of men being treated and controlling BP level is significantly less than of women: according to the study Boytsov S.A., et al. (2014), only 14,4% of hypertensive men successfully control the BP level vs one third of women with the same disease [9]. In rural residents, HTN prevalence, according to the same study, was higher regardless of sex.

The prevalence of obesity in the ESSE-RF study, on the contrary, was higher among the female population. However, the growth rate of obesity in men is significantly higher than in women: in men, increment of obesity since 2003 has more than doubled, in women — only by a few percent [8]. Obesity is not only associated with an increase in BP, but also with an increase in the number of ineffectively treated patients [14], which affects the frequency of HTN. Thus, the rather high frequency of wide QRS obtained in rural residents according to current study may be associated with a higher prevalence and worse control of obesity and HTN in this category of patients.

The parallelism of changes in QRS duration and the prevalence of obesity, increased BP and CAD (Figure 4) suggests the relationship of these phenomena. However, the relationship of these diseases with a decrease in ventricular depolarization and/or conduction disorders, which causes a lengthening of QRS ⩾110 ms, needs to be clarified in further studies.

Study limitations. To assess the prevalence of LVH in this study, generally accepted ECG criteria were used, namely Minnesota codes 3-1 and 3-3, corresponding to the Sokolov-Lyon voltage criteria, which are not sensitive enough.

Conclusion

The prevalence of QRS ⩾110 ms being an unfavorable prognostic ECG indicator was 17,2% among people aged 25-64 in the ESSE-RF study (18,5% in men and 16,2% in women).

QRS duration ⩾110 ms, like most other ECG disorders (except for ST-T wave abnormalities), prevails in men and increases with age.

The greater prevalence of wide QRS among men compared with women is due to the predominance of "preblock" QRS duration (110-119 ms) in male sample, and not cases of bundle branch blocks.

The results suggest that the greater prevalence of wide QRS in rural residents is due to the higher frequency of obesity, high BP and CAD in this category of population. However, this supposal requires further verification.

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Markers of vascular damage depending on the blood pressure level: data of the population study ESSE-RF

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Aim. To evaluate the relationship of prehypertension (preHTN) with vascular wall damage and decreased renal function depending on cardiovascular risk in a representative sample of Russian population.

Material and methods. As a part the ESSE-RF study in 4 regions (St. Petersburg, Tomsk, Tyumen, the Republic of North Ossetia), 7042 participants aged 25-64 were additionally examined for state of vessels. All participants signed informed consent and completed the approved questionnaires. Anthropometry, fasting glucose and blood pressure (BP) levels were assessed. BP was measured by the OMRON monitor (Japan) twice on the right hand in a sitting position; average BP was calculated. The optimal BP was considered 120/80 mm Hg, preHTN — 120-139/80-89 mm Hg, HTN — ≥140/90 mm Hg or antihypertensive therapy. The 10-year risk of fatal cardiovascular diseases was determined according to the SCORE charts. Glomerular filtration rate (GFR) was calculated using the CKD-EPI equation. Investigation of vessels was performed using a vascular screening system VaSera, Fukuda Denshi. Cardio-ankle vascular index (CAVI) and ankle-brachial index (ABI) was determined. Statistical analysis was performed using SPSS Statistics 20.

Results. The analysis included data of 6906 participants, among which women predominated (n=4531; 65,6%). An increase in the prevalence of subclinical vascular lesion according to CAVI was detected with a BP increase from optimal to preHTN and HTN (0,06, 0,19 and 0,75, respectively). According to ABI, this pattern was not observed (0,24, 0,22 and 0,54, respectively). The prevalence of ABI <0,9 was greatest in the HTN group and did not significantly differ between patients with preHTN and optimal BP. After the exclusion of 1610 patients belonging to the groups of high and very high cardiovascular risk, the prevalence of subclinical vascular lesion was reevaluated. With a BP increase from optimal to preHTN and HTN in the low-risk groups of cardiovascular events, an increase in the prevalence of subclinical vascular lesions was also observed only according to CAVI (0,11, 0,28 and 0,62, respectively). Due to the low prevalence of chronic kidney disease (CKD) in the general population (n=7), the analysis of CKD prevalence in groups by BP level was not carried out. According to linear regression analysis (adjusted for sex, age, body mass index, total cholesterol level), significant associations of systolic BP with GFR, CAVI, and ABI were not detected in the groups of optimal BP, preHTN, and HTN.

Conclusion. Regardless of cardiovascular risk grade, an increase in the prevalence of subclinical vascular lesions was detected with an increase in BP from optimal to preHTN and HTN only according to CAVI. The prevalence of decreased ABI did not significantly differ between patients with preHTN and optimal BP. No association of GFR reduction with preHTN has been identified. No association of GFR reduction with preHTN has been identified.

Key words: prehypertension, vascular lesion, cardio-ankle vascular index, vascular index.

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In 2003, the Joint National Committee for Prevention, Detection, Evaluation and Treatment of High Blood Pressure (BP) (JNC 7) introduced the concept of "prehypertension" (preHTN). PreHTN includes a range of systolic BP (SBP) of 120-139 mm Hg, diastolic BP (DBP) of 80-89 mm Hg and is considered a risk factor for hypertension (HTN) [1]. It is known that the association of BP and cardiovascular mortality is significant with blood pressure of 115/75 mm Hg and more. With an increase in BP for every 20/10 mm Hg the risk of cardiovascular death doubles [2].

Over the past 15 years, with the results of new studies, the standing of preHTN has been reinforced as a condition associated with target organ damage (TOD), cardiovascular morbidity and mortality. In the National Health and Nutrition Examination Survey, preHTN is defined as a risk factor for cardiovascular disease and stroke, especially in case of one or more other risk factors (hypercholesterolemia, obesity, diabetes and/or smoking) [3]. Qureshi AI, et al. analyzed the data of the Framingham Heart Study and determined the relationship of preHTN with the risk of myocardial infarction (MI) and coronary artery disease (CAD), and did not revealed associations between preHTN and stroke [4]. However, the Women's Health Initiative study demonstrated the association of preHTN with fatal cardiovascular events and strokes in postmenopausal women [5].

Unlike optimal BP, preHTN increases the risk of both chronic kidney disease (CKD) [6] and end-stage kidney disease [7]. Literature data on the vascular wall characteristics in patients with preHTN are contradictory. An analysis of the Framingham Heart Study did not reveal an association of a decrease in the ankle-brachial index (ABI) with the preHTN risk [4]. In later

Table 1

Sex-specific characteristics of the subjects

Parameter	Total (n=6906)	Men (n=2375)	Women (n=4531)	p (men vs women)
Age, years	50,0 [38,0;57,0]	54,0 [42,0;57,0]	48,0 [36,0;58,0]	<0,0001
Smoking, n (%)	2526 (36,7%)	1607 (67,7%)	919 (20,3%)	<0,0001
BMI, kg/m^2	28,3±5,8	27,6±4,7	28,6±6,3	<0,0001
BMI, kg/m^2	27,1 [24,4;33,7]	27,0 [23,4;36,7]	27,3 [24,5;34,0]	
BMI ⩾30 kg/m^2, n (%)	2360 (34,3%)	660 (28,0%)	1700 (37,7%)	<0,0001
WC ⩾102 cm for men and ⩾88 cm for women, n (%)	2638 (38,3%)	660 (27,9%)	1978 (43,8%)	<0,0001
SBP, mm Hg	132,5±19,6	135,6±18,3	130,8±20,0	<0,0001
DBP, mm Hg	81,8±11,2	83,8±11,7	80,8±10,8	<0,0001
Antihypertensive therapy, n (%)	2183 (31,6%)	575 (24,2%)	1608 (35,5%)	<0,0001
Total cholesterol, mmol/l	5,5±1,2	5,4±1,2	5,6±1,2	<0,0001
Total cholesterol >4,9 mmol/L*, n (%)	4327 (69,4%)	1286 (65,1%)	3041 (71,4%)	<0,0001
Reception of statins, n (%)	208 (3,1%)	62 (2,7%)	146 (3,3%)	0,08
Diabees, n (%)**	470 (7,5%)	149 (7,5%)	321 (7,5%)	0,51
Creatinine, mmol/l	66,5 [60,4;73,3]	72,6 [65,9;81,0]	63,4 [58,8;71,0]	
GFR, ml/min/1,73 m^2	104,1 [91,7;115,3]	91,0 [81,5;101,2]	110,0 [97,4;117,9]	
GFR ⩽60 ml/min/1,73 m^2, n (%)	7 (0,1%)	5 (0,3%)	2 (0,04%)	<0,0001

Note: * — lipid-lowering therapy, ** — blood glucose ⩾7,1 mmol/l and/or glucose-lowering therapy.
Abbreviation: WC — waist circumference.

Table 2

Prevalence of patients with high and very high risk of CVE depending on BP levels

Parameter	Optimal BP (n=1380)	PreHTN (n=2098)	HTN (n=3428)	Total (n=6906)	P
Diabetes, n	20 (1,6%)	65 (3,6%)	385 (12,3%)	470 (7,5%)	<0,0001
History of stroke, n	9 (0,7%)	18 (0,9%)	91 (2,7%)	118 (1,7%)	<0,0001
History of MI, n	6 (0,4%)	17 (0,8%)	90 (2,6%)	113 (1,6%)	<0,0001
SCORE ⩾5%, n	28 (2,2%)	168 (9,1%)	987 (31,5)	1183 (18,9%)	<0,0001
Total of patients with high and very high risk, n	62 (4,8%)	243 (13,2%)	1305 (41,3%)	1610 (25,7%)	<0,0001

publications by Indian and Scandinavian authors, the relationship between preHTN both with a decrease in ABI [8] and an increase in the cardio-ankle vascular index (CAVI) was determined [9]. In the Russian population, the association of preHTN with renal dysfunction and vascular wall damage has not been previously analyzed.

The aim of this study was to assess the association of preHTN with vessel wall lesions and decreased renal function depending on cardiovascular risk (CVR) in a representative sample of the Russian population.

Material and methods

As a part of the multicenter observational study ESSE-RF, in 2012-2013 a sex- and age-stratified, random sample of people 25-64 years old was formed. In 4 regions, 7042 participants underwent an additional examination of blood vessels. Data of 6906 participants were suitable for analysis (St. Petersburg — 1596 people, Tomsk — 1560, Tyumen — 1631, Republic of North Ossetia — 2119). All participants signed informed consent. Respondents were interviewed using a standard questionnaire consisting of 12 modules containing information on lifestyle, comorbidity and therapy.

BP was measured with an Omron automatic monitor (Japan) on the right hand in a sitting position, after a 5-minute rest. BP was measured twice with an interval of 2-3 minutes; the analysis includes the average of two measurements.

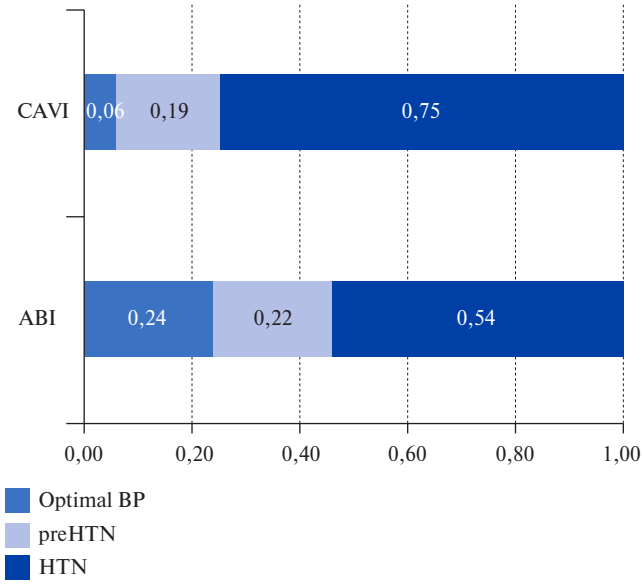

Figure 1. Prevalence of subclinical vascular injury (CAVI ⩾9 and ABI <0,9) in the general population depending on BP levels.

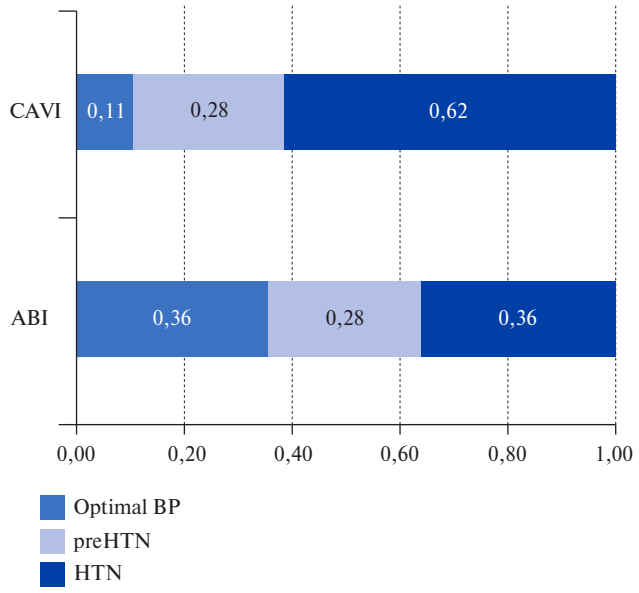

Figure 2. Prevalence of subclinical vascular injury (CAVI ⩾9 and ABI <0,9) in patients with low and moderate risk of CVE depending on BP levels.

Depending on the BP level and use of antihypertensive therapy, the following groups were identified according to the 2013 ESH/ESC guidelines for the management of arterial hypertension: optimal BP (BP <120/80 mm Hg), preHTN (120/80⩽ BP <140/90 mm Hg) and HTN (BP ⩾140/90 mm Hg and/or antihypertensive therapy) [10]. This classification of BP levels was used to increase the statistical significance of the calculations. PreHTN included groups of normal and high-normal BP.

All participants underwent anthropometry. Fasting blood tests of the lipid profile, glucose, and creatinine (Abbott Architect 8000 analyzer (USA), reagents manufactured by Roche-diagnostics) was carried out. Body mass index (BMI) was calculated using the Quetelet's equation; glomerular filtration rate (GFR) was estimated using the CKD EPI equation.

Based on age, sex, levels of SBP, total cholesterol, and smoking status, a 10-year risk of fatal cardiovascular diseases was determined according to the SCORE risk charts.

Vascular examination was performed using a VaSera screening system (Fukuda Denshi); CAVI and ABI was estimated. The vascular examination technique was described in detail in a previous publication [11].

For data processing, standard descriptive statistics were used (mean, standard error of the mean in case of normal distribution and median, 25 and 75 percentiles in case of nonnormal distribution). To assess associations, multivariate models of binary logistic regression and multiple linear regression were used. Mathematical and statistical data analysis was performed using the software package SPSS 20.0 (SPSS Inc., USA).

The study was supported by the Grant of President of Russian Federation on state support of leading scientific schools of the Russian Federation NS-5508.2018.7 (agreement № 075-15-2019-161 dated 23.05.2019).

Results

The analysis included data of 6906 participants (women — 4531; 65,6%). The characteristics of participants with an assessment of sex differences are presented in Table 1.

The men smoked more often, took antihypertensives less often, and had significantly lower values of GFR. Among women, obesity and hyperlipidemia were significantly more often diagnosed.

The prevalence of patients with a high and very high risk of cardiovascular events (CVE) (diabetes, stroke, history of MI or SCORE ⩾5%) depending on BP levels is presented in Table 2. Due to the low prevalence of CKD in the general population (n=7), analysis of CKD prevalence depending on BP levels was not performed.

With an increase in BP from optimal to preHTN and HTN, the prevalence of diabetes, stroke, MI, and the number of patients with high risk of CVE increases. In patients with preHTN, a high risk is approximately 3 times more likely than in participants with optimal BP.

Table 3

Association of HTN with a high risk of cardiovascular diseases and TOD (binary logistic regression; results are presented as odds ratio [95% confidence interval])

Parameter	HTN
SCORE ⩾5%	3,34 [2,72;4,10], p=0,0001
Diabetes	2,30 [1,76;3,01], p=0,0001
History of stroke	1,97 [1,19;3,26], p=0,009
History of MI	1,95 [1,11;3,40], p=0,02
CAVI ⩾9	1,84 [1,51;2,25], p=0,0001
ABI <0,9	1,40 [0,98;2,01], p=0,07

The prevalence of subclinical vascular injury in the general population depending on the BP levels is shown in Figure 1.

An increase in the prevalence of subclinical vascular lesion according to the CAVI was detected with BP increase from optimal to preHTN and HTN; according to the ABI, this pattern was not observed. The prevalence of ABI <0,9 was highest in the HTN group and does not significantly differ between patients with preHTN and optimal BP.

After the exclusion of 1610 subjects, belonging to high and very high-risk groups of CVE, the prevalence of subclinical vascular injury was reevaluated. The results are presented in Figure 2.

With an increase in BP from optimal to preHTN and HTN in the low-risk groups of CVE, there is an increase in the prevalence of subclinical vascular damage only according to CAVI.

According to linear regression adjusted for sex, age, BMI, and total cholesterol, SBP in the preHTN and HTN groups was associated with SCORE risk (β=0,03 [0,02; 0,04] and 0,08 [0,07; 0,08], respectively). No significant associations of SBP with GFR, CAVI, and ABI were found in the groups of optimal BP, preHTN, and HTN.

Table 3 presents the results of a binary logistic regression adjusted for sex, age, smoking, obesity (BMI ⩾30 kg/m^2) and hypercholesterolemia (total cholesterol ⩾4,9 mmol/l).

In binary logistic regression, the association of optimal BP and preHTN with TOD was not detected. HTN is significantly associated with a high SCORE risk, diabetes, a history of stroke and/or MI, and subclinical vascular injury according to the CAVI.

Discussion

According to the ESSE-RF study (Russian population), with an increase in BP from optimal to preHTN and HTN, the prevalence of patients with high and very high CVR and subclinical vascular lesions increases.

The definition and concept of preHTN was developed after extended discussion and debates of JNC 7 participants. The idea was to consider preHTN as a risk factor for HTN development and recommend not to initiate drug therapy, but emphasize the need for lifestyle modification [1].

Increased BP is often accompanied by impaired carbohydrate metabolism: permeability of the endothelial barrier and oxidative stress contribute to pancreatic β-cell dysfunction and insulin resistance [12]. In Iran from 2009 to 2014, Khosravani A, et al. observed 2941 participants without HTN and diabetes. The five-year incidence rate of diabetes among individuals with preHTN was 12,7%, while the logistic regression results were not significant [13].

Our study revealed an increase in diabetes prevalence with BP increase from optimal to preHTN and HTN. Logistic regression did not reveal a significant relationship between preHTN and diabetes, while the presence of HTN increased the diabetes risk in the Russian population.

The high prevalence of CKD is now recognized as an urgent public health problem worldwide. HTN is one of the main reasons of CKD. A meta-analysis by Garafallo C, et al. revealed a relationship of preHTN and HTN with CKD. At the same time, an increase in SBP and DBP for every 10 mm Hg increases the risk of reducing GFR [6]. According to a meta-analysis of 6 studies with 1003793 participants by Huang Y, et al., preHTN compared with optimal BP significantly increases the likelihood of end-stage kidney disease [7]. According to our data, assessment of CKD prevalence depending on the BP levels and logistic regression analysis did not reveal significant relationships. Perhaps this is due to the low prevalence of CKD (0,1% in the studied Russian population).

In the structure of cardiovascular mortality, stroke and MI take a leading position. Meta-analysis of 17 studies with 591664 subjects by Huang Y, et al. revealed that preHTN increased the risk of CAD [14].

Results were more significant in studies with follow-up >10 years. It is important that the preHTN-associated risk of CAD was higher in Western than in Asian participants. Authors also revealed that 8,4% of CAD cases could be prevented if the predisposition to HTN was removed in Asian patients, and this proportion increases to 24,1% in Western subjects. Huang Y, et al. performed a meta-analysis of 19 studies with 762393 participants, which confirmed an increased risk of stroke in patients with preHTN compared with optimal BP [15]. Significant differences between groups by sex and ethnicity were not identified. In our study, there was an increase in the history of stroke and MI with BP increase from optimal to preHTN and HTN. Association with history of strokes and MI was found only for participants with HTN.

In patients with preHTN, endothelial dysfunction is recorded. According to small study with 53 respondents with optimal BP and 65 with preHTN by Thitiwuthikiat P, et al., association of a combination of hyperuricemia and preHTN with subclinical vascular injury according to CAVI test (⩾9) was revealed [9]. The prospects of diagnosing subclinical vascular lesions according to ABI test (<0,9) is controversial. In 2005, Qureshi AI, et al. analyzed data of the Framingham Heart Study, according to which a significant relationship between preHTN and ABI <0,9 was not identified [4]. According to a later study with 70 participants by Rubio-Guerra AF, et al. (2017), a relationship was found between preHTN and ABI <0,9 [8].

Conclusion

1. In the Russian population, with an increase in BP from optimal to preHTN and HTN, there is an increase in the number of patients with high and very high risk. In patients with preHTN, markers of high CVR are found about 3 times more often than in subjects with optimal BP.

2. Regardless of CVR grade, an increase in the prevalence of subclinical vascular lesions was detected with an increase in BP from optimal to preHTN and HTN only according to CAVI. The prevalence of decreased ABI did not significantly differ between patients with preHTN and optimal BP.

3. The prevalence of impaired renal function in the Russian population is low. No association of GFR reduction with preHTN has been identified.

Relationships and Activities. The study was supported by the Grant of President of Russian Federation on state support of leading scientific schools of the Russian Federation NS-5508.2018.7 (agreement № 075-15-2019-161 dated 23.05.2019).

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Cardioprotective diet: prevalence, associations and prevention reserves

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Most traditional risk factors for cardiovascular disease (CVD) are diet dependent and are caused by an imbalanced nutrition. A healthy diet and individual eating habits have a significant protective effect against CVD.

Aim. To study the prevalence of dietary habits with protective effects against CVD in the adult population.

Material and methods. The analysis was performed using data of representative samples in 13 Russian regions of male and female population aged 25-64 years (n=19520; men — 7329, women — 12191). The response rate was about 80%. The diet was assessed by the frequency of consumption of certain foods. The cardioprotective diet included: daily consumption of vegetables and fruits, weekly — fish products, the use of only vegetable oils in cooking, and consumption of low-fat dairy. The presence of all 4 eating habits was considered Ideal Diet (ID), 1-3 habits — Intermediate Diet (ImD), none of listed habits — Bad Diet (BD).

Results. The ImD was the most common — 85,8%. However, there were slight regional differences — from 80,1% in the Ivanovo Oblast to 91,0% in the Tyumen Oblast (p<0,001). The prevalence of ID was 7,0%; more common — among women (p<0,001), urban residents (p<0,001), people with higher education (p<0,001) and unemployed participants (p=0,016). It increases with age (p<0,001). The highest rate of ID was noted in St. Petersburg (13,8%) and Primorsky Krai (10,5%), the lowest — in the Volgograd (3,6%) and Tyumen Oblasts (3,5%), in the Republic of North Ossetia (3,4%). BD was more common in men (p<0,001), among people aged 25-34 years (p<0,001), less educated (p<0,001) and low-income (p <0,001) people. The prevalence of BD in the general population was 7,2% and varies from 3,1% in the Voronezh Oblast to 13,6% in the Volgograd Oblast. Individuals with hyperglycemia (50%), abdominal obesity (20%) and general obesity (18%), dyslipidemia (15%) and history of CVD (22%) were more likely to have ID. Persons with hyperglycemia (17%), abdominal obesity (13%), general obesity (11%), dyslipidemia (8%) and history of CVD (9%) were more likely to have ImD.

Conclusion. A low prevalence of cardioprotective diet in the population was revealed. Only individual habits are widespread; however, a small part of Russians follow all cardioprotective habits.

Key words: cardioprotective diet, nutrition, protective eating habits, dietary habits.

Relationships and Activities: none.

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Cardiovascular disease (CVD) is the leading cause of death in Russia and in the world. Most conventional CVD risk factors (RF) are diet-dependent and are caused by imbalanced nutrition. Epidemiological studies revealed nutritional factors with a protective effect against CVD [1, 2]. Such dietary factors are determined at the levels of certain nutrients, basic food groups, and food habits. This made it possible to create recommendations for target population levels [3], develop special diets, such as DASH diet [4], and use protective properties of food in guidelines on management of CVD and diabetes [5-7], as well as in prognostic indices and indicators of ideal cardiovascular health [8] and a healthy lifestyle [9].

According to experts of the World Health Organization (WHO), about a third of all CVD are due to inappropriate feeding with inadequate consumption of fruits and vegetables and excessive intake of animal fats [10]. Whereas daily taking recommended amount of vegetables and fruits and adequate consumption of animal fats reduce all-cause and cardiovascular mortality [11, 12]. The daily intake of vegetables and fruits is the most significant protective factor of nutrition. Thus, according to the World Bank experts, among 7 factors specifying premature mortality and the loss of healthy life years in Russia, along with already formed diet-related RF, such as hypertension (HTN), hypercholesterolemia (HCE) and overweight, there is behavioral habit — insufficient consumption of fruits and vegetables [13]. Dietary patterns with high intake of fruits and vegetables and low amount of animal fats are associated with lower cardiovascular, cancer, and all-cause mortality [14-16].

One of the first significant initiatives was organized by the American Heart Association, proposing 7 indicators to assess ideal cardiovascular health [8]. The proposed concept of ideal cardiovascular health pays more attention to a healthy lifestyle and RF, increasing morbidity and mortality, rather than the disease itself. It is this approach that seems appropriate also in assessing the resources and priorities of prevention programs.

The aim was to study the prevalence of dietary habits with protective effects against CVD in the adult population.

Material and methods

The analysis was performed using data of representative samples in 13 Russian regions (Voronezh, Ivanovo, Volgograd, Vologda, Kemerovo, and Tyumen oblasts; Samara, Orenburg, Vladivostok, Tomsk, and St. Petersburg; Republic of North Ossetia-Alania, Krasnoyarsk Krai) of male and female population aged 25-64 years (n=19520; men — 7329, women — 12191) as a part of ESSE-RF study. The medical ethics committees of all participating centers approved this study. All participants signed informed consent. The response rate was about 80%.

To assess nutrition and eating habits, we used standard questionnaire on the frequency of taking basic food groups (red meat, poultry, fish and seafood, sausage products and deli meats, pickled products, cereals and pasta, raw vegetables and fruits, legumes, pastry products and sweets, dairy products: milk, kefir, yogurt, sour cream/cream, cottage cheese, cheese) according to 4 consumption criteria — "not use/rarely"; "1-2 times/month"; "1-2 times/week" and "daily/almost daily". High-fat dairy products were defined in accordance with regulatory documents [17]. Criteria for assessing the adequacy of consumption and adherence to a healthy diet were given according to WHO guidelines [18].

The following eating habits were included the cardioprotective diet: daily consumption of vegetables and fruits, weekly — fish products, the use of only vegetable oils in cooking, and intake of dairy products, at least 2 of which were low-fat. The presence of all 4 eating habits was considered Ideal Diet (ID), 1-3 habits — Intermediate Diet (ImD), none of listed habits — Bad Diet (BD).

The income level was estimated by the answer to the question — "How do you assess your family's wealth compared to others?". The answers "very poor" and "relative poor" were classified as "low income", and the answers "average", "relatively wealthy" and "very wealthy" — as "moderate or high income".

HTN was recorded with a systolic blood pressure (BP) ⩾140 mm Hg and/or diastolic BP ⩾90 mm Hg, or in case of regular antihypertensive therapy.

Obesity was established with a body mass index (BMI) ⩾30 kg/m^2. Abdominal obesity (AO) was diagnosed with waist circumference >102 cm in men and >88 cm in women.

HCE was diagnosed with a total cholesterol >5,0 mmol/l, or in case of lipid-lowering therapy. Hypertriglyceridemia (HTG) was established with triglycerides >1,7 mmol/l. Hyperglycemia (HG) was revealed with fasting blood glucose >6,1 mmol/l, or in case of glucose-lowering therapy.

The category "CVD in history" included respondents who noted in form one of the following conditions: stroke, myocardial infarction, coronary artery disease, arrhythmias, and other heart diseases.

Statistical processing included univariate assessment of statistical significance of differences using the Pearson's chi-squared test. For a multivariate assessment of associations between RF and eating habits, we used logistic regression adjusted for age, marital status, occupation, income level, and place of residence. The odds ratio (OR) and the 95% confidence interval (CI) were calculated. Statistical analy-

Table 1

Characteristics of subjects (%, n)

		BD	ImD	ID	p
Total sample		7,2 (1411)	85,8 (16738)	7,0 (1371)	–
Sex	women	5,8 (708)	86,0 (10481)	8,2 (1002)	<0,001
	men	9,6 (703)	85,4 (6257)	5,0 (369)	
Age	25-34 years old	10,1 (418)	84,7 (3512)	5,2 (218)	<0,001
	35-44 years old	7,9 (307)	85,8 (3348)	6,3 (248)	
	45-54 years old	6,5 (356)	86,1 (4674)	7,4 (402)	
	55-64 years old	5,5 (330)	86,2 (5204)	8,3 (503)	
Family	no	7,3 (503)	85,2 (5884)	7,5 (518)	0,14
	yes	7,2 (908)	86,0 (10854)	6,8 (853)	
	not married	8,1 (236)	85,0 (2478)	6,9 (202)	0,056
	married/civil marriage	7,2 (908)	86,0 (10854)	6,8 (853)	
	divorced/separate	6,5 (167)	85,3 (2199)	8,2 (212)	
	widower/widow	7,1 (100)	85,5 (1207)	7,4 (104)	
Education	lower than higher	8,1 (891)	86,3 (9529)	5,6 (623)	<0,001
	higher	6,1 (520)	85,1 (7209)	8,8 (748)	
Job	no	6,4 (300)	86,1 (4058)	7,5 (352)	0,016
	yes	7,5 (1111)	85,6 (12680)	6,9 (1019)	
Income	low	11,2 (235)	84,2 (1767)	4,6 (96)	<0,001
	moderate or high	6,8 (1176)	85,9 (14971)	7,3 (1275)	
Place of residence	urban	7,0 (1103)	85,6 (13541)	7,4 (1173)	<0,001
	rural	8,3 (308)	86,3 (3197)	5,4 (198)	
Region	Krasnoyarsk Oblast	7,4 (102)	87,3 (1196)	5,3 (72)	<0,001
	Primorsky Krai	4,0 (76)	85,5 (1627)	10,5 (200)	
	Volgograd Oblast	13,6 (160)	82,8 (974)	3,6 (42)	
	Vologodskaya Oblast	5,3 (80)	87,2 (1322)	7,5 (114)	
	Voronezh Oblast	3,1 (46)	87,9 (1301)	9,0 (133)	
	Ivanovo Oblast	10,5 (182)	80,1 (1387)	9,4 (162)	
	Kemerovo Oblast	4,1 (60)	87,6 (1287)	8,3 (122)	
	Samara Oblast	11,4 (174)	84,5 (1293)	4,1 (63)	
	St. Petersburg	4,5 (65)	81,7 (1193)	13,8 (202)	
	Orenburg Oblast	3,6 (52)	90,6 (1309)	5,8 (84)	
	Tomsk Oblast	10,6 (155)	84,3 (1234)	5,1 (75)	
	Tyumen Oblast	5,5 (75)	91,0 (1248)	3,5 (48)	
	Republic of North Ossetia	11,5 (184)	85,1 (1367)	3,4 (54)	

sis was performed using the software package Statistica 10. Differences were considered significant at $p<0,05$.

Results

The characteristics of participants are presented in Table 1. The ImD was the most common — 85,8%. However, there were slight regional differences — from 80,1% in the Ivanovo Oblast to 91,0% in the Tyumen Oblast. The prevalence of ID was more common among women, urban residents, people with higher education and unemployed participants. It increases with age. The highest rate of ID was noted in St. Petersburg and Primorsky Krai, the lowest — in the Volgograd and Tyumen Oblasts, in the Republic of North Ossetia. BD was more common in men, among people aged 25-34 years, less educated and low-income people. The prevalence of BD in the general population varies from 3,1% in the Voronezh Oblast to 13,6% in the Volgograd Oblast. Of the 13 regions examined, 5 was characterized by BD prevalence >10%, i.e., every

Table 2

Prevalence of risk factors among people with protective eating habits, %

Parameter	Use of only vegetable oils			Daily consumption of vegetables/fruits			Recommended fish consumption			Low-fat dairy products		
	No, n=1391	Yes, n=18129	p	No, n=7883	Yes, n=11637	p	No, n=6795	Yes, n=12725	p	No, n=8867	Yes, n=10653	p
HTN	41,9	48,0	<0,001	45,6	48,9	<0,001	43,7	49,6	<0,001	47,5	47,5	0,99
Obesity	26,5	32,5	<0,001	29,3	33,9	<0,001	28,9	33,7	<0,001	31,3	32,7	0,038
AO	28,0	37,4	<0,001	32,7	39,5	<0,001	32,9	38,8	<0,001	35,0	38,2	<0,001
HG	12,8	13,8	0,28	12,3	14,8	<0,001	10,3	13,8	<0,001	12,8	14,6	<0,001
HTG	26,2	26,1	0,96	26,4	25,9	0,45	25,8	26,3	0,46	26,5	25,8	0,28
HCE	51,2	56,9	<0,001	54,7	57,7	<0,001	54,2	57,7	<0,001	54,8	57,9	<0,001
CVD	25,4	30,7	<0,001	27,6	32,1	<0,001	30,2	30,3	0,81	28,8	31,6	<0,001

10th resident of this region did not have even one of the protective eating habits.

In the Russian population, protective eating habits are more often observed in individuals with dietary RF (Table 2). This is more often seen in relation to the recommended intake of vegetables/fruits and fish products, as well as the use of vegetable oils in cooking, less often in low-fat dairy products. Taking low-fat dairy products is characteristic of only people paying attention to the dietary fats and having lipid metabolism disorders and/or obesity. However, this was noted only in relation to dairy products, while the consumption of animal fats remains without adequate attention. So, the habit of using only vegetable oils in cooking was more often observed among people with HTN, obesity, AO, HCE and history of CVD, while among people with HG and HTG it does not differ from people without RF. Also, there was no difference in the level of fish intake depending on HTG and history of CVD. The most common protective eating habit among people with dietary RF was daily consumption of fruits and vegetables, with the exception of people with HTG. The most motivated for the healthy diet were people with obesity, AO and HCE. Among them, all four mentioned protective habits were more often present.

The presence of dietary RF increased adherence not only to certain protective eating habits, but also to their complex. It is these associations that were noted in the logistic regression analysis. Thus, participants with HG (by 50%), AO (by 20%), obesity (by 18%), dyslipidemia (by 15%), and history of CVD (by 22%) more often adhered to ID. Similar but less pronounced associations were observed among individuals with ImD. Thus, individuals with HTN (by 17%), AO (by 13%), obesity (by 11%), dyslipidemia (by 8%) and history of CVD (by 9%) more often adhered to ImD. The highest adherence to the cardioprotective nutrition was observed among subjects with HTN, both to the ID and ImD. The results of the logistic regression are presented in Table 3.

The structure of most common model (ImD) is shown in Figure 1, and the prevalence its components is presented in Figure 2. The habit of using only vegetable oils is a mainstay of ImD. Also, more than half of people with ImD adhered to recommended intake of fish products, fruits and vegetables. Despite the fact that in the ImD structure, the intake of low-fat dairy products is less common compared to other components, in general, this parameter is quite high for the population. Further analysis revealed that such a high percentage of taking low-fat dairy products related only certain products. Thus, the intake of low-fat cottage cheese and sour cream was observed in 58,8% and 52,5%, respectively, and low-fat liquid dairy products (milk, kefir, yogurt) and cheese only in 28,8% and 29,8%, respectively.

A combination of 3 components was noted in less than a third of subjects with ImD, and a combination of 2 components — less than half (41,1%). Rather large proportion of individuals adhered to ImD had only one eating habit — 27,8%.

Discussion

Current analysis was performed using the same criteria as in the national cross-sectional population study FINRISK, conducted in Finland in 2007 among a population aged 25-74 years [19]. Given the high similarity of eating habits in Russia and Finland, it was interesting to compare it in relation to cardioprotective effects and evaluate the contribution of Finnish population preventive programs in changing dietary patterns. It is worth emphasizing that the prevalence of ID in the Finn-

Table 3

Associations of diets with risk factors

Parameter	ID, n=2782		ImD, n=18149	
	OR (95% CI)	p	OR (95% CI)	p
HTN	1,05 (0,90; 1,17)	0,31	1,04 (0,97; 1,11)	0,26
Obesity	1,18 (1,07; 1,30)	0,0012	1,11 (1,03; 1,18)	0,0032
AO	1,20 (1,08; 1,32)	<0,001	1,13 (1,05; 1,20)	<0,001
HG	1,50 (1,30; 1,72)	<0,001	1,17 (1,06; 1,29)	0,0014
HTG	1,05 (0,95; 1,16)	0,36	1,02 (0,95; 1,09)	0,57
HCE	1,07 (0,76; 1,17)	0,17	1,01 (0,95; 1,07)	0,77
HDL	1,15 (1,03; 1,29)	0,014	1,08 (1,01; 1,16)	0,047
LDL	1,02 (0,93; 1,13)	0,62	1,02 (0,96; 1,08)	0,53
History of CVD	1,22 (1,10; 1,35)	<0,001	1,09 (1,02; 1,17)	0,017

Note: adjusted for gender, age, educational status, marital status, occupation, income level, place of residence, region; reference group — individuals with BD.

Abbreviations: CI — confidence interval, HDL — high density lipoproteins, LDL — low density lipoproteins.

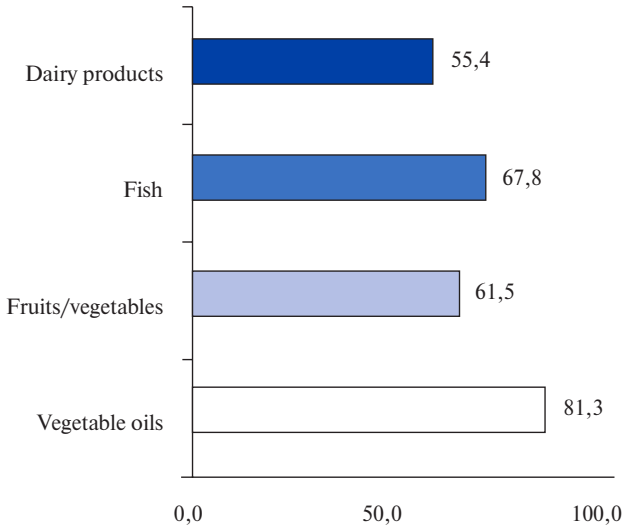

Figure 1. Structure of the components of Intermediate Diet (%).

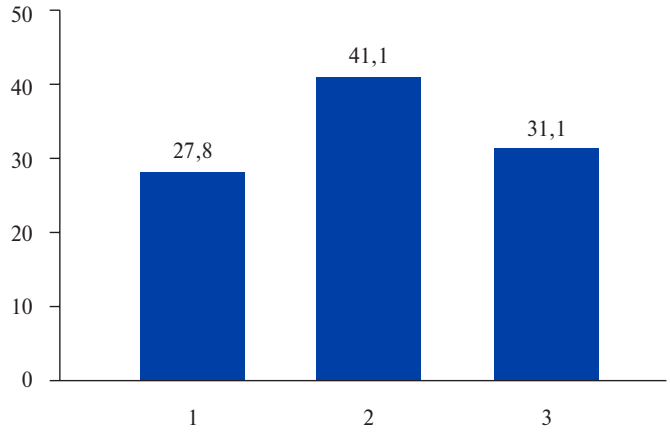

Figure 2. Combination of components of Intermediate Diet (%).

ish population is many times higher — 12,6% among women and 24,1% among men vs 8,2% and 5,0%, respectively, in Russia. It is interesting to note that in Russia a more protective dietary pattern is observed in women, while in Finland — in men. Differences were revealed also revealed in relation to ImD and BD. Thus, according to the FINRISK 2007 study, the proportion of people adhered to ImD was 73,5% among women and 65,3% among men [19], while in Russia this indicator is much higher — 86,0% and 85,4%, respectively, and do not have sex differences. BD among women in Russia (5,8%) is observed less common than in Finland (13,9%) [19], while among men the indicators are comparable — 9,6% vs 10,6%, respectively. Of course, the lower proportion of women with BD is due to the widespread habit of using vegetable oils in cooking [20]. But higher ID and lower ImD proportions in the Finnish population indicate a higher prevalence of protective eating habits, which may reflect the effectiveness of national preventive projects and programs. Moreover, in Finland there is a higher proportion of people not only with certain eating habits, but also with protective dietary pattern in general. In Russia, the modification of dietary habits towards a

healthy model only observed in individuals with developed dietary RF for CVD, which this study confirmed.

The structure of ImD makes it possible to identify "problems" of Russian eating habits and priorities for preventive activities. The low prevalence of subjects with three and two components in ImD allows us to conclude that the prospects for increasing the proportion of people with ID are very low. This because these people need to not only learn about the effectiveness of one or two eating habits, but also introduce them into daily practice to belong to ID group. Of course, the daily intake of certain foods should be a priority in a healthy diet. Therefore, it is advisable to shift the emphasis of specialists to the popularization of daily consumption of fruits and vegetables and the use of low-fat dairy products. The popularization of taking fish and fish products also remains relevant, however, it should be borne in mind that the recommended levels of consumption differ significantly. So, the recommended level of fish consumption is at least 2 per week (200 g), while for fruits and vegetables — 5 per day (400 g) [18]. Particular attention of people should be attracted to the use of low-fat dairy products, since these foods are consumed daily. Russians choose low-fat dairy products of only certain forms (sour cream, cottage cheese), which are consumed much less than liquid dairy products (milk, kefir, yogurt, etc.). They prefer milk and dairy products with higher fat content, which significantly increases the atherogenesis. The relevance of changing this habit is also emphasized by the fact that dairy products are the "basis" for the creation of certain dietary pattern in Russia [21], which further justifies drawing attention to raising public awareness of the need for using only low-fat dairy products [18].

Currently, studies on developing population-based Healthy Eating Index is conducted in Russia [22]. However, the developed methods have significant differences with the presented results. So, it is proposed to use quantitative components for calculating the Index, while in this analysis we used frequency characteristics, which are easier to collect in most epidemiological and clinical studies. Although the methodological differences do not allow a comparison of the results, it should be emphasized that the development of different approaches for assessing dietary patterns is necessary for prediction and determining the priorities of population-based prevention programs.

Conclusion

This study identified very low prevalence of cardioprotective eating habits in the Russian population. Only certain habits are widespread, of which so far, the dietary pattern is formed in a small number of Russians. At the same time, relevant points were also noted for the popularization of cardioprotective eating habits, which specifies the focus and scope of preventive counseling and set specific tasks for population-based preventive programs and public health.

Relationships and Activities: none.

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The prevalence of traditional risk factors for cardiovascular disease in the Omsk region: data of the ESSE-RF2 study

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Aim. To study the prevalence of some traditional risk factors for cardiovascular disease (CVD) in the Omsk region.

Material and methods. The prevalence of traditional risk factors for CVD in a representative sample of the Omsk region population aged 25-64 years (n=1648) was estimated as a part of the ESSE-RF2 study in 2017.

Results. It was established that the mean age of CVD detection in the Omsk region is 46,3 years, the prevalence of overweight is 35,0%, obesity — 30,3%. Abdominal obesity was detected in 56,8% of subjects. Smoking was reveled in 21,2% of the population, former smoking — 20,0%. Alcohol consumption more than 2 times a month was observed in one third of respondents (30,5%). In the group of healthy people, compared with CVD patients, the percentage of smokers and alcohol consumers was detected significantly more often: smoking — 25,2±1,26% vs 17,1±0,86% and 32,9±1,6% vs 28,1±1,4%, respectively. Perhaps it was the diseases the reason for smoking cessation and alcohol abstinence among people with CVD. It should be noted that among 70% of alcohol consumers, both with/without CVD, strong drinks were the preferred type of alcohol.

Hypertension (HTN) was observed in 47,9% of subjects, and in 43,1% the diagnosis was verified. In 4,8% of HTN individuals, blood pressure increase was detected for the first time in this study.

The prevalence of diabetes of both types in the Omsk region was 6,7%, and in group A (with CVD) it was much higher than in group B (without CVD): 10,7% vs 2,8%. Type 2 diabetes prevailed in people with CVD (p=0,000005). This was not characteristic of type 1 diabetes.

Conclusion. The most common risk factors for CVD in the Omsk region population were HTN (47,9%), abdominal obesity (56,8%), a positive family history of early CVD (62,0%), alcohol consumption over the past 12 months (71,7%) and strong alcohol drinking (72,0%). However, a significant portion of the subjects (41,3%) consumed alcohol no more than 1 time per month.

Key words: risk factors, cardiovascular diseases, smoking, alcohol consumption, abdominal obesity, hypertension.

Relationships and Activities. The study was funded by the federal budget. Omsk State Medical University participated in an open competition for conducting this study in the Omsk region, which resulted in the conclusion of a civil contract № 2/4/17000062 of May 24, 2017.

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In recent years, in high-income countries, age-standardized death rates from cardiovascular disease (CVD) have decreased sharply. Among the factors contributing to such a reduction in mortality was a decrease in smoking prevalence, blood pressure (BP) normalization, and improved healthcare [1, 2].

A high-risk strategy is the main approach of primary prevention of CVD, which include identifying patients with a high risk of CVD [3]. This approach is particularly relevant in Russia, where the prevalence and mortality from CVD is significantly higher than in most countries of Europe and USA [3]. It can be assumed that in different Russian regions, due to economic, climatic and geographical differences and behavioral patterns of the population, traditional CVD risk factors (RF) may have different distribution and, as a result, significance in disease prevention.

The aim was to study the prevalence of some traditional risk factors for CVD in the Omsk region.

Material and methods

In 2017, as part of a multicenter observational study ESSE-RF2, a screening study of the Omsk region population with single protocol for all participating centers was conducted [4].

According to the Protocol requirements [4], a representative sample of the population of Omsk and Omsk Oblast (n=2000) was formed by cluster sampling. Following healthcare facilities took part in the study: A. N. Kabanov City Clinical Hospital № 1; City Polyclinic № 10; City Clinical Hospital № 3; City Polyclinic № 4; City Polyclinic № 11.

Then, 20 locality health centers of mentioned healthcare facilities were randomly selected for participation in the study: 15 — urban (5 from each district) and 5 from the rural facility — Omsk Central District Hospital. Then households included in the sample was randomized (n=1000). Men and women permanently residing in selected households aged 25-64 years were invited to the survey. The quantitative composition of participants was controlled according to the eight age-sex strata (men and women — 25-34 years, 35-44 years, 45-54 years, 55-64 years). Characteristics of the invitation, the response rates, the reasons and structure of denials were reflected in our previous articles [5, 6].

Of the created representative sample, 1648 people were examined. The response rate was 84,0% [5].

We evaluated the prevalence of the following traditional RF for CVD [3]:

1) Male gender;

2) Positive family history of early CVD: fatal or nonfatal CVD (myocardial infarction, stroke), and/or documented hypertension (HTN) in first-degree relatives up to 55 years old in men and up to 65 years old in women;

3) Overweight (body mass index (BMI) ⩾25 kg/m^2) and obesity (BMI ⩾30 kg/m^2);

4) Abdominal obesity (AO) was considered as an increase in waist circumference ⩾94 cm in men and ⩾80 cm in women;

5) Smoking. Smokers were those who smoked at least one cigarette per day or quit smoking <1 year ago;

6) Alcohol. Three criteria were evaluated: “alcohol intake over the past 12 months”; “frequency of alcohol consumption per month” (“>2 times”); “prevailing type of alcohol” (“strong”);

7) HTN. Hypertensive subjects were those who answered in the affirmative the question: “Have you ever been told by a doctor or other medical professional that you have high BP?”.* Increased office BP ⩾140 and/or ⩾90 mm Hg was considered as a possible HTN;

8) Type 2 diabetes (T2D). Subjects with diabetes were those who answered in the affirmative the question: “Have you ever been told by a doctor that you have/had diabetes?”.

Sex, age, family history of CVD, the presence of HTN and T2D, smoking status, frequency, type and intensity of alcohol consumption were evaluated according to standardized questionnaires of the study.

Since the ESSE-RF study in the Omsk region was conducted on the basis of outpatient healthcare facilities, the survey was performed by the primary care physician. Thus, all verified cases of elevated BP were considered as a history of HTN.

Resting BP was measured before the survey, in the sitting position with the right arm supported on the table at the heart level using automatic BP monitor. Systolic BP (SBP)/diastolic BP (DBP) considered the average of two measurements taken at interval of 5 min.

Obesity was determined by measuring height and weight, followed by BMI calculation.

To assess the significance of non-modifiable RF for CVD such as sex, age, positive family history of early CVD, the sample was divided into

* All affirmative answers to the question about whether the respondent had high BP before the examination were verified by the primary care physician.

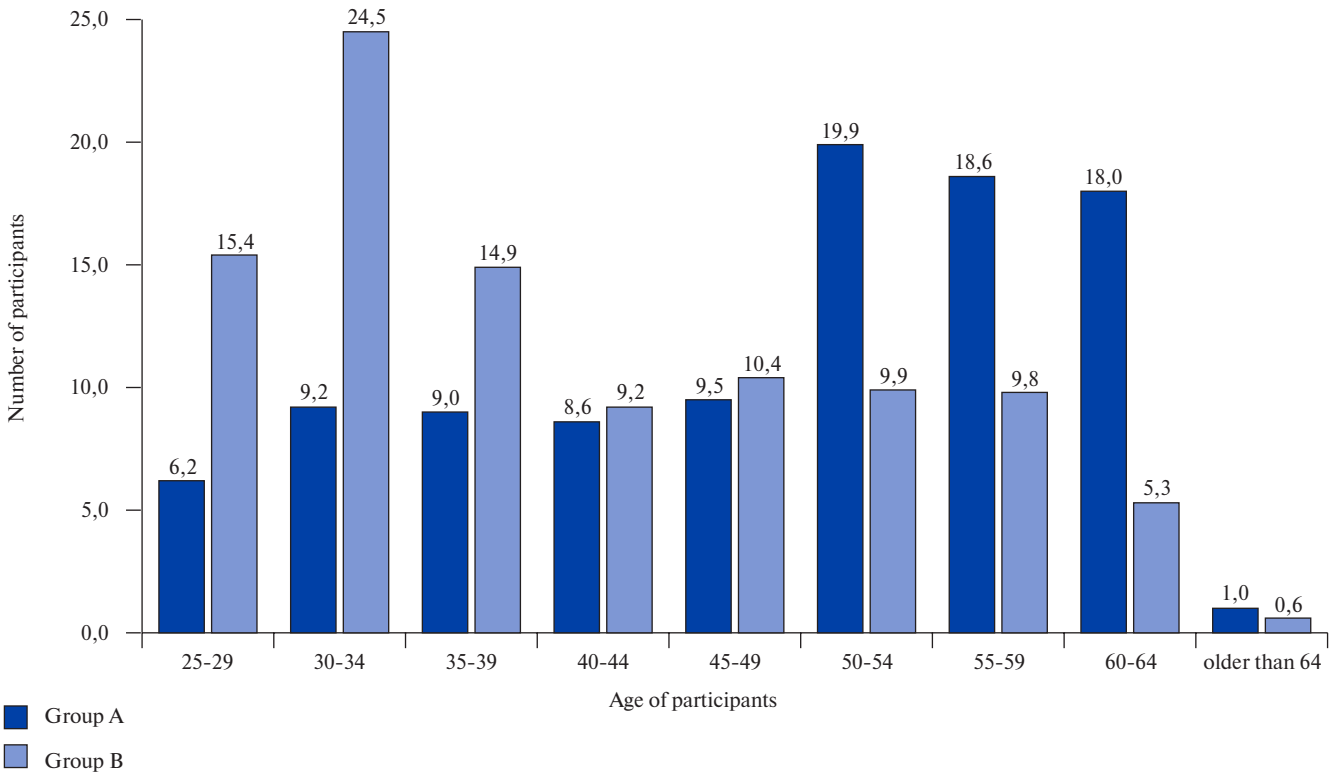

Figure 1. Age-specific distribution of participants (%).

two groups: group A (n=811) — subjects with cardiovascular disease (HTN, myocardial infarction, stroke, heart failure, coronary artery disease, cardiac arrhythmias) and group B (n=837) — subjects without CVD.

We used observational epidemiological (case-control, cross-cectional) and statistical research methods. The significance of the factors was assessed by odds ratio (OR) with 95% confidence interval (CI). For data processing, the spreadsheet program MS Excel and the open source OpenEpi (http://www.openepi.com/Menu/OE_Menu.htm) were used. To describe the prevalence of RF in groups, the mode (Mo) and median (Me) values were used. In each study group, the prevalence of RF was calculated for all patients and separately for men and women. Differences were considered significant at $P<0,05$.

This study was performed in accordance with the Helsinki Declaration and Good Clinical Practice standards. The ESSE-RF2 study was approved by the Independent Ethical Committee of National Medical Research Center for Preventive Medicine. The medical ethics committees of all participating centers approved this study. All patients signed informed consent.

Results and discussion

Age-specific distribution of the participants is shown in Figure 1. As shown in the Figure, among the subjects <50 years old, there are more patients without CVD (group B) compared to group A. Then there is an almost twofold increase in the number of patients with CVD (group A) compared to group B. In group A there were 44,4% of men (n=360) and 55,6% of women (n=451); in group B there was a comparable sex composition: 45,6% (n=382) and 54,4% (n=455), respectively. The predominance of women in both groups (906 women vs 742 men) is apparently associated with a more responsible attitude to their own health. A similar sex ratio was obtained by us for the urban and rural population of the same region in previous studies [5, 6].

The mean age of participants with CVD (group A) was 48,7 years (95% CI 46,3÷51,1) and group B (without CVD) — 41,0 years (95% CI 39,0÷43,1). Significant differences between these groups by age are explained by a known more common development of CVD at an older age: the earliest age in a subject with CVD was 46,3 years (men — 45,8 years; women — 46,6 years). The mean age in

Table 1

Prevalence and significance of RF for CVD in the population of the Omsk region

№	Risk factor	Overall in region, n=1648		Subjects with CVD (Group A), n=811		Subjects without CVD (Group B), n=837		OR (95% CI) between 5 and 7	P Significance of differences between 5 and 7
		абс	%	абс	%	абс.	%		
1	Men >45 years old	432	26,2	255	31,4	177	21,0	1,710 (1,369÷2,136)	0,000002
2	Women >55 years old	241	14,7	182	22,4	59	7,0	3,815 (2,793÷5,212)	<0,0000001
3	Positive family history of early CVD	1022	62,0	558	68,8	464	54,8	1.254 (1,162÷1,355)	<0,0000001
4	Overweight (25⩽BMI<30)	576	35,0	299	37,0	277	33,0	1,126 (0,986÷1,285)	0,0779
5	Obesity (BMI ⩾30)	500	30,3	332	41,0	168	20,0	2,061 (1,759÷2,416)	<0.0000001
6	Abdominal obesity WC ⩾94 cm in men, ⩾80 cm in women	936	56,8	589	72,6	347	41,5	1,771 (1,616÷1,940)	<0,0000001
7	Current smoking	350	21,2	139	17,1	211	25,2	0,687 (0,567÷0,832)	0,0001006
8	Former smoking	329	20,0	183	22,6	146	17,5	1,308 (1,076÷1,589)	0,006786
9	Hypertension	711	43,0	711	87,7	0	0	-	-
10	First smoking experience at the age <18 years	168	10,2	87	10,7	81	9,7	1,122 (0,815÷1,543)	0,481
11	Alcohol consumption over last 12 months	1182	71,7	588	72,5	594	71,0	1,079 (0,870÷1,337)	0,489
12	Frequency of alcohol intake per month: >2 times	503	30,5	228	28,1	275	32,9	0,799 (0,648÷0,986)	0,037
13	Prevailed type of alcohol — strong	1186	72,0	597	73,6	589	70,4	1,175 (0,947÷1,457)	0,143
14	Both types of diabetes	110	6,7	87	10,7	23	2,8	3,946 (2,518÷6,184)	<0,0000001
15	Type 2 diabetes	89	5,4	78	9,6	11	1,3	1,875 (1,216÷2,890)	0,000005
16	Type 1 diabetes	21	1,3	9	1,1	12	1,4	0,782 (0,332÷1,847)	0,574

Abbreviations: CI — confidence interval, BMI — body mass index, WC — waist circumference, O**K** — odds ratio, CVD — cardiovascular disease.

groups A and B did not differ between men and women: group A — 48,2 (95% CI 45,8÷50,6) vs 49,1 (95% CI 46,6÷51,6) years, in group B — 41,3 (95% CI 39,2÷43,4) vs 40,0 (95% CI 38,0÷42,0) years, respectively. Thus, the development of CVD in the Omsk region can be expected from 48 years for men and 49 years for women. However, according to the National guidelines, age as RF is considered to be 55 years for men and 65 years for women [3]. This fact requires further study.

A positive family history of early CVD in first-degree relatives (<55 years for men and <65 years for women) was detected in 62,0% of respondents (Table 1). In group A, this indicator was significantly higher than in group B — 68,8% vs 54,8%, p<0,0000001. This indicates a high proportion of people with a positive family history of early CVD (>60%) and the need for additional early preventive measures.

A more detailed analysis showed that 16,0% (n=130) of group A subjects had a positive family history of myocardial infarction, 57,3% — stroke (n=465), 17,3% — HTN (n=140). In group B, a similar distribution was as follows: 9,4% (n=79), 44,2% (n=370) and 16,7% (n=140), respectively. This may indicate the need for a careful attitude of respondents without CVD and with positive family history of

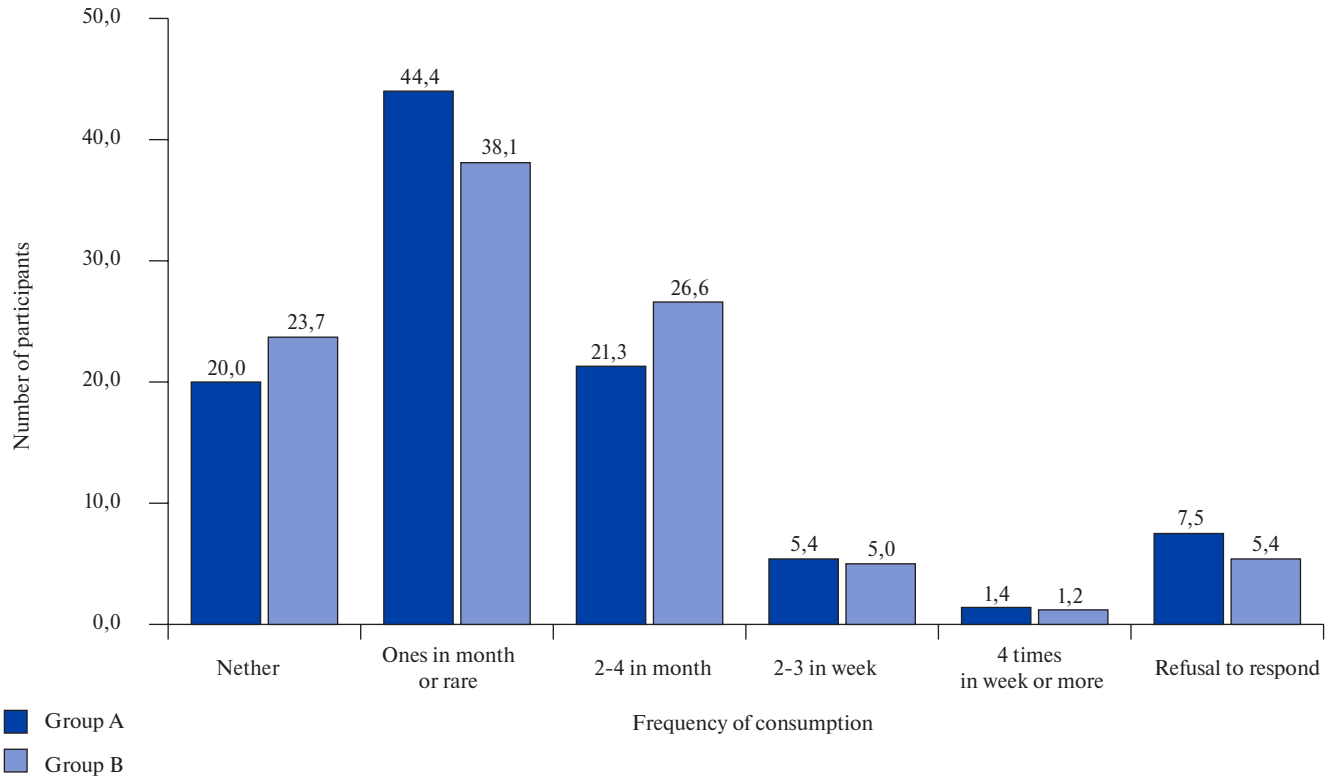

Figure 2. Frequency of alcohol consumption (%).

CVD to their own health and an early change in lifestyle.

The proportion of respondents with overweight and obesity (BMI ⩾25) was 65,3% (n=1076), of which overweight — 35,0% (n=576), obesity — 30,3% (n=500) (Table 1). The same prevalence of obesity in Russian population was obtained in the ESSE-RF study: 29,7% [7] and 33,4% [8].

Among people with CVD, the prevalence of overweight did not differ significantly from people without CVD: 37,0% vs 33,0%, but obesity (BMI ⩾30) was 2 times more common in group A than in group B (41,0% vs 20,0%) (Table 1).

However, BMI does not reflect the differences between muscle and adipose tissue, as well as the distribution of the latter. Waist circumference (WC) is a more valuable predictor of both CVD and diabetes. AO amounted to 56,8% in the Omsk region (Table 1), which is comparable to the national data — 55% [8]. As in other regions of Russia [8], Omsk women are significantly more likely to suffer from AO compared with men: 63,4% (n=574) and 48,8% (n=362), respectively. It is noteworthy that the prevalence of AO significantly exceeds the prevalence of obesity in BMI both in the population and in both study groups (Table 1). This fact indicates the importance of measuring WC as an indicator defining such an important and widely spread RF as AO. In both groups A and B, AO prevailed among women compared with men: in group A — 44,7% (n=359) vs 29,3% (n=238), in group B — 26,5% (n=221) vs 15,1% (n=126), respectively. Thus, in the Omsk region, AO among CVD patients compared with people without CVD is significantly more common: men — OR 1,97 (95% CI 1,62-2,39, p<0,0000001), women — OR 1,70 (95% CI 1,48-1,94, p<0,0000001).

Smoking was detected in 21,2% (n=350) of the Omsk region population (Table 1). Compared with the data of the ESSE-RF study in 2013-2014 (27,7%) and the Russian Federal State Statistics Service in 2011 (25,7%), the value obtained in this study is quite "favorable" and is closer to the low prevalence compared to other Russian regions [9]. According to the ESSE-RF study, only three regions have lower prevalence of smoking: the Republic of North Ossetia-Alania, the Tyumen and Samara Oblasts (18,7%, 20,0% and 20,7%, respectively). In the other eight regions of Russia participating in the

ESSE-RF study, this parameter is higher and even reaches 32,1% (Tomsk region) and 34,6% (Kemerovo region) [9].

It is noteworthy that 20,0% (n=329) of the population were former smokers, and this number is comparable to the number of current smokers, which is an encouraging fact (Table 1).

Among smokers and former smokers, more than 95% of participants smoked every day in both groups (group A — 95,6%, group B — 96,7%). First smoking experience at the age <18 years in group A was in 26,6%, in group B — in 22,7% of respondents. This fact confirms the known data that the earlier a person begins to smoke, the more likely it can affect the development of CVD.

There were lower number of current smokers in group A than in group B (17,1% vs 25,2%, respectively, p=0,0001). It is obvious that a sick person rather breaks bad habits than an individual without diseases. This is also indicated by the fact that the proportion of former smokers among CVD patients is significantly higher than in the group without CVD (22,6% vs 17,5%, respectively; p=0,006). It is encouraging that the proportion of never smokers not depend on the presence/absence of CVD. In the Omsk region, the prevalence of this indicator in groups A and B were close: 60,3% (n=489) and 57,3% (n=480), respectively.

Over the past 12 months, alcohol consumption was detected in 71,7% of respondents in the Omsk region (Table 1). A significant part of participants consume alcohol mainly 1 time/month and less often — 41,3% (group A — 44,4% and group B — 38,1%) (Figure 2). A third (30,5%) of respondents consumes alcohol more than 2 times/month. People with CVD (group A) were significantly less likely to consume alcohol compared to group B (28,1% vs 32,9%, p<0,037), which can probably be explained, as in smokers, by a greater motivation for patients to break bad habits compared to healthy people (Table 1). It should be noted that in both groups strong drinks prevailed (Table 1), such as vodka, cognac, etc. (73,6% vs 70,4%), which generally corresponds to Russian traditions and the trend of alcohol consumption in Russia described in earlier studies [9-11].

HTN is today considered the most important RF for other CVD and, at the same time, an independent disease [3]. The proportion of people informed by a doctor or other medical professional that they have high BP was 43,1% (Table 1). Since all these cases were documented, the obtained value can be considered the prevalence of HTN in the region. There were also 79 subjects (4,8%) who answered in the negative and who had high office BP (SBP and/or DBP ⩾140/90 mm Hg). Given these cases, the proportion of people with high BP in the Omsk region reaches 47,9% (n=790).

The mean SBP in patients with CVD was 132,4 mm Hg (95% CI 125,8÷139,0), DBP — 84,0 mm Hg (95% CI 79,8÷88,2). Similar parameters in the group of subjects without CVD were lower: 119,6 mm Hg (95% CI 113,6÷125,6) and 76,1 mm Hg (95% CI 68,0÷75,2), respectively. If we take into account that all persons with established HTN were included in group A, and all of them used antihypertensive therapy before inclusion in the study, then the mean BP in the group can be a tool to assess the therapy efficiency. Given the value of mean BP in individuals with CVD (group A) who did not reach the target level (<130/80 mm Hg), we may indicate the low effectiveness of antihypertensive treatment.

Diabetes is another disease that is considered RF for CVD [3]. The prevalence of both types of diabetes in the Omsk region was 6,7%, and among patients with CVD (group A), the odds for having diabetes were much higher than in group B (without CVD): OR 3,95 (2,52÷6,18) (Table 1). In group A, the prevalence of T2D in comparison with group B was significantly higher (p=0,000005), which is not the case for type 1 diabetes.

Study limitation. Analysis of RF was limited to the age range of 25-64 years according to the Protocol requirements [4]. Alcohol as a risk factor was evaluated only by the frequency of consumption (over 12 months, per month) and the preferred type of drink.

Conclusion

Among the Omsk region population, the most common risk factors for CVD were HTN (47,9% — overall; 43,1% — according to ambulatory medical record), AO (56,8%), positive family history of early CVD (62,0%), alcohol consumption over the past 12 months (71,7%). However, a significant part of subjects (41,3%) consumed alcohol no more often than 1 time/month. All of these indicators, including T2D, are significant CVD-associated R for the population of the Omsk region.

Current smokers and alcohol consumers (at least 2 times/month) prevailed in the group of healthy people. This is probably due to a change in the lifestyle of people with CVD and higher motivation to break bad habits in order to regain

health. Both groups had the same preferred type of alcohol: 73,6% of healthy people and 70,4% of people with CVD preferred strong drinks.

Data on RF for CVD, which are widespread among the population of the Omsk region, can be useful for creating regional programs for monitoring, screening and primary prevention of CVD.

Relationships and Activities. The study was funded by the federal budget. Omsk State Medical University participated in an open competition for conducting this study in the Omsk region, which resulted in the conclusion of a civil contract № 2/4/17000062 of May 24, 2017.

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Correlation of excess salt intake identified by the survey with urine sodium level and blood pressure: data of ESSE-RF study

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Aim. To study the association of blood pressure (BP) and hypertension (HTN) with salt intake estimated by the survey and the urinary Na^+ concentration among men and women 25-64 years old, examined within the ESSE-RF and ESSE-RF-2 studies.

Material and methods. Representative samples of the Russian population aged 25-64 years were examined. At the first phase in 2012-2014, 21888 people (men — 38,2%) were included, and at the second phase in 2017 — 6714 people (men — 44,7%). The response rate was 80%. We used standard questionnaire. Adding more salt and the consumption of salted foods (sausages, deli meats, and pickled foods) in the criteria "daily or almost daily" was considered excess salt intake (ESI). BP measurement was carried out in a sitting position on the right hand. BP was measured twice with an interval of about 2-3 minutes. HTN was diagnosed at a systolic BP (SBP) ≥140 mm Hg and/or diastolic BP ≥90 mm Hg, or in case of antihypertensive therapy. In ESSE-RF-2, an analysis of the morning urine was additionally performed. Na^+ was determined using the EX-Ds ion-selective electrolyte analyzer. All participants were stratified by the quintiles of urine sodium level. Data analysis was performed using the software package R 3.6.1. The models of linear and logistic regression were used. The differences were considered at $p<0,05$.

Results. The average level of SBP significantly increases with an increase in Na^+ in urine: 1,04 (0,60-1,48) mm Hg for the quintile of sodium distribution ($p<0,001$), the odds of HTN increases by 1,11 (1,05-1,17) times for the quintile ($p<0,001$). Questionnaire components of ESI are also significantly related to urinary Na^+ levels. The consumption of sausages and deli meats has the greatest effect, causing an increase in the average Na^+ level by 11,59 (7,06-16,12) mmol/l ($p<0,001$). The applied point scale is significantly related to urine sodium level and predicts HTN no worse than Na^+ in the urine ($p=0,15$ for the difference hypothesis). One point on the scale increases the Na^+ level by an average of 7,51 (5,01-10,02) mmol/l, SBP by an average of 0,74 (0,41-1,07) mm Hg and the odds of HTN by 1,1 (1,06-1,15) times ($p<0,001$ for all).

Conclusion. In the pattern of ESI components, processed meat and sausage products take first place in terms of association strength with urine sodium. The questionnaire used to assess the proportion of people with ESI can be recommended for assessing this risk factor during screening. ESI detected by the questionnaire is associated with elevated BP and urinary Na^+ values.

Key words: hypertension, blood pressure, excess salt intake, urine sodium level, ESSE-RF, risk factors.

Relationships and Activities: none.

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Excess salt intake (ESI) refers to behavioral risk factors (RF) associated with the eating habits of modern humans. The contribution of this RF to cardiovascular mortality is 12% [1]. Despite the World Health Organization guidelines on the daily intake of salt <5 g (2 g/day of sodium), the average consumption in the world is about 10 g/day (3,95 g/day of sodium) [2]. An analysis conducted within the The Global Burden of Disease (GBD) study showed that in 13 studies included in the analysis, salt intake ranged from 6,75 to 10,66 g/day, i.e., exceeded the recommended values in all regions [3].

The relationship between ESI and blood pressure (BP) level has been was studied for many years. The history of research was analyzed in detail by N. Poteshkina (2011, 2013) in reviews [4, 5]. Mentioned relationship was confirmed in the American population within the Multiple Risk Factor Intervention Trial (MRFIT). An international study by the Intersalt Cooperative Research Group (INTERSALT), in addition to the relationship, revealed a dose-dependent effect of salt intake on BP, which increases with age. A similar relationship was noted within the Norfolk Cohort of the European Prospective Investigation into Cancer (EPIC-Norfolk) [6]. In the International Study of Micro- and Macro-Nutrients and Blood Pressure (INTERMAP), in addition to the above, the relationship between the amount of salt consumed and the mortality rate due to stroke was confirmed. An increase in salt intake was associated with an increase in the hypertension (HTN) prevalence in the population. Moreover, the Prospective Urban Rural Epidemiology study (PURE) showed that the relationship between BP and salt intake is manifested precisely in regions with higher level of salt intake (>5 g/day) [7].

Some studies focused on the role of reducing salt intake in lowering BP at the population level. So, He FJ and Macgregor GA (Cochrane Systematic Review, 2013) observed a moderate decrease in salt intake over 4 weeks, associated with a significant BP decrease both among people with HTN and without it [8]. The decrease in salt intake in the UK from 2003 to 2011 explain the blood pressure decrease at the population level in the country [9]. Thus, reducing the level of salt intake among population is one of the important components of a multidimensional approach to HTN control. However, this poses the question of estimating salt intake by the population.

There are no many population-based studies evaluating salt intake and the prevalence of ESI in Russia. One of these studies is INTERSALT, con-

ducted in the last quarter of 20th century. According to this trial, the average salt intake in Russia in those years was 9,46 g/day. There was also sample monitoring of the diet of the population conducted by the Federal State Statistics Service in 2013 and 2018 in all subjects of Russia [10]. Salt consumption in this study was studied by questioning. The interviewers in this study were not medical professionals, but previously they all had a special interview on the rules for collecting information. BP and urine were not assessed. According to the ESSE-RF study, this RF amounted to 49,9% according to first section of the study [11].

When studying eating habits, including ESI, at the population level, a researcher must solve the question of the significance of results obtained by questioning. In short-term studies with large sample, original validated questionnaires are used to evaluate the RF. At the same time, the amplification of screening techniques by laboratory tests significantly increases the total cost of the study. Among laboratory methods for assessing urinary Na^+, the first place is the 24-hour urinary sodium excretion. However, there are difficulties with the preparation of a subject and the cost, which is high on a scale of population study. From this point of view, despite some distortion of result due to unbalanced salt intake during the day [12], the determination of Na^+ in the morning urine seems technically more feasible. At the same time, the predictive value of this technique is discussed by many researchers [13].

The aim was to study the association of BP and HTN with salt intake estimated by the survey and the urinary Na^+ concentration among men and women 25-64 years old, examined within the ESSE-RF and ESSE-RF-2 studies.

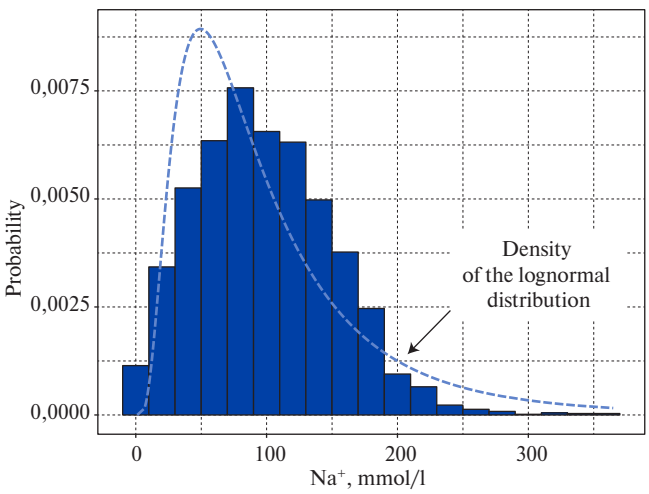

Figure 1. Histogram of urinary sodium distribution.

Material and methods

Representative samples of the Russian population aged 25-64 years were examined. At the first phase in 2012-2014, 21888 people (8354 men and 13534 women) from Volgograd, Vologda, Voronezh, Ivanovo, Kemerovo, Orenburg, Tomsk, Tyumen Oblasts, Krasnoyarsk Krai, Primorsky Krai, Republic of North Ossetia, St. Petersburg were included. At the second phase in 2017 — 6714 people (3000 men and 3714 women) from Krasnodar Krai, Omsk and Ryazan Oblasts, Republic of Karelia). A systematic stratified multistage random sample was used, created according to Kish selection grid, features of which were described in detail earlier [6, 14]. The response rate was about 80%. The study was approved by the Independent Ethics Committee of the National Medical Research Center for Therapy and Preventive Medicine. Each participant signed informed consent. For all participating regions, the same research tools were provided.

All subjects were interviewed according to a single standard questionnaire, created on the basis of adapted international methods. The analysis included the region and place of residence: (urban/rural area), age groups (25-34, 35-44, 45-54 and 55-64 years), level of education (below secondary, secondary and above secondary), income level, habits, anamnestic data. The module for assessing diet and eating habits included a standard questionnaire on the frequency of taking basic food groups with a partial semi-quantitative assessment of food intake, which was descripted in detail earlier [15]. Adding more salt in ready-to-eat meals and the consumption of salted products (sausages, deli meats or pickled products) in categories "daily" or "almost daily" was considered ESI. The components used in ESI were included in the score: the presence of one of them was equal to 1 point, two — 2 points, three — 3 points.

BP measurement was carried out in the sitting position with the right arm using Omron automatic BP monitor. The level of BP (systolic BP (SBP) and diastolic BP (DBP)) was measured twice with an interval of about 2-3 minutes. The analysis took into account the average of two measurements. HTN was considered at SBP ⩾140 mm Hg and/or DBP ⩾90 mm Hg, or when the subjects took antihypertensive drugs.

In two regions participating in ESSE-RF-2 (Krasnodar Krai and Ryazan Oblast), an analysis of urine was additionally performed. The collection of morning urine was carried out according to standard recommendations — on day before, vegetables and fruits that discolored urine (beets, carrots, etc.) and diuretics were excluded. Electrolytes (sodium (Na) and potassium (K)) in urine were determined by the ion selective electrode technique using an EX-Ds

Table 1

Characteristics of Na^+ levels in the morning urine in the age groups of men and women

Age groups	Men*			Women		
	N	Mean ± standard deviation	Median [Q25; Q75]	N	Mean ± standard deviation	Median [Q25; Q75]
25-34	449	103,17±53,67	97,2 [65,8; 136,7]	539	91,35±52,17	84 [51,2; 124,4]
35-44	388	105,02±56,68	100,9 [64,13; 139,8]	483	93,79±50,66	86,25 [58,63; 126,5]
45-54	399	108,54±54,13	107,2 [67,9; 149]	503	88,43±47,79	82,6 [51,8; 122,4]
55-64	384	110,05±53,80	107,4 [71,4; 145,6]	523	92,9±50,06	88,9 [54,6; 126,75]
25-64	1620	106,62±54,6	103,0 [66,85; 142,6]	2048	91,65±50,10	85,7 [54,10; 125,60]

Note: * — mean level increases with age (p=0,033).
Abbreviation: Q — quantile.

Table 2

Associations of excess salt intake according to the questionnaire with urinary sodium level. Results of a univariate regression analysis adjusted for sex and age

ESI and its components	Average increase in urinary Na^+ (CI 95%)	p
Adding more salt in ready-to-eat meals	7,44 (3,33-11,55)	<0,001
Daily/almost daily consumption of sausages and deli meats	11,59 (7,06-16,12)	<0,001
Daily/almost daily intake of pickled foods	6,77 (0,71-12,83)	0,0286
Score of ESI components*	7,51 (5,01-10,02)	<0,001
ESI in general	11,34 (5,75-16,94)	<0,001

Note: * — coefficient shows the average increase in urinary Na^+ (mmol/l) with an increase in score of 1.
Abbreviations: CI — confidence interval, ESI — excess salt intake.

electrolyte analyzer (JOKOH CO., LTD., Japan). All participants were stratified by the quintiles of urinary Na^+ (<50,76, <80,2, <109,18, <142,60, <364,90 mmol/l).

Statistical analysis was performed using the software package R 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). To assess the association of questionnaire scores and levels of urinary Na^+ with SBP, DBP and HTN, linear and logistic regression were used, both with/without sex and age adjustment. The null hypothesis was verified by Wals test. The parameter effect in the linear regression model was estimated by its coefficient, in logistic regression model — the odds ratio (OR). The quality of linear regression predictions was estimated by coefficient of determination (R^2). The quality of logistic regression predictions was evaluated using the area under ROC curve (AUC). Comparison of linear regression models was carried out by the Wuong test [16]; AUC was compared using the bootstrap method for the pROC package [17]. The differences were considered significant at p<0,05.

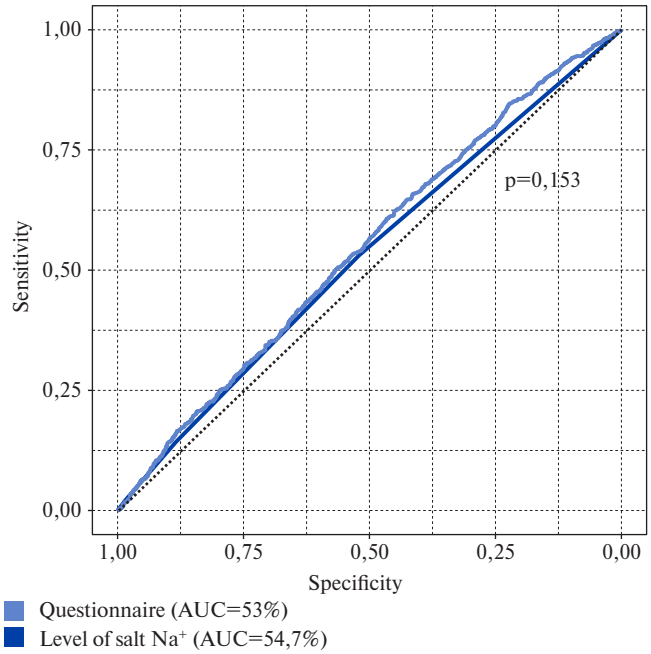

Figure 2. ROC analysis of the association of hypertension with urinary Na+ levels and questionnaire data.

Table 3

The relationship between the components of salt intake (according to the questionnaire) and SBP, DBP and HTN in ESSE-RF-1 and ESSE-RF-2 studies. Results of a univariate regression analysis adjusted for sex and age

	ESSE-RF-1						ESSE-RF-2					
	SBP		DBP		HTN		SBP		DBP		HTN	
	Coefficient	p	Coefficient	p	OR	p	Coefficient	p	Coefficient	p	OR	P
Adding more salt in ready-to-eat meals	0,01 (-0,5-0,52)	0,98	0,25 (-0,05-0,55)	0,10	1,09* (1,03-1,16)	0,0058	0,13 (-0,71-0,98)	0,76	-0,13 (-0,67-0,41)	0,64	1,09 (0,97-1,22)	0,15
Daily/almost daily consumption of sausages and deli meats	1,78* (1,17-2,39)	<0,001	1,16* (0,8-1,52)	<0,001	1,19* (1,11-1,28)	<0,001	1,0 (-0,002-2)	0,051	1,35* (0,71-1,99)	<0,001	1,24* (1,09-1,42)	0,0013
Daily/almost daily intake of pickled foods	0,61 (-0,21-1,44)	0,15	-0,16 (-0,65-0,33)	0,52	0,98 (0,89-1,09)	0,76	1,19 (-0,2-2,58)	0,092	1,11* (0,21-2)	0,015	1,08 (0,89-1,29)	0,44
Score of ESI components†	0,74* (0,41-1,07)	<0,001	0,48* (0,29-0,68)	<0,001	1,1* (1,06-1,15)	<0,001	0,65* (0,11-1,19)	0,019	0,64* (0,29-0,99)	<0,001	1,14* (1,06-1,22)	<0,001
ESI in general	1,38* (0,69-2,07)	<0,001	0,85* (0,44-1,26)	<0,001	1,18* (1,09-1,29)	<0,001	0,61 (-0,6-1,81)	0,32	0,98* (0,21-1,76)	0,013	1,2* (1,02-1,41)	0,027

Note: * — significant associations, † — coefficient shows the average salt increase with an increase in score of 1.

Abbreviations: HTN — hypertension, DBP — diastolic blood pressure, ESI — excess salt intake, SBP — systolic blood pressure, OR — odds ratio.

Results

ESSE-RF-2 study was performed later, however, in addition to the questionnaire, Na^+ in the morning urine was analyzed in 2 regions. The distribution of Na^+ is shown in Figure 1; the characteristics of Na^+ distribution depending on sex and age are shown in Table 1. Linear regression showed a significant increase in the average values of Na^+ with age in men (p=0,033), but not in women. In men, Na^+ levels are on average higher than in women (p<0,001).

Associations of SBP, DBP and HTN with the quintiles of urinary sodium distribution were statistically significant. The average level of SBP is incrementally increased by 1,04 (0,60-1,48) mm Hg for each quintile of Na^+, the average level of DBP — by 0,61 (0,33-0,88) mm Hg. The odds for HTN increases by 1,11 (1,05-1,17) times per quintile.

Further, according to ESSE-RF-2, an analysis was made on the relationship between the salt intake and urinary sodium (Table 2). The components of ESI were considered each separately: the adding more salt in ready-to-eat meals, daily/almost daily consumption of sausages and deli meats, and pickled products. Among these components, the most significant is the consumption of sausages and deli meats, which increased Na^+ by an average of 11,59 (7,06-16,12) mmol/l. Then the components of salt intake were included in the developed score. With a score increase of one point, Na^+ in urine increased on average by 7,51 (5,01-10,02) mmol/l. In general, ESI as RF increased the sodium level by an average of 11,34 (5,75-16,94) mmol/l. To find out how much predictive power is lost when using questionnaire data instead of urinary sodium, we compared their predictive performance in regression models. The level of urinary Na^+ explains 1,4% of the SBP variation, while the questionnaire accounts for 0,35%, which is significantly (p<0,001) worse. On the other hand, the level of urinary sodium predicts the HTN with AUC of 54,7%, while the questionnaire with AUC of 53% and the differences are not significant (p=0,15) (Figure 2).

An analysis of the relationship between BP values and HTN with salt intake components characterizing according to the questionnaire was carried out within ESSE-RF-2 and ESSE-RF studies with a large total sample size (Table 3). The most pronounced effect was shown by the consumption of processed meat, while adding more salt significantly affected only HTN in the ESSE-RF sample. Consumption of pickled products showed significant association only with DBP in the ESSE-RF-2 sample. The score of ESI components is reliable for all parameters in both studies — the OR for HTN — 1,18 (1,09-1,29) in ESSE-RF and 1,14 (1,06-1,22) in ESSE-RF-2.

Discussion

The main result of this analysis is the identification of associations of BP levels and hypertension with urinary Na^+ concentration, as well as the associations of urinary sodium and components of ESI obtained using the questionnaire. Each of the questionnaire components had a significant effect on BP and/or HTN. The closest relationship was observed with the consumption of meat and sausage products: their effect on the salt level was about 2 times stronger than the effect of the remaining two components. However, the introduction of a score taking into account the double effect of meat and sausage products did not lead to a significant increase in predictive performance. The salt intake variables obtained using the questionnaire were associated with HTN and BP. The predictive power of the questionnaire for HTN was 1,57 times lower than of a laboratory test, but this difference was not statistically significant. The close relationship between the consumption of meat and sausage products and urinary sodium level is of particular concern, because a study of the eating habits of Russians showed that about a quarter of men and a fifth of women consume it daily or almost daily [15]. The obtained relationships of eating habits, urinary sodium level, and parameters characterizing hypertension specifies the population-based prevention strategies. A previous analysis showed a significant increase in the HTN prevalence among men in recent years [15]. Among the RF associated with this growth, not only the increase in male obesity [18] is noteworthy, but also the dietary characteristics among men — high salt content in the food, adding more salt, higher consumption of sausages, pickled products, meat and sausage products, savory snacks [15]. It is noteworthy that among men included in the analysis, urinary sodium levels were higher compared to women.

American researchers also noted the negative role of processed meat products, noting that about 70% of Na^+ enters the body as part of processed and ultra-processed foods [19]. At the same time, salt remains an indispensable component of products made from processed meat, alternatives to which have not yet been developed [20].

The study of the population aspects of HTN control in Russia remains extremely relevant. Despite the known methods for diagnosing this disease, the availability of medications for its treatment, an increase in HTN is noted in Russia, and the proportion of people with high BP is 33,8% [21, 22]. In recent years, it has been noted that ESI has a negative effect not only on BP, but also independently affects target organs — heart, kidneys, brain, and bone mineral density [23].

There are few works evaluating salt intake using laboratory tests in Russia; such studies are more limited and are performed on certain categories of patients, but not on a population level. In the ESSE-RF study, the questioning was used, supplemented in ESSE-RF-2 by determining the level of Na^+ in morning urine. Although a positive relationship has been shown between age and average Na^+ levels in the morning urine only among men. The use of some drugs (nonsteroidal anti-inflammatory drugs, antitumor agents, diuretics, antibiotics, and a number of others) may affect its values — both increasing and decreasing Na^+ levels.

The question of using a morning urine to evaluate Na^+ remains debatable. This method was used as part of the PURE study in samples from 18 countries — a 24-hour urinary sodium excretion and further analysis using the Kawasaki formula were performed on the morning urine [7]. However, despite the fact that about 90% of the salt is excreted with urine, this process is unbalanced during the day [12]. Therefore, an assessment of morning urine may not provide true values and lead to underestimation. However, the researchers noted a correlation between one-time and 24-hour collection of urine, which allows the use of a regression coefficient of 0,375 to recalculate it [5]. The study on validation of data obtained in one-time urine collection in comparison with a 24-hour sample revealed the correlation of these parameters not at the individual level, but at the population level [24].

The International Consortium for Quality Research on Dietary Sodium/Salt (TRUE) [12] indicated the futility of using this method to calculate the 24-hour intake of Na^+. However, in population studies, an important problem is not only the predictive power of method, but also the complexity of collecting material and cost for analysis with a large number of respondents. Thus, the use 24-hour urinary sodium seems to be possible to use only on certain categories of individuals, but not on screening nationwide. Less expensive, but also less accurate is the analysis of a morning urine, but this method also increases the cost of the study with a large number of patients. In this case, the predictive value of survey is very important. Questionnaires studying salt intake by the semi-quantitative method or by evaluating the daily nutrition are most optimal in epidemiological studies and are widely used in the world. Thus, the survey method is used to assess the proportion of people with ESI in epidemiological monitoring using the STEPS method (WHO) [25]. The survey method allows identifying the proportion of people taking much salt and the individual dietary components that are present in excess. At the same time, the daily intake of Na^+ is not calculated.

Study limitations: the analysis was carried out within cross-sectional study, which does not allow us to assess the contribution of ESI to HTN. Analysis of Na^+ levels was performed on a morning urine.

Conclusion

In the pattern of ESI components, processed meat and sausage products take first place in terms of association strength with urine sodium. In population-based prevention programs aimed at reducing the BP levels, it is advisable to include measures reducing salt intake, paying particular attention to informing the population about the importance of reducing use of processed meat products.

The questionnaire used in population studies allows to estimate the proportion of people with ESI and its individual components. ESI detected by the questionnaire is associated with elevated BP and urinary Na^+ values, which justifies the use of this tool for epidemiological studies. High prevalence of ESI in the population may indirectly indicate the ineffectiveness of population-based preventive measures to reduce salt intake and its effect on BP in the population. However, it is not possible to use the questionnaire to calculate Na^+ consumption.

Relationships and Activities: none.

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Chaotic global analysis of heart rate variability following power spectral adjustments during exposure to traffic noise in healthy adult women

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Aim. Previous studies have described the substantial impact of different types of noise on the linear behaviour of heart rate variability (HRV). Yet, there are limited studies about the complexity or nonlinear dynamics of HRV during exposure to traffic noise. Here, we evaluated the complexity of HRV during traffic noise exposure via six power spectra and, when adjusted by the parameters of the Multi-Taper Method (MTM).

Material and methods. We analysed 31 healthy female students between 18 and 30 years old. Subjects remained at rest, seated under spontaneous breathing for 20 minutes with an earphone turned off and then the volunteers were exposed to traffic noise through an earphone for a period of 20 minutes. The traffic noise was recorded from a busy urban street and the sound involved car, bus, trucks engineers and horn sounds (71-104 dB).

Results. The results stipulate that CFP3 and CFP6 are the best metrics to distinguish the two groups. The most appropriate power spectra were, Welch and MTM. Increasing the DPSS parameter of MTM increased the performance of both CFP3 and CFP6 as mathematical markers. Adaptive was the preferred type for Thomson's nonlinear combination method.

Conclusion. CFP3 with the adaptive option for MTM, and increased DPSS is designated as the best mathematical marker on the basis of five statistical tests.

Key words: autonomic nervous system, cardiovascular physiology, cardiovascular system, noise, noise occupational, nonlinear dynamics.

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Traffic noise exposure can be unpleasant and distracting, which may have effects on physiological variables. It is often found in hazardous situations as a result of industrialization and urbanization [1]. Hence, the scientific research literature has previously investigated the effects of different types of noise on autonomic nervous system (ANS) by investigating heart rate variability (HRV) [1].

The consecutive heart beats (RR-intervals) derived from the electrocardiograph (ECG) have been demonstrated to fluctuate in an irregular and chaotic manner [2]. Here, the objective is to estimate the possible pathological risks that traffic noise exposure during driving in women poses to the individual by evaluating the heart rate variability (HRV). To complete this we enforced the Shannon Entropy [3] and Detrended Fluctuation Analysis (DFA) [4] algorithms to six alternate power spectra to understand which exhibited the greatest parametric sensitivity. At the outset, Garner and Ling [5] computed the spectral Entropy 5and spectral Detrended Fluctuation Analysis (sDFA) [5], and these were based on the Welch power spectrum [6, 7]. Later, the *high spectral* Entropy (*hs*Entropy) [8] and *high spectral* Detrended Fluctuation Analysis (*hs*DFA) [8]; were formulated founded on the Multi-Taper Method (MTM) power spectrum [9]. Yet, here further parameters based on Covariance [10], Burg [10], Yule-Walker [11] and the Periodogram [12] are computed. By implementing six different power spectra we hope to accomplish results of greater significance by parametric and non-parametric statistics and, the three effect sizes (discussed later) when equating the control subjects to those experiencing exposure to traffic noise via an earphone. It would then be possible to reach a clinical diagnosis quicker and provide the required treatment earlier.

Chaotic global techniques are more responsive to erraticism in dynamical systems than those based on linear, time-domain, geometric methods, frequency domain or the nonlinear measurements [2]. Chaotic behaviour in biological systems typically indicates normal physiological status; while a reduction of chaotic tendencies could be a pathophysiological marker [13]. Such computations are beneficial when assessing surgical patients [13], particularly if sedated [14, 15] or incapable of indicating discomfort as with sleep apnea [16] or those with "air hunger" [17, 18]. We expected the subjects exposed to traffic noise to perform in a nonlinear manner equivalent to persons with cardiac arrest [19], epileptic seizures [20, 21], chronic obstructive pulmonary disease (COPD) [22] or attention deficit hyperactivity disorder (ADHD) [8].

The advantage for constructing the correlation with HRV is that it can provide a benchmark of the potential risks of the dynamical diseases [23] in the traffic noise exposure group. HRV is a simple, reliable and inexpensive technique to continuously record the ANS. Therefore, we aimed to evaluate nonlinear HRV through chaotic global analysis during exposure to traffic noise.

Material and methods

All method and materials were exactly as in the study by Alves M, et al. [24], which followed the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines. Our study previously published [24] described information regarding setting, variables, study design, participants, measurements, data sources, quantitative variables description, statistical methods and potential sources of bias.

Ethical approval and informed consent. All procedures were performed in accordance with the 466/2012 resolution of the National Health Council of December 12th 2012 and all subjects signed a confidential informed consent letter. All experimental protocols were inspected and approved by the Research Ethics Committee in Research of UNESP/Marilia through the Brazilian online platform (Number 5406).

Six Power Spectra. Formerly, we computed the Welch and Multi-Taper Method (MTM) power spectras. De Souza NM, et al. [25] described the application of the Welch power spectrum to achieve chaotic globals in subjects with type I diabetes mellitus. Yet, it was anticipated that since the MTM is an adaptive and nonlinear technique, and as such has a reduced amount of spectral leakage it would potentially be more sensitive to chaotic responses. The *high spectral* Entropy (*hs*Entropy) and *high spectral* Detrended Fluctuation Analysis (*hs*DFA) via the MTM power spectrum have been applied in studies on malnutrition [26], youth obesity [27] and ADHD [8]. Throughout all of the studies we applied the MTM power spectrum to generate the third parameter spectral Multi-Taper Method (sMTM) [5]. This quantifies the extent of broadband noise in the system associated with increasing chaotic response. This parameter remains unchanged throughout all the subsequent analysis.

In this study, when calculating spectral Entropy (*hs*Entropy for MTM) or spectral DFA (*hs*DFA for MTM) we enforce six different power spectra (Welch, MTM, Covariance, Burg, Yule-Walker and Periodogram) to give six variants of these parameters. There are seven different non-trivial permutations of three chaotic globals. The Chaotic Forward Parameters (CFP1 to CFP7) enables seven different combinations of chaotic globals to be applied to ensure optimum chaotic response. Initially whilst assessing the

effects of the six power spectra all three chaotic global values have equal weighting of unity. The settings for these six power spectra are described next.

When we compute spectral Entropy and sDFA via Welch's method the parameters are set at: (i) sampling frequency of 1Hz, (ii) 50% overlap, (iii) a Hamming window and the number of discrete Fourier transform (DFT) point to use in the power spectral density (PSD) estimate is the greater of 256 or the next power of two greater than the length of the segments, and (iv) there is no detrending.

Then, with MTM, the parameters are set as the following: (i) sampling frequency of 1Hz; (ii) time bandwidth for the discrete prolate spheroidal sequences (DPSS) often referred to as slepian sequences [28] is 3; (iii) FFT is the larger of 256 and the next power of two greater than the length of the segment (iv) Thomson's adaptive nonlinear combination method to combine individual spectral estimates is applied.

The Periodogram power spectral density estimate is a nonparametric estimate of a wide-sense stationary random process using a rectangular window. The number of points in the discrete Fourier transform (DFT) is a maximum of 256 or the next power of two greater than the signal length.

Finally, for the Covariance, Burg and Yule-Walker methods the order is of the autoregressive model (AR) used to produce the power spectra density estimate and is set to 16. A default discrete Fourier transform (DFT) length of 256 is applied.

Nonlinear & statistical analysis

Chaotic Globals & CFP1 to CFP7. Spectral Entropy [5] (*hs*Entropy for the MTM) is an algorithm founded on the unevenness of the amplitude and frequency of the power spectrums peaks. Shannon entropy [3] is the function applied to the cited power spectrum. We compute the Shannon entropy for three values attained from three various power spectra. So, the power spectra at three test settings: (a) a sine wave, (b) uniformly distributed random variables, and (c) the oscillating signal from the subjects exposed to traffic noise. The three values are reduced proportionately so that their sum of squares is equal to one. Spectral Entropy (*hs*Entropy for the MTM) is the median value of the three.

DFA was derived in 1995 [4]. It can be executed on time-series where the mean, variance and autocorrelation adjust with time. sDFA (or, *hs*DFA for MTM) is where DFA is applied to the frequency rather than time. To acquire sDFA (or, *hs*DFA for MTM) we estimate the spectral adaptation in precisely the same manner as with Spectral Entropy (or, *hs*Entropy for MTM). Yet, DFA is the algorithm enforced onto the appropriate power spectrum.

Spectral Multi-Taper Method (sMTM) [5] is derived from elevated broadband noise intensities generated in MTM power spectra by irregular and often chaotic signals. sMTM is the area beneath the power spectrum but above the baseline.

CFP1 to CFP7 are applied to RR-intervals from the control subjects and those undergoing traffic noise exposure. sDFA (and *hs*DFA) respond to chaos contrariwise to the others, so we subtract its value from unity. There are seven non-trivial permutations of the three chaotic globals [8].

One-Way Analysis Of Variance & Kruskal-Wallis Tests. Parametric statistics accept that datasets are normally distributed, so they use the mean as a measure of central tendancy. If we are unable to normalize the data we should not compare means. To prove normality we assessed the Anderson-Darling [29], Ryan-Joiner [30] and Lilliefors [29] tests. The Anderson-Darling test for normality applies an empirical cumulative distribution function, but the Ryan-Joiner test is a correlation-based test comparable to Shapiro-Wilk [31]. The Lilliefors test is particularly useful when studies have small sample sizes. Yet, in this study results were inconclusive throughout so we cannot declare that the observations are normally or non-normally distributed. So, we apply parametric and non-parametric tests of significance. Those chosen were the one-way analysis of variance (ANOVA1) [32] and the Kruskal-Wallis [33] tests of significance, respectively.

Cohen's d_s, Hedges's g_s and Glass's Δ Tests. Cohen's d_s [34] is the leading subcategory of effect sizes. It refers to the standardized mean difference between two groups of independent observations for the appropriate sample [35]. It is founded on the sample means and gives a *biased* estimate of the population effect size [36].

In the algebraic formula for Cohen's d_s, the numerator is the variation between the means of two groups of observations. The denominator is the pooled standard deviation. These differences are squared. Then, they are summed and divided by the number of observations minus one for bias (hence, *Bessel's correction*) in the estimate of the population variance. Finally, the square root is applied.

$$Cohen's\ d_s = \frac{\overline{X}_1 - \overline{X}_2}{\sqrt{\frac{(n_1-1)SD_1^2 + (n_2-1)SD_2^2}{n_1+n_2-2}}}$$

Cohen's d_s is often denoted as the *uncorrected* effect size. The *corrected* effect size is *unbiased* and may be termed Hedges's g_s [37]. The difference between Cohen's d_s and Hedges's g_s is tiny especially in sample sizes greater than 20 [38]. Its algebraic formula is beneath. The same subscript letter in Hed-

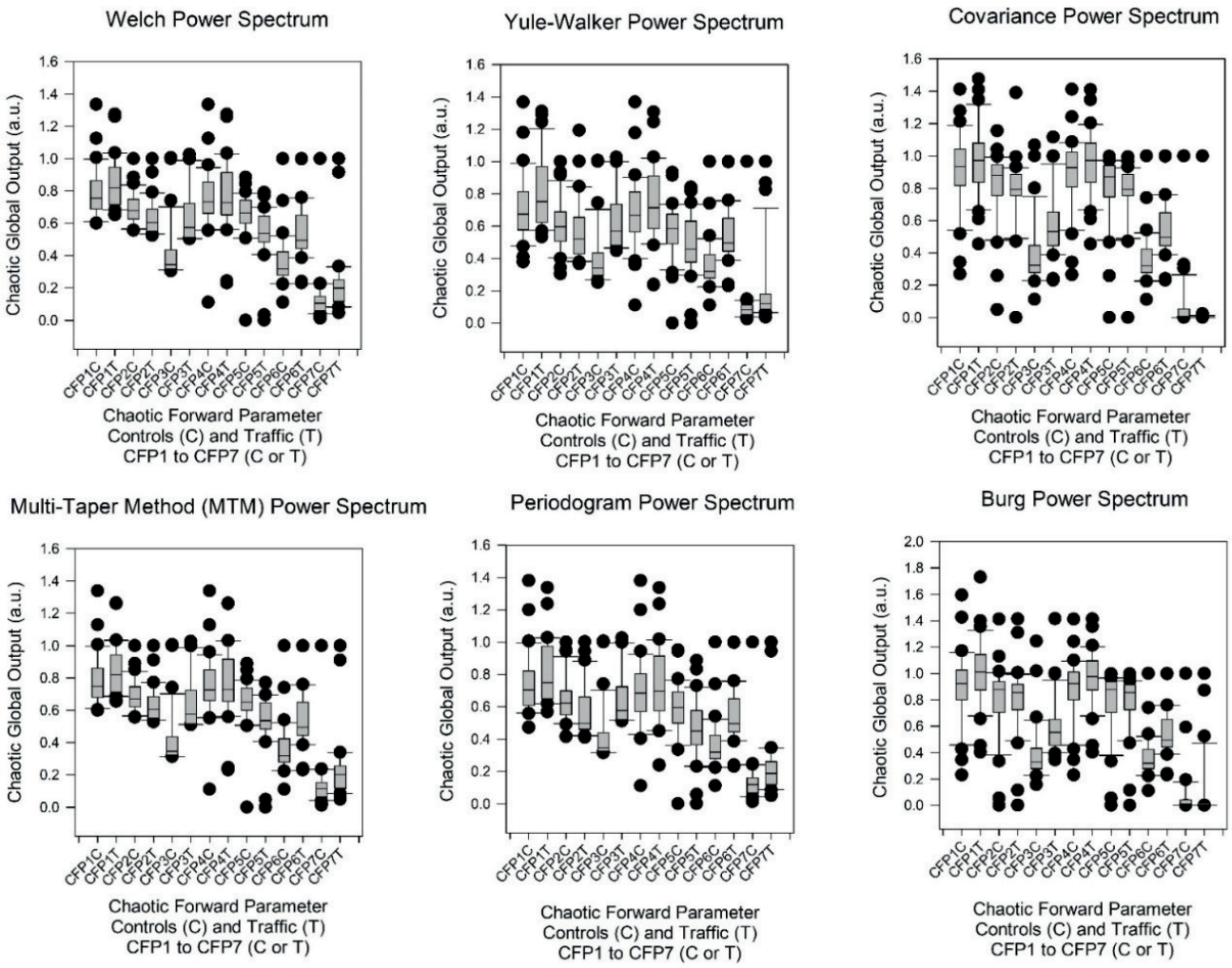

Figure 1. The boxplots of the seven combinations of chaotic forward parameters (CFP 1 to 7) for the six power spectra density (PSD) estimates (Welch, MTM, Burg, Covariance, Yule-Walker and Periodogram) of 500 RR intervals in control subjects (CFPx C) and traffic noise exposed subjects (CFPx T).

Note: the point closest to the zero is the minimum and the point farthest away is the maximum. The point next closest to the zero is the 5th percentile and the point next farthest away is the 95th percentile. The boundary of the box closest to zero indicates the 25th percentile, a line within the box marks the median (not the mean), and the boundary of the box farthest from zero indicates the 75th percentile. The difference between these points is the inter-quartile range (IQR). Whiskers (or error bars) above and below the box indicate the 90th and 10th percentiles respectively.

ges's g_s is applied to distinguish the different calculations; as is the case here for Cohen's d_s.

$$Hedges's\ g_s = Cohen's\ d_s \times \left[1 - \frac{3}{4(n_1+n_2)-9}\right]$$

Finally, when the standard deviations differ substantially between conditions, Glass's Δ delta may be suitable [39]. This calculates the control group's standard deviation alone, and the experimental group is avoided.

For all effects' sizes but particularly with Cohen's d_s the extents are nominated as 0,01> very small effect; 0,20> small effect; 0,50> medium effect; 0,80> large effect; 1,20> very large effect; 2,00> huge effect. These are based on the standards provided by Cohen [34] and, Sawilowsky [40].

CFP3 & CFP6 — MTM Spectrum only

Thomson's nonlinear combination methods & DPSS. Now we assess the outcome of manipulating Thomson's nonlinear combination settings on the MTM spectra. There are three options. They are "adapt", "eigen", or "unity" and are the weights on individual tapered power spectral density (PSD) estimates. The default "adapt" is the adaptive frequency-dependent weights. The "eigen" method weights each tapered PSD estimate by the eigenvalue (frequency concentration) of the corresponding Slepian taper. The "unity" method weights each tapered PSD estimate equally [41].

Table 1

Chaotic responses (CFP 1 to CFP 7) derived via six power spectra (Welch, MTM, Burg, Covariance, Yule-Walker & Periodogram) for control subjects (n=31) and those undergoing traffic noise exposure (n=31)

Power Spectrum	CFP (1 to 7)	ANOVA1	Kruskal-Wallis	Glass's Δ Delta	Hedges g_s	Cohen's d_s
MTM	CFP1	0,1243	0,0704	0,3982	0,3910	0,3960
	CFP2	0,0395	0,0043	-0,5625	-0,5280	-0,5347
	CFP3	<0,0001	<0,0001	1,2210	1,2720	1,2882
	CFP4	0,5739	0,4182	0,1531	0,1418	0,1436
	CFP5	0,0121	0,0011	-0,6905	-0,6487	-0,6569
	CFP6	<0,0001	<0,0001	1,1530	1,0984	1,1124
	CFP7	0,0748	0,0016	0,5156	0,4548	0,4606
Burg	CFP1	0,1291	0,0621	0,3798	0,3860	0,3909
	CFP2	0,9282	0,9047	0,0229	0,0227	0,0230
	CFP3	0,0007	<0,0001	0,9064	0,9023	0,9138
	CFP4	0,1105	0,0727	0,3921	0,4063	0,4115
	CFP5	0,9506	0,7039	-0,0153	-0,0156	-0,0158
	CFP6	<0,0001	<0,0001	1,1530	1,0984	1,1124
	CFP7	0,7956	0,0911	0,0737	0,0653	0,0661
Welch	CFP1	0,1410	0,0981	0,3846	0,3741	0,3789
	CFP2	0,0321	0,0045	-0,5955	-0,5503	-0,5572
	CFP3	<0,0001	<0,0001	1,2163	1,2649	1,2810
	CFP4	0,6067	0,5310	0,1409	0,1298	0,1315
	CFP5	0,0108	0,0013	-0,7091	-0,6599	-0,6683
	CFP6	<0,0001	<0,0001	1,1530	1,0984	1,1124
	CFP7	0,0745	0,0013	0,5177	0,4552	0,4610
Yule-Walker	CFP1	0,0927	0,0898	0,4429	0,4285	0,4340
	CFP2	0,3877	0,1699	-0,2478	-0,2182	-0,2210
	CFP3	<0,0001	<0,0001	1,2084	1,2130	1,2285
	CFP4	0,3343	0,2752	0,2540	0,2441	0,2472
	CFP5	0,0659	0,0412	-0,4878	-0,4698	-0,4758
	CFP6	<0,0001	<0,0001	1,1530	1,0984	1,1124
	CFP7	0,1050	0,0021	0,5142	0,4129	0,4181
Periodogram	CFP1	0,1769	0,1571	0,3473	0,3427	0,3471
	CFP2	0,0915	0,0152	-0,4715	-0,4302	-0,4356
	CFP3	<0,0001	<0,0001	1,2312	1,2754	1,2916
	CFP4	0,5996	0,5590	0,1402	0,1324	0,1341
	CFP5	0,0118	0,0041	-0,6958	-0,6517	-0,6600
	CFP6	<0,0001	<0,0001	1,1530	1,0984	1,1124
	CFP7	0,0757	0,0022	0,5194	0,4533	0,4591
Covariance	CFP1	0,2100	0,2233	0,3085	0,3178	0,3219
	CFP2	0,6217	0,1165	-0,1238	-0,1244	-0,1260
	CFP3	0,0012	<0,0001	0,8479	0,8558	0,8666
	CFP4	0,1417	0,1132	0,3520	0,3735	0,3782
	CFP5	0,7448	0,2370	-0,0771	-0,0820	-0,0831
	CFP6	<0,0001	<0,0001	1,1530	1,0984	1,1124
	CFP7	0,4265	0,0060	-0,1980	-0,2008	-0,2033

Note: table of results for the chaotic responses (CFP 1 to CFP 7) derived via six power spectra (Welch, MTM, Burg, Covariance, Yule-Walker & Periodogram) for those control subjects (n=31) and those undergoing traffic noise exposure (n=31). We computed the significance (p-value) by parametric and nonparametric techniques: One way Analysis of Variance (ANOVA1) and Kruskal-Wallis tests of significance, respectively. We also calculated the effect sizes Glass's Δ Delta, Hedges g_s and Cohen's d_s. We assessed 500 RR-intervals throughout.

Table 2

The properties of the discrete prolate spheroidal sequences (DPSS) value (2 to 13) on the effect sizes Glass's Δ Delta, Hedges g_s and Cohen's d_s

DPSS Value	CFP3 *adaptive*			CFP6 *adaptive*		
	Glass's Δ delta	Hedge's g_s	Cohen's d_s	Glass's Δ delta	Hedge's g_s	Cohen's d_s
2	1,2101	1,2707	1,2869	1,1366	1,0912	1,1050
3	1,2221	1,2734	1,2896	1,1530	1,0984	1,1124
4	1,2197	1,2709	1,2871	1,1464	1,0943	1,1082
5	1,2324	1,2849	1,3012	1,1580	1,1053	1,1193
6	1,2406	1,2935	1,3099	1,1666	1,1137	1,1278
7	1,2423	1,2950	1,3115	1,1682	1,1149	1,1290
8	1,2442	1,2969	1,3134	1,1706	1,1172	1,1314
9	1,2442	1,2974	1,3139	1,1699	1,1174	1,1316
10	1,2436	1,2969	1,3134	1,1690	1,1168	1,1310
11	1,2440	1,2973	1,3138	1,1692	1,1171	1,1313
12	1,2435	1,2968	1,3133	1,1684	1,1165	1,1307
13	1,2451	1,2984	1,3149	1,1706	1,1183	1,1325

Note: the properties of the discrete prolate spheroidal sequences (DPSS) value (2 to 13) on the effect sizes Glass's Δ Delta, Hedges g_s and Cohen's d_s when comparing chaotic globals CFP3 and CFP6 for control subjects and those undergoing traffic noise exposure (both n=31). The remaining parameters are set as (a) sampling frequency of 1Hz; is (b) a discrete Fourier transform (DFT) length of 256 or the next power of two greater than the length of the segment (c) Thomson's "*adaptive*" nonlinear combination method to combine individual spectral estimates is applied. 500 RR-intervals were assessed thoughout.

Moreover, we simultaneously assess the effect of changing the settings of the DPSS from 2 to 13. A DPSS equal to 1, indicates the conventional Blackman and Tukey [42, 43] Fast Fourier Transform (FFT), so is excluded.

DPSS affects the adaptation properties of the tapers with the intention of reducing spectral leakage. Whilst assessing the outcomes of the Thomson's nonlinear combinations settings and the levels of DPSS on the chaotic response the sampling frequency is fixed at 1Hz for the MTM and Fast Fourier Transform of length 256 is enforced. We assessed the outcomes of DPSS (2 to 13) and Thomson's nonlinear combinations ("adaptive", "eigen" and "unity"). Throughout the analysis there are 500 RR-intervals. We assessed CFP3 and CFP6. These are the only groupings significant under the default conditions and with all six power spectra.

Results

ANOVA1, Kruskal-Wallis & Effect Sizes

We have computed the seven permutations of the three chaotic globals CFP1 to CFP7 for 31 female subjects; both controls and those exposed to traffic noise via the earphone. We achieved this with 500 RR intervals throughout. The statistical results are illustrated in the six boxplots, one for each power spectrum as in Figure 1.

As of Table 1 we detected that the combinations CFP3 and CFP6 behave equally during all six power spectra. All CFP3 and CFP6 for Welch, MTM, Covariance, Burg, Yule-Walker and Periodogram have similar reponses. They have a $p<0,001$ for the ANOVA1 and Kruskal-Wallis tests of significance and, have large to very large effect sizes by all three measures — Glass's Δ Delta, Hedges g_s and Cohen's d_s. They demonstrate an *increase* in chaotic response when comparing the controls to the traffic noise exposed group.

With MTM and Welch power spectra there are also significant results for CFP2 ($p<0,05$, medium effect sizes) and CFP5 ($p<0,01$, large effect sizes). Be that as it may, as revealed by the negative effect sizes the traffic noise exposed subjects exhibit a *decrease* in response when comparing control to the traffic noise exposed subjects. The Welch and MTM power spectra perform similarly throughout. MTM has the slightly better levels of significance when compared by the three effect sizes. It is not possible to distinguish between the two on the basis of the ANOVA1 and Kruskal-Wallis tests as the both give $p<0,001$. This is the advantage of calculating the effect sizes in this study.

Next the Periodogram power spectra has a significant result for CFP5 ($p<0,01$, medium effect size), yet the effect size value is *negative* and so responds in the opposite direction to those it calculated for CFP3 and CFP6. Those values which give negative values for the effect sizes can be ignored. They are responding incorrectly and have the lesser significances than CFP3 and CFP6.

Table 3

The properties of the discrete prolate spheroidal sequences (DPSS) value (2 to 13) on the effect sizes called Glass's Δ Delta, Hedges g_s and Cohen's d_s

DPSS Value	CFP3 *eigen*			CFP6 *eigen*		
	Glass's Δ delta	Hedge's g_s	Cohen's d_s	Glass's Δ delta	Hedge's g_s	Cohen's d_s
2	1,2024	1,2638	1,2798	1,1291	1,0847	1,0985
3	1,2205	1,2725	1,2887	1,1508	1,0960	1,1100
4	1,2232	1,2744	1,2906	1,1503	1,0964	1,1103
5	1,2253	1,2778	1,2940	1,1497	1,0976	1,1116
6	1,2322	1,2852	1,3015	1,1565	1,1046	1,1186
7	1,2347	1,2877	1,3040	1,1588	1,1067	1,1208
8	1,2371	1,2900	1,3064	1,1616	1,1093	1,1234
9	1,2379	1,2913	1,3077	1,1621	1,1104	1,1245
10	1,2381	1,2915	1,3079	1,1620	1,1105	1,1246
11	1,2388	1,2922	1,3087	1,1627	1,1113	1,1254
12	1,2390	1,2924	1,3088	1,1627	1,1114	1,1255
13	1,2405	1,2939	1,3103	1,1647	1,1131	1,1272

Note: the properties of the discrete prolate spheroidal sequences (DPSS) value (2 to 13) on the effect sizes called Glass's Δ Delta, Hedges g_s and Cohen's d_s when comparing chaotic globals CFP3 and CFP6 for control subjects and those undergoing traffic noise exposure (both n=31). The remaining parameters are set as with Table 2 with the exception that Thomson's "*eigen*" nonlinear combination method to combine individual spectral estimates is applied. Again, 500 RR-intervals were used for the calculations throughout.

Table 4

The effects of discrete prolate spheroidal sequences (DPSS) value (2 to 13) on Glass's Δ Delta, Hedges g_s and Cohen's d_s

DPSS Value	CFP3 *unity*			CFP6 *unity*		
	Glass's Δ delta	Hedge's g_s	Cohen's d_s	Glass's Δ delta	Hedge's g_s	Cohen's d_s
2	1,2040	1,2647	1,2808	1,1297	1,0849	1,0987
3	1,2223	1,2736	1,2898	1,1526	1,0972	1,1112
4	1,2226	1,2735	1,2897	1,1491	1,0955	1,1094
5	1,2257	1,2782	1,2944	1,1495	1,0978	1,1118
6	1,2334	1,2864	1,3027	1,1575	1,1057	1,1198
7	1,2357	1,2887	1,3051	1,1597	1,1077	1,1218
8	1,2381	1,2911	1,3075	1,1627	1,1104	1,1246
9	1,2388	1,2922	1,3086	1,1629	1,1113	1,1254
10	1,2387	1,2922	1,3086	1,1627	1,1113	1,1254
11	1,2394	1,2929	1,3094	1,1633	1,1120	1,1261
12	1,2395	1,2929	1,3094	1,1632	1,1120	1,1262
13	1,2412	1,2946	1,3111	1,1655	1,1139	1,1281

Note: the effects of discrete prolate spheroidal sequences (DPSS) value (2 to 13) on Glass's Δ Delta, Hedges g_s and Cohen's d_s when relating chaotic globals CFP3 and CFP6 for control subjects (n=31) and those undergoing traffic noise exposure (n=31). We used 500 RR-intervals throughout. The remaining parameters are as with Table 2 and 3 with the exception that Thomson's "*unity*" nonlinear combination method to combine individual spectral estimates is applied.

Now we assess the consequence that the DPSS has on the significance of the results. We use the three effect sizes (Glass's Δ Delta, Hedges g_s and Cohen's d_s) here, as when we calculate the ANOVA1 and Kruskal-Wallis they all perform equally with $p<0,001$. Therefore, it is very difficult to distinguish which values perform best. The range of statistical outcomes is unable to discriminate between their results.

When we calculate the effect sizes the values are similar throughout with all values greater than 1,08 (large effect size) and the majority over 1,20 (very

large effect size). It is evident that the values for both CFP3 and CFP6 and for the three options of Thomson's nonlinear combination methods to combine individual spectral estimates ("adapt", "eigen" and "unity"), increase slightly with increasing DPSS. Effect sizes for CFP3 are greater and therefore more significant than CFP6. So increasing DPSS increases the significance of the results. So a DPSS of 13 where there is a reduced amount of spectral leakage and more adaptation (compared to FFT of Blackman-Tukey, DPSS of 1), is able to distinguish between the two groups in a more statistically significant manner. The mathematical markers are more efficient.

Discussion

We can recognize from the results above that the most robust parameters throughout are CFP3 and CFP6. This was the situation for all six power spectra. MTM, Welch and Periodogram did have other groups which were significant but they responded in the inappropriate manner regarding their chaotic response.

So, for three of the power spectra — Welch, MTM and Periodogram all predicated on the Fast Fourier Transform, and all are non-parametric methods. It is expected that CFP3 would be the most statistically robust parameter. It has the best values when assessed by the three effect sizes. It is notable that the Welch and MTM power spectra perform very similarly, as would be expected. A Periodogram spectrum is able to give consistent results with higher noise levels than the other two. But it is the least sophisticated algorithm that we applied in this study [12]. Despite the Periodogram matching the MTM and Welch it is rejected because, it is a blunt tool; the MTM and Welch have more parameters which can be modified to achieve better responses. The main ones we assessed are for MTM and are the DPSS (2 to 13) and Thomson's nonlinear combination methods to combine individual spectral estimates ("adapt", "eigen" and "unity").

For the other three power spectra, all are parametric methods — Burg, Covariance and Yule-Walker and the results are mostly comparable, marginally less significant when assessed by effect sizes. The order of the power spectra has little influence over the results. Here we set the orders to 16. These are more computer processor intensive algorithms, and so slower to calculate. It is recommended where possible to use the non-parametric techniques.

Returning to MTM we call these derivatives *high spectral* Entropy (*hs*Entropy) and *high spectral* Detrended Fluctuation Analysis (*hs*DFA) and they do *slightly* outperform those derived from the Welch power spectrum. Yet, the MTM power spectrum excels with regards to the various parameters which define the spectrum. For instance, the time bandwidth for the DPSS can be adjusted and Thomson's "adaptive" nonlinear combination method to combine individual spectral estimates can be attuned to the "eigenvalue" or "unity" settings.

This flexiblity enables the possibility of increasing the significance of CFP3 and CFP6 derived from MTM power spectra. It is statistically valuable to increase the DPSS to 13 and, thus outperformed those with lower DPSS when compared by the three effect sizes (see Tables 2 to 4). Adjustments of Thomson's nonlinear combinations method appears limited but "adapt" is the slightly better performer on the three effect sizes (also, Tables 2 to 4). Having time-series which are longer, and increasing the number of subjects for both control and traffic noise exposed subjects could be advantageous.

The chaotic global metrics CFP3 (and CFP6), imposed on the HRV of women exposed to traffic noises and compared to the control groups are capable of statistically discriminating the variation between them. They demonstrate an *increase* in chaotic response when comparing the controls to the traffic noise exposed group. The results are more significant for CFP3 than CFP6, and the best performers are the Welch and MTM power spectra. When the DPSS is elevated for the MTM power spectrum the mathematical marker is improved; with increased effect sizes. The MTM power spectra is advocated as the best way of calculating chaotic globals with highest DPSS set at 13. The three Thomson's nonlinear combination methods to combine individual spectral estimates settings had a minimal consequence, but the "adapt" option was slightly improved on the basis of the three effect sizes. It is accepted that longer time-series and increasing the number of subjects could be useful and, likely increase the statistical significance of the results.

Conclusion

Nonlinear HRV analysis through global chaotic approach detected changes in heart rhythm during traffic noise exposure, indicating increased nonlinear HRV during auditory stimulation.

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