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Primary and residual cardiometabolic risk factors among young adults in a Russian city

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Abstract

Background Cardiovascular diseases are a leading cause of mortality and a significant contributor to temporary and permanent disabilities worldwide. This study aimed to investigate the burden of primary and residual cardiometabolic risk factors in a sample of young adults in the Russian city of Kazan.

Methods This case-control study used the Cardiometabolic Disease Staging (CMDS) classification system, which has been validated in several countries. The study included 191 individuals aged 25–44 years who met the inclusion criteria but did not meet any exclusion criteria. Data collection involved a patient card with questions from the World Health Organization's STEPS instrument, face-to-face patient interviews, and a physical examination. Anthropometric assessments included height, weight, and waist circumference measurements. Body composition was evaluated using bioelectrical impedance measurements. Patients also underwent in-depth laboratory biochemical analyses.

Results The study cohort was comprised of 97 females (50.8%) and 94 males (49.2%). The median age of participants was 35.00 years [IQR: 30.00–39.00]. The study cohort showed an increase in all anthropometric parameters, with abdominal obesity and overweight reaching 100% in the CMDS 3. Apart from atherogenic lipids and raised blood pressure, other risk factors that precipitate residual risk and were not part of CMDS, such as insulin levels, insulin resistance, leptin values, and hyperuricemia, increased as CMDS levels increased.

Conclusions The prevalence of cardiometabolic risk factors was high in young adults in Kazan. This study highlights the need for the early identification and management of cardiometabolic risk factors in young adults to prevent the development of cardiovascular diseases later in life.

Keywords Cardiometabolic risk factors, Cardiometabolic disease staging, Obesity, Dysglycemia, Prediabetes, Dyslipidemia, Hypertension

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Background

Cardiovascular diseases (CVDs) are a leading cause of disability and mortality worldwide [1]. The number of deaths due to CVDs has increased from 12.4 million in 1990 to 19.8 million in 2022. In 2019, CVDs were responsible for approximately 35 million years lived with disability (YLD) and resulted in 358 million years of life lost (YLL) [2, 3]. Most CVD-related deaths are attributed to ischemic heart disease, stroke, and hypertension [3]. Common risk factors associated with CVD deaths include cardiometabolic risk factors such as hypertension, dysglycemia, dyslipidemia, high body mass index (BMI), and tobacco use [3, 4]. These data provide a grim picture of adults aged 45 years and above. However, the picture for young adults may not be very different, as recent studies have indicated a growing trend of cardiometabolic diseases in young adults globally [3, 5–7]. These results highlight the importance of risk assessment in early adulthood [8]. While new risk factors are being studied, new approaches are also being developed for their early identification [9]. Although there is no universally accepted system for assessing cardiometabolic risk, several countries have designed broad guidelines [10, 11].

The Cardiometabolic Disease Staging (CMDS) classification system has been validated in North America, South America, and Europe. Furthermore, a recent study on the CMDS model suggested that it had a similar or superior ability to predict the 10-year risk of major adverse cardiovascular events (MACE) [12, 13]. This system is noteworthy for its simplicity, which makes it a strong candidate for use in primary care settings. Moreover, CMDS has been employed in studies involving young adults, making it a rational choice for use in this age group [14–16]. Although CMDS can effectively classify a wide range of risks for diabetes, cardiovascular disease mortality, and all-cause mortality regardless of BMI, limited data are available on changes in insulin resistance, leptinemia, visceral obesity, C-reactive protein, uric acid, creatinine, and natriuretic peptide levels in young people with different cardiometabolic risks [17, 18]. These residual factors play a key role in increasing the cardiometabolic risk and the associated changes. Furthermore, few studies have focused primarily on young adults in the context of cardiometabolic risk factors in the Russian Federation, which faces a higher burden of cardiometabolic disease. The goal of this study was to investigate the burden of primary and residual cardiometabolic risk factors in a sample of young adults in the Russian city of Kazan.

Methods

Study setting, design, and participants

This study was conducted at a primary care center affiliated with Kazan State Medical University. The sample size was calculated using the application Epi Info v5.5.11 for iOS. Participants were selected based on their BMI (normal weight, overweight, and obesity). The study power was set at 80% and a two-sided confidence level of 95%. The prevalence of overweight and obesity was considered based on the national study by Balanova et al. [19] The required sample size was 180. We oversampled patients considering that some participants would drop out. This case-control study included 191 patients. A two-stage random sampling process was employed to ensure representativeness and minimize selection bias. First, a primary care center was randomly selected by inputting the names of all primary care centers in Kazan into the randomization tool. After choosing the primary care center, the study subjects were randomly selected based on their medical record numbers. This approach was designed to achieve a representative sample and reduce potential biases in the selection process.

Inclusion criteria

The inclusion criterion was participants aged 25–44 years who provided voluntary informed consent to participate in this study.

Exclusion criteria

The exclusion criteria included patients with psychiatric illness that hampered the interview process; the presence of verified cardiometabolic diseases (type 2 diabetes mellitus, coronary artery disease, congestive heart failure, atrial fibrillation, chronic kidney disease); antiphospholipid syndrome and autoimmune inflammatory diseases; the presence of verified oncological disorders; decompensatory states of concomitant diseases or conditions (liver disease, kidney disease, etc.), acute infectious diseases, diseases of the endocrine system, and other diseases and conditions that are secondary causes of obesity; medical implants, including a pacemaker, silicone implants, and metal prostheses; and pregnant and lactating women.

Data collection

We designed a patient card that included questions from the World Health Organization's STEPS instrument [20] to assess noncommunicable disease risk factors. During patient interviews, a thorough history, physical examination, and analysis of the patient's medical documentation were recorded on the patient card. Physical examination was performed according to the guidelines. Height was measured using a stadiometer. Weight and body composition were evaluated using bioelectrical impedance with a Tanita BC-601 body composition monitor (Tanita Corporation, Japan). Visceral fat rating in the range of 1–12 was considered normal, whereas 13–59 was recorded as excess visceral fat [21]. BMI was calculated and

categorized according to the World Health Organization classification [22]. Waist circumference was measured at the midpoint between the iliac crest and lower edge of the rib cage [23]. The blood pressure was measured on a clinically validated sphygmomanometer (Omron M2 Basic, Japan), by following instructions prescribed in the guidelines.

The workup was performed using fasting venous blood samples obtained from a single certified laboratory. Samples were collected by trained phlebotomists using standard venipuncture techniques. Blood was drawn into appropriate collection tubes (e.g. serum separator tubes, EDTA tubes) depending on the tests to be performed. Lipid profile analysis was performed on a Beckman Coulter AU480 (Beckmann Coulter Inc., Brea, USA) automated chemistry analyzer. Total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-c) and low-density lipoprotein cholesterol (LDL-c) were measured using enzymatic colorimetric method. Fasting plasma glucose was measured using hexokinase method. Oral glucose tolerance test was performed by giving 75 g glucose load and measuring 2-hour post-load glucose. Glycated hemoglobin (HbA1c) was measured by automated immunoturbidometric test using Randox RX series kits (United Kingdom). Insulin levels measured by chemiluminescent immunoassay on Siemens Immulite 1000 analyzer (Siemens, Germany). Other biochemical tests such as serum high-sensitivity CRP (hsCRP) was measured by immunoturbidimetric assay; uric acid was measured by uricase enzymatic colorimetric method; and serum creatinine was measured by kinetic method on Beckmann Coulter AU480 analyzer. Leptin and N-terminal pro-brain natriuretic peptide (NT-proBNP) were measured by enzyme immunoassay on Siemens Immulite 1000 analyzer. Thorough quality control protocols were in place. In internal quality control, samples were run with each batch. Instruments regularly went calibration and maintenance.

Cardiometabolic risk factors

Cardiometabolic risk was determined according to CMDS based on the presence of the following cardiometabolic risk factors [15]:

(1) Abdominal obesity, determined by waist circumference (WC) ≥ 80 cm and/or waist-to-hip ratio (WHR) > 0.85 in females and ≥ 94 cm and/or WHR > 0.9 in males; (2) raised blood pressure, defined as systolic blood pressure (SBP) ≥ 130 mmHg and/or diastolic blood pressure (DBP) ≥ 85 mmHg or on antihypertensive therapy; (3) low HDL-c, defined as HDL-c < 1.2 mmol/L in females and < 1.0 mmol/L in males or on lipid-lowering therapy; and (4) fasting hypertriglyceridemia, defined as triglycerides ≥ 1.7 mmol/l or on lipid-lowering medication.

Participants were classified into the following CMDS stages [15]: Stage 0, individuals without any risk factors, that is, who were metabolically healthy; Stage 1 (low risk), individuals who had one or two of the above-listed risk factors; Stage 2 (medium risk), three or more metabolic abnormalities listed above, or the presence of prediabetes, defined as impaired fasting glucose (IFG, venous glucose 6.1–6.9 mmol/L) or impaired glucose tolerance (IGT −2-h venous glucose 7.8–11.0 mmol/L); Stage 3 (high risk), the presence of three or more metabolic risk factors listed above and prediabetes; and Stage 4 (end-stage disease), when the subject had a confirmed diagnosis of type 2 diabetes mellitus (T2DM) and/or vascular disease (coronary artery disease, stroke, peripheral artery disease, etc.). T2DM was defined as self-reported T2DM, a fasting glucose level ≥ 7 mmol/L, or the use of antidiabetic therapy.

Individuals with CMDS 4 (a total of six patients) were excluded from the study. All analyses were performed on 185 individuals.

Additionally, we considered other risk factors that precipitate residual risk. The reference insulin levels were in the range of 3–27 μU/ml. According to the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), insulin resistance was confirmed when the value was > 2.52 [24]. The reference leptin concentrations were in the range of 3.7–11.1 ng/ml. An NT-proBNP level > 125 pg/ml was considered elevated. Hyperuricemia was diagnosed when serum uric acid level was > 360 μmol/L. The glomerular filtration rate (GFR) was calculated using the CKD-EPI formula and categorized according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [25]. The non-high-density lipoprotein cholesterol (non-HDL-c) level was calculated by subtracting the HDL-c value from the total cholesterol content. An elevated level was considered to be > 3.4 mmol/L [26]. hsCRP levels > 3 mg/L were defined as elevated. The visceral adiposity index (VAI) was estimated with respect to age [27]. The atherogenicity index was calculated as the ratio of non-HDL to HDL cholesterol.

Ethical approval

The study was approved by the local ethics committee of Kazan State Medical University (Protocol # 6 dated June 22, 2021).

Statistical analysis

All statistical analyses were performed using the SPSS 26 software (IBM Corp. Released 2019. IBM SPSS Statistics for Macintosh, Version 26.0. Armonk, NY: IBM Corp.). Normality was assessed using the Kolmogorov-Smirnov test. As the data were not normally distributed, nonparametric tests were performed. The Mann-Whitney U test was used to compare two independent groups and the

Kruskal-Wallis test was used to compare three or more groups. Continuous variables are presented as medians and interquartile ranges [IQRs: 25th-75th percentiles]. Descriptive statistics were used to obtain frequencies and percentages for categorical variables, and significant differences in categorical variables were tested using Pearson's chi-squared test or Fisher's exact test. A p value (two-tailed) was set at $p<0.05$.

Results

The study cohort was comprised of 97 females (50.8%) and 94 males (49.2%). The sex distributions across various CMDS are depicted in Fig. 1.

The median age of participants was 35.00 [IQR: 30.00–39.00] years. We did not observe statistically significant differences in the age of the study subjects across the different CMDS, either in the general or sex-based cohorts ($p=0.096–0.568$). Given the normal distribution of females and males, further analysis across various CMDS was conducted in the overall cohort. The characteristics of the main and residual cardiometabolic risk factors across various CMDS are presented in Tables 1 and 2.

Considering that abdominal obesity is one of the criteria used in CMDS staging, it is self-explanatory that it was absent in CMDS 0. However, it is worth noting that 16,2% of individuals in the same group were overweight. As CMDS progressed, the prevalence of abdominal obesity and BMI≥25 kg/m^2 reached 100% in CMDS 3. Table 2 shows the increase in the median values of all anthropometric parameters.

The excess visceral fat level and body fat percentage significantly increased from CMDS 0 to CMDS 3 and were comparable with anthropometric data. Bioimpedance analysis revealed a relatively low prevalence of excess visceral fat in patients with CMDS 1 and 2. However, every fourth patient with CMDS 3 had excess visceral fat level. Interestingly, despite the presence of individuals with higher BMIs and body fat percentages in the CMDS 0 group, they did not have excess visceral fat levels.

Similarly, the proportion of individuals with high blood pressure increased from CMDS 0 to 3. Moreover, in the CMDS 3 group, the frequency of raised blood pressure was more than 50%. A similar rise in frequency with increasing cardiometabolic risk has been observed for the diagnosis of hypertension. We also noted that, with an increase in the CMDS stage, the median values of SBP and DBP significantly increased (Table 2).

Analysis of lipid profile derangements from CMDS 0 to 3 (Table 1) revealed an increase in the frequency of hypercholesterolemia and hypertriglyceridemia, increased LDL-c levels, and decreased HDL-c levels. Notably, hypertriglyceridemia and decreased HDL-c levels were not observed in the CMDS 0 group. In the CMDS 3 group, hypertriglyceridemia, increased LDL-c levels, and decreased HDL-c levels were observed more frequently than increased total cholesterol levels. As the CMDS progressed, the atherogenic lipids increased,

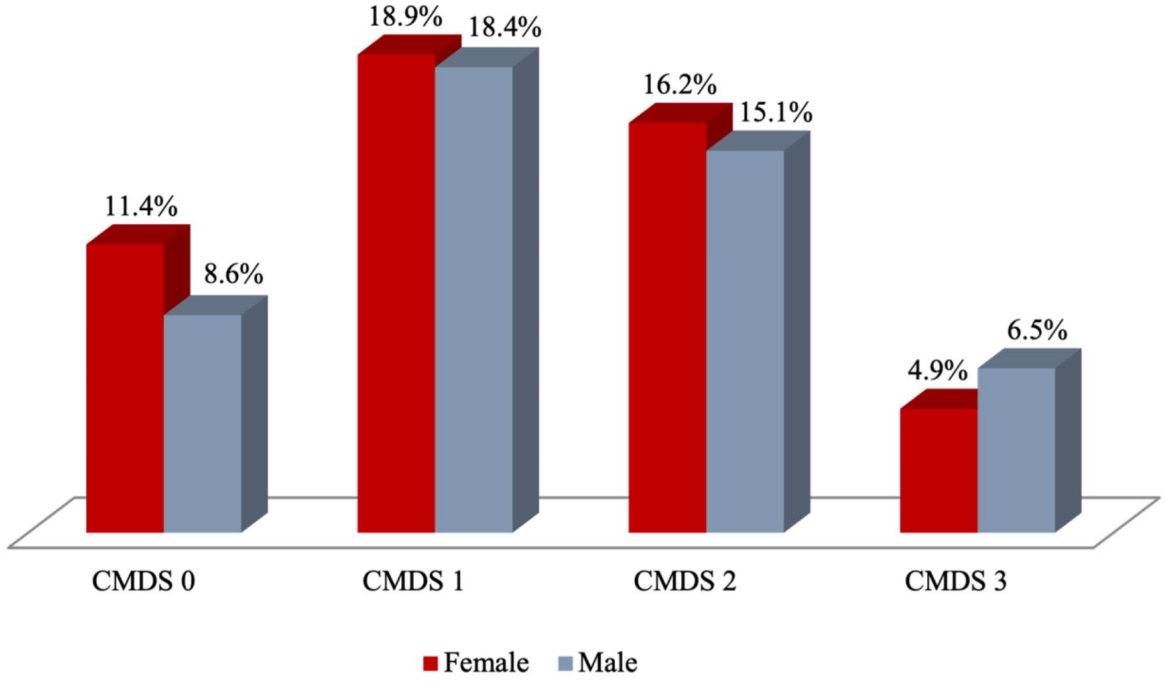

Fig. 1 Prevalence of CMDS (%). Differences among sex categories are presented using a chi-square test

Table 1 Frequency of cardiometabolic risk factors in individuals with different stages of CMDS

Parameter	CMDS 0 (*n* = 37)	CMDS 1 (*n* = 69)	CMDS 2 (*n* = 58)	CMDS 3 (*n* = 21)	*p* value
	1	2	3	4	
	n (%)	*n* (%)	*n* (%)	*n* (%)	
Anthropometry and Bioimpedance analysis					
BMI ≥ 25 kg/m^2	6 (16.2)	52 (75.3)	43 (74.1)	21 (100)	< 0.001
BMI ≥ 30 kg/m^2	0 (0)	26 (37.7)	20 (34.5)	15 (71.4)	< 0.001
WC ≥ 80 cm in females	0 (0)	29 (42.0)	19 (32.8)	9 (42.9)	< 0.001
WC ≥ 94 cm in males	0 (0)	15 (21.8)	16 (27.6)	11 (52.3)	< 0.001
WHR > 0.85 in females	0 (0)	11 (15.6)	9 (15.5)	6 (28.6)	< 0.001
WHR > 0.9 in males	0 (0)	11 (15.6)	9 (15.5)	9 (42.9)	< 0.001
Abdominal obesity	0 (0)	47 (68.1)	36 (62.0)	21 (100)	< 0.001
Increased body fat percentage	13 (35.1)	45 (65.2)	41 (70.7)	19 (90.5)	< 0.001
Visceral fat level > 12	0 (0)	4 (5.8)	2 (3.4)	5 (23.8)	< 0.001
Blood pressure					
SBP ≥ 130 mmHg	0 (0)	19 (27.5)	19 (32.8)	11 (52.4)	< 0.001
DBP ≥ 85 mmHg	0 (0)	17 (24.6)	17 (29.3)	13 (61.9)	< 0.001
Diagnosis of hypertension	0 (0)	11 (15.9)	10 (17.2)	8 (38.0)	0.010
Diagnosis of hypertension + patients on AHT	0 (0)	4 (5.8)	1 (1.7)	4 (19.0)	0.010
Lipid profile					
Total cholesterol ≥ 5 mmol/l	9 (24.3)	29 (42.0)	29 (50.0)	11 (52.3)	0.025
Triglycerides ≥ 1.7 mmol/l	0 (0)	4 (5.8)	14 (24.1)	15 (71.4)	< 0.001
↓HDL (in females < 1.2 mmol/l; in males < 1.0 mmol/l)	0 (0)	16 (23.1)	18 (31.0)	14 (66.7)	< 0.001
LDL > 3 mmol/l	18 (48.7)	39 (56.6)	34 (58.6)	18 (85.7)	0.086
Non-HDL-c > 3.4 mmol/l	12 (32.4)	36 (52.1)	35 (60.3)	16 (76.1)	0.014
Atherogenic index > 3	4 (10.8)	24 (34.8)	27 (46.5)	18 (85.7)	0.262
Glycemic profile					
Impaired fasting glucose (IFG)	0 (0)	0 (0)	0 (0)	2 (9.52)	0.538
Impaired glucose tolerance (IGT)	0 (0)	0 (0)	19 (32.8)	16 (76.1)	< 0.001
IFG + IGT	0 (0)	0 (0)	19 (32.8)	16 (76.1)	< 0.001
HOMA-IR > 2.52	1 (2.7)	15 (21.7)	14 (24.1)	14 (66.7)	< 0.001
Hyperinsulinemia > 27 µU/ml	0 (0)	3 (4.3)	4 (6.9)	1 (4.8)	< 0.001
Other risk factors					
CRP > 3 mg/l	1 (2.7)	23 (33.3)	12 (20.7)	12 (57.1)	< 0.001
Leptin > 11.1 ng/ml	17 (45.9)	34 (49.3)	36 (62.1)	19 (90.5)	0.009
NT-proBNP > 125 ng/ml	10 (27)	9 (13)	6 (10.3)	2 (9.5)	0.166
Uric acid > 360 µmol/l	6 (16.2)	20 (28.9)	17 (29.3)	13 (61.9)	< 0.001
GFR ≥ 120 ml/min/1.73 m^2	0 (0)	3 (4.35)	1 (1.7)	0 (0)	0.538
GFR 90–119 ml/min/1.73 m^2	29 (78.4)	40 (57.9)	37 (63.8)	15 (71.4)	0.178
GFR 60–89 ml/min/1.73 m^2	8 (21.6)	25 (36.2)	20 (34.4)	5 (23.8)	0.313

Note: n = number of participants with deranged parameters, % – proportion of subjects with deranged parameters presented as percentages. BMI – body mass index, WC – waist circumference; WHR – waist-to-hip ratio, SBP – systolic blood pressure, DBP – diastolic blood pressure, AHT – antihypertensive therapy, HDL – high-density lipoprotein, LDL – low-density lipoprotein, non-HDL-c: non-high-density lipoprotein cholesterol, IGT – impaired glucose tolerance, IFG – impaired fasting glucose, HOMA-IR – homeostasis model assessment of insulin resistance, NT-proBNP – N-terminal pro-brain natriuretic peptide, CRP – C-reactive protein, GFR – glomerular filtration rate

which was confirmed by the rise in the frequency of elevated non-HDL cholesterol and the atherogenicity coefficient, reaching 76.1% and 85.7%, respectively, in CMDS 3. The changes in the quantitative parameters reflected an increase in the incidence of dyslipidemia from CMDS 0 to 3 (Table 1). There was a tendency toward an increase in total cholesterol and atherogenic lipids, a decrease in HDL-c, and an increase in the atherogenicity coefficient and non-HDL-c. This was confirmed using the Kruskal–Wallis test.

Prediabetes was diagnosed only in CMDS groups 2 and 3, as it is a criterion for these two stages. However, when comparing the frequency of dysglycemia in these two groups, a significantly higher prevalence (76,1%) was found in patients with CMDS 3 (Table 1). Although insulin resistance is not a criterion for determining the stage of CMDS, it was interesting to observe an increase

Table 2 Median values of cardiometabolic risk factors in individuals with different stages of CMDS

Parameter	CMDS 0 (*n* = 37)	CMDS 1 (*n* = 69)	CMDS 2 (*n* = 58)	CMDS 3 (*n* = 21)	*p* value
	1	2	3	4	
	Me [25–75%]	Me [25–75%]	Me [25–75%]	Me [25–75%]	
Anthropometry and Bioimpedance analysis					
BMI, kg/m^2	23.40 [21.65–24.40]	27.70 [24.90-31.95]	27.95 [24.07–31.25]	32.70 [28.45–38.75]	< 0.001
WC in females, cm	72.50 [70.25-76.00]	87.00 [83.00–99]	83.00 [77.50-98.25]	101.50 [91.50–110.00]	< 0.001
WC in males, cm	83.00 [79.37–86.50]	92.00 [84.75–102]	94.00 [84.00–98.00]	103.50 [96.50-118.50]	0.004
WHR in females	0.73 [0.70–0.74]	0.83 [0.78–0.87]	0.78 [0.74–0.88]	0.93 [0.81–1.01]	< 0.001
WHR in males	0.82 [0.80–0.86]	0.88 [0.84–0.93]	0.87 [0.84–0.91]	0.94 [0.88–0.98]	< 0.001
Body fat percentage, %	24.70 [16.75–32.60]	32.00 [21.40–40.10]	29.60 [21.47–38.80]	33.20 [24.90–39.40]	0.020
Visceral fat level	4.00 [2.50-5.00]	7.00 [5.00–8.00]	7.50 [5.00–10.00]	11.00 [7.50–13.00]	< 0.001
Visceral adiposity index	0.71 [0.58–0.95]	1.10 [0.86–1.47]	1.49 [0.74–2.24]	3.08 [2.19–4.63]	0.001
Blood pressure					
SBP, mmHg	117.5 [109.2–123.0]	121.0 [113.0-130.0]	120.5 [109.0-134.0]	131.0 [117.5-140.5]	0.002
DBP, mmHg	71.50 [65.2–76.5]	78.0 [70.0-84.5]	76.5 [68.7–87.0]	85.0 [77.0-99.5]	< 0.001
Lipid profile					
Total cholesterol, mmol/l	4.5 [3.8–5.0]	4.7 [4.0–5.5]	5.03 [4.3–5.8]	5.0 [4.5–5.7]	0.025
Triglycerides, mmol/l	0.6 [0.5–0.8]	1.0 [0.7–1.1]	1.1 [0.7–1.7]	2.3 [1.4–2.7]	< 0.001
HDL, mmol/l	1.4 [1.2–1.5]	1.3 [1.1–1.4]	1.2 [1.0-1.5]	1.0 [0.9–1.1]	< 0.001
LDL, mmol/l	2.9 [2.2–3.2]	3.1 [2.5–3.7]	3.4 [2.6–3.8]	3.4 [3.0-3.9]	0.071
Non-HDL-c, mmol/l	3.0 [2.45–3.55]	3.49 [2.68–4.14]	3.75 [2.88–4.82]	3.92 [3.32–4.67]	< 0.001
Atherogenic index	2.12 [1.73–2.51]	2.71 [2.08–3.30]	2.9 [2.41–3.78]	3.76 [3.02–4.68]	< 0.001
Glycemic profile					
Glucose, mmol/l	4.20 [3.80–4.47]	4.40 [4.00-4.70]	4.20 [3.90–4.60]	4.60 [3.99–5.15]	0.047
Glycated hemoglobin (HbA1c), %	5.10 [4.90–5.40]	5.20 [5.00-5.40]	5.90 [5.50-6.00]	6.00 [5.95–6.20]	< 0.001
Insulin, μIU/ml	5.44 [4.16–7.28]	8.57 [4.99–12.60]	8.37 [5.71–13.75]	17.30 [12.00-21.95]	< 0.001
HOMA-IR	1.00 [0.68–1.33]	1.67 [0.88–2.46]	1.58 [1.09–2.74]	3.31 [2.33–4.75]	< 0.001
Other risk factors					
Uric acid, mmol/l	305.8 [240.5-345.2]	305.8 [265.1-366.4]	305.7 [263.7-369.3]	393.6 [282.9–473]	0.018
Leptin, ng/ml	9.14 [2.91–17.75]	13.97 [4.30-33.21]	14.83 [5.12–25.56]	24.79 [9.66–34.81]	0.021
NT-proBNP, ng/ml	78 [52.8–134]	63.7 [40.2-103.5]	60.3 [44.7–89.4]	75.2 [41.8–97.8]	0.200

Table 2 (continued)

Parameter	CMDS 0 (*n* = 37)	CMDS 1 (*n* = 69)	CMDS 2 (*n* = 58)	CMDS 3 (*n* = 21)	*p* value
	1	2	3	4	
	Me [25–75%]	Me [25–75%]	Me [25–75%]	Me [25–75%]	
CRP, mg/l	0.71 [0.58–0.95]	1.10 [0.86–1.47]	1.49 [0.74–2.24]	3.08 [2.19–4.63]	0.002
GFR ml/min/1.73 m^2	102.5 [71.3–85.5]	91.5 [82.25–106.5]	96 [78.7–114]	81 [69–91]	0.322

Note: n = number of participants in a particular group, Me – median [interquartile range, 25th–75th percentile], p value – p value obtained from the Kruskal–Wallis test. BMI – body mass index, WC – waist circumference; WHR – waist-to-hip ratio, SBP – systolic blood pressure, DBP – diastolic blood pressure, HDL – high-density lipoprotein, LDL – low density lipoprotein, non-HDL-c: non-high-density lipoprotein cholesterol, HOMA-IR – homeostasis model assessment of insulin resistance, NT-proBNP – N-terminal pro-brain natriuretic peptide, CRP – C-reactive protein, GFR – glomerular filtration rate

in its frequency and median values from CMDS 0 to 3. Every fifth patient with CMDS 1 had insulin resistance; that is, these young patients already had a greater risk of cardiometabolic diseases. Despite the absence of statistically significant differences in the frequency of hyperinsulinemia with increasing cardiometabolic risk, insulin levels significantly increased from CMDS 0 to 3.

We also noted an increase in the prevalence of hyperuricemia, leptinemia, elevated CRP levels, and their median values as the CMDS stage progressed.

The frequency of lower N-terminal pro-brain natriuretic peptide levels, as well as its median values from CMDS 0 to 3 were also noted.

The GFR was assessed at different levels. No significant differences were detected in the changes in the GFR within the CMDS group.

Discussion

From CMDS 0 to 3, the frequency and median values of parameters associated with obesity increased, mainly the frequency of increased waist circumference, waist–hip ratio, abdominal obesity, visceral fat level, and BMI. The obtained results were consistent with those of the authors who designed the CMDS [14]. Similar results were obtained by Jia et al., who studied the relationship between obesity and cardiometabolic risk in the Chinese population. An increase in cardiovascular risk, individual cardiometabolic risk factors, and metabolic syndrome has been established in obese individuals [28]. Thus, it can be inferred that individuals with higher CMDS stages may face compounded risks over time, potentially accelerating the development of cardiovascular diseases and metabolic disorders.

Recent studies have suggested that visceral obesity triggers dysmetabolic processes and a general proinflammatory state, thus acting as an independent factor of cardiometabolic risk. The best method for assessing abdominal obesity is still being debated [29]. Our study used two criteria: waist circumference and waist–hip ratio. Our results showed that these two criteria complement each other, thereby improving the detection of abdominal obesity. Our results are consistent with those of other studies [30].

One of the crucial parameters for determining adiposity dysfunction associated with cardiometabolic risk is the visceral adiposity index (VAI). The sex-specific calculation formula is based on parameters such as BMI, waist circumference, triglycerides, and HDL-c. Our results demonstrated a statistically significant increase in the frequency of increased VAI from CMDS 0 to 3, suggesting its utility in estimating cardiometabolic risk [29].

Higher leptin levels were significantly more common with an increase in CMDS. This was accompanied by an increase in the body fat percentage and visceral fat level, which may be a manifestation of an increase in adiposopathy [31]. In a study conducted in Novosibirsk among people aged 25–35 years, leptinemia was associated with the following cardiometabolic risk factors: higher waist circumference, higher hip circumference, BMI ≥ 25 kg/m^2, raised blood pressure, and elevated triglyceride concentrations. These patients showed an increase in the incidence of metabolic syndrome and a decrease in high-density lipoprotein cholesterol levels [32]. The increasing prevalence elevated leptin levels, and visceral adiposity as discussed above trigger a cascade, contributing to insulin resistance, inflammation, and endothelial dysfunction, thereby exacerbating cardiometabolic risks over time.

Over one-third of the individuals in the CMDS 3 group were diagnosed with hypertension. However, only 19% of the patients in this group received antihypertensive therapy, which is consistent with the nationwide trend [33]. Undertreatment of known risk factors, such as uncontrolled hypertension, if not addressed promptly, could lead to various worse long-term outcomes, such as coronary artery disease, heart failure, and atrial fibrillation.

Prediabetes results in macrovascular disorders and increased atherogenesis, which increase the likelihood of cardiovascular disease [4]. In our study, there was a significant increase in the risk of CMDS 2 to 3 due to prediabetes alone.

Apart from the risk factors included in the CMDS, we conducted an extensive work-up that included other

factors, such as leptin, insulin resistance, NT-proBNP, CRP, uric acid, and GFR. The results showed a negative trend, both in the frequency and deviation of the median values of all studied cardiometabolic risk factors. This reflects an increase in all dysmetabolic processes and an increase in risk.

Recent literature suggests that there is not only a simultaneous increase in the number and severity of risk factors but also a negative synergistic effect, potentiating the risks [34–36], which is in line with our results. It should be noted that the risk factors not included in the CMDS staging were also observed in CMDS 0, specifically, an increase in LDL-c (48.7%), non-HDL-c (32.4%), total cholesterol (24.3%), and BMI ≥ 25 kg/m^2 (16.2%), which is consistent with the staging concept of the authors themselves [37, 38].

The utility of CRP measurement for risk stratification was highlighted Ridker et al., which identified a subgroup of patients at risk for cardiovascular disease who were not considered for statins at the time of the study but benefited when randomized to a statin [39]. These data are consistent with those of our study. In our cohort, a significant increase in the frequency of CRP was found with increasing cardiometabolic risk. Individuals with obesity and concomitant dysmetabolic disorders have a proinflammatory state [34]. These changes play an essential role in the development of cardiometabolic diseases. In our cohort, in addition to a significant increase in the frequency of elevated CRP levels, an increase in the median CRP value was noted with increasing CMDS. As suggested in the literature, systemic inflammation is associated with residual risk, which is common in patients with cardiovascular diseases and potentially leads to poorer long-term cardiovascular outcomes [40].

On analyzing NT-proBNP levels, we found lower values in individuals with CMDS 3, which is consistent with the data of other authors. With an increase in cardiometabolic risk in the groups, the prevalence of obesity also increased, and the average values of NT-proBNP decreased. This may be explained by natriuretic peptide deficiency in asymptomatic, obese individuals as well as people with insulin resistance [41–43]. The association between obesity and low NT-proBNP levels was first demonstrated in a study involving 318 individuals by Mehra et al. [44]. Furthermore, it has also been demonstrated that relative deficiency of natriuretic peptide levels among obese individuals contribute to higher cardiometabolic diseases susceptibility [41–43].

Hyperuricemia occurred in 30.3% of the patients in the general cohort, and its frequency increased with increasing cardiometabolic risk. The increasing prevalence of hyperuricemia with higher CMDS stages suggests an additional pathway for cardiovascular risk. Asymptomatic hyperuricemia is common among young adults, which is consistent with our results. Literature suggests it has been associated with hypertension, metabolic syndrome, and kidney disease, potentially contributing to worse long-term outcomes [45].

Kidney function may be significantly altered in patients with cardiometabolic disorders. Its well known that hyperfiltration is an early marker of kidney damage, and in later stages the kidney function declines. Therefore, we assessed the change in GFR at three ranges: GFR 90–120 ml/min/1.73 m^2; <90 ml/min/1.73 m^2; and ≥120 ml/min/1.73 m^2. We did not find any significant differences in the GFR changes within the CMDS group.

These results may improve the understanding of comprehensive risk assessments in various CMDS, and may play a crucial role in developing screening and management strategies from a primary prevention perspective. The presence of multiple residual risk factors even in lower CMDS stages highlights the importance of early screening and intervention. Addressing these risks in young adults could potentially prevent or delay the onset of cardiometabolic diseases later in life. Furthermore, it would be interesting to longitudinally track changes in the cardiometabolic risk over time. In summary, our results present data obtained using physical, anthropometric, and laboratory methods to determine the cardiometabolic health of young adults in Kazan, Russia.

Strengths and limitations

This study has several strengths. First, to the best of our knowledge, this is the first study originating from Russia that has performed a comprehensive assessment of cardiometabolic risk factors in young adults. The study used a combination of questionnaires, physical examinations, and laboratory tests to gather comprehensive data from the participants. As a result, we have a detailed picture of both the primary and residual risk factors in young adults, offering a holistic view of cardiometabolic health. Second, the study employed the CMDS classification system, which has been validated in multiple countries, enhancing the reliability and comparability of the results. Third, by targeting individuals aged 25–44 years, this study addresses an important gap in the research on cardiometabolic risk factors in younger populations.

Our study has several limitations. First, the case–control study design is prone to selection bias, which may limit the generalizability of the results. Second, we conducted a study in a single city, which may limit its applicability to other regions or countries. Third, there may be other factors influencing cardiometabolic risk that were not measured or accounted for in this study. Fourth, there was a lack of long-term follow-up data. Without longitudinal data, the study cannot assess how these risk factors translate into actual cardiovascular events or mortality. Finally, despite the use of standardized protocols, there is

always some potential for errors in clinical and laboratory measurements. We attempted to minimize them by using validated, regularly calibrated instruments with stricter quality control measures. Furthermore, strict adherence to guidelines and standard operating procedures ensured minimal to negligible variation in measurements or results.

Overall, in our view, the results provide a valuable contribution to the understanding of cardiometabolic risk in young adults, with its comprehensive approach being a major strength.

Conclusions

This study on cardiometabolic risk factors provided valuable insights into cardiometabolic risk in young adults in Russia, where the population's median age is approximately 40 years. We used CMDS staging to comprehensively assess cardiometabolic risk. Our findings highlight the high prevalence of cardiometabolic risk factors, even in young adults, underscoring the urgent need for early screening and intervention strategies. The use of CMDS classification proved effective in identifying individuals at various levels of risk, including those with additional risk factors contributing to residual risk. Our data confirmed a simultaneous increase in the number and severity of risk factors and the presence of a negative potentiation of risk. Thus, the presented results justify the use of the CMDS classification at the screening and primary prevention stages of cardiometabolic diseases to identify groups with the most significant abnormalities in fat, lipid, and carbohydrate metabolism and to develop differentiated approaches for their management and follow-up. These results can directly inform public health policies by: (1) advocating comprehensive cardiometabolic risk assessment in young adults, incorporating both traditional and emerging risk factors. (2) emphasizing the importance of early detection programs targeting young adults. (3) guiding the development of tailored intervention strategies based on CMDS stages, allowing for more precise and cost-effective resource allocation. (4) highlighting the need for a multifaceted approach to risk reduction, addressing not only primary risk factors but also those contributing to residual risk. (5) providing a model for similar studies in other countries, enabling global comparisons and the development of internationally applicable strategies. (6) demonstrating the value of extensive clinical and laboratory assessments in identifying at-risk individuals who may appear healthy by conventional standards. By implementing these findings, public health systems globally can work towards reducing the long-term burden of cardiometabolic diseases through early, targeted interventions in young adult populations.

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Author contributions
AVS contributed to the research design and implementation, analysis of the results, and writing of the manuscript. SP, GRM, ZRA, ARN, TYK, and ASF collected, cleaned, and prepared the data. AVS, TYK, ASF, ARN, GRM, ZRA, and SP analyzed the data. AVS conceived the original manuscript and supervised the project. SP wrote the first draft of the manuscript, AVS, ARN, TYK, GRM, ZRA, and ASF, and edited the manuscript. All authors approved the final version of the manuscript.

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Data availability
The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval and consent to participate
The study protocol was designed in accordance with the ethical guidelines of the 1975 Declaration of Helsinki. It was then discussed and approved by the local ethics committee of Kazan State Medical University vide protocol No. 6 on June 22, 2021. Participation in the study was voluntary, and participants signed an informed consent form to participate in the study. The participants were informed about the study in an easy-to-understand language and confidentiality was guaranteed. The participants were also apprised of potential risks during laboratory examinations. The participants had access to their results and the option to opt out of the study at any time.

Consent for publication
The participants were assured of the full anonymity of their data. The participants provided voluntary consent to use their data for publication and other presentation purposes.

Competing interests
The authors declare no competing interests.

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