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Early structural and functional left ventricular disorders in young patients with hypertension: a role of insulin resistance

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Cardiac remodeling refers to factors that increase the risk of cardiovascular events in patients with hypertension (HTN). Changes in myocardial structure and function can be caused not only by hemodynamic causes, but also a number of metabolic disorders.

Aim. To analyze the associations of insulin resistance and left ventricular (LV) remodeling in a cohort of young patients with untreated uncomplicated hypertension and high normal blood pressure (BP).

Material and methods. The presented cohort cross-sectional study included 105 subjects. We analyzed clinical, demographic and anthropometric characteristics, performed a biochemical panel (creatinine, potassium, lipid profile, glucose, insulin, uric acid) with the estimation of insulin resistance scores (HOMA-IR, METs-IR, TyG), a glycosylated hemoglobin test. Urine albumin-to-creatinine ratio was determined. Office and 24-hour ambulatory BP measurement and two-dimensional speckle-tracking echocardiography were performed in all patients.

Results. The median age was 23 years (men — 85%); 51% of participants were overweight or obese, 39% had dyslipidemia, 21% — insulin resistance. Signs of LV remodeling were observed in 38 (40%) subjects: 32 (34%) — concentric remodeling, 5 (5%) — concentric LV hypertrophy (LVH), 1 (1%) — eccentric LVH. Defects of LV systolic global longitudinal strain (GLS) were observed in 44 (47%) young patients with HTN and preHTN. Stepwise multivariate regression analysis revealed that the TyG index was an independent predictor of LV GLS defects (b=0,38, p=0,001).

Conclusion. In a cohort of young patients with HTN and high normal blood pressure, there is a high prevalence of insulin resistance, metabolic disorders, and early signs of LV remodeling and subclinical systolic dysfunction. The TyG index, available for estimation by routine biochemical tests, is an independent factor affecting the LV GLS.

Key words: hypertension, young patients, prehypertension, insulin resistance, left ventricular hypertrophy, left ventricular strain, left ventricular systolic global longitudinal strain, two-dimensional speckle-tracking echocardiography.

Relationships and Activities: not.

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The high prevalence of hypertension (HTN) in young people and little evidence of a decrease in the absolute risk of cardiovascular events (CVE) with long-term antihypertensive therapy in young people require further study of this issue and search for a favors of early drug use. In 2018, an analysis of the prospective cohort study CARDIA with long-term follow-up (median — 19 years) was published, which included people <40 years of age. This work confirmed the increased risk of CVE in people with blood pressure (BP) >130/80 mm Hg compared with normotension individuals [1]. One of the independent predictors of unfavorable prognosis is left ventricular hypertrophy (LVH). The Framingham study showed that an increase in left ventricular (LV) mass for every 50 g increases the relative cardiovascular risk in women by 49%, and in men by 57% [2]. Not only hemodynamic, but also metabolic factors contribute to the development of LVH. Both in experimental and in clinical studies, the contribution of insulin resistance to development of myocardial structural and functional changes has been confirmed. The American Association of Clinical Endocrinologists has created a concept for dysglycemia-based chronic disease, where insulin resistance is defined as the first stage, followed by prediabetes, type 2 diabetes, and vascular complications. [3].

Since LVH is more likely associated with LV diastolic dysfunction, and LV contractility are usually not impaired [4], special attention should be paid to more sensitive methods for diagnosing a decrease in LV systolic function. The prognostic value of LV strain changes, estimated by speckle tracking echocardiography, as well as the search for effective preventive strategies in young people with HTN and preHTN, remain the debating point. Cardiac magnetic resonance imaging (MRI) remains the gold standard technique for assessing myocardial strain, but its practical use is limited by cost and low availability. The use of 2D speckle tracking echocardiograpy allows to quantify the global and regional contractile function of the myocardium. This technique has already been introduced into current guidelines on examination of patients with cardiomyopathies, patients after heart transplant, in case of chemotherapy-induced cardiotoxicity. However, the prospects of its use in young HTN patients requires further study. The aim of this study was to analyze the associations of insulin resistance and LV remodeling in a cohort of young patients with untreated uncomplicated HTN and preHTN.

Material and methods

During the medical screening, students and employees of the RUDN University aged 18 to 45 years (n=965) were doubly measured for office BP with 2-week interval. Fifty-seven (5,9%) individuals were diagnosed with HTN, 64 (6,6%) participants had high normal BP. The study was approved by the ethics committee of the RUDN University. Of the 121 people mentioned, 105 agreed to continue participating in the study and signed informed consent. They underwent 24-hour ambulatory BP monitoring. White-coat HTN was revealed in 11 patients who were excluded from further follow-up. Laboratory and instrumental examinations was performed for 94 patients with uncomplicated essential HTN diagnosed by office and 24-hour ambulatory BP measurement. The inclusion criteria were clinic BP ⩾140/90 mm Hg and/or average 24-hour BP ⩾130/80 mm Hg and/or average daytime BP ⩾135/85 mm Hg and/or average nocturnal BP ⩾120/70 mm Hg. There were following exclusion criteria: history of CVD (myocardial infarction or unstable angina, stroke, hospitalization due to heart failure); atrial fibrillation; glomerular filtration rate <45 ml/min (CKD-EPI equation); secondary HTN; white coat HTN; exacerbation/decompensation of chronic diseases; type 2 diabetes; limb amputation.

We collected anamnestic, demographic, and anthropometric data. Assessment of salt, fast food, and alcohol consumption was carried out by a structured questionnaire. Levels of creatinine, potassium, lipids, glucose, insulin, and uric acid were determined. We also assessed glycated hemoglobin (HbA_{1c}), as well as urine albumin/creatinine ratio.

Assessment of insulin resistance. We used Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) proposed by Matthews DR, et al. (1985) [5]. The HOMA-IR was calculated as follows: HOMA-IR = fasting serum insulin (μU/ml) × fasting plasma glucose (mmol/l)/22,5. The threshold of insulin resistance was considered as exceeding the 75th percentile of its cumulative population distribution in non-diabetic adult population aged 20-60 years; HOMA-IR >2,7 was considered confirmation of insulin resistance.

Alternative methods for assessing insulin resistance were:

— Triglyceride-glucose index (TyG) proposed by Simental-Mendía L, et al. (2008) and calculated as ln (fasting triglycerides (mg/dl) × fasting glucose (mg/dl/2)). The threshold for normal glucose tolerance were TyG level of 8,29 [6].

— The Metabolic Score for Insulin Resistance (METS-IR) proposed by Bello-Chavolla O, et al. and calculated as ln ((2*Fasting glucose)+fasting TG)*BMI)/(ln (HDL-Cl), where TG are triglycerides, BMI — body mass index, HDL-C — high density lipoprotein cholesterol [7].

Echocardiography. We myocardial structure and function by standard echocardiography on a

Table 1

Clinical and demographic characteristics of young subjects with uncomplicated essential hypertension

Parameter	n=94
Age, years	23 [21; 25]
Men, n (%)	80 (85)
Race:	
Caucasians, n (%)	85 (90,5)
Negroids, n (%)	5 (5,3)
Mongoloids, n (%)	3 (3,2)
Hispanic/Latino, n (%)	1 (1,0)
Family history of early CVD, n (%)	32 (34)
Family history of HTN, n (%)	67 (71)
Body weight, kg	81,8±17,0
BMI, kg/m^2	25,9±4,8
BMI ⩾25 kg/m^2, n (%)	48 (51)
BMI ⩾30 kg/m^2, n (%)	16 (17)
WC, cm	88,3±13,5
Abdominal obesity, n (%)	30 (32)
TC, cm	100,9±10,9
WC/TC	0,86 [0,78; 0,91]
TC/height	0,48 [0,44; 0,54]
Smoking, n (%)	36 (38)
Fast food ⩾1 time/week, n (%)	45 (48)
Salt >5 g/day, n (%)	45 (48)
eGFR (SKD-EPI), ml/min/1,73 m^2	100,7±15,4
Urine albumin/creatinine ratio, mg/g	4 [0; 7]
TC, mmol/L	4,6±1,0
LDL-C, mmol/L	2,7±0,8
HDL-C, mmol/L	1,3±0,4
TG, mmol/L	0,9 [0,7; 1,4]
Dyslipidemia, n (%)	37 (39)
Uric acid, μmol/L	345,8±70,8
Glucose, mmol/L	4,9 [4,7; 5,3]
Insulin, μU/ml	8,1 [5,4; 12,3]
HOMA-IR	2,0±1,2
TyG	8,3±0,6
METS-IR	38,0±8,3
HbA_{1c}, %	5,1±0,3

Abbreviations: BMI — body mass index, WC — waist circumference, TC — thigh circumference, eGFR — estimated glomerular filtration rate, TC — total cholesterol, LDL-C — low density lipoprotein cholesterol, HDL-C — high density lipoprotein cholesterol, TG — triglycerides.

VIVID-7 ultrasound system (General Electric, USA). We used B-mode, M-mode, pulse wave (PW) and continuous wave (CW) Doppler, colour flow mapping with assessment of end-dastolic and end-systolic LV dimensions, end-diastolic and end-systolic volumes, stroke volume (SV), LV ejection fraction (EF), interventricular septum (IVS) and LV posterior wall (PW) thickness at diastole, left (LA) and right atrial (RA) sizes, LA volume index, RV size, pulmonary artery systolic pressure (PASP). LV mass was calculated by the Devereux R (1986) formula and indexed to body surface area (m^2) [8]. The criteria for LV hypertrophy were LV mass index (LVMI) ⩾95 g/m^2 in women, ⩾115 g/m^2 in men. Classification of LV remodeling types was carried out according to Ganau A (1992) method [9]. To evaluate diastolic function, we determined the peak E, the E/A ratio, average peak e', E/e'avg ratio, left atrial volume index, and tricuspid regurgitation peak velocity. All patients underwent an assessment of LV global longitudinal strain (GLS) using a speckle-tracking echocardiography. Apical four-, two- and three-chamber views were obtained. LV GLS was calculated automatically. Normal values of LV GLS were considered at >-20% [10]

The 24-hour ambulatory BP monitoring was performed according to a standard technique using a BPlab monitor with Vasotens technology (OOO Petr Telegin, Nizhny Novgorod, Russia).

Statistical analysis. Statistical processing was carried out using the software package SPSS 10.0. Normally distributed quantitative variables are presented as m±SD. For non-normally distributed quantitative variables, the median (Me) and 25; 75 percentiles (interquartile range — IQR) were used. Significance of differences was evaluated by Wilcoxon and Mann-Whitney tests. Data comparison in three subgroups was carried out using one-way analysis of variance, as well as the Kruskal-Wallis test with Bonferroni adjustment or Tukey's test. To assess the relationship, the Spearman's Rank or the linear Pearson's correlation coefficients were calculated. Differences were considered significant at $p<0,05$.

Results

The clinical and demographic characteristics of participants are presented in Table 1. The median age was 23 years (men — 85%). More than half of the subjects had overweight or obesity, and an abdominal distribution of excess fat was observed in 32%. We also revealed that 34% of participants had a family history of early CVE. Dyslipidemia was detected in 39%. More than a third of patients were smokers. Two-thirds of patients (67%) had masked HTN. Office systolic BP (SBP) was 133,4±15,7 mm Hg; diastolic BP (DBP) — 77,5±12,7 mm Hg. The average 24-hour SBP were 134,3±14,5 mm Hg, DBP — 77,0 [73,0; 85,5].

Table 2

Comparison of LV structural and functional parameters depending on the distribution between the quartiles of insulin resistance indices

HOMA-IR					
	1st quartile (n=21)	2nd quartile (n=23)	3rd quartile (n=23)	4th quartile (n=22)	p
BMI, kg/m^2	21,2±2,2	23,3±1,6	27,1±2,0	31,9±3,9	<0,001
WC, cm	75,9±7,8	81,3±6,6	90,9±5,9	105,5±9,2	<0,001
LVEF, %	60,3±5,2	60,0±4,6	59,4±5,4	60,8±5,6	NA
IVS thickness, cm	1,0 [0,8; 1,1]	0,9 [0,9; 1,1]	1,0 [0,9; 1,1]	1,0 [0,9; 1,1]	NA
LVPW thickness, cm	1,0 [0,8; 1,1]	1,0 [0,9; 1,1]	1,0 [0,9; 1,1]	1,0 [0,9; 1,1]	NA
LVMI, g/m^2	81,6 [71,4; 87,5]	86,4 [71,6; 95,6]	83,9 [78,0; 104,4]	88,0 [82,8; 100,7]	NA
RWT	0,39±0,05	0,41±0,08	0,45±0,09	0,43±0,11	NA
LV GLS, %	-20,5±1,5	-20,1±1,3	-19,9±2,6	-20,0±3,0	NA
METS-IR					
	1st quartile (n=23)	2nd quartile (n=24)	3rd quartile (n=23)	4th quartile (n=23)	p
BMI, kg/m^2	21,2±2,2	23,3±1,6	27,1±2,0	31,9±3,9	<0,001
WC, cm	75,9±7,8	81,3±6,6	90,9±5,9	105,5±9,2	<0,001
LVEF, %	61,4±5,3	60,3±5,3	59,3±4,7	59,5±4,9	NA
IVS thickness, cm	0,9 [0,8; 1,0]	0,9 [0,8; 1,0]	1,0 [0,9; 1,1]	1,0 [1,0; 1,2]	<0,001
LVPW thickness, cm	0,9 [0,8; 1,0]	0,95 [0,9; 1,1]	1,0 [0,9; 1,1]	1,1 [1,0; 1,2]	<0,001
LVMI, g/m^2	81,5 [63,1; 89,4]	87,5 [71,7; 96,4]	86,8 [80,5; 101,2]	87,0 [78,0; 109,1]	NA
RWT	0,38±0,06	0,41±0,09	0,41±0,05	0,47±0,12	0,003
LV GLS, %	-20,9±2,2	-20,2±2,0	-19,9±1,4	-19,4±2,8	NA
TyG					
	1st quartile (n=23)	2nd quartile (n=23)	3rd quartile (n=25)	4th quartile (n=23)	p
BMI, kg/m^2	23,8±3,5	24,9±5,0	26,9±5,5	27,8±4,0	0,015
WC, cm	82,1±10,2	82,3±11,9	92,2±13,6	95,3±12,9	0,001
LVEF, %	60,6±4,9	60,0±5,4	60,4±5,1	59,6±4,8	NA
IVS thickness, cm	0,9 [0,8; 1,0]	1,0 [0,8; 1,0]	1,0 [0,9; 1,1]	1,0 [0,9; 1,2]	NA
LVPW thickness, cm	0,9 [0,8; 1,0]	1,0 [0,9; 1,1]	1,0 [0,9; 1,1]	1,1 [1,0; 1,2]	0,012
LVMI, g/m^2	87,3 [68,7; 101,9]	81,7 [74,4; 89,7]	86,2 [78,1; 93,8]	88,4 [81,0; 111,9]	NA
RWT	0,37±0,06	0,42±0,07	0,42±0,09	0,45±0,11	0,014
LV GLS, %	-21,1±2,4	-20,5±1,6	-19,9±1,7	-18,6±2,3	0,003

Abbreviations: IVS — interventricular septum, LVPW left ventricular posterior wall, LVMI — LV mass index, RWT — relative wall thickness, LV GLS — left ventricular global longitudinal systolic strain.

LV remodeling were found in 38 (40%) participants: concentric remodeling — 32 (34%), concentric LVH — 5 (5%), eccentric LVH — 1 (1%). In order to assess LV dysfunctional impairment, LVEF was determined. Preclinical LV systolic dysfunction with normal LVEF was observed in 44 (47%) young people with HTN and preHTN.

To identify early disorders of carbohydrate metabolism, HbA_{1c}-level was evaluated; there were subjects with HbA_{1c} >5,7% (prediabetes). Insulin resistance (HOMA-IR >2,7) was diagnosed in 20 (21%) patients. Insulin sensitivity was also determined using TyG and METS-IR. The sample was divided into quartiles for each of three insulin resistance indices (Table 2). In the obtained subgroups, we compared clinical, demographic, anthropometric characteristics, laboratory data and parameters of myocardial structure and function. In subgroups, there were no significant differences in the age and sex patterns, the levels of clinic and average 24-hour

Table 3

Comparison of subgroups depending on insulin resistance and overweight/obesity

	Normal BMI, no IR (n=32)	Increased BMI, no IR (n=18)	Normal BMI, IR (n=14)	Increased BMI, IR (n=30)	p
Age, years	23,5±1,4	24,2±2,1	23,9±3,3	27,1±1,4	NA
Sex, f (%)	7 (22)	2 (11)	2 (14)	3 (10)	NA
BMI, kg/m^2	21,8±0,3	28,7±0,4	22,8±0,6	29,8±0,3	<0,001
WC, cm	77,5±6,4	94,4±9,0	80,2±7,6	99,9±10,6	<0,001
TC, cm	92,7±9,5	106,7±12,3	94,3±6,2	108,0±9,7	<0,001
SBPcl, mm Hg	130,5±14,5	128,7±10,9	136,7±15,1	137,4±17,6	NA
DBPcl, mm Hg	76,5±11,7	73,2±8,6	79,7±14,1	80,2±13,5	NA
SBP24, mm Hg	133,6±12,3	132,8±12,4	134,5±13,9	136,3±16,0	NA
DBP24, mm Hg	82,1±9,2	75,4±4,0	81,3±13,9	80,3±14,0	NA
LVMI, g/m^2	82,0 [69,3; 91,8]	82,6 [77,8; 102,1]	87,0 [75,4; 94,1]	87,0 [79,9; 109,8]	NA
RWT	0,38±0,07	0,41±0,05	0,42±0,09	0,46±0,10	0,007
LV GLS, %	-20,9±2,3	-20,7±1,2	-19,1±1,5	-19,2±2,2	0,005

Abbreviations: BMI — body mass index, WC — waist circumference, TC — thigh circumference, SBPcl — clinic systolic blood pressure, DBPcl — clinic diastolic blood pressure, SBP24 — average 24-hour systolic blood pressure, DBBP24 — average 24-hour diastolic blood pressure, LVMI — left ventricular mass index, RWT — relative wall thickness, LV GLS — left ventricular global longitudinal systolic strain.

Table 4

Correlation of insulin resistance indices with anthropometric and demographic characteristics

	HOMA-IR	TyG	METS-IR
Age, years$^{\#}$	0,012	0,178	0,202
BMI, kg/m^2	0,248*	0,323*	0,928**
WC, cm	0,373**	0,456**	0,852**

Note: $^{\#}$ — ρ (Spearman's), rest — r (Pearson's) * — p<0,05, ** — p<0,01.
Abbreviations: BMI — body body mass, WC — waist circumference.

Table 5

Multivariate regression analysis of the association of LV GLS with clinical, hemodynamic and echocardiographic parameters

	b	p
TyG	0,38	0,001
METS-IR	-0,18	0,49
WC	0,11	0,66
Office SBP	0,12	0,62
Average office BP	0,29	0,22
LVMI	0,13	0,36

Abbreviations: WC — waist circumference, SBP — systolic blood pressure, LVMI — left ventricular mass index.

SBP and DBP, LVEF. In all cases, from the lower quartile to the upper, an increase in BMI, waist circumference (WC), and proportion of individuals with abdominal obesity was noted. Lipid metabolism disorders were more significantly expressed in the upper quartile using HOMA-IR. LVMI, thicknesses of IVS and PW, relative wall thickness (RWT), LV global longitudinal strain (GLS) remained

unchanged depending on the HOMA-IR quartile. No significant differences in LVMI between quartiles were obtained for the other two insulin resistance indices. In this case, the RWT increased from the lower to the upper quartile of METS-IR and TyG. For the latter, more significant LV strain aggravation in the upper quartile was also demonstrated.

Then we identified 4 subgroups depending on the simultaneous presence of two characteristics: insulin resistance (TyG) and overweight or obesity (BMI $\geqslant$25 kg/m^2). For this analysis, we used TyG because it had a more significant relationship with LV remodeling parameters than HOMA-IR and did not show a direct dependence on BMI like METS-IR. In the first group, there were no participants with both insulin resistance and overweight/obesity, in the second and third groups, there were deviations of only one of the characteristics: BMI $\geqslant$25 kg/m^2 without insulin resistance or normal BMI with insulin resistance, respectively. Patients from the fourth subgroup were characterized by both insulin resistance and overweight/obesity. The threshold of the TyG was 8,29. The comparison of subgroups are presented in Table 3.

RWT and LV GLS significantly differed between groups. For LVMI, only a tendency to a larger value in individuals with insulin resistance was recorded. When dividing the sample only by presence of insulin resistance, the differences in LVMI were not significant (p=0,087). Multiple comparison of RWT and LV GLS between subgroups using the Bonferroni adjustment revealed significant differences only between the first and fourth subgroups.

The correlation analysis showed that all three insulin resistance indices had relationships with obesity by BMI and WC (Table 4). Associations of HOMA-IR with LV structural characteristics were significant only in relation to LVPW thickness (r=0,238, p<0,05) and RWT (r=0,235, p<0,05). For TyG and METS-IR, stronger relationships were established with LV remodeling parameters, such as IVS and LVPW thicknesses, RWT, LV GLS. The relationship with LVMI was significant only for METS-IR.

For the variables with strongest relationships, we performed a univariate regression analysis, where one of the insulin resistance indices acted as a predictor variable, and one of LV characteristics — as a dependent variable. TyG was significant predictor of changes in LV GLS (r=0,46, p=0,005), LVMI (r=0,32, p=0,02), IVS thickness (r=0,31, p=0,03), LVPW thickness (r=0,30, p=0,03), and METS-IR — LV GLS (r=0,46, p=0,005), LVMI (r=0,42, p=0,002), IVS thickness (r=0,52, p=0,00006), LVPW thickness (r=0,44, p=0,001), and RWT (r=0,31, p=0,03). The HOMA-IR was not associated with LV GLS, but there were associations with LVMI (r=0,40, p=0,003), IVS thickness (r=0,48, p=0,0004), and LVPW thickness (r=0,38, p=0,006), and RWT (r=0,33, p=0,02).

In order to assess the contribution of anthropometric, metabolic, hemodynamic factors to the subclinical change in LV systolic function, a multivariate regression analysis was performed. Age and sex were not significant predictors of LV GLS changes and were not included in the model. The TyG, METS-IR, HOMA-IR, WC, office SBP, average office BP, and LVMI were used as predictors, and LV GLS was a dependent variable (Table 5). The TyG (b=0,38, p=0,001) was an independent predictor of impaired LV GLS. Thus, after the inclusion of SBP, WC, and LVMI in the regression equation, the TyG remained a significant factor of LV GLS decrease.

Discussion

There is no position statement on the therapy need for young people with uncomplicated HTN, since it is difficult to conduct a study evaluating the prognosis in such patients due to the long waiting time for hard endpoints [11]. Nevertheless, a number of epidemiological studies with a long follow-up period have confirmed that in young patients with BP >130/80 mm Hg, as well as in older age groups, there is a clear relationship between BP and the long-term risk of CVE and mortality [12, 13]. Perhaps the early initiation of therapy can prevent more severe HTN and HTN-mediated organ damage, usually not undergoing a complete regression without timely treatment [14, 15].

In this population, it is necessary to search for indicators of structural and functional disorders caused by HTN, preferably before the LVH — one of the independent factors of an unfavorable prognosis. As one of these indicators, LV GLS can be used. In the study by Navarini S, et al., when comparing the HTN and normotension children and adolescents (mean age — 14 and 11 years) without changes in LV volumetric parameters and LVEF, a significant decrease of LV GLS in the HTN group was revealed [16]. In another study, Sengupta S, et al. found that patients with HTN, compared with non-HTN individuals, have a decrease of LV peak longitudinal strain in the subendocardial and subepicardial regions, and of circumferential strain — in the subepicardium. LV radial strain does not differ between the groups. The subendocardial-to-subepicardial gradient of circumferential deformation correlated with the radial strains. Despite reduced longitudinal shortening, LV wall thickening

in patients with HTN occurs later due to relatively preserved circumferential shortening [17]. In our study, early impairment of systolic function, assessed by reduced LV strain, was detected in almost half of young HTN people with hypertension and high normal BP. Assessment of prevalence of various remodeling types revealed a predominance of RWT increase without LVMI increase, that is, concentric LV remodeling.

One of the interesting findings was the high frequency of masked HTN (67%). This can be explained by the fact that the median age of participants was 23 years, and the prevalence of masked HTN among young patients is higher than among middle-aged people.

In routine practice, medical screening of healthy individuals does not require 24-hour BP monitoring, while masked HTN is much more likely associated with disorders of carbohydrate and lipid metabolism and asymptomatic target organ damage compared with true normotension [18, 19]. In this regard, we analyzed the prevalence of insulin resistance by HOMA-IR, which was rather high — every fifth had signs of impaired insulin sensitivity. The determination of insulin levels is not included in the routine examination of a HTN patient, which does not allow the HOMA-IR to be calculated. Therefore, a search for new screening tests is needed to assess insulin sensitivity. These tools are TyG and METS-IR, calculated using the lipids and glycemia levels. The predictive value of the TyG was demonstrated by da Silva A, et al. — the frequency of symptomatic coronary artery disease was 16% higher in the upper TyG tertile (9,9±0,5) compared with the lower one (8,3±0,3) [20].

The effect of insulin resistance on the myocardial structure and function has been confirmed in some clinical studies. Thus, in two cross-sectional population studies, a correlation was found between the extent of insulin resistance increase, estimated by the HOMA-IR, and the severity of LVH estimated by MRI data [21, 22] In another large cross-sectional study, the association of higher HOMA-IR values with LV GLS decrease was observed, and the relationship was not dependent on the obesity [23]. In the study by Lin JL, et al. (2018), a significant relationship between insulin resistance and LV remodeling in the Chinese population was obtained, and there were also no differences in groups and BMIs above and below 23 kg/m^2 [24]. In the CARDIA study, according to echocardiography 25 years after the initial examination, individuals with impaired glucose tolerance compared with normoglycemia subjects had the larger LV RWT and the lower LV GLS [13]. The limitations of the CARDIA study include a comparative statistical analysis of LV remodeling parameters only in groups that differ in the severity of impaired glucose metabolism (normoglycemia, impaired glucose tolerance, diabetes mellitus) without assessing the effect of insulin resistance. A prospective analysis of LV remodeling changes depending on the presence/absence of insulin resistance was performed by Cauwenberghs N, et al. [25]. This study demonstrated that higher levels of insulin and its increase during the 5-year follow-up in middle-aged people were associated with a more severe impairment of LV strain, LVEF decrease, deterioration in LV diastolic function (E/e'), and increased LVMI. Additional studies are needed to confirm the validity of such tendencies in young people with preHTN and HTN.

In our study, dividing the group by METS-IR and TyG quartiles showed an increase in RWT from the group with lowest values to the group with highest values of indices, and a more significant decrease in LV strain was determined in the group of upper TyG quartile. Similar data was also confirmed in the correlation analysis, where associations of IVS and LVPW thicknesses, RWT and LV GLS with METS-IR and TyG were found; HOMA-IR had associations with RWT and LVPW thickness. With a weaker relationship between the TyG and structural parameters, its correlation with LV GLS was found to be stronger with a higher significance compared to METS-IR and, especially, HOMA-IR, which had a slight association with LV GLS. An important question is, what specifies the early LV remodeling in young HTN people to a greater extent — obesity or insulin resistance. In the group without insulin resistance and obesity, the values of RWT and LV GLS were low, significantly increasing from the group of obesity without insulin resistance to the group of insulin resistance without obesity, being the highest in the group with both factors. In group of individuals with preHTN and hypertension, a rather high frequency of abdominal obesity was observed — 32%, while a BMI of $\geqslant$30 kg/m^2 was recorded in 17% of these patients. Moreover, the inclusion of WC in regression model for assessing the TyG role in early LV structural and functional changes did not reduce its prognostic value; the TyG remains an independent predictor of LV GLS decrease in young people with HTN.

The modern model for reducing the CVE risk focuses on the early, preclinical diagnosis of cardiovascular diseases and the primary prevention of complications. Nevertheless, relevant therapeutic algorithms are developed only for patients with already developed diseases. The exceptions are guidelines for smoking cessation and dyslipidemia

treatment, and the lipid-lowering therapy is associated with a decrease in CVE risk by only 30% [26]. A number of researchers explain the maintenance of residual risk with statin therapy by a decrease in insulin sensitivity [27-30]. It is known that long before the development of symptomatic cardiovascular diseases, myocardial remodeling onsets. An important role in the development and progression of myocardial damage (metabolic cardiomyopathy) can be played by insulin resistance. Under the ischemia, increased pressure load, and myocardial damage, insulin-resistant myocytes assimilate glucose worse and caused an impairment of myocardial adaptability [31]. Compensatory enhancement of fatty acid metabolism is accompanied by increased oxygen consumption, decreased cardiac myocyte efficiency, lipotoxicity, free-radical changes, subclinical inflammation, micro- and macrovasculopathy [32, 33]. In this regard, modern clinical guidelines focus on the early detection and prevention of risk factors such as HTN, obesity, and carbohydrate metabolism disorders [34]. Additional prospective studies are required to assess the prospects for non-drug and drug therapy of HTN and insulin resistance in young people with increased BP.

Conclusion

In a cohort of young patients with HTN and high normal blood pressure, there is a high prevalence of insulin resistance, metabolic disorders, and early signs of LV remodeling and subclinical systolic dysfunction. The TyG index, available for estimation by routine biochemical tests, is an independent factor affecting the LV GLS in young people with preHTN and HTN. This index retains its predictive value even with WC use in the regression equation. Since early disorders of carbohydrate metabolism can make a significant contribution to cardiovascular disease progression, they should be taken into account when developing preventive strategies. Prospective studies are required to study the effectiveness of antihypertensive therapy for young people with HTN and impaired LV GLS in order to reduce the CVE risk.

Relationships and Activities: not.

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