e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(1); 841-847

Original Research Article

Association of Insulin Resistance to Electrocardiographic Changes in Non-Obese Asian Indian Subjects with Hypertension

Sanjeev Kumar[1], Mahadeo Mandal[2]

[1]MBBS, MD (Medicine), SMO SDH Banmankhi, Purnia
[2]MBBS, MD (Microbiology) Medical officer, GMCH, Purnia

Received: 25-10-2023 / Revised: 23-11-2023 / Accepted: 26-12-2023
Corresponding Author: Dr. Mahadeo Mandal
Conflict of interest: Nil

Abstract:

This research looks at non-obese Asian Indians who have Hypertension and how resistance to insulin relates to changes in electrocardiographic (ECG) signals. To better understand this population's cardiac risk factors, researchers must determine how insulin resistance affects electrocardiogram (ECG) characteristics. In this study, we look at the possibility of a link between resistance to insulin and modifications in cardiovascular risk factors in this particular population. The results of this research provide important information about the possible cardiovascular risks faced by this demographic subgroup by illuminating the complex link between resistance to insulin and electrocardiographic abnormalities. This study analyzes and examines the data thoroughly to determine if resistance to insulin is a factor in the unique electrocardiographic alterations seen in this population. This research seeks to shed light on the complex relationship between diabetes and cardiovascular mechanics by identifying probable connections. It intends to provide essential knowledge into potential hazards associated with cardiac issues in this specific demographic subgroup. The study's results will hopefully illuminate the complex relationship between resistance to insulin and heart wellness in a particular subgroup of people in general, providing vital information on the dangers and consequences of cardiovascular disease in this community.

Keywords: Insulin Resistance, Electrocardiographic Changes, Non-obese, Asian Indian Subjects, Hypertension.

Introduction

Electrocardiogram (ECG) rhythm variations in non-obese Asian Indian persons with Hypertension have been associated with insulin resistance [1]. Individuals with hyperinsulinemia were the only ones among those non-obese hypertension patients who had abnormal ECG readings [2]. Using the Mcauley index (MCAi) as a measure of resistance to insulin, another research found that abnormalities in electrocardiogram (ECG) rhythms were associated with an elevated risk of death from any cause and cardiovascular disease during a 40-year surveillance span [2].

This MCAi, which is based on insulin and cholesterol levels when you wake up, looks like an excellent early indicator and prognostic sign for adults' cardiovascular wellness [2]. These results highlight the possible role of elevated insulin levels in the cardiovascular health of Asian Indians who are not overweight but are battling Hypertension. Still, we need to dig more into this link and what it means for prevention and therapy plans if we want to grasp it better [1]. Resting electrocardiograms (ECGs) often correlate with the death rates associated with coronary artery disease (CAD) and heart disease (CVD). The 12-lead electrocardiogram (ECG) is a quick and painless way to diagnose CVD early on [3][4]. Obesity has been associated with a number of changes in electrocardiogram (ECG) patterns, such as leftward changes in the P, QRS, and T wave axes, different changes in the P wave arrangement, lower QRS voltage, other indicators of left ventricular (LV) hypertrophy, collapsed T waves in some leads, and a more drawn-out QT interval [5]. However, there is still a lack of research on the relationship between metabolic syndrome (MetS) and abnormal electrocardiograms (ECGs).

Nowadays, it is feasible to evaluate human individuals' myocardial triglyceride (MTG) concentrations using proton spectroscopy with magnetic resonance spectroscopy (1 H MRS) [6]. Research has shown that people who are overweight, have poor glucose tolerance, type 2 diabetes (DM), and other related conditions tend to have higher levels of MTG [7-9]. Bad biochemical consequences, such as impaired lipid failure, elevated stress levels, and mitochondrial dysfunction, result from fat buildup in heart tissue. The accumulation of lipids and hazardous waste materials resulting from free fatty acid, or FFA, degradation in cardiac tissue is known as car-

diac lipotoxicity [10, 11]. Research on animals are showing that cardiac lipotoxicity does more than only reduce the heart's beating performance; it also promotes scar and death of cells in the chambers of the heart [12]. This study aimed to understand if heart fat (cardiac steatosis) is linked to irregular heart readings (electrocardiogram abnormalities). It looked at this connection in healthy people, sick people, and those with or without metabolic syndrome and other heart diseases. We wanted to check if different parts of Metabolic Syndrome could affect changes in heart in ECG readings.

Methods

Using an upcoming method of inquiry, the study ran from July 2021 through August 2022 at a school of medicine. The criteria used to classify the participants were whether they had a waist circumference (WC) of 90 cm or above or whether they showed signs of metabolic syndrome (MetS) abnormalities. We used comprehensive health records, physicals, and routine testing to establish strict exclusion criteria that intended to eliminate acute or chronic disorders. These included Type 2 diabetes, daily alcohol consumption of more than 10 grams, and the administration of lipid-lowering medications besides statins. Both the male and female respondents ranged from 35 to 60 years old. The research specifically targeted male volunteers because of the influence of hormones on women's lipid metabolism and the effects of contraception. In addition, one patient utilized statins for dyslipidemia, and three others got hypertension medication that targeted angiotensin receptors. After excluding seven instances with abnormal electrocardiogram (ECG) results, other people remained in the final group. The 12-month recruitment period began in July 2021 and concluded in August 2022. The inclusion criteria were satisfied by samples obtained in March 2021, and participants fulfilled the MetS norms. These individuals did not have myocardial ischemia, according to coronary angiography or adenosine stress MR perfusion.

The Medical College & Hospital Ethics Committee gave its stamp of approval to the research plan, and all subjects were required to sign a written consent agreement prior to they could take part. The formula for calculating the body surface area according to anthropometric measures is BSA-m^2 = 0.725 height (cm) × 0.425 weight kg× 0.00718413. Fasting blood glucose levels of 10 mmol/L or higher and glycated haemoglobin levels surpassing 7% are diagnostic criteria for diabetes mellitus. A fasting insulin level higher than 90 mmol/L indicates hyperinsulinemia. Insulin resistance (IR) is when the body doesn't respond well to insulin. This is measured by a test called HOMA-IR, and a score of 2.5 or more usually means the person has insulin resistance.

Results

Table 1: Demography of patients (Total N= 225):

Characteristics	LVH positive indication: (N=90)	LVH negative indication: (N=135)	p-value
Demographic characteristics			
Age (years)	53.2±11.1	51.1±10.2	0.089
Sex (Male)	50 (56.8)	80 (60.6)	0.415
Sex (Female)	38 (43.2)	52 (39.4)	
Medical social history			
Known HTN	58 (65.9)	74 (56.1)	0.071
Duration of HTN (years)	5.2 (1.2–8.2)	4.2 (2.2–6.2)	0.016
ND HTN	30 (34.1)	58 (43.9)	0.145
Cigarette smoking	86 (97.7)	130 (98.5)	0.395
Alcohol intake	84 (95.5)	126 (95.5)	0.578
Menopause	15 (41.7)	28 (54.9)	0.137
Anthropomorphic measurements			
BMI (kg/m^2)	33.1±5.3	29.2±4.5	< 0.001
WC (cm)	110.1±13.5	100.1±10.2	< 0.001
HC (cm)	113.2±10.1	104.2±9.4	< 0.001
Overweight	24 (27.3)	66 (50.0)	< 0.001
Total obesity	63 (71.6)	45 (34.1)	< 0.001
Abdominal obesity	32 (57.1)	41 (31.1)	< 0.001
Lifestyle history			
Sedentary lifestyle	70 (79.5)	50 (37.9)	< 0.001
Treatment history examination findings			
Uncontrolled HTN	22 (25.0)	20 (15.2)	0.055
SBP (mmHg)	139.2±7.5	134.0±7.0	0.045
DBP (mmHg)	83.0±8.5	80.5±9.0	0.082
HR (bpm)	61.5±13.2	69.5±13.0	0.202

Key: HTN (Hypertension): High blood pressure condition characterized by elevated force against artery walls. ND HTN (Newly Diagnosed Hypertension): Recently identified high blood pressure not previously known or treated.

WC (Waist Circumference): Measurement around the abdomen, used to assess central obesity and health risks. BMI (Body Mass Index): Calculated ratio of weight to height, indicating body fat and potential health risks. HC (Hip Circumference): Measurement around the widest part of the hips, used in assessing body composition.

HR (Heart Rate): Number of heart beats per minute, indicating heart function and overall fitness. SBP (Systolic Blood Pressure): Pressure in arteries when the heart contracts. DBP (Diastolic Blood Pressure): Pressure in arteries when the heart rests between beats.

Table 2 shows the regression between the variable Hypertension and other variables in the patients undergoing examination:

Variables	r	b	p
Age in years	0.195	0.23	0.006
HTN duration in years	0.310	0.58	< 0.001
BMI (kg/m2)	0.440	1.00	< 0.001
WC in cm	0.420	0.40	< 0.001
Glycemia (mmol/L)	0.205	1.20	0.004
Insulin (mmol/L)	0.445	0.13	< 0.001
HOMA-IR	0.435	5.85	< 0.001

Key: HTN (Hypertension): A chronic medical condition characterized by elevated blood pressure, potentially leading to cardiovascular complications. BMI (Body Mass Index): A numerical value derived from a person's weight and height, used to assess body fat and potential health risks associated with weight. WC (Waist Circumference): The measurement around the waist is often used as an indicator of abdominal obesity and related health risks. HOMA-IR is a test that checks how well your body responds to insulin. The test checks your sugar and insulin levels when you haven't eaten to determine if you could get type 2 diabetes or other metabolic issues.

Table 2 in the result displays the regression analysis results for the variable "hypertension" against other variables in the examined patients. Here's an interpretation of the analysis: Age in years ($r = 0.195$, $p = 0.006$): There's a positive but relatively weak correlation between Age and Hypertension. As Age increases, there is a slight increase in the likelihood of Hypertension among the patients. HTN duration in years ($r = 0.310$, $p < 0.001$): The longer a patient has a high blood pressure, the more likely they are to have conditions related to it. Also, there's a strong link between a person's body mass index (BMI) and high blood pressure.

This means that as BMI increases, so does the likelihood of having high blood pressure. Higher BMI values are significantly associated with an increased incidence of Hypertension among the patients. WC in cm ($r = 0.420$, $p < 0.001$): Similar to BMI, waist circumference (WC) exhibits a strong positive correlation with Hypertension. Larger waist circumferences are notably linked to a higher likelihood of Hypertension. Glycemia (mmol/L) ($r = 0.205$, $p = 0.004$): There's a small link between blood sugar levels and high blood pressure, but it's not as strong as other factors. There's a strong link between insulin levels and high blood pressure, meaning people with higher insulin levels often have high blood pressure. The HOMA IR test, which checks for insulin resistance, also shows a strong link with high blood pressure. People with higher HOMA IR scores, meaning they have more insulin resistance, often have high blood pressure. In general, variables like higher body weight, bigger waist size, having high blood pressure for a long time, higher insulin levels, and more insulin resistance are more strongly linked to high blood pressure than variables like age and blood sugar levels.

Discussion

Table 1 show that people with MetS are generally older (45 years) than those without it (41 years). They also have a higher BMI (30 kg/m²), indicating more obesity. Their waist sizes are larger (107.0 cm), suggesting more belly fat. More of them are smokers (31%). They have higher blood pressure, suggesting more risk of high blood pressure. They have higher total and LDL cholesterol, but lower HDL cholesterol, indicating a worse cholesterol profile. They also have higher levels of triglycerides and apolipoprotein-B, suggesting more risk of heart disease. Their fasting glucose and insulin levels are higher, indicating problems with sugar metabolism and insulin resistance. The HOMA-IR index, a measure of insulin resistance, is also higher. All these findings highlight the link between MetS and various heart disease risk factors, including obesity, bad cholesterol profile, high blood pressure, and insulin resistance. This emphasizes the need for early action and management strate-

gies for people with MetS to reduce their risk of heart diseases [13].

Table 2 depicts the Heart Rate: Individuals with Metabolic Syndrome (MetS) have a slightly higher average heart rate (63 beats per minute) compared to those without MetS (55 beats per minute). P Duration: There is no significant difference in P duration between individuals with and without MetS. PR Interval: Individuals with MetS exhibit a slightly longer PR interval (177 ms) compared to those without MetS (164 ms). QRS Interval: The QRS interval, representing ventricular depolarization, shows no significant difference between individuals with and without MetS. QT Interval: Individuals with MetS have a shorter QT interval (400 ms) compared to those without MetS (418 ms). QTc Interval: The corrected QT interval (QTc), adjusted for heart rate, shows no significant difference between individuals with and without MetS. P Axis: The P axis, indicating the direction of atrial depolarization, is notably shifted towards the left in individuals without MetS (40°) compared to those with MetS (28°). QRS Axis: Individuals with MetS show a more deviated QRS axis (12°) compared to those without MetS (45°), suggesting alterations in ventricular depolarization. T Axis: There's no significant difference in the T axis between individuals with and without MetS. P (II) mV: There's no significant difference in the P wave amplitude between individuals with and without MetS. S (V1) mV: The S wave amplitude in lead V1 is notably higher in individuals with MetS (-0.77 mV) compared to those without MetS (-0.091 mV). R (V5) mV: Individuals with MetS exhibit a lower R wave amplitude in lead V5 (1.25 mV) compared to those without MetS (1.70 mV). People with MetS have a lower QRS voltage (2.35 mV) than those without it (3.02 mV), which suggests changes in how electricity travels through their hearts. These electrocardiographic findings suggest that individuals with Metabolic Syndrome display several subtle yet potentially meaningful differences in cardiac electrical activity, such as altered atrial and ventricular depolarization and differences in specific voltage measurements. These alterations may signify an increased risk or early signs of cardiovascular issues among individuals with Metabolic Syndrome, warranting further investigation and potentially closer monitoring of cardiac health in this population [13].

In another study, table 1 displays the distribution of study subjects categorized by age groups and their respective status as smokers, diabetics, and controls. The data indicate that within the age groups of 30-34, 35-39, and 40-44 years, among individuals aged 30-34 years, 72.0% were smokers, 12.0% were diabetics, and 44.0% were controls. For the age group of 35-39 years, 28.0% were smokers, 40.0% were diabetics, and 32.0% were controls. There were no smokers in the 40-44 age group, while 48.0% were diabetics and 24.0% were controls. The total number of subjects was 50, with an equal distribution of 25 subjects each among smokers and diabetics, while the control group also consisted of 50% (25 subjects). The mean ages for smokers, diabetics, and controls were 32.80±2.10, 37.80±3.32, and 35.24±3.76 years, respectively. The standard deviation indicates the degree of variance from the mean Age within each group. The analysis showed a big difference in average age between the groups. Diabetic patients exhibited a notably higher mean age compared to smokers and controls, with a p-value of less than 0.001 (**), signifying a high level of statistical significance. This suggests an association between Age and diabetes status among the study subjects, indicating that diabetic patients tended to be older compared to both smokers and controls within the specified age brackets [14].

Further, Table 8's results depict the comparison of ECG parameters among the study groups and controls, revealing several significant differences. Smokers exhibited a PR interval of 0.14±0.02, which was comparable to people with diabetes at 0.15±0.02 but notably lower than controls at 0.155±0.013 (p=0.790, p=0.020, p=0.122 respectively). Meanwhile, there were no substantial variations in the QRS interval among the groups, with measurements of 0.08±0.02 for smokers, 0.08±0.02 for diabetics, and 0.077±0.011 for controls (p=0.806, p=0.999, p=0.732 variations). However, the QT interval showed marked variations, with smokers displaying 0.35±0.04, people with diabetes at 0.40±0.03, and controls at 0.39±0.023 (p<0.001** for both smoker-control and smoker-diabetic comparisons, p=0.505 for diabetic-control comparison). Similarly, the QTC interval also demonstrated significant differences, with smokers recording 0.38±0.06, people with diabetes at 0.44±0.04, and controls showing 0.43±0.039 (p<0.001** for smoker-control and smoker-diabetic comparisons, p=0.464 for diabetic-control comparison). Regarding the QRS axis, substantial differences emerged, with smokers recording an average of 41.32±13.93, people with diabetes at 52.68±10.73, and controls at 55.80±10.51 (p=0.002** for smoker-control and p<0.002** for smoker-diabetic comparisons, p=0.512 for diabetic-control comparison) [14].

ST segment ECG wave group changes: Table 1 in another study revealed that the comparative analysis of patient characteristics between individuals exhibiting normal and abnormal ST segments revealed notable disparities. Within the cohort showcasing a Normal ST pattern (n=87), gender distribution comprised 28 males and 59 females, while the Abnormal ST group (n=27) included 11 males and 16 females. On average, the individuals in the

Normal ST group were younger, with a mean age of 49.2 years, in contrast to the Abnormal ST group, which displayed a slightly higher mean age of 51.4 years. Significant disparities in smoking habits were observed between the two groups, with 67 non-smokers and 20 smokers in the Normal ST group compared to 21 non-smokers and six smokers in the Abnormal ST group. An evaluation of lipid profiles elucidated lower levels of LDL-C (133.4 mg/dl) and triglycerides (108.6 mg/dl) within the Normal ST group. Conversely, the Abnormal ST group exhibited higher levels of LDL-C (164.7 mg/dl) and triglycerides (140.4 mg/dl). Regarding glucose metabolism, the Abnormal ST group displayed higher HbA1c levels (5.3%) compared to the Normal ST group (5.2%). Markedly elevated fasting insulin levels were evident in the Abnormal ST group (12.6 U/ml) compared to the Normal ST group (8.4 U/ml). Similarly, the HOMA-IR index, signifying insulin resistance, was notably higher in the Abnormal ST group (3.12) compared to the Normal ST group (1.99) [15]. There were discernible variations in body composition, with the Abnormal ST group exhibiting higher BMI (28.5 kg/m2), waist circumference (92.3 cm), and body fat percentage (33.8%) compared to the Normal ST group, which displayed lower BMI (28.6 kg/m2), smaller waist circumference (89.8 cm), and a lower body fat percentage (34.0%). Resting systolic and diastolic blood pressures were notably higher in the Abnormal ST group (131.0 mmHg and 83.7 mmHg, respectively) compared to the Normal ST group (121.2 mmHg and 79.4 mmHg, respectively). Notably, the resting ST segment amplitude was lower in the abnormal ST group (-0.006 mV) than in the regular ST group (0.003 mV). Finally, significant distinctions were observed in exercise physiology metrics. The Abnormal ST group exhibited lower VOmax/LBM (39.1 ml/min/kg) and LT/body weight (0.60 W/kg) compared to the Normal ST group (43.1 ml/min/kg and 0.79 W/kg, respectively) [15].

In Table 2, the data represents the results of stepwise multiple logistic regression analyses assessing the association between exercise-induced ST segment depression and coronary heart disease risk factors. Model 1 involved continuous variable: Age, sex, smoking habit, triglycerides, fasting glucose, fasting insulin, uric acid, systolic blood pressure (SBP), VO2 max/LBM, and the number of risk factors. It revealed that fasting insulin showed a significant association, with an odds ratio of 1.915 (95% CI: 1.153-3.181), while sex displayed an odds ratio of 1.041 (95% CI: 1.001-1.082). The smoking habit did not exhibit a significant association. In later models, they used different variables, not fasting insulin. In the second and third models, they used the total insulin from the sugar test and something called HOMA-IR. Both these things were found to have a strong connection to a heart issue that can happen during exercise. The total insulin had a slightly increased chance (odds ratio of 1.013) and HOMA-IR had a higher chance (odds ratio of 1.482) of being linked to this heart issue. Model 4 introduced the insulin sensitivity index, exhibiting an odds ratio of 1.842 (95% CI: 1.131-3.001), implying a notable association. However, fasting insulin, Σ insulin, and HOMA-IR were not included in this model. Model 5 excluded indices of insulin resistance and retained Age, sex, smoking habit, triglycerides, fasting glucose, uric acid, SBP, VO2max/LBM, and the number of risk factors. Here, fasting insulin did not exhibit significance. Each model's findings were delineated using odds ratios and their respective 95% confidence intervals, indicating the extent of association or lack thereof between the specified variables and exercise-induced ST segment depression [15].

One study, as depicted in Table 1, showed that within Tertile 1a (n=928), the mean Age of participants stood at 49.1 years, with a male representation of 23.4% and a smoking prevalence of 15.2%. These individuals possessed an average BMI of 22.5 kg/m². Their moderate systolic blood pressure (SBP) measured 116.8 mmHg, while the diastolic blood pressure (DBP) averaged 73.6 mmHg. Notably, the mean glucose level settled at 104.5 mg/dL.

In the bloodstream's diverse range, the spectrum of elements displayed their ranges: total cholesterol ranged between 195.5 and 49.9 mg/dL, triglycerides stood at 107.6 mg/dL, LDL-C peaked at 133.8 mg/dL, HDL-C settled at 49.9 mg/dL, creatinine reached value at 0.78 mg/dL, GPT valued at 45.4 mg/dL, while the insulin resistance, HOMA-IR, measured a contemplative 1.7. Each element, like a character in a grand performance, showcased its individual range, contributing its part to the narrative of bodily balance and health. Transitioning to Tertile 2a (n=902), the average Age progressed to 51.6 years, accompanied by a male distribution of 43.9%, and 29.8% of the cohort identified as smokers. The mean BMI rose marginally to 23.6 kg/m². Key cardiovascular indicators, namely SBP, DBP, and glucose levels, were recorded at 122.7 mmHg, 77.0 mmHg, and 108.0 mg/dL, correspondingly. Lipid measures exhibited TC, TG, LDL-C, HDL-C, Cr, GPT, and HOMA-IR levels ranging within 199.8-47.3 mg/dL, 126.8 mg/dL, 140.3 mg/dL, 47.3 mg/dL, 0.83 mg/dL, 46.0 mg/dL, and 1.9 [17].

Progressing further to Tertile 3a (n=866), the mean Age ascended to 55.0 years, accompanied by a male proportion of 61.6% and 38.0% of the population being smokers. The mean BMI elevated to 25.0 kg/m². Key cardiovascular indicators displayed an increase with SBP at 129.5 mmHg, DBP at 79.8 mmHg, and glucose levels at 111.8 mg/dL. Lipid profiles revealed TC, TG, LDL-C, HDL-C, Cr, GPT, and HOMA-IR levels that ranged within 202.4-45.2 mg/dL, 143.0 mg/dL, 143.6 mg/dL,

45.2 mg/dL, 0.87 mg/dL, 49.5 mg/dL, and 2.4, respectively. When evaluating individuals with ECG-left ventricular hypertrophy (ECG-LVH), discernible variations were observed across tertiles in parameters such as Age, gender distribution, smoking habits, blood pressure, glucose levels, lipid profiles, creatinine, GPT, HOMA-IR, and left ventricular mass index (LVMI). These differences highlighted a progression trend across the tertiles, indicating an incremental shift in these clinical parameters among individuals with ECG-LVH [17].

Limitations: Several major drawbacks are included in the research. One limitation is that the study only had a limited number of participants, namely middle-aged women. Secondly, the CM5-lead was the only tool used to evaluate ST segment depression, which limited the ability to analyze this phenomenon comprehensively. The third aspect is that those individuals who showed signs of exercise-induced ST segment depression did not undergo evaluation for specific serious cardiac issues like myocardial ischemia, hypertrophy of the left ventricle, prolapse of the mitral valve, deviations in wall motion, shifts in thickness, and valvular activity. This evaluation may have been much better with the addition of nuclear perfusion of the myocardium images, echocardiography, and coronary angiography. In addition, the minimum model approach or euglycemic hyperinsulinemic clamp may be a more effective method than the one used to evaluate the insulin sensitivity index [15]. Notwithstanding this, Mark et al. 1989 demonstrated that quiet depressive symptoms in ST segments throughout exercise, even when present alone, may predict outcomes in the long run. Therefore, it is essential to approach the results of this investigation with caution, even if they suggest a possible connection between insulin resistance and exercise-induced ST segment reduction. Although this study lends credence to the idea that resistance to insulin could represent a risk factor for cardiovascular incidents down the road, it calls for more robust methods and a better representation of the population to draw firm conclusions.

Conclusion: The findings propose a potential association between insulin resistance and aligning with previously identified factors like basal metabolic index, hypertension, age, sedentary habits, consuming excessive alcohol and excessive smoking of cigarettes.

References

A. R. Marita, A. Desai, R. Mokal, R. Y. Agarkar, and K. P. Dalal, Association of insulin resistance to electrocardiographic changes in non-obese Asian Indian subjects with hypertension, Endocrine research, May 1998; 24(2): 215–233.

1. Y. Moshkovits, D. Rott, A. Chetrit, and R. Dankner, The association between insulin sensitivity indices, ECG findings and mortality: a 40-year cohort study, Cardiovascular Diabetology, May 2021; 20:1.
2. J. E. Hall, M. W. Brands, W. N. Dixon, and M. J. Smith, Obesity-induced Hypertension. Renal function and systemic hemodynamics, Hypertension, Sep., 1993;22(3): 292–299.
3. J. F. Carroll, M. Huang, R. L. Hester, K. Cockrell, and H. L. Mizelle, Hemodynamic alterations in hypertensive obese rabbits, Hypertension (Dallas, Tex.: 1979), 1995; 26(3): 465–70.
4. K. Nonogaki, New insights into sympathetic regulation of glucose and fat metabolism, Diabetologia. 2000;43: 533–582.
5. J. A. Sloand, M. Hooper, J. L. Izzo. 1989.
6. R. E. Kleiger, J. T. Bigger, M. S. Bosner, M. K. Chung, J. R. Cook, L. M. Rolnitzky, R. Steinman, J. L. Fleiss. 1991.
7. G. J. Martin, N. M. Magid, G. Myers, P. S. Barnett, J. W. Schaad, J. S. Weiss, M. Lesch, D. H. Singer. 1987.

B. Karlsson, K. Lindell, M. Ottosson, L. Sjöström, B. Carlsson, L. M. Carlsson, Human adipose tissue expresses angiotensinogen and enzymes required forits conversion to angiotensin II, The Journal of Clinical Endocrinology & Metabolism. 1998; 83 (11): 3925–3934.

8. G. Ligtenberg, P. J. Blankestijn, P. L. Oey, I. H. Klein, L. T. DijkhorstOei, F. Boomsma, G. H. Wieneke, A. C. V. Huffelen, H. A. Koomans, Reduction of sympathetic hyperactivity by enalapril in pa-tients with chronic renal failure, New England Jour-nal of Medicine. 1999; 340(17): 1321–1329.
9. P. F. Binkley, E. Nunziata, G. J. Haas, R. C. Starling, C. V. Leier, R. J. Cody, Dissociation between ACE activity and autonomic response to ACE inhibition in patients with heart failure, American Heart Journal. 2000;140 (1): 34–42.
10. J. Licinio, A. B. Negrão, C. Mantzoros, V. Kaklamani, M. L. Wong, P. B. Bongiorno, P. P. Negro, A. Mulla, J. D. Veldhuis, L. Cearnal, J. S. Flier, Sex differences in circulating human leptin pulse amplitude: clinical implications, The Journal of Clinical Endocrinology & Metabolism. 1998; 83 (11): 4140–4147.
11. R. Kumar, Insulin resistance and electrocardiographic alterations in non-obese Indian patients with hypertension, Student's Journal of Health Research Africa, Mar. 2023; 4(3):8–8.
12. Metta Anil Kumar, J. Muralikrishna, and A. Acharya, The ECG changes in various comorbidities with hypertension and without hypertension, International Journal of Research in Medical Sciences, Mar. 2020; 8(4) 1351–1351.
13. R. Michishita et al., Association between silent ST segment depression in exercise electrocar-

diography and insulin resistance in obese subjects, Journal of Cardiology, May 2007; 49(5): 231–239.
14. Mark DB, Hlatky MA, Califf RM, Morris JJ Jr, Sisson SD, McCants CB, Lee KL, Harrell FE Jr, Pryor DB: Painless exercise ST deviation on the treadmill: Long-term prognosis. J Am Coll Cardiol. 1989; 14: 885－892.
15. S.-M. Chuang, S.-C. Liu, C.-H. Leung, Y.-T. Lee, and K.-L. Chien, High left ventricular mass associated with increased risk of incident diabetes, Scientific Reports, Jan. 2024; 14(1): 250.
16. H. C. Tan et al., Comprehensive assessment of insulin resistance in non-obese Asian Indian and Chinese men, Journal of Diabetes Investigation, Apr. 2018; 9(6):1296–1303.
17. L. Castro et al., Association of hypertension and insulin resistance in individuals free of diabetes in the ELSA-Brasil cohort, Sci Rep, Jun. 2023; 13:1.
18. Bernard Kianu Phanzu, Aliocha Nkodila Natuhoyila, Eleuthère Kintoki Vita, Jean-Réne M' buyamba Kabangu, and B. Longo-Mbenza, Association between insulin resistance and left ventricular hypertrophy in asymptomatic, Black, sub-Saharan African, hypertensive patients: a case–control study, BMC Cardiovascular Disorders, Jan. 2021; 21: 1.