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Effects of insulin resistance on cardiovascular risk factors in obese and non-obese patients

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ABSTRACT

Objectives: Objectives: It is known that insulin resistance increases cardiovardiovascular risk. But it could not obviously be understood whether insulin resistance itself or the metabolic syndrome parameters, like obesity, that already exist in most of them, are responsible for this increased risk. Our aim is to determine cardiovascular risks in obese and non-obese insulin-resistant patients.

Methods: One hundred thirty-nine patients were included in the study. They were divided into 4 groups: Group 1 (having obesity and insulin resistance), Group 2 (having only insulin resistance but not obesity), Group 3 (having obesity but not insulin resistance), and Group 4 (having neither obesity nor insulin resistance). Patients having any systemic disease were excluded. Insulin resistance is calculated via Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) formula. Electrocardiographic, echocardiographic and lipid parameters of these patients were compared.

Results: High-density lipoprotein (HDL) levels of Group-4 were higher than Group 1 and Group 2. There was no statistical difference in HDL cholesterol levels between Group 3 and the others. Triglyceride and very low-density lipoprotein levels were higher in Group 1. There was no difference in P wave dispersion between the groups. In echocardigraphy, epicardial fat tissue thickness of Group 1 was significantly higher. Prevalance of diastolic dysfunction was higher in Group 1 compared to Group 4.

Conclusion: Insulin resistance itself is a risk factor for low HDL levels independent of obesity. When obesity is added to insulin resistance, other cardiovascular risk factors appear, like high triglyceride levels, increase in epicardial fat tissue thickness and presence of diastolic dysfunction. Early detection of insulin resistance may alert us to the risks of cardiovascular diseases.

Keywords: Insulin resistance, cardiovascular risk factors, obesity, high-density lipoprotein

Insulin resistance defines biological responsiveness to both endogenous and exogenous insulin in the body. In clinical practice, mostly the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) formula is used to determine insulin resistance. It may be accepted as insulin resistance when

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HOMA-IR is calculated above 2.7. [1, 2].

Metabolic syndrome (MS) is a collection of cardiometabolic risk factors that includes obesity, insulin resistance, hypertension, and dyslipidemia [3]. In many cases, metabolic syndrome or insulin resistance is accompanied by obesity. To determine obesity, mostly body mass index (BMI) and waist circumference measurements are used. BMI over 30 kg/m2 shows obesity.

It is well known that obesity and metabolic syndrome are important risk factors for cardiovascular diseases. The relation between metabolic syndrome and cardiovascular diseases is thought to be based on insulin resistance and the hyperinsulinemia following it [4]. However, insulin resistance and all the components of metabolic syndrome are accepted as cardiac risk factors.

There are many studies in the literature that shows an increased risk of hypertension, dyslipidemia, heart failure, coronary artery diseases, and arrhythmias in patients with metabolic syndrome or insulin resistance [5-10]. Also, diastolic and systolic functions of the heart are worse affected in those groups of patients.

In many of those studies, patients with insulin resistance or metabolic syndrome also have increased body mass index. As a result, it couldn't obviously be understood whether insulin resistance itself or obesity, which is seen in most of them, is responsible for cardiovascular risks in these patients. To our knowledge, there are no studies evaluating cardiac risks in obese and non-obese patients with insulin resistance.

Our aim in this study is to observe obese and non-obese insulin-resistant patients in terms of determining cardiovascular risks in this group.

METHODS

One hundred and thirty-nine patients, who were admitted to the outpatient clinic of Internal Medicine for some reason without acute inflammatory or infectious disease that could change blood sugar and insulin levels and known systemic diseases were included in the study. The demographic features of patients are shown in Table 1. These patients were divided into 4 groups: Group 1 (Patients that have both obesity and insulin resistance), Group 2 (Patients that only have insulin resistance but not obesity), Group 3 (Patients that only have obesity but not insulin resistance), and Group 4 (Patients without obesity and insulin resistance; control group). These groups were matched in terms of age and sex.

All the subjects were evaluated first for the presence of any systemic disease. Patients that have diabetes mellitus, hypertension, coronary artery disease, heart failure, kidney failure, renal failure, cardiac arrhythmias, hypothyroidism, hyperthyroidism, valvular heart disease, electrolyte imbalance, age under 20 and over 70 were excluded.

The patients underwent complete physical examination and laboratory tests including fasting blood glucose, insulin, glycated hemoglobin (HbA1c), urea, creatinine, hemogram, aspartate aminotransferase, alanine aminotransferase, total cholesterol, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglyceride, free t4, thyroid stimulating hormone, sodium, potassium, calcium, and magnesium. Insulin resistance is calculated via HOMA-IR formula. The formula HOMA-IR = fasting glucose(mg/dL) × insulin (U/mL) /405 was used to determine the HOMA-IR score. Patients having HOMA-IR values over 2.7 were accepted as insulin resistant. Body mass indexes (BMI) were calculated for each of the patients. The physical examinations and medical evaluations of the patients were done by the same doctor [1, 2].

Also, patients were evaluated by electrocardiography (ECG) and echocardiography. P wave dispersions in ECG were calculated. Echocardiography was performed by a cardiologist. In echocardiography, the left ventricular mass index, epicardial fat tissue thickness, myocardial performance index, sol atrial volume, and E/E' were the main parameters. Patients were also investigated whether they had diastolic dysfunction. Standard parasternal, apical, and subcostal views were used using a 3. 5 MHz transducer from the VIVID 5S GE Medical System in Istanbul, Turkey, for the two-dimensional echocardiography. Measurements were made in the parasternal long-axis view of the left atrium (LA), left ventricular end-diastolic diameter (LVEDD), and interventricular septum diameter (IVSD). Using a two-dimensional picture of the LV chamber during systole and diastole in the 4- and 2-chamber apical views, the left ventricular ejection fraction was determined using Simpson's formula. The diagnosis of left ventricular hypertrophy (LVH) was

Table 1. Distribution of demographical features

	Mean±SD	Min-Max
Age (year)	46.81±8.75	25-68
Height (cm)	162.28±7.85	146-186
Weight (kg)	78.77±16.63	49-133
BMI (kg/m^2)	29.89±5.87	19-47
Waist circumference (cm)	95.35±13.17	72-132
Gender	**n**	**%**
Female	113	81.3
Male	26	18.7

BMI=Body mass index, SD=standard deviation, Min=minimum, Max=maximum

made using the algorithm suggested by the American Society of Echocardiography (ASE) for predicting LV mass from 2D linear LV measures and indexed to body surface area (the cut-off values were LVMI >115 g/m^2 for men and >95 g/m^2 for women) [11]. The pulsed-wave Doppler gate was positioned in the LV at the level of the mitral valve margins, and mitral valve inflow was captured in the apical 4-chamber view. We measured the phase E deceleration time and the E/A ratio. The flow pattern via the aortic and mitral valves could be registered and the isovolumic diastolic time could be calculated simultaneously with the apical 5-chamber image. Mitral annular velocity was measured using tissue Doppler imaging in the apical views. The sample volume was adjusted as necessary (often 5-10 mm) to cover the longitudinal excursion of the mitral annulus during diastole, with the sample being placed at or within 1 cm of the septal insertion sites of the mitral leaflets. Additionally, the E/E' ratio and mitral septal annulus early diastolic velocity (septal E') were computed. LA volume measured by biplane area-length method: Orthogonal apical views, apical four and two-chamber views are obtained for determination of LA area and length. The length is determined from the middle of the plane of the mitral annulus to the posterior wall. Left atrial volume is calculated on the basis of the algorithm 0.85×A1×A2/L; where A1 and A2 are the areas of LA in four and 5 two-chamber views and L is the shortest of the lengths obtained from the orthogonal views and indexed to body surface area.

Epicardial adipose tissue (EAT) measurement by

Table 2. Age and gender distribution of groups

	Group 1 (Obese + IR) (n = 37)	Group 2 (IR) (n = 32)	Group 3 (Obese) (n = 32)	Group 4 (Control) (n = 38)	P value
Age (years)					
Mean±SD	46.97±9.11	46.63±8.03	47.63±10.59	46.13±7.44	0.913[a]
Median (Min-Max)	47 (28-68))	46.5 (31-64))	49 (25-65)	46.5 (29-61)	
Gender, n (%)					
Female	29 (78.4)	25 (78.1)	27 (84.4)	32 (84.2)	0.842[b]
Male	8 (21.6)	7 (21.9)	5 (15.6)	6 (15.8)	

IR=insulin resistance, SD=standard deviation, Min=minimum, Max=maximum. [a]One Way Anova Test, [b]Pearson Chi-Square Test

echocardiography is defined as an echo-free space above the right ventricular free wall by transthoracic echocardiography and measured the thickness from the anterior aspect of the right ventricular free wall through parasternal long axis window.

The study obtained approval from the local ethic committee (no: 89513307/1009/ 284 and date: 06.05.2014)nd it has been carried out as per the Helsinki Declaration. All the participants gave informed consent before they were included in the study.

Statistical Analysis

The statistical analysis was conducted using the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) application. The Oneway Anova test was used for the intergroup comparisons of parameters with normal distribution during the evaluation of the study data, regarding the comparisons of quantitative data as well as descriptive statistical methods (Mean, Standard deviation, median, frequency, and ratio), and the Tukey HSD test was used to determine the group causing the difference. When comparing parameters between groups that did not have a normal distribution, the Kruskal-Wallis test was utilized, and the Mann-Whitney U test was used to identify the group that caused the difference and to evaluate the performance of the two groups. For the comparison of qualitative data, Yates Continuity Correction and Pearson Chi-Square tests were applied. At a significance level of $P<0.05$, the data were assessed using a 95% confidence interval.

RESULTS

A total of 139 participants, 81.3% (n=113) female and 18.7% (n=26) male, aged between 25-68 years, were included in this study. Demographic parameters are shown in Table 1. The patients were divided into 4 groups according to the presence of insulin resistance and obesity. The age and sex distribution of the groups are shown in Table 2. Lipid profiles, P wave dispersion in ECG, and echocardiography parameters were compared between the groups.

Laboratory parameters were shown in Table 3, and lipid profile distributions of the groups were shown in Table 4. There was no statistically meaningful difference between the groups in LDL-cholesterol and total cholesterol levels ($P>0.05$). HDL-cholesterol levels of Group 4 were higher than Group 1 and Group 2

Table 3. Distribution of laboratory findings

	Mean±SD	Min-Max
Glucose (mg/dL)	95.60±10.00	76-121
HbA1c (%)	5.44±0.36	4.2-6.4
Insulin (µU/mL)	12.56±6.79	3.3-38.9
Urea (mg/dL)	27.65±6.79	13-51
Creatinine (mg/dL)	0.67±0.15	0.24-1.22
AST (U/L)	22.30±7.29	12-61
ALT (U/L)	24.83±20.71	6-209
Total cholesterol (mg/dL)	224.84±42.89	123-359
LDL cholesterol (mg/dL)	144.52±34.66	72-217
HDL cholesterol (mg/dL)	53.19±12.31	27-92
Triglyceride (mg/dL)	135.48±90.92	26 – 678
VLDL cholesterol (mg/dL)	26.96±17.94	6-136
HOMA-IR	2.99±1.72	0.74-11.10

HbA1c= glycated hemoglobin, AST= aspartate aminotransferase, ALT= alanine aminotransferase, HDL=high density lipoprotein, VLDL=very low density lipoprotein, HOMA-IR= Homeostatic Model Assessment of Insulin Resistance, SD=standard deviation, Min=minimum, Max=maximum

Table 4. **Lipid profile of groups**

		Group 1 (Obese + IR) (n=57)	Group 2 (IR) (n=36)	Group 3 (Obese) (n=17)	Group 4 (Control) (n=35)	P value	P value (1-2)	P value (1-3)	P value (1-4)	P value (2-3)	P value (2-4)	P value (3-4)
Total cholesterol (mg/dL)	Mean±SD	223.30±45.51	230.38±40.18	217.09±42.76	228.18±43.22	**0.607**[a]	0.904	0.933	0.961	0.607	0.997	0.706
	Median (Min-Max)	218 (154-359)	240.5 (139-291)	213 (123-290)	226 (147-326)							
LDL Cholesterol (mg/dL)	Mean±SD	138.47±33.14	151.03±37.43	143.47±32.86	145.97±35.62	**0.526**[a]	0.463	0.934	0.790	0.827	0,933	0.991
	Median (Min-Max)	140.5 (86-211)	152.5 (81-217)	141.5 (73-216)	152 (72-212)							
HDL Cholesterol (mg/dL)	Mean±SD	49.41±13.25	50.75±9.44	52.91±9.54	5918±13.69	**0.003**[a]	0.965	0.610	**0.003**	0.885	**0,018.**	0.124
	Median (Min-Max)	49 (27-83)	49 (36-69)	51.5 (37-78)	57.5 (37-92)							
Triglyceride (mg/dL)	Mean±SD	172.08±116.51	148.19±99.47	104.13±48.15	115.53±68.22	**0.004**[c]	0.273	**0.002**	**0.007**	**0.019***	0.075	0.934
	Median (Min-Max)	138 (49-678)	115.5 (59-481)	87.5 (30-234)	93 (26-289)							
VLDL cholesterol (mg/dL)	Mean±SD	34.46±23.38	29.06±18.8	20.84±9.72	23.05±13.60	**0.003**[c]	0.243	**0.002**	**0.006**	**0.021***	0.068	0.953
	Median (Min-Max)	28 (10-136)	23.5 (12-96)	17.5 (6-47)	18.5 (8-58)							

SD=standard deviation, Min=minimum, Max=maximum, [a]Oneway Anova Test (post hoc Tukey HSD), [c]Kruskal Wallis Test (post hoc Mann Whitney U test)

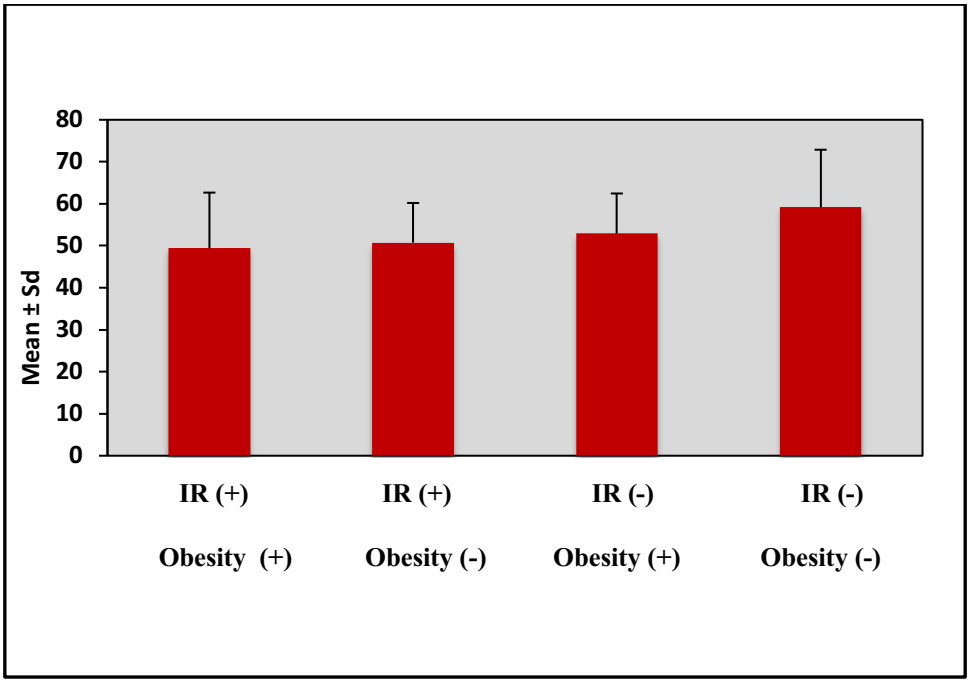

Fig. 1. HDL cholesterol level distribution of groups.

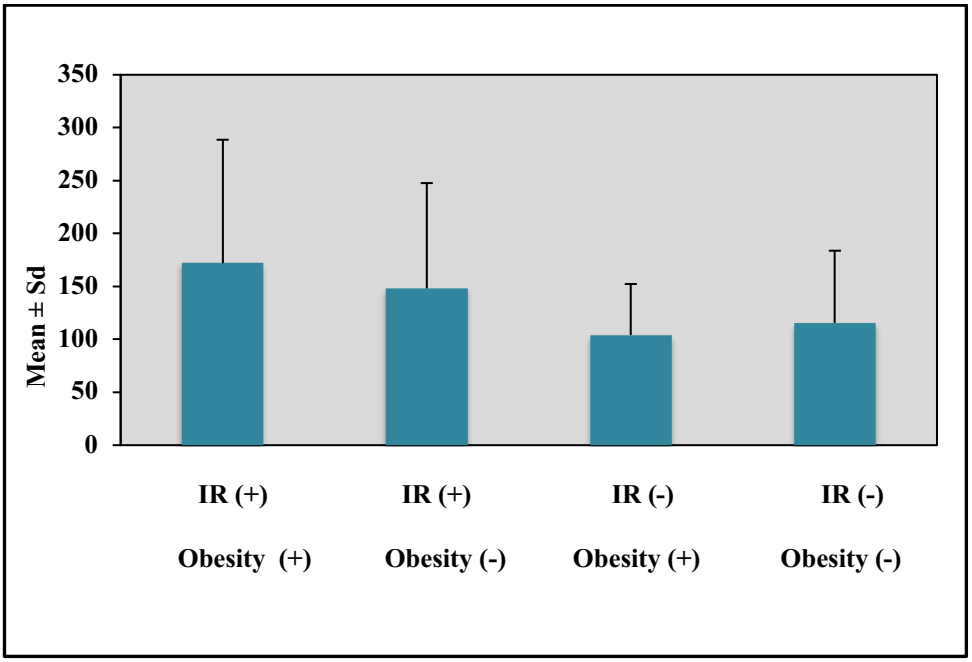

Fig. 2. Triglyceride level distribution of groups.

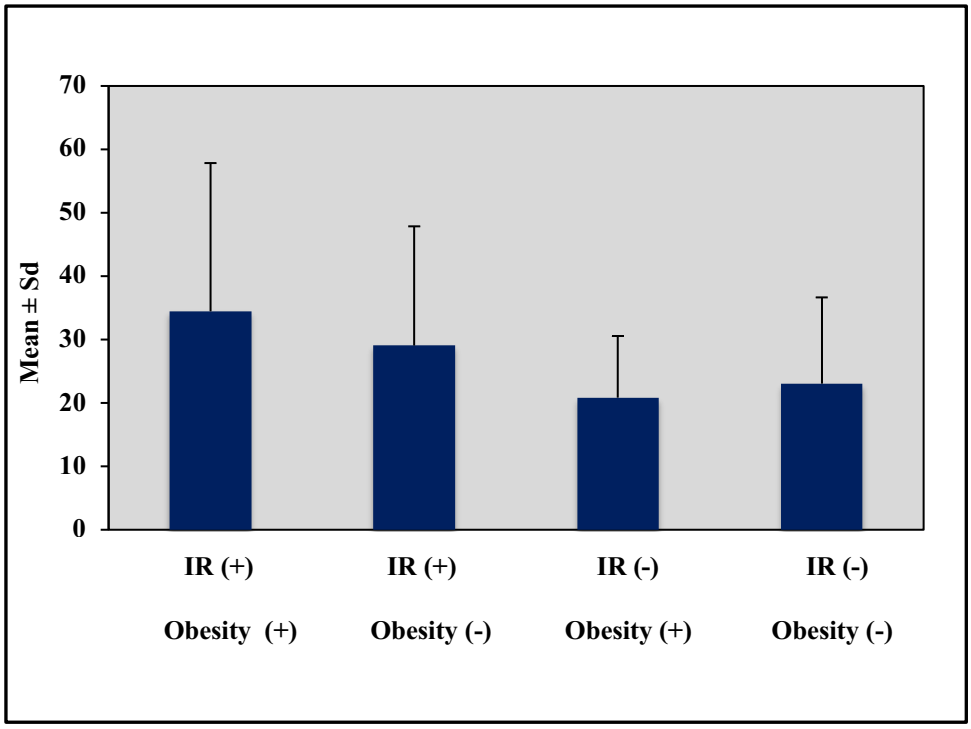

Fig. 3. VLDL cholesterol level distribution of groups.

(P<0.05). No statistical difference was detected in HDL cholesterol levels between Group 3 and the others (Fig. 1). Triglyceride and VLDL-cholesterol levels of Group 1 were higher than Group 3 and Group 4 (P<0.01). Triglyceride and VLDL-cholesterol levels of Group 2 were higher than Group 3 (P<0.05). (Figs. 2 and 3).

The results of echocardiography parameters were shown in Table 5. There was no difference in P wave dispersion, left ventricular mass index, myocardial performance index, and E/E ratio between the groups (P>0.05). Epicardial fat tissue thickness of Group 1 was significantly higher than Group 2, Group 3, and Group 4 (P<0.01) (Fig. 4). Left atrial volumes of Group 2 were statistically lower than Group 3 and Group 4 (P<0.05) (Fig. 5).

The prevalence of diastolic dysfunction was higher in Group 1 compared to Group 4 (P<0.01). (Fig. 6). The distribution of echocardiography parameters of all the groups were shown in Table 6

DISCUSSION

The leading cause of death in the world continues to be diseases of the cardiovascular system. Cardiovascular diseases (CVD) include hypertension, coronary heart disease, congestive heart failure, atherosclerosis, cerebrovascular diseases, peripheral artery diseases, and conditions that often occur in combination. In 2012 and 2013, CVD was estimated to result in 17.3 million deaths worldwide on an annual basis [12, 13].

Table 5. Distribution of echocardiography parameters

	Mean±SD	Min-Max
Left ventricular mass index (g/m^2)	71.40±15.13	37-134
Epicardial fat tissue thickness (mm)	2.39±1.22	1-6
Myocardial performance index	0.41±0.10	0.14-0.70
Left atrial volüme (mL/m^2)	17.49±4.42	7-30
E/E'	6.55±1.69	3.40-11.20
Diastolic dysfunction	**n**	**%**
No	82	59.0
Yes	57	41.0

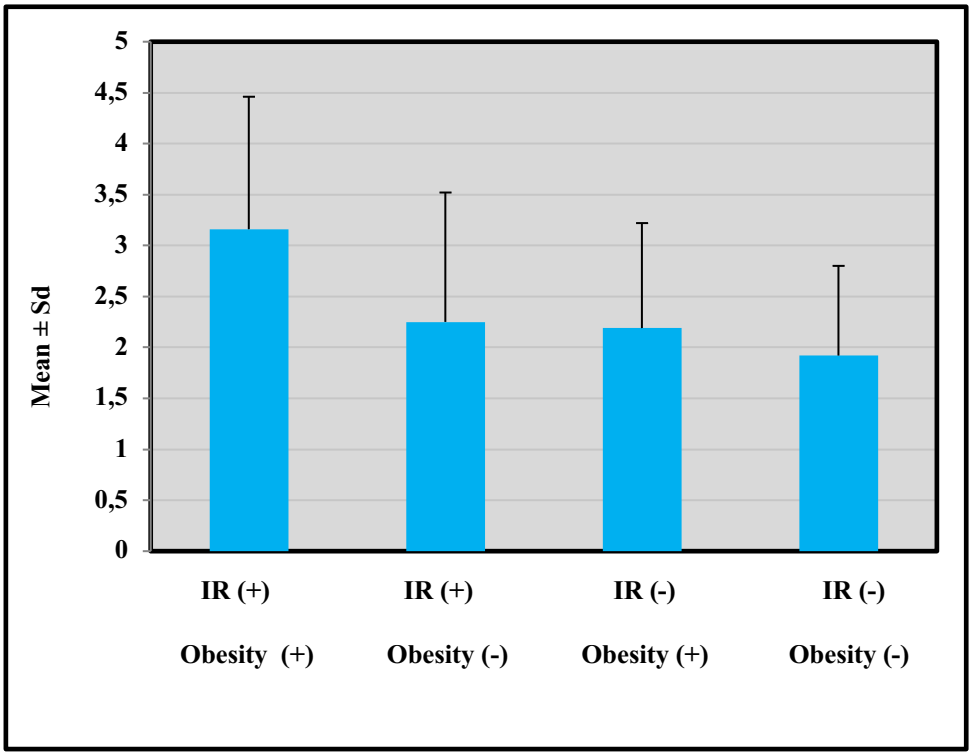

Fig. 4. Epicardial fat tissue thickness distribution of groups.

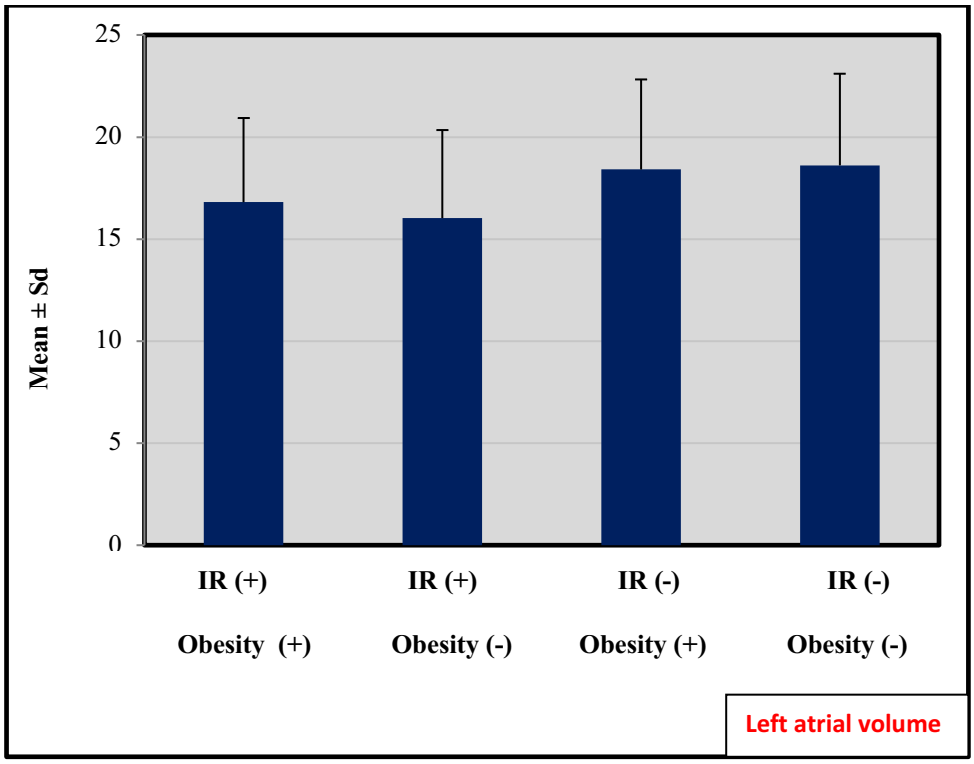

Fig. 5. Left atrial volume distribution of groups.

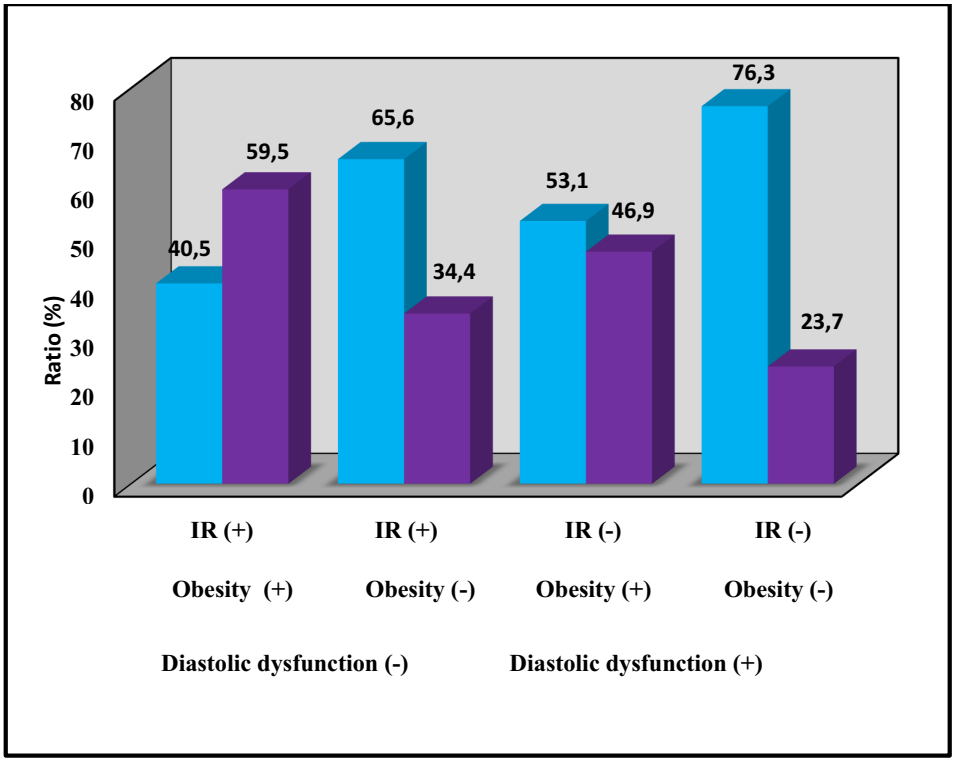

Fig. 6. Presence of diastolic dysfunction distribution of groups.

And this number of deaths is expected to reach 23 million by the year 2030. Many individuals in the general population have one or more risk factors for CVD. The five leading modifiable risk factors (hypercholesterolemia, diabetes, hypertension, obesity, and smoking) are estimated to be responsible for more than half of cardiovascular mortality [14]. The increase in risk when multiple risk factors are present has been noted in several studies [15, 16].

Many risk factors for CVD are modifiable by specific preventive measures. In this study we focused on insulin resistance that can later lead to diabetes mellitus, which is reported as a coronary heart disease risk equivalent, thereby elevating it to the highest risk category. It has also been suggested as an important risk factor in the development of metabolic syndrome, a cluster of abnormalities comprising glucose intolerance, dyslipidemia, high blood pressure, and impaired fibrinolysis activity that is associated with an increased risk of developing type 2 diabetes mellitus and CVD. For this reason, detecting insulin resistance, diagnosing patients in the prediabetic stage, and taking preventive measures by modifying environmental risk factors may reduce total cardiovascular mortality in the population. There are many studies that show increased cardiovascular risk in insulin-resistant patients [17, 18].

Obesity is the most important cause of insulin resistance and also a component of metabolic syndrome. It is well demonstrated that obesity is a risk factor for type 2 diabetes and CVD [19]. In the literature, studies made about insulin resistance and metabolic syndrome mostly contain obese individuals also. This close association between insulin resistance and obesity has made it difficult to establish whether insulin resistance, independent of obesity, is associated with cardiovascular risk. But it must be borne in mind that there are also non-obese insulin-resistant individuals.

Our study aimed to see the cardiovascular risks of non-obese insulin-resistant patients. For this purpose, we looked at the lipid profiles of these patients and performed ECG, and echocardiography on each of them. Then we compared the results with the control and the obese group.

In the lipid profile, we saw that obesity alone does not contribute to a decline in HDL levels. But insulin resistance alone, without obesity, triggers low HDL levels. In patients having both insulin resistance and

Table 6. **Echocardiography parameters of groups**

		Group 1 (Obese + IR) (n=37)	Group 2 (IR) (n=32)	Group 3 (Obese) (n=32)	Group 4 (Control) (n=38)	P value	P value (1-2)	P value (1-3)	P value (1-4)	P value (2-3)	P value (2-4)	P value (3-4)
Left ventricular mass index (g/m^2)	Mean±SD	76.38±17.47	68.91±14.11	71.69±15.53	68.42±12.18	**0.094**[a]	0.168	0.564	0.102	0.879	0.999	0.799
	Median (Min-Max)	76 (37-134)	66.5 (49-113)	69.5 (47-120)	46-101 (66)							
Epicardial fat tissue thickness (mm)	Mean±SD	3.16±1.30	2.25±1.27	2,19 ± 1,03	1.92±0.88	**0.001**[c]	**0.003**	**0.002**	**0.001**	0.955	0.382	0.318
	Median (Min-Max)	3 (1-6)	2 (1-6)	2 (1-5)	2 (1-4)							
Myocardial performance index	Mean±SD	0.4±0.10	0.45±0.10	0.4±0.13	0.4±0.08	**0.130**[a]	0.173	0.998	1.000	0.264	0.181	0.999
	Median (Min-Max)	0.39 (0.24-0.7)	0.4 (0.2-0.7)	0.39 (0.14-0.7)	0.4 (0.2-0.56)							
Left atrial volüme (mL/m^2)	Mean±SD	16.81±4.12	16.03±4.31	18.41±4.41	18.61±4.49	**0.041**[a]	0.878	0.425	0.281	**0.030**	**0.014**	0.997
	Median (Min-Max)	16 (9-27)	16 (7-25)	18.5 (11-27)	18 (8-30)							
E/E'	Mean±SD	6.85±1.56	6.25±1.99	7.00±1.79	6.14±1.34	**0.080**[a]	0.442	0.983	0.253	0.279	0.993	0.143
	Median (Min-Max)	6.5 (4.4-11)	5.7 (3.8-11.2)	6.75 (4.1-11)	6.05 (3.4-10)							
P wave dispersion (ms)	Mean±SD	31.89±11.98	34.38±13.66	34.38±9.14	34.74±13.7	**0.722**[c]	0.482	0.247	0.394	0.780	0.912	0.876
	Median (Min-Max)	40 (20-60)	40 (20-60)	40 (20-40)	40 (20-60)							
Diastolic dysfunction, n (%)	No	15 (40.5)	21 (65.6)	17 (53.1)	29 (76.3)	**0.012**[b]	0.066	0.422	**0.004**	0.445	0.471	0.074
	Yes	22 (59.5)	11 (34.4)	15 (46.9)	9 (23.7)							

SD=standard deviation, Min=minimum, Max=maximum, [a]One way Anova Test (post hoc Tukey HSD), [b]Pearson Chi-Square Test, [c]Kruskal Wallis Test (post hoc Mann Whitney U test)

obesity, HDL - cholesterol levels were lower than the control group. Neither insulin resistance nor obesity alone correlates with triglyceride levels. But in non-obese insulin-resistant patients, triglyceride levels are found higher than in the obese, insulin-sensitive group. When obesity and insulin resistance come together, triglyceride levels reach to significantly higher levels compared to control group.

Results detected in triglyceride were also valid for VLDL-cholesterol. There was no statistically meaningful difference between the groups in LDL-cholesterol and total cholesterol levels. These results were similar to the ones found in the study done by Piché *et al*. [20] in 2005. But differently, our study showed that insulin resistance is a risk factor for low HDL-cholesterol levels independent of obesity. Also, triglyceride levels in insulin-resistant non-obese patients were found higher than insulin-sensitive obese patients. This suggested that insulin resistance may be a more important risk factor for high triglyceride levels than obesity.

The diminished antilipolytic activity of insulin can be used to explain the independent role of insulin resistance in the variation in triglyceride concentrations. This causes a rise in the amount of free fatty acids in the blood and their flow to the liver, which can promote the synthesis of triglycerides [21]. Another study found that the dysregulation of intramyocellular fatty acid metabolism was related to insulin resistance in the skeletal muscle of healthy, young, thin, insulin-resistant offspring of people with type 2 diabetes. These changes in fatty acid metabolism might serve as a connection between insulin resistance and hypertriglyceridemia [22].

In a different study conducted in 2003 by Nieves *et al*. [23], they discovered that non-obese insulin-resistant patients had different lipid-lipoprotein profiles than non-obese insulin-sensitive individuals (higher concentrations of triglycerides, LDL cholesterol, and apo-B, and lower concentrations of HDL cholesterol). In the electrocardiography of patients, there was no meaningful difference between groups in terms of P wave dispersion. In echocardiography, we found that neither obesity nor insulin resistance alone has an independent risk for developing diastolic dysfunction. But when they are seen together, diastolic dysfunction prevalence increases. Carvalho *et al*. [24] discovered that people with increased insulin resistance had lower diastolic function measures in their study. In addition, Dinh *et al*. [25] showed that insulin resistance was a separate factor in the development of LVDD in a sample of chosen non-diabetic patients undergoing elective coronary angiography. In another study performed by Russo *et al*. [26], they demonstrated an independent association between LVDD and obesity.

Subclinical left ventricular diastolic dysfunction (LVDD) is widespread in the population and is known to be a significant indicator of long-term mortality and heart failure. The identification of these asymptomatic abnormalities in left ventricular function and the early detection of its primary risk factors are of particular importance, according to current heart failure recommendations [27]. According to certain research, changes in diastolic function, which are already present in pre-diabetic patients [28], may be linked to the condition of insulin resistance and occur before the onset of diabetes. MS, also known as insulin resistance syndrome, is a collection of risk factors for cardiovascular disease that have been demonstrated to work in concert to raise the chance of unfavorable cardiovascular events as well as to cause subclinical alterations in heart structure and function. Indeed, LVDD is more common among patients with metabolic syndrome [29].

In our study, like diastolic dysfunction, it is found that obesity or insulin resistance alone are not directly related to increased epicardial adipose tissue (EAT) thickness. But when they are seen together, this causes an increase in EAT thickness.

EAT is a part of the visceral fat deposit. It has endocrine, paracrine, vasocrine, and inflammatory effects and is related to metabolic syndrome, insulin resistance, coronary artery disease, and hypertension [30, 31]. EAT produce various cytokines and vasoactive peptides such as free fatty acids, interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), angiotensin II, and plasminogen activator inhibitor, all of which increase the cardiovascular risk [32]. In patients with significant coronary artery disease, higher levels of chemokines and cytokines were detected in epicardial fat tissue [33]. Also, a relationship between EAT thickness and coronary artery calcification score and severity of coronary heart disease was detected in a study by Picard *et al*. [34].

Limitations

Main limitations of this study is its low sample size and being unable to rule out contribution of genetic factors which are very important for cardiovascular risk determinants.

CONCLUSION

In conclusion, early detection of insulin resistance may alert us to the risks of cardiovascular diseases. Insulin resistance itself is a risk factor for low HDL-cholesterol levels independent of obesity. We should also consider cardiovascular risk factors in cases of insulin resistance not accompanied by obesity and we should screen these patients for dyslipidemia. When obesity is added to insulin resistance, other cardiovascular risk factors appear, like high triglyceride levels, an increase in epicardial fat tissue thickness, and the presence of diastolic dysfunction. Future studies will evaluate whether administering medications that boost insulin sensitivity can enhance the structure and function of the myocardium, particularly diastolic function, or have a positive impact on the lipid profile.

Authors' Contribution

Study Conception: BAT, GF, KSF; Study Design: GF, KSF, TU; Supervision: GF, ÖK; Funding: GF; Materials: BAT, NPT, KSF; Data Collection and/or Processing: BAT, NPT; Statistical Analysis and/or Data Interpretation: BAT, TU, NPT; Literature Review: ÖK, BAT, GF; Manuscript Preparation: BAT, GF, TU and Critical Review: ÖK, GF.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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