

ORIGINAL ARTICLE

Predictive power of different obesity measures for the presence of diastolic dysfunction

Farklı obezite ölçümlerinin diyastolik fonksiyon bozukluğunun varlığını öngörme gücü

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ABSTRACT

Objective: Body mass index (BMI) and waist circumference (WC) as measures of obesity have some limitations. The aim of this study was to evaluate whether one measure could predict the presence of diastolic dysfunction (DD) more accurately than the other measures.

Methods: A total of 91 obese patients without any other risk factors for DD were prospectively enrolled. Echocardiographic examination was performed. DD was defined and categorized according to recent guidelines. The study participants were divided into 2 groups according to the presence of DD. Weight, height, and WC were measured; BMI and waist-to-hip ratio (WHR) were calculated; and a body shape index (ABSI) was calculated as $WC/(BMI^{2/3} \times height^{1/2})$. The associations between ABSI, BMI, WHR, and WC and the presence of DD were examined using logistic regression analyses. Analysis of covariance was used to examine the differences.

Results: WC and BMI were significantly greater in subjects with DD ($p=0.049$ and 0.051 , respectively). A greater BMI, WC, and WHR increased the risk of the presence of DD (BMI-DD: odds ratio [OR]=1.096, $p=0.024$; WC-DD: OR=1.059, $p=0.007$; WHR-DD: OR=2.363, $p=0.007$). After adjustment for age and sex, only BMI continued to be significantly associated with DD ($p=0.031$). ABSI was not associated with DD.

Conclusion: After adjustment for age and sex, BMI was the only predictor of DD in obesity. Despite its limitations, BMI may still be a potentially more accurate measure of DD compared with other obesity measures.

ÖZET

Amaç: Vücut kitle indeksi ve bel çevresinin obezitenin değerlendirilmesinde bazı kısıtlılıkları vardır. Bu çalışma bir obezite ölçümünün diyastolik disfonksiyonun (DD) varlığını diğer obezite ölçümlerinden daha doğru öngörüp öngörmediğini değerlendirmeyi amaçladı.

Yöntemler: Diyastolik disfonksiyon için herhangi bir risk faktörü olmayan 91 obez denek çalışmaya alındı. Ekokardiyografik inceleme yapıldı. DD, en güncel kılavuzlara göre tanımlandı ve sınıflandırıldı. Denekler DD varlığına göre iki gruba ayrıldılar. Kilo, boy ve bel çevresi (BÇ) ölçüldü. Vücut kitle indeksi (VKİ) ve bel kalça oranı (BKO) hesaplandı. Bir vücut şekil indeksi (VŞİ), $BÇ/(VKİ^{2/3} \times boy^{1/2})$ denkleminde hesaplandı. Lojistik regresyon analizi ile VŞİ, VKİ, BKO ve BÇ'nin DD ile ilişkisini inceledik. İki grup arasındaki farkın incelenmesi için kovaryans analizi kullanıldı.

Bulgular: Bel çevresi ve VKİ, DD'si olan deneklerde anlamlı olarak artmıştı (sırasıyla, $p=0.049$ ve 0.051). Artmış VKİ, BÇ ve BKO DD olma riskini arttırdı [BMI-DD: odds oranı (OR)=1.096, $p=0.024$; WC-DD: OR=1.059, $p=0.007$; WHR-DD: OR=2.363, $p=0.007$]. Yaş ve cinsiyet düzeltilmesinden sonra sadece VKİ anlamlı olarak DD ile ilişkili olmaya devam etti ($p=0.031$). VŞİ DD ile ilişkili değildi.

Sonuç: Yaş ve cinsiyet düzeltilmesinden sonra VKİ obezitede DD'nin tek öngördürücüsü idi. Tüm kısıtlılıklarına rağmen VKİ halen potansiyel olarak DD'nin diğer obezite ölçümleri içinde en doğru ölçümü olabilir.

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Obesity is a well-known risk factor for diastolic dysfunction (DD).^[1] Although body mass index (BMI) is widely used as a measure of obesity, it has potential weaknesses. To partly overcome these weaknesses, waist circumference (WC) is used as an indicator of abdominal fat accumulation. However, WC reflects not only abdominal fat accumulation but also overall body size (height and weight). Chronic heart failure is a major health problem with an increasing prevalence, morbidity, and mortality throughout the world. DD may account for more than half of these cases.^[1] At present, echocardiography is the best non-invasive tool to evaluate diastolic function and to estimate filling pressures. Identifying obese individuals who are at high risk for DD is potentially of significant benefit, so that preventive measures can be applied. Findings concerning the relationship between several obesity measures and cardiovascular disease morbidity or mortality have been inconsistent.^[2,3] Krakauer et al.^[4] described a new obesity measure, a body shape index (ABSI), which quantifies abdominal adiposity relative to BMI and height. To date, several cohort studies have evaluated the ABSI regarding the prediction of morbidity and mortality.^[5-7] One indicated that the ABSI was significantly associated with total stroke incidence in men, while BMI was not.^[5] Another reported that among different obesity measures, ABSI revealed a stronger association with total, cardiovascular, and cancer mortality.^[8] Another demonstrated that ABSI was the strongest predictor of all-cause mortality among the obesity measurements.^[9] Others found that ABSI was valuable for the prediction of the development of diabetes^[6] or hypertension,^[7] although the predictive power was no better than WC or BMI. The aim of this study was to examine the predictive power of ABSI, BMI, WC, and waist-to-hip ratio (WHR) for DD in obese individuals without any cardiovascular risk factors.

METHODS

Patients

The study design was prospective, and included 91 obese individuals without any cardiovascular risk factors. The exclusion criteria were coronary artery disease (visible coronary stenosis >20% in at least 1 coronary artery on angiography, myocardial infarction, and/or percutaneous or surgical re-vascularization), stroke, transient ischemic attack, peripheral arterial

disease, moderate (>2+) valvular regurgitation or any valvular stenosis, any rhythm other than sinus rhythm, systolic dysfunction (ejection fraction <50%), insufficient echocardiographic imaging, myocardial wall thinning or motion abnormalities (seen on echocar-

diography and suggestive of previous myocardial infarction), anemia, renal failure, hepatic failure, pregnancy or lactation, regular use of alcohol, current or past smoking, any systemic inflammatory condition, history of risk factors for DD (including hypertension, atherosclerotic cardiovascular disease, diabetes mellitus, obstructive sleep apnea, hyperlipidemia, and metabolic syndrome), and major systemic or psychiatric disease. The study participants were not taking any medication, including oral contraceptive pills. This study was approved by the medical ethics committee of the participating university (protocol number: 60116787/020/27531) and was conducted in accordance with the Helsinki Declaration. Informed consent was obtained from all of the members of the study group.

The participants were weighed and their height was measured, and then body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Obesity was defined as BMI >30 kg/m². ABSI was calculated as WC / (BMI^{2/3}height^{1/2}), with WC and height in meters.^[4] WC (cm) was measured midway between the lowest rib and the iliac crest while the participants were standing upright. Fasting plasma glucose and insulin level measurements were obtained for all of the participants. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the following formula: (fasting plasma glucose X fasting plasma insulin) / 22.5.^[10] The state of insulin resistance was determined using the cutoff value of 2.7.

Echocardiographic analysis

A comprehensive echocardiography examination was performed for each participant while at rest in the left

Abbreviations:

ABSI	A body shape index
BMI	Body mass index
BSA	Body surface area
CI	Confidence interval
E/e'	Ratio between early mitral inflow velocity and mitral annular early diastolic velocity
DD	Diastolic dysfunction
HOMA-IR	Homeostasis model assessment of insulin resistance
LV	Left ventricle
TR	Tricuspid regurgitation
WC	Waist circumference
WHR	Waist-to-hip ratio
OR	Odds ratio

lateral decubitus position using standard views on a Vivid 7 echocardiography device (GE Healthcare, Inc. Chicago, IL, USA). Left ventricle (LV) internal dimensions and wall thickness were measured using 2-dimensional M-mode guided echocardiographic tracings obtained at mid-chordal level in the parasternal long-axis view according to the American Society of Echocardiography criteria.^[11] The LV ejection fraction was calculated using the modified Simpson method. Mitral inflow velocities were obtained with pulse-wave Doppler ultrasound in the apical 4-chamber view with the sample volume positioned at the tips of the mitral valve leaflets. The peak early and late diastolic mitral inflow velocity and maximal tricuspid regurgitation (TR) velocity were measured and averaged over 3 cardiac cycles. The ratio of early diastolic to late diastolic mitral inflow velocities was calculated. The E wave deceleration time and isovolumetric relaxation time were measured. Myocardial velocity profiles of the lateral and septal mitral annuli were obtained by positioning the sample volume at the junction of the mitral annulus and the respective wall. The peak mitral annular early diastolic velocities were measured and averaged over 2 consecutive cardiac cycles. The mean value of the septal and lateral annulus early diastolic velocity was calculated. The ratio between early mitral inflow velocity and mitral annular early diastolic velocity was calculated (E/ϵ). Maximal left atrial volumes were obtained with the apical 4-chamber view and the disc summation method at the mitral valve opening and indexed for body surface area (BSA). The type and severity of DD was classified according to the combination of LV diastolic parameters, including transmitral inflow, myocardial tissue velocity, isovolumetric relaxation time, deceleration time, E/ϵ mean septal-lateral, maximal TR velocity, and maximal LA volume index.^[12-15] Grade I DD was defined as an E/A ratio of ≤ 0.8 along with a peak E velocity of ≤ 50 cm/second, an E/A ratio of ≤ 0.8 with a peak E velocity of >50 cm/second, an E/A of $0.8 - <2$ with 2 of 3 or all 3 of the following criteria below the cutoff values: average $E/\epsilon >14$, maximal TR velocity >2.8 m/second, and maximal LA volume index of >34 mL/m². Grade II DD was characterized as $E/A \leq 0.8$ with peak E velocity of >50 cm/second or $E/A 0.8 - <2$ with 2 of 3 or all of the previously mentioned criteria meeting the cutoff values.^[13] All of the echocardiographic results were analyzed by a single cardiologist (Y.T.Y.) who was blinded to

the clinical and laboratory characteristics of the patients. Intraobserver variability of $<5\%$ was accepted for the echocardiographic measurement.

Statistical analysis

The statistical software package, PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA), was used to perform all analyses. Continuous and categorical data were reported as mean \pm SD and percentages, respectively. Intergroup comparisons were performed using an independent samples t-test (e.g., age) or the Mann-Whitney U-test for continuous variables, and a chi-square test for categorical variables (e.g., sex).

Normal distribution of the data was assessed with the Shapiro-Wilk test. Analysis of covariance for adjustment was applied for age and to examine differences between groups with and without DD, because age differed between the groups. Therefore, the results of the analysis of covariance were given with standard error values in the tables. A sex category was not included in the analysis of covariance because the sex distribution did not differ significantly between the groups. To determine the risk factors influencing DD, binary and multiple logistic regression methods were used. Both age and sex were included in logistic regression models. Statistical significance was determined at $p < 0.05$.

RESULTS

The sample included 91 asymptomatic obese individuals with no risk factors for DD. The participants were divided into 2 groups according to the presence of DD as per the recent guidelines.^[1] There were 49 subjects with normal diastolic function and 42 with grade I DD (impaired relaxation). Clinical and laboratory characteristics are listed in Table 1. Age, WC, and BMI were significantly greater in subjects with DD ($p < 0.001$, 0.049, and 0.051, respectively). The WC value differed between groups both before and after adjustment for age. The WHR differed between groups only before adjustment for age. The BMI value differed only after adjustment for age. Therefore, BMI can be considered to have a significant effect on DD. The ABSI measurement did not differ between groups either before or after adjustment for age.

The binary logistic regression analysis results are provided in Table 2. Before the adjustment for age and

Table 1. Clinical and laboratory characteristics of the patients (n=91)

	Diastolic dysfunction (+) (n=42)		Diastolic dysfunction (-) (n=49)	
	Mean±SE	Mean±SE	Mean±SE	p
Age, years	47±2	36±2		<0.001*†
Male, n (%)	9 (21%)	5 (10%)		0.139‡
Waist circumference (cm)	108±2	103±2		0.049*§
Waist circumference-hip ratio	0.68±0.01	0.65±0.01		0.119§
Body mass index (kg/m ²)	37±1	34±1		0.051*§
Height (cm)	159±1	159±1		0.613§
Weight (kg)	94±3	87±2		0.038*§
A body shape index	0.78±0.01	0.77±0.01		0.824§
Laboratory measurements				
Total cholesterol (mg/dL)	190.47±6.38	196.4±5.79		0.514§
HDL-C (mg/dL)	44.54±2.39	53.57±2.17		0.009*§
LDL-C (mg/dL)	112.89±5.12	116.7±4.64		0.601§
Triglycerides (mg/dL)	170.45±15.85	131.44±14.37		0.086§
Fasting glucose (mg/dL)	97.8 ±1.92	99.74±1.74		0.477§
Insulin (uIU/mL)	13.28±1.28	15.5±1.13		0.222§
HOMA-IR	3.2±0.34	3.88±0.3		0.151§
Creatinin (mg/dL)	0.66±0.02	0.63±0.02		0.352§
Echocardiographic indices				
TR velocity (m/s)	1.92±0.03	1.92±0.03		0.212§
LA volume index (ml/m ²)	28±1	17±0		<0.001*§
MV-inflow				
MV-E (m/s)	0.77±0.03	0.82±0.03		0.283§
MV-A (m/s)	0.74±0.02	0.65±0.02		0.632§
E/A ratio	1.06±0.05	1.29±0.05		0.003*§
Deceleration time (m/s)	266±5	203±4		<0.001*§
IVRT (m/s)	149±3	66±2		<0.001*§
Tissue Doppler				
e' septal (m/s)	0.065±0.003	0.13±0.003		<0.001*§
e' lateral (m/s)	0.08±0.02	0.16±0.01		0.001*
e' mean septal-lateral (m/s)	0.1±0.01	0.13±0.01		0.055§
E/e' mean septal-lateral	9.5±0.37	6.29±0.34		<0.001*§

HDL-C: High-density lipoprotein cholesterol; IVRT: Isovolumic relaxation time; LDL-C: Low-density lipoprotein cholesterol; HOMA-IR: Homeostasis model assessment of insulin resistance; LA: Left atrial; MV-A: Mitral valve late diastolic inflow; MV-E: Mitral valve early diastolic inflow; e': Early diastolic tissue velocity; E/e': Ratio between early mitral inflow velocity and mitral annular early diastolic velocity; SE: Standard error; TR: Tricuspid regurgitation.

*p<0.05 statistically significant; †: Independent samples t-test; ‡: Chi square test; §: Analysis of covariance (Covariates appearing in the model are evaluated at age=41.14 years).

gender, BMI, WC, and WHR appeared to have a significant effect on DD, while ABSI did not have any effect on DD. After adjustment for age and gender, only BMI had a significant effect on DD (Table 2). A greater BMI increased the risk for DD 1.104 times. WC and WHR

had no effect on DD after adjustment for age and gender. The intra-observer variability was less than 5% for all of the echocardiographic measurements.

The agreement between predictions for DD based on the constructed models and the actual results for

Table 2. Binary and multiple logistic regression analyses to determine the effects of variables on diastolic dysfunction

Model	Variables	SE	Wald	<i>p</i>	OR	95% CI for EXP(B)	
						Lower	Upper
Univariate	BMI	0.041	5.082	0.024*	1.096	1.012	1.186
Univariate	ABSI	0.448	1.844	0.174	1.838	0.764	4.424
Univariate	WC	0.021	7.196	0.007*	1.059	1.016	1.104
Univariate	WHR	0.321	7.168	0.007*	2.363	1.259	4.433
Multivariate Model 1	Age	0.024	13.333	<0.001*	1.09	1.041	1.141
	Gender	0.728	2.713	0.1	3.319	0.796	13.833
Multivariate Model 2	BMI	0.046	4.637	0.031*	1.104	1.009	1.209
	Age	0.025	13.881	<0.001*	1.097	1.045	1.153
	Gender	0.812	1.087	0.297	2.331	0.475	11.442
Multivariate Model 3	ABSI	0.597	0.059	0.809	0.865	0.268	2.791
	Age	0.024	12.445	<0.001*	1.088	1.038	1.14
	Gender	0.739	0.393	0.531	1.589	0.374	6.756
Multivariate Model 4	WC	0.025	3.195	0.074	1.045	0.996	1.097
	Age	0.024	11.225	0.001*	1.085	1.034	1.137
	Gender	0.731	1.517	0.218	2.461	0.587	10.314
	WHR	0.372	2.77	0.096	1.859	0.896	3.857

ABSI: A body shape index; BMI: Body mass index; CI: Confidence interval; OR: Odds ratio; SE: Standard error; WC: Waist circumference; WHR: Waist-to-hip ratio. *Significant.

Table 3. Agreement between the constructed models for diastolic dysfunction and the actual results

	CCR	Sensitivity	Specificity	PPV	NPV	Kappa (<i>p</i>)	McNemar
Model 1	75.6	68.3	81.6	75.7	75.5	0.503 (<0.001)	0.523
Model 2	72.1	69.2	74.5	69.2	74.5	0.437 (<0.001)	1
Model 3	70.9	66.7	74.5	68.4	72.9	0.412 (<0.001)	1
Model 4	76.7	71.8	80.9	75.7	77.6	0.529 (<0.001)	0.824

CCR: Correct classification ratio; NPV: Negative predictive value; PPV: Positive predictive value.

DD was statistically significant (Table 3). The best result was predicted with Model 4 (age, gender, WHR). However, when examined with the results of logistic regression analysis, BMI provided better results than WHR in terms of consistency. The correct classification ratio and Kappa values were very similar in Models 1 and 4, indicating that the predictions of WHR and BMI for DD were very close.

DISCUSSION

The main findings of this study are: (1) WC and BMI were significantly greater in subjects with DD, (2) a greater BMI, WC, and WHR, but not ABSI, were as-

sociated with DD, and (3) after adjustment for age and gender, BMI was the variable that predicted DD in obesity. BMI can still be a useful tool to identify DD in obese individuals without risk factors, despite its limitations.

To the best of our knowledge, this study is the first to look at ABSI as a predictor for DD in obese individuals without any risk factor for DD. Heart failure has been a rapidly growing epidemic in recent years. DD and its progression are independent predictors of the incidence of heart failure.^[16] Obesity is defined as an excess of body fat and is a known risk factor for DD.^[11] Obesity is associated with altered LV remodeling,

possibly due to increased hemodynamic load, neurohormonal activation, and increased cytokine production.^[17] It is important to identify high-risk individuals early to recognize those who need further evaluation. DD may be affected not only by the amount of body fat, but also by its distribution. Various studies have reported that patients with more abdominal fat will have higher risks of cardiovascular disease and other related diseases including hypertension, type 2 diabetes, and high cholesterol.^[18,19] In the present study, BMI predicted the presence of DD better than other obesity indices. Lai et al.^[20] have recently demonstrated that increased visceral adiposity may be associated with DD. They used multidetector computed tomography to quantify visceral adiposity. However, for quantifying abdominal obesity, WC has the advantage of being a simple anthropomorphic measure requiring only a measuring tape. ABSI uses the basic inputs of WC, height, and weight. However, in this study, neither WC nor ABSI predicted DD better than BMI after adjusting for age and gender. In light of the limited availability and high cost of more complex biochemical, genetic, or imaging technology, BMI can still be a useful tool in an improved assessment of risk related to obesity and body composition. Numerous studies have examined the relationship between different indices of obesity and DD.^[21-23] In a previous study of healthy volunteers, WC and BMI were both independently associated with LV DD.^[21] One study showed that WC was second only to age in impact on an independent association with E/A in a population sample with a high prevalence of excess adiposity.^[24] Another study indicated that increased WHR had a stronger association with lower LV ejection fraction and LV DD than BMI.^[22] Russo et al.^[23] reported that increased BMI was associated with worse LV diastolic function independent of LV mass and associated risk factors. In another study, it was found that only WC remained significantly associated with LV DD after the adjustment for age, gender, and risk factors.^[21] Another study found BMI to be an independent predictor of LV DD, along with age, hypertension, and diabetes mellitus.^[25] In contrast, Krishnan et al.^[26] found no correlation between BMI and LV wall thickness, fractional shortening, or pulmonary artery systolic pressure.

Obesity indices cannot fully distinguish visceral fat from subcutaneous fat. It is not clear which of these obesity indices has a stronger association with

DD. The results of epidemiological studies that have reported this characteristic of anthropometric indices are inconsistent. In this study, BMI was a better predictor of DD than WHR, ABSI, or WC. Krakauer and Krakauer^[3] have shown that despite small differences in the odds ratios, total mortality was considerably better predicted by ABSI than by BMI, WC, WHR, or waist-to-height-ratio. Though there are a small number of studies evaluating the potential of ABSI to predict the risk of mortality or diseases, there is no consensus if this measure is better than BMI or WC. He and Chen^[6] found ABSI to be independently capable of anticipating the onset of diabetes mellitus among a Chinese population, although it was not more accurate than BMI and WC. Other studies have also not observed ABSI to be better than WC and/or BMI in the evaluation of the risk of cardiovascular disease,^[27] cardiovascular disease mortality,^[2] incident hypertension,^[28] diabetes,^[29] dyslipidemia,^[29] or metabolic syndrome.^[27] One study did not demonstrate ABSI as a predictor of cardiovascular disease.^[30] Recently, one study showed that among other anthropometric measures, ABSI had a stronger relationship to total, cardiovascular, and cancer mortality. However, the added predictive value of ABSI in the prediction of mortality was limited.^[8] In contrast, a study conducted among a European population indicated that WC and WHR were stronger predictors for CVD mortality than BMI and ABSI.^[2] ABSI had not been found to add consistently to the predictive values of other anthropometric measures in cardiovascular disease prediction.^[9] Another study conducted in a middle-aged, and older Indonesian population group reported that ABSI was less strongly associated with incident hypertension than WC and BMI.^[28] In contrast, in a sample of Portuguese adolescents, ABSI explained variance in blood pressure better than WC and BMI. As such, when examining the effect of weight status on blood pressure, considering use of ABSI alongside BMI would be justified.^[31] The underlying mechanism of these conflicting results is not clear. However, ethnic and gender differences might be a possible explanation for some of the contrasting findings. Another possibility may be patients' clinical characteristics, i.e., the presence of other risk factors for DD. For example, in participants with multiple comorbidities, central obesity has been found to be associated with adverse cardiac mechanics.^[32] Most of these studies do not appear to have transformed ABSI

into age and sex specific z scores as previously advocated.^[4] Correction for age is particularly relevant, since mean ABSI increases from the youngest to the oldest adults by about 2 standard deviations of young adult ABSI.

Limitations

Our study had limitations. The study was cross-sectional in design. There was no long-term follow-up of the patients. We did not evaluate diastolic function invasively. The predictive power of obesity indices could not be assessed for different severity levels of DD, as the 42 patients with DD in this study were all classified as grade I DD (impaired relaxation). We did not perform 24-hour blood pressure monitoring or a glucose tolerance test in every patient to rule out hypertension and diabetes, respectively. Other limitations were the small sample size, which was predominantly female and precluded gender analysis. Larger-scale, longitudinal studies that include obese patients without any cardiovascular risk factors are needed to confirm the present findings.

Conclusion

In this study, we demonstrated that all 3 obesity measures, but not ABSI, determined the presence of DD. BMI showed the strongest association with DD. It may be a more accurate measure for identifying DD and could therefore better inform and guide treatment to improve obesity-related health.

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Keywords: A body shape index; body mass index; diastolic dysfunction; obesity; waist circumference; waist-to-hip ratio.

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