Do female patients with metabolic syndrome have masked left ventricular dysfunction?

Metabolik sendromlu kadınlarda gizli sol ventrikül disfonksiyonu mu var?

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ABSTRACT

Objective: Metabolic syndrome (MS) is a condition, which is recognized as raising the risk of cardiovascular disease. The aim of our study is to estimate the left ventricular functions by atrioventricular plane displacement (AVPD), myocardial performance index (MPI) and conventional methods in patients with MS who were diagnosed according to NCEP (ATP III) criteria.

Methods: Fifty-three female patients with MS (mean age 53.1±6.9 years) and 30 healthy female subjects (mean age 52.8±6.3 years, p>0.05) underwent complete echocardiographic assessment. All of the subjects had no heart and pulmonary diseases. The systolic mitral AVPD was recorded at 4 sites (septal, lateral, anterior, and posterior) by M-mode echocardiography and left ventricle ejection fraction (LVEF) was calculated from the AVPD-mean (EF-AVPD). The LVEF was also established by biplane Simpson's (EF-2D) and Teichholz's methods (EF-T). Left ventricular MPI was calculated as (isovolumic contraction time + isovolumic relaxation time) / aortic ejection time by Doppler echocardiography.

Results: Patients with MS showed mild left ventricular diastolic dysfunction (DD) in comparison to healthy subjects. The EF-2D and EF-T in patients with MS and healthy subjects were not different significantly and were within normal limits. Patients with MS showed LV global dysfunctions compared to healthy subjects (MPI: 0.56±0.12 and 0.46±0.11 respectively, p<0.01). Both the septal, anterior, lateral and posterior part of the atrioventricular plane values and also AVPD-mean during systole were statistically lower in patients with MS (12.85±1.76 mm) as compared with controls (14.65±2.19 mm, p<0.05). EF-AVPD in patients with MS was statistically lower (65.58 ±11.95%) as compared with healthy subjects (74.45±11.07 %, p<0.01).

Conclusion: Female patients with MS had both left ventricular DD and a global dysfunction with an increased MPI. The EF-2D and EF-T were not different significantly between patients and controls, but patients with MS had a relatively reduced EF-AVPD. The AVPD method may indicate a systolic dysfunction with a relatively lower AVPD-mean and relatively lower EF-AVPD. The presence of global dysfunction in patients with MS may lead to heart failure. *(Anadolu Kardiyol Derg 2005; 5: .283-8)*

Key words: Metabolic syndrome, atrioventricular plane displacement, myocardial performance index.

ÖZET

Amaç: Metabolik sendrom (MS), kardiyovasküler hastalık riskini artırdığı kabul edilen bir durumdur. Bu çalışmanın amacı, NCEP (ATP III) kriterlerine göre MS tanısı konmuş hastalarda, sol ventrikül fonksiyonlarını atriyoventriküler plan yer değişimi (AVPD), miyokardiyal performans indeksi (MPİ) ve konvansiyonel metodlarla değerlendirmektir.

Yöntemler: Metabolik sendromlu 53 kadın hasta (ortalama yaş 53.5±6.9 yıl) ve 30 sağlıklı kadın (ortalama yaş 52.7±6.3 yıl, p>0.05) tam ekokardiyografik değerlendirmeye alındı. Olguların hiçbirinde kalp ve akciğer hastalığı yoktu. Sistolik mitral AVPD 4 bölgeden (septal, lateral, anteriyor ve posteriyor) M-mod ekokardiyografi ile ölçüldü ve ortalama AVPD'den sol ventrikül ejeksiyon fraksiyonu (EF) hesaplandı (EF-AVPD). Sol ventrikül EF, ayrıca biplan Simpson (EF-2D) ve Teichholz (EF-T) metodlarıyla da değerlendirildi. Miyokardiyal performans indeksi, Doppler ekokardiyografi ile (isovolümik kontraksiyon zamanı + isovolümik relaksasyon zamanı) / aortik ejeksiyon zamanı) formülünden hesaplandı.

Bulgular: Metabolik sendromlu kadınlar, sağlıklı kişilerle kıyaslandığında hafif sol ventrikül diyastolik disfonksiyonu (DD) gösterdiler. Hasta ve kontrol gruplarında EF-2D ve EF-T anlamlı fark oluşturmadı ve normal sınırlardaydı. Metabolik sendromlu hastalar sağlıklı kişilere göre sol ventrikül global disfonksiyonu gösterdiler (MPİ sırasıyla 0.56±0.12 ve 0.46±0.11, p<0.01). Hem septal, anteriyor, lateral ve posteriyor atriyoventriküler plan ve hem de ortalama sistolik AVPD, MS'lu hastalarda, sağlıklı kişilere göre anlamlı olarak daha düşüktü (sırasıyla 12.85±1.76 mm ve 14.65±2.19 mm, p<0.05). Yine MS'lu hastalarda EF-AVPD, kontrol grubuna göre, istatistiksel olarak daha düşüktü (sırasıyla %65.58 ±11.95 ve %74.45±11.07, p<0.01).

Sonuç: Metabolik sendromlu kadın hastalar hem sol ventrikül DD'na ve hem de artmış MPİ değerleriyle global disfonksiyona sahiptiler. Hasta ve kontrol gruplarında EF-2D ve EF-T anlamlı fark oluşturmadı; ancak MS'lu hastalar, göreceli olarak azalmış EF-AVPD değerlerine sahiplerdi; AVPD metodu, göreceli olarak düşük ortalama AVPD ve EF-AVPD değerleri ile sistolik disfonksiyona işaret edebilir. Metabolik sendromlu hastalarda aynı zamanda global disfonksiyonun varlığı, kalp yetersizliğine yol açabilir. *(Anadolu Kardiyol Derg 2005; 5: 283-8)*

Anahtar kelimeler: Metabolik sendrom, atriyoventriküler plan yer değişimi, miyokardiyal performans indeksi

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Introduction

Metabolic syndrome (MS) (1), dysmetabolic syndrome or insulin-resistance syndrome (2) or syndrome X as it was initially designated (3), which is closely linked to insulin resistance, is a condition which is recognized as raising the risk of cardiovascular disease. It was originally described by Reaven (3) as a quartet of hypertension, glucose intolerance and dyslipidemia (high triglyceride, low high-density lipoprotein-cholesterol (HDL-C)), with insulin resistance or hyperinsulinemia. Central obesity is often associated (4). The new National Cholesterol Education Program (NCEP) guidelines (Adult Treatment Panel (ATP) III) (5) recognized MS as a secondary target of risk-reduction therapy and selected to define MS when three or more of certain five risk determinants are present.

The left ventricular (LV) systolic and diastolic functions are closely related to mortality and morbidity. Arterial hypertension (HT), evidence of left ventricular hypertrophy (LVH), and coronary artery disease (CAD) are independent predictors of diastolic dysfunction (DD). In addition to these factors, DD is related to high body mass index (BMI), high body fat mass, and diabetes mellitus (DM) (1-5). In a previous study, we suggested that insulin resistance might be an important factor causing LV dysfunction and wall thickness in non-diabetic patients with HT(6,7). Diastolic dysfunction precedes LV systolic impairment and accounts alone for about 30–40% of patients with LV failure (8). Early recognition and appropriate therapy of DD is advisable to prevent further progression to heart failure (HF) and death (9,10).

Several echocardiographic methods provide quantitative analysis of LV volumes and ejection fraction (EF) based on the precise tracing of endocardial borders (11-14). In M-mode echocardiography Teichholz's formula is the most commonly used equation for calculation of EF, based on short axis diameter reduction. Simpson's rule is the most commonly used two-dimensional (2D) echocardiographic method for estimation of EF. The short-axis systolic diameter reduction, the long-axis shortening, and a combination of these have been used for calculation of left ventricular EF. Doppler tissue imaging of the mitral annulus may be used to determine LV systolic and diastolic functions. However, technically limited studies prohibit such direct analysis, and alternative techniques must be applied.

The mitral atrioventricular plane displacement (AVPD) method has been shown to be a reliable and simple technique to study left ventricular systolic function in patients, because the mitral annulus can be visualized in almost all patients even if the endocardial borders are difficult to trace (15-24). The contraction of LV involves both a reduction in diameter of the cylindrical portion and a shortening alone the longitudinal axis of the chamber. During ventricular systole the AV plane moves towards the apex of the heart, while during diastole the AV plane rapidly ascends towards the left atrium (17,18). The mitral AVPD also may reflect the left ventricular diastolic function (23). However, myocardial performance index (MPI, Tei index) reflects LV global (systolic and diastolic) functions (25). A relationship between MPI and left ventricular geometry was established in hypertensive patients, and the left ventricular global dysfunction was more advanced in patients with concentric hypertrophy than the other LV geometric patterns (26).

In order to show if the patients with MS have masked systolic dysfunction or not, we aimed to assess the left ventricular functions by AVPD, MPI and conventional methods in these patients who were diagnosed according to NCEP (ATP III) criteria (5).

Methods

Study population

Fifty-three female patients with MS (mean age 53.5±6.9 years) and 30 healthy female subjects (mean age 52.7±6.3 years, $p>0.05$) underwent complete echocardiographic assessment. All of the subjects in both groups had no heart and pulmonary diseases based on physical examination, and also their electrocardiograms were normal, and in sinus rhythm. All of them underwent treadmill exercise test and the test was normal. Systolic (SBP) and diastolic (DBP) blood pressures were measured in the sitting position on the right arm using an aneroid sphygmomanometer (Erka, Germany), after at least 5 min of rest. First appearance and disappearance (phase V) of Korotkoff's sounds were used to define the pressures. Readings were recorded to the nearest even number, and the mean of two recordings 3 min apart was computed. Heart rate per minute (HR) was measured in the sitting position. Waist circumference (WC) was measured with the subject standing and wearing only underwear, at the level midway between the lower rib margin and the iliac crest, while that of the hip was measured at the level of the greater trochanters. Body mass index (BMI) was calculated by a computer as weight divided by height squared (kg/m^2). After an overnight fasting (at least 12 hours) blood glucose (FBG), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) were analysed with commercial kits (Abbott, USA) by an autoanalyser (Aeroset, USA). On the other hand, in non-diabetic subjects 75 g oral glucose tolerance test was performed.

Identification of MS conformed to the definition used by the NCEP (ATP III)(5), namely when three or more of the following five risk determinants were present: WC (in men >102 cm, in women >88 cm), TG ≥150 mg/dl, HDL-C (in men <40, in women <50 mg/dl), blood pressure (≥130 / ≥85 mmHg), and FBG ≥110 mg/dl.

Echocardiographic measurements

All measurements were performed with the subjects in the left lateral decubitus position by M-mode, two-dimensional (2D), and Doppler ultrasound echocardiography according to the recommendations of the American Society of Echocardiography (27-29). The ultrasound equipment used was Contron Sigma Iris with a 2.5–MHz probe. Basic measurements of LV dimensions in diastole and systole, thickness of interventricular septum (IVS) and posterior wall (LVPW), and also LV mass (LVM) using Devereux formula were measured by the M-mode technique (30). LVM was divided with body surface area to obtain left ventricular mass index (LVMI). Left ventricular EF by Simpson's biplane method (EF-2D) was calculated as (diastolic volume-systolic volume)/(diastolic volume). Also, left ventricular EF was calculated as Teichholz's short axis method (EF-T). Early (E) and atrial (A) transmitral maximal flow velocities, the ratio (E/A) and deceleration time of E was registered. Isovolumic relaxation time was measured by the continuous wave Doppler technique. The velocity of mitral flow propagation (VPR) was estimated using color Doppler M-mode (31). The left ventricular MPI was calculated as (isovolumic contraction time + isovolumic relaxation time) / aortic ejection time) (25).

From apical 4- and 2-chamber views the displacement of the AV plane towards the apex in systole was recorded at 4 sites in

the left ventricle using M-mode, according to the methods of Willenheimer and colleagues (21). The regional displacement (mm) was the distance covered by the AV plane between the position most remote from the apex (corresponding to the onset of contraction) and the location closest to the apex (corresponding to the end of contraction, including any post-ejection shortening), that is, the full extent of the displacement. The septal and lateral AVPD were measured in the four-chamber view and anterior and posterior AVPD-in the two-chamber view. The mean value of the AVPD from the above 4 sites (AVPD-mean) expressed in mm was calculated from the above four sites. All measurements were performed on three consecutive beats and the mean values were given. No measurements were made within five cycles of an ectopic beat.

Left ventricular EF was calculated using the regression equation by Alam et al, (22) describing the relation between the left ventricular EF, determined by radionuclide ventriculography, and echocardiographically assessed AVPD:

EF_{AVPD} = (5.5 X mean AVPD) - 5

Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences version 10.0 (SPSS-10.0) for Windows packet program. Results were given as mean±standard deviation, differences between measurements were assessed using independent t- test. Correlations between variables were tested assuming a linear relationship. A P-value<0.05 was considered significant.

Results

Basic characteristics of patients and healthy subjects

Characteristics of patients with MS and healthy subjects are shown in Table 1. Patients with MS had significantly higher WC (p<0.001), higher BMI (p<0.01), higher SBP (p<0.01) and DBP (p<0.01), higher FBG (p<0.01) and TG (p<0.001) but, had lower HDL-C (p<0.001) than healthy female subjects. However, waist-to-hip ratio (WHR) and HR were not different statistically between patients and controls (p>0.05).

Table 1. Basic characteristics of patients with metabolic syndrome (MS) and healthy subjects

	Patients with MS (n=53)	Healthy subjects (n=30)	p
Mean age	53.5±6.9	52.7±6.3	NS
WC (cm)	101.3±10.7	90.4±11.7	0.001
WHR	0.88±0.5	0.86±0.4	NS
BMI (kg/m^2)	31.5±4.7	27.9±4.7	0.01
HR (pulse/min)	76.0±10.2	78.4±7.4	NS
SBP (mmHg)	132.1±22.9	118.8±10.9	0.01
DBP (mmHg)	83.5±10.2	76.6±6.8	0.01
FBG (mg/dl)	112.2 ± 33.4	90.0 ± 10.2	0.01
Insulin (UIU/ml)	10.3±4.8	8.6±2.9	NS
TG (mg/dl)	146.9±60.7	93.2±41.1	0.001
HDL-C (mg/dl)	41.3±6.9	53.8±13.1	0.001
TC (mg/dl)	205.0±42.8	198.2±39.3	NS

BMI: Body, mass index, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, HDL-C: High-density lipoprotein cholesterol, HR: Heart rate per minute, NS: Not significant, SBP: Systolic blood pressure, TG: Triglyceride, TC: Total cholesterol, WC: Waist circumference, WHR: Waist-to-hip ratio

Basic echocardiographic parameters

Assessment of left ventricular diameters and functions in patients with MS and healthy subjects was shown in Table 2 and 3 respectively. Thickness of IVS, LVPW and LVM in patients were higher than in controls (p<0.05 for all). However, LVMI did not differ significantly between patients and controls (p>0.05). Although parameters of diastolic function were in normal limits in healthy subjects, patients with MS had mild DD. Systolic functions by conventional method (EF-2D and EF-T) were not different significantly between patients (69.2±4.7% and 68.3±3.5%) and controls (70.6±4.5%, p>0.05 and 70.1±4.0%, p>0.05) and were in normal limits in both groups. On the other hand, patients with MS showed LV global dysfunctions compared to healthy subjects (MPI: 0.56±0.12 and 0.46±0.11 respectively, p<0.01).

AVPD

The displacements at four sites (septal, anterior, lateral and posterior part of the atrioventricular plane) in both groups were

Table 2. Assessment of left ventricular mass and diameters by echocardiography in patients with metabolic syndrome (MS) and healthy subjects

	Patients with MS (n=53)	Healthy subjects (n=30)	p
Left atrium (mm)	37.7±3.6	35.1±4.6	0.01
IVS Thickness (mm)	10.8±1.4	10.0±1.4	0.05
LVPW Thickness (mm)	10.5±1.1	9.8±1.2	0.05
LVM (g)	210.4±48.7	182.3±45.3	0.05
LVMI (g/m^2)	114.8±23.4	105.9±22.7	NS
LVED Diameter (mm)	47.3±4.7	45.7±3.7	NS
LVES Diameter (mm)	29.2±3.8	27.6±2.9	NS
LVED Volume (ml)	104.3±23.5	98.3±20.3	NS
LVES Volume (ml)	32.3±9.8	28.5±8.7	NS

IVS: Interventricular septum, LVED: Left ventricular end diastolic, LVES: Left ventricular end systolic, LVM: Left ventricular mass, LVMI: Left ventricular mass index, LVPW: Posterior left ventricular wall, NS: Not significant

Table 3. Assessment of left ventricular functions by echocardiography in patients with metabolic syndrome (MS) and healthy subjects

	Patients with MS (n=53)	Healthy subjects (n=30)	p
Systolic functions			
EF-2D (%)	69.2±4.7	70.6±4.5	NS
EF-T (%)	68.3±3.5	70.1±4.0	NS
EF-AVPD (%)	65.6±12.0	74.5±11.1	0.01
FS (%)	39.1±4.1	39.9±4.0	NS
Diastolic functions			
E-vel. (m/s)	0.8±0.2	0.8±0.2	NS
A-vel. (m/s)	1.1±1.4	0.7±0.2	NS
E/A ratio	0.9±0.3	1.2±0.4	0.001
DT (ms)	237.2±36.0	208.5±50.1	0.01
IVRT (ms)	108.2±23.0	79.8±16.7	0.001
VPR (cm/s)	45.0±23.2	92.3±50.6	0.001
Global function			
MPI	0.56±0.12	0.46±0.10	0.01

A- vel.: late mitral flow velocity, DT:deceleration time, E- vel.: early mitral flow velocity, E/A ratio: ratio of early and late mitral flow velocities, EF-AVPD: left ventricular ejection fraction by atrioventricular plane displacement method, EF-2D: left ventricular ejection fraction in 2 dimensional echocardiography, EF-T: ejection fraction by Teicholz, FS: fraction shortening, IVRT: isovolumic relaxation time, MPI: myocardial performance index, VPR: mitral flow propagation, NS: nonsignificant

shown in Table 4. Both the septal, anterior, lateral and posterior part of the atrioventricular plane values and also AVPD-mean during systole were statistically lower in patients with MS (12.8±2.2 mm) as compared with healthy subjects (14.5±2.0 mm, p<0.01). The EF-AVPD was statistically lower in patients (65.6±12.0 %) as compared with healthy subjects (74.5±11.1 %, p<0.01).

Correlations

Significantly positive correlations were shown between EF-AVPD and EF-2D (r =0.707, p<0.01) and EF-T (r =0.818, p<0.01) (Fig.1). Also, a significantly positive correlation was shown between EF-2D and EF-T (r =0.645, p<0.01). However, EF-AVPD was negatively correlated with MPI (r = -0.500, p<0.01) (Fig.2).

Discussion

It is well known that important cardiovascular risk factors, such as hypertension, glucose intolerance, hyperinsulinemia, dyslipidemia, and obesity, often cluster in the same individuals. Therefore, the existence of a syndrome involving these disorders has been proposed in which insulin resistance has been suggested to be of particular importance (3,32,33). An association between this insulin resistance syndrome and left ventricular hypertrophy (LVH) has recently been found (32,33). Characteristically, cardiac hypertrophy is secondary to hypertension, but some degree of cardiac hypertrophy can also be found in normotensive obese subjects (24), in patients with ischemic heart disease (35), and in diabetic patients (36). Insulin resistance could influence myocardial morphology and function in several ways, because insulin resistance is associated with hyperinsulinemia, which is known to induce growth of myocardial tissue in vitro (34).

In our study, in patients with MS, IVS and LVPW thicknesses, left atrial diameter and LVM were found to be increased, but not LVMI in comparison to healthy subjects. Mild left ventricular DD was shown in patients with MS compared with healthy subjects. Although the EF-2D and EF-T between patients with MS and healthy subjects were not different significantly, and were in normal limits; AVPD-mean during systole and EF-AVPD were statistically lower in patients with MS compared with healthy subjects. Also, patients with MS had statistically higher MPI than healthy subjects reflecting left ventricular global dysfunction. These results show that the patients with MS and apparently preserved systolic function, as assessed by conventional methods, may have an unrecognized reduction in left ventricular contractility, and suggest left ventricular global dysfunction in addition to presence of mild DD.

In our study patients DD might be dependent on risk determinants (especially blood pressure, FBG and abdominal obesity) of metabolic syndrome. However, none of the patients with MS had clinically overt CAD, and all of them had electrocardiographically normal treadmill exercise tests. A strong correlation between BMI and, in particular, an elevated body fat mass with HT and LVH was demonstrated (34). The correlation between an elevated fat mass and diastolic dysfunction may result from pressure overload and a disproportional increase of IVS and LVPW thickness in obese individuals. This is also in agreement with our findings.

Most traditional echocardiographic methods for determining left ventricular EF have some disadvantages, limiting their use (17,18). Long axis fibres are mainly subendocardial and more prone to ischaemia, implying that abnormalities of AVPD may occur earlier in the disease process and represent more subtle alterations in ventricular function. The systolic mitral AVPD is quite different from left ventricular EF and other conventional measurements of left ventricular systolic function. The contrac-

Table 4. Assessment of left ventricular systolic function by AVPD method in patients with metabolic syndrome (MS) and healthy subjects

	Patients with MS (n=53)	Healthy subjects (n=30)	p
AVPD-septal (mm)	12.5±1.9	14.0±2.2	0.01
AVPD-lateral (mm)	13.1±2.7	15.1±2.2	0.01
AVPD-anterior (mm)	12.8±2.5	14.3±2.1	0.01
AVPD-posterior (mm)	12.9±2.5	14.4±2.1	0.01
AVPD-mean (mm)	12.8±2.2	14.5±2.0	0.01
EF-AVPD (%)	65.6±12.0	74.5±11.1	0.01

AVPD: Atrioventricular plane displacement, EF-AVPD: Left ventricular ejection fraction from atrioventricular plane displacement method.

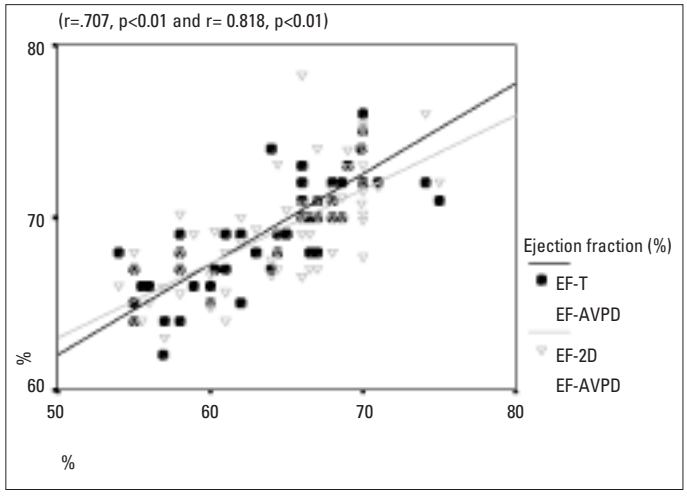

Figure 1. Correlations between EF-AVPD and EF-2D

EFAVPD: Left ventricular ejection fraction by atrioventricular plane displacement method, EF-2D: Left ventricular ejection fraction in 2 dimensional echocardiography, EF-T: Left ventricular ejection fraction by Teichholz's method

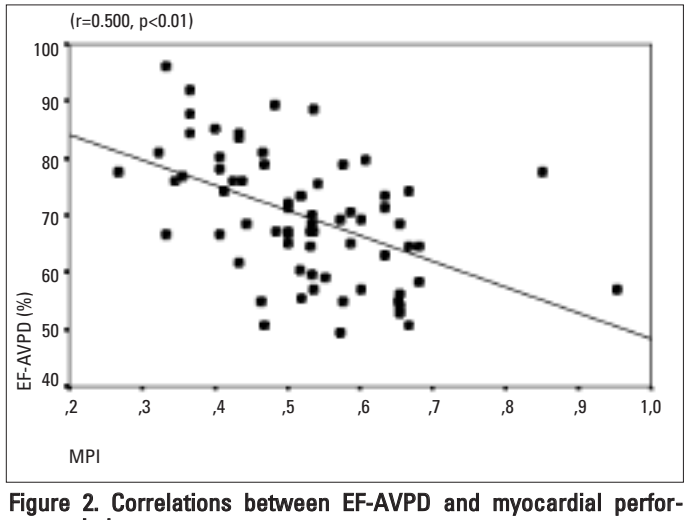

Figure 2. Correlations between EF-AVPD and myocardial performance index

EFAVPD: Left ventricular ejection fraction by atrioventricular plane displacement method, MPI: Myocardial performance index

tion of left ventricle involves both a reduction in diameter of the cylindrical portion and a shortening alone the longitudinal axis of the chamber. The left ventricular pump function has traditionally been attributed mainly to the circumferentially orientated myocardial fibres (17-20). The mitral AVPD may better reflect left ventricular systolic function and may ultimately prove to be a more accurate prognostic indicator than EF despite left ventricular asymmetry, since it is determined in four different regions (the septal, lateral, posterior and anterior regions) of the left ventricle, and since it may evaluate the total shortening along the left ventricular long axis in the respective regions. However, the correlation between AVPD and reliable indices of left ventricular systolic function is very strong (r values> 0.8) (21,22). The correlations between AVPD and EF-2D and EF-T were significantly strong in our study patients ($r = 0.707$, $p<0.01$ and $r = 0.818$, $p<0.01$, respectively). More important, reduced systolic mitral AVPD is a powerful predictor of poor prognosis (20,21). Mortality is significantly higher when the AVPD is less than 10 mm with a substantial mortality increase when AVPD is less than 7 mm (21). However, in our study population there was no subject who had an AVPD< 10 mm.

The predominant role of HT for the development of diastolic heart failure was initially established by the Framingham Heart Study (37). Diastolic dysfunction in hypertensive patients can occur even in the absence of structural myocardial abnormalities and represents usually myocyte dysfunction with impaired isovolumic relaxation. Left ventricular diastolic filling is a complex event that is influenced by several factors, such as preload, heart rate, left ventricular relaxation, left ventricular compliance, left atrium contraction force and afterload (32). Thus, left ventricular DD might be the result of a variety of impairments.

Hypertension commonly occurs in type 2 DM, and contributes importantly to the heightened risk of cardiovascular, renal, and retinal disease (36). Diabetes mellitus might predispose to left ventricular systolic and diastolic dysfunctions independently of concurrent coronary or rheumatic heart disease (38). Histology in diabetics is largely indistinguishable from changes found in hypertensive left ventricular disease. Specific myocardial disease in DM commonly is called “diabetic cardiomyopathy”. The pathogenesis is unclear, although possible mechanisms include the synergistic impact of hypertension plus chronic derangement of myocardial metabolism, with increased free fatty acid oxidation and decreased glucose utilisation (39).

Left ventricular systolic and/or diastolic functions provide prognostic information in patients. So, the AVPD method may indicate a systolic dysfunction with a relatively lower AVPD-mean and relatively lower EF-AVPD in patients with MS compared with healthy subjects. This indicated the presence of normal, but statistically significant decrease of left ventricular systolic function by AVPD method in patients with MS. Diastolic abnormalities may represent an early cardiac abnormality in subjects with such risk factors who may develop, as a consequence, functional abnormalities of the heart including DD. Also significantly higher MPI in patients with MS may reflect left ventricular global dysfunction. It might be suggested that DD might be combined with systolic dysfunction rather than presence of isolated diastolic dysfunction in patients with MS.

As a result, our findings may suggest that female patients with MS who have DD may prone to develop systolic dysfunction also. So, the presence of global dysfunction in patients with MS may lead to heart failure. The mitral AVPD and MPI may be useful and simple non-invasive methods for the estimation of left ventricular systolic and global functions in patients with MS.

Study limitations

One of the our study limitations is that there are no other more sophisticated markers of diastolic function available such as Doppler tissue imaging of mitral annular motion or pulmonary venous flow signals. Since the ventricular systolic and/or diastolic functions provide prognostic information in the patients with MS, our results should be further confirmed with larger prospective studies.

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