# Assessment of longitudinal left ventricular systolic function by different echocardiographic modalities in patients with newly diagnosed mild-to-moderate hypertension

*Yeni tanı konulmuş hafif ve orta derecede hipertansiyonu olan hastalarda sol ventrikül longitüdinal fonksiyonunun değişik ekokardiyografik modaliteler ile değerlendirilmesi*

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## ABSTRACT

**Objective:** Standard echocardiographic methods reflect chamber dynamics and do not provide a direct measure of myocardial fiber shortening. Therefore we evaluated longitudinal left ventricular myocardial function by tissue Doppler echocardiography; strain (S), strain rate (SR), tissue Doppler velocity (TDV) in newly diagnosed mild to moderate hypertensive patients.

**Methods:** Our cross-sectional and observational study population consisted of 57 patients and 48 normotensive control subjects. Patients with obesity, diabetes mellitus, regional wall motion abnormality, secondary hypertension and a history or clinical evidence of cardiovascular disease, arrhythmias or conduction abnormalities were excluded from the study. Ejection fraction, endocardial fractional shortening ($_eFS$), meridional end-systolic stress ($_mESS$), stress-adjusted $_eFS$ (observed /predicted $_eFS$) were measured by M-mode echocardiography. Relationship between the left ventricular mass index and mESS was assessed by Pearson's linear regression model.

**Results:** Hypertensive patients had significantly decreased longitudinal myocardial function compared to control subjects determined by septal (-1.25±0.30 vs. -1.02±0.33, p<0.001) and lateral (-1.20±0.28 vs. 1.02±0.41, p<0.01) SR (1/s) measurements. However, there was no significant correlation between the $_mESS$ and strain-strain rate measurements in both normal and hypertensive subjects.

**Conclusions:** Early impairment in longitudinal left ventricular systolic function can be expected despite normal endocardial left ventricular function indicated by M-mode echocardiography in patients with newly diagnosed and never treated mild to moderate hypertension. *(Anadolu Kardiyol Derg 2010; 10: 247-52)*

**Key words:** Longitudinal myocardial function, strain, strain rate, hypertension

## ÖZET

**Amaç:** Standart ekokardiyografik yöntemler odacık dinamiklerini yansıtmakla beraber miyokart liflerinin kısalması ile ilgili doğrudan bilgi sağlamamaktadır. Bu nedenle yeni tanı konulmuş hafif orta derecede hipertansiyon hastalarında sol ventrikül longitüdinal miyokart fonksiyonunu doku Doppler ekokardiyografi ile strain (S), strain rate (SR), doku Doppler velosite (TDV) kullanarak inceledik.

**Yöntemler:** Enine- kesitli ve gözlemsel çalışmamızın popülasyonu 57 hasta ve 48 normotansif kontrol olgusundan oluşmaktaydı. Obezite, diyabetes mellitus, bölgesel duvar hareket bozukluğu, sekonder hipertansiyon ve kardiyovasküler hastalık öyküsü, aritmiler ve ileti bozuklukları öyküsü veya klinik kanıtı olan hastalar çalışmadan dışlandı. Ejeksiyon fraksiyonu, endokardiyal fraksiyonel kısalma ($_eFS$), meridyonel sistol sonu stres ($_mESS$), stres ile düzeltilmiş $_eFS$ (gözlemlenen/öngörülen $_eFS$) M-mod ekokardiyografi ile ölçüldü. Sol ventrikül kütle indeksi ve $_mESS$ arasındaki ilişki Pearson doğrusal regresyon modeli ile incelendi.

**Bulgular:** Hipertansif hastalar kontrol olguları ile karşılaştırıldığında septal (-1.25±0.30 ve 1.02±0.33, p<0.001) ve lateral (-1.20±0.28 ve 1.02±0.41, p<0.01) SR (1/s) ölçümleri ile belirlenen belirgin olarak azalmış longitüdinal miyokart fonksiyonuna sahiptiler. Bununla birlikte, hem normal hem de hipertansif olgularda, $_mESS$ ve strain-strain rate ölçümleri arasında belirgin korelasyon yoktu.

**Sonuç:** Yeni tanı konulmuş ve tedavi edilmemiş hafif orta dereceli hipertansiyon olgularında M-mode ekokardiyografi ile normal endokardiyal sol ventrikül fonksiyonuna rağmen longitüdinal sol ventrikül sistolik fonksiyonunda erken bozulma beklenebilir. *(Anadolu Kardiyol Derg 2010; 10: 247-52)*

**Anahtar kelimeler:** Longitüdinal miyokart fonksiyonu, strain, strain rate, hipertansiyon

## Introduction

Myocardial fibers shorten in either longitudinal or circumferential direction. The fibers responsible for short-axis shortening and thickening of the left ventricle are circumferentially located at the midwall. The longitudinally orientated fibers are predominantly located at the subendocardium and they are responsible for long-axis shortening and twisting of the left ventricle (1). Standard echocardiographic measurements, such as endocardial fractional shortening ($_e$FS) and ejection fraction (EF), reflect chamber dynamics and they are not direct measurements of the longitudinal fiber function (2). It has been suggested that assessment of the left ventricular contractile function by using standard M-mode echocardiography tends to overestimate longitudinal systolic performance in hypertensive patients (3-6).

Strain (S) and strain rate (SR) are derived from tissue Doppler echocardiography. Strain is a method, which measures myocardial deformation and SR measures the rate of the deformation (7). Tissue Doppler velocity (TDV) has also the potential to assess left ventricle contractile function. Recent studies revealed that myocardial strain by Doppler echocardiography might represent a new, powerful method for quantifying regional myocardial function (7, 8). This method is less influenced by tethering effects than Doppler tissue imaging, but it is markedly load-dependent (8). Different from S and SR rate, TDV is dependent of whole heart translation and tethering (9). Although some analysts claim that myocardial SR imaging is a superior method for the evaluation of longitudinal left ventricular systolic function, others also suggest that TDV is a well-established method for quantitative analysis of longitudinal systolic function (2, 9-12).

Diminished contractile reserve in hypertensive patients is associated with increased cardiovascular risk. Recent studies reported early impairment of circumferential left ventricular function, which may be documented by reduced midwall performance. Hypertensive patients with normal or supranormal standard M-mode systolic measurements may have impaired longitudinal systolic function. Additionally, endocardial fractional shortening, which measures circumferential function, is strictly influenced by left ventricle geometry and radial thickening. The measurements based on standard M-mode echocardiographic methods are controversial in the assessment of systolic myocardial function (13-16). There is no enough information about whether using physiologically more appropriate echocardiographic methods lead to different interpretations of longitudinal left ventricular systolic function than those derived from standard M-mode echocardiography in hypertensive patients. Recent studies established that longitudinal myocardial function evaluated by S and SR echocardiography deteriorates earlier than circumferential myocardial function in subjects with pathologic and/or physiologic left ventricular hypertrophy (10-12).

We hypothesized that longitudinal myocardial function may be impaired even in the early phases of hypertension, and we investigated the longitudinal myocardial systolic function by S and SR imaging in both normotensive and newly diagnosed never treated mild to moderate hypertensive subjects.

## Methods

### Patient characteristics and study protocol

We enrolled 57 consecutive patients (30 men and 27 women; mean age 48±9 years) with newly diagnosed and never treated mild-to-moderate hypertension and 48 normotensive control subjects (26 men and 22 women; mean age 46±9 years) in this cross-sectional and observational study. Subjects with obesity (BMI>30), diabetes mellitus, regional wall motion abnormality, secondary hypertension anamnesis and a history or clinical evidence of cardiovascular diseases (e.g. ischemic heart disease, heart valve disease), arrhythmias or conduction abnormalities and/or older than 65 years were excluded from the study. Patients who had cardiovascular risk factors underwent an exercise stress test before enrollment. Patients with positive test result according to the ACC/AHA exercise stress test guidelines were excluded (17). The study protocol was approved by the local institutional Ethics committee. All subjects gave written informed consent before participating.

Hypertension was diagnosed and classified according to the 7th report of the 'Joint National Committee' (18). None of the patients had ever taken antihypertensive treatment. Patients were included into the study if their supine systolic blood pressure (BP) and diastolic BP were persistently between 140-159 and 90-100 mmHg respectively on three consecutive visits, 1 week apart. The baseline BP value was defined as average of three measurements taken at 5-minute intervals at the third visit.

### Standard echocardiographic examination

Echocardiograms were recorded in supine position turned 30° on the left side, using commercially available echocardiographic machine (Vivid 7, GE Systems, Oslo, Norway) with a 2.5 MHz transducer. Two-dimensional guided M-Mode echocardiograms were obtained just below the mitral valve leaflets at the chordal level. All echocardiograms were recorded and stored in a hard disk and were analyzed later. Septal and posterior wall thickness and left ventricle chamber dimensions were measured according to the American Society of Echocardiography (ASE) guidelines. The left ventricle mass index (LVMI) was determined by the ASE-recommended formula.

'LVMI $(g/m^2)$=(1.04[(IVST+LVID+PWT)$^3$-LVID$^3$]-13.6)/ body surface area'.

The LVMI ≥95 gm/m$^2$ in female and ≥115 gm/m$^2$ in male were accepted as left ventricular hypertrophy. Relative wall thickness (RWT=2x LVPWd/LVDd) was calculated in patients with left ventricular hypertrophy for geometry analysis. Hypertrophy was accepted as eccentric if RWT<0.42 and concentric if RWT ≥0.42 (19). Ejection fraction (EF) was derived from diastolic and systolic left ventricular volumes calculated with Teichholz's formula (20).

Endocardial fractional shortening ($_e$FS%) was calculated as:

$$_e\text{FS\%}=100 \times (\text{LVID}_d-\text{LVID}_s)/\text{LVID}_d$$

where LVID was left ventricular internal dimension; $_d$ was end-diastole; $_s$ was end-systole. Three consecutive cardiac cycles were measured and average values were obtained.

Meridional end-systolic stress($_m$ESS) was calculated by use of systolic blood pressure (SBP) during the echocardiographic examination using the following formula (13):

$$_mESS = \frac{0.334 \times SBP \times LVID_S}{PWT_s \times \{1+(PWT_s/LVID_s)\}}$$

where PWT was posterior wall thickness. The relationship between $_e$FS and $_m$ESS was obtained from our normotensive population data as:

**Predicted** $_e$FS=122.55-1.64x$_m$ESS

Midwall fractional shortening ($_m$FS%) was calculated according to the formula (13);

mFS%=100x[(LVID$_d$+H$_d$/2) - (LVID$_s$+ H$_s$/2)] / (LVID$_d$+H$_d$/2)
h=(PWT+IVS)/2.

Circumferential end-systolic stress ($_c$ESS) was calculated using SBP during echocardiographic examination using the following formula (21):

$$_cESS= \frac{SBPx(LVID_s/2)^2x\{1+(LVID_s/2+PWT_s)^2/(LVID_s/2+PWT_s/2)^2\}}{(LVID_s/2 + PWT_s)^2-(LVID_s/2)^2}$$

The relationship between $_m$FS and $_c$ESS was obtained from our normotensive population data as:

**Predicted** $_m$FS=102.20-0.95x$_c$ESS

To calculate predicted $_m$FS and $_e$FS, we calculated constant values in the equation y=a+bχ with the regression formula (a, b=constant values; χ=$_c$ESS or $_m$ESS; y= $_m$FS or $_e$FS).

a=mean y-(bxmean χ), b= Σ(χ-mean χ) (y-mean y)/Σ(χ-mean χ)$^2$

To evaluate afterload-independent longitudinal systolic performance of the left ventricle, we used the ratio of the $_e$FS calculated from M-mode echocardiographic measurements to that predicted from $_m$ESS. We also used the ratio between the observed $_m$FS and the predicted from $_c$ESS for afterload-independent circumferential systolic performance.

### Pulsed tissue Doppler velocity

Pulsed TDV analysis of the mitral annulus was performed in the apical 4-chamber view. Guided by 2-dimensional echocardiography, a 5 mm sample volume was placed at the septal and lateral sites of the annulus. Settings were adjusted for a frame rate between 120 and 180 Hz, and a cine loop of 3 to 5 consecutive heart beats was recorded. Care was taken to obtain an ultrasound beam parallel to the direction of mitral annulus motion. The peak of myocardial systolic wave was determined at each annular level. All the measurements were calculated from 3 consecutive cycles and average of 3 measurements was recorded.

### Strain and strain rate imaging

Analysis was performed on a commercially available computer (Echopac, GE Systems, Oslo, Norway). Because SR imaging is angle-dependent, and longitudinal velocities are the highest in the basal segments of the left ventricle and diminish towards the apex, laterobasal region and basal septum were preferred for SR analysis.

For all strain parameter measurements, the sample volume, oval and 12-x6-mm in size, was placed in basal inner half of the left ventricle myocardium at the septum and the lateral wall to keep the angle between the Doppler beam and the endocardium smaller than 30°. The peak systolic S at each site was determined as the difference in S measured from the onset of the QRS complex to the nadir of the S tracing. The SR is the percentage of deformation per second and is expressed in $s^{-1}$ or $^{1/}s$. For S and SR, average of three measurements obtained from 3 consecutive cycles was recorded. Every echocardiographic analysis was done by the same investigator who was unaware of the subjects' clinical status. Both strain and strain rate measurements were reproducible and the intraobserver variability was found as 5% in our study.

### Statistical analysis

All statistical analyses were performed by a computer using the SPSS V10.0 system (Statistical Package for the Social Sciences INC., Chicago, Illinois, USA). Patients' data are presented with descriptive statistics as frequencies and as means±standard deviation. Differences in normally distributed continuous variables were tested by an unpaired Student's t test. Categorical data were compared with a Chi-square test. The Mann-Whitney U test was used to compare abnormally distributed continuous variables. Pearson's linear regression was used to determine whether correlations exist between left ventricle mass index and $_m$ESS with contractile parameters. In all tests a p-value of <0.05 was considered statistically significant.

## Results

Demographic findings (age, sex, body surface area, baseline heart rate) were similar in both hypertensive patients and healthy control subjects. LVMI was found increased in hypertensive patients (p<0.001) (Table 1). Of the 57 hypertensive patients, 39 (68%) had left ventricular hypertrophy. Left ventricular hypertrophy was concentric and eccentric in 23 (58.9%) and 16 (39.1%) patients respectively.

There were no statistically significant differences between the normotensive and hypertensive subjects with respect to EF, $_e$FS, and $_m$FS calculated from M-mode echocardiography. In addition, stress-adjusted (observed/predicted) $_e$FS and $_m$FS

**Table 1. Baseline characteristics**

| Variables | Normal (n=48) | Hypertensive (n=57) | p* |
|---|---|---|---|
| Age, years | 46.39±9.54 | 48.96±9.54 | 0.15 |
| Male/female, n | 26/22 | 30/27 | 0.51 |
| Systolic BP, mmHg | 114.16±10.12 | 156.42±16.23 | <0.001 |
| Diastolic BP, mmHg | 74.45±6.58 | 97.28±7.99 | <0.001 |
| Body surface area, m$^2$ | 1.82±0.18 | 1.88±0.21 | 0.13 |
| LV mass index, gr/m$^2$ | 88.14±14.09 | 121.07±27.35 | <0.001 |
| Heart rate, beats/min | 68.14±10.78 | 68.45±9.93 | 0.87 |

Data are presented as proportions and mean±standard deviation

*- unpaired Student's t test, Chi-square test

BP - blood pressure, LV - left ventricle

were not statistically different in both groups (Table 2). Significant inverse correlations were seen between $_e$FS and $_m$ESS in both normal subjects (r=-0.712, p<0.001) and hypertensive patients (r=-0.617, p<0.001) (Fig.1, Fig.2).

Septal and lateral basal systolic myocardial velocities measured via tissue Doppler were similar in both hypertensive patients and controls. However, septal and lateral systolic S and SR values, which demonstrate longitudinal myocardial function, were significantly decreased in hypertensive patients (p<0.001 and p<0.01, respectively) (Table 2). In both normal and hypertensive groups, neither mESS nor LVMI was statistically correlated with strain and strain rate measurements (Table 3, Table 4).

## Discussion

This study established the presence of an early impairment in longitudinal myocardial function, determined by strain and
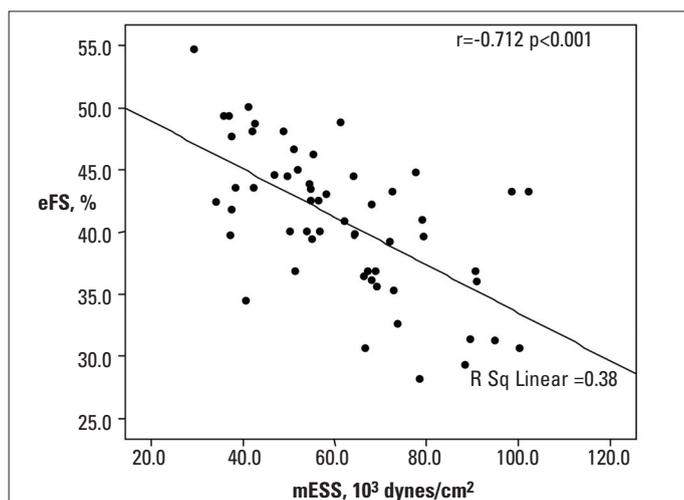


**Figure 1. Correlation between the mESS and endocardial FS in the patient group**
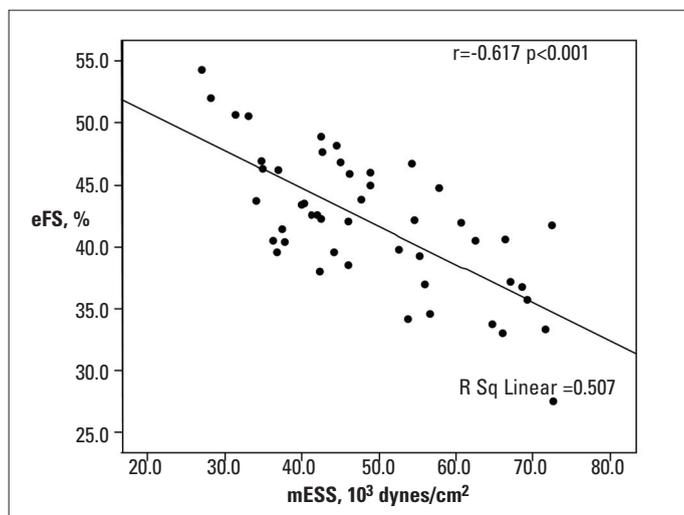FS - fractional shortening, mESS - meridional end-systolic stress



**Figure 2. Correlation between the endocardial FS and mESS in the control group**
FS - fractional shortening, mESS - meridional end-systolic stress

**Table 2. Echocardiographic measurements of the subjects**

| Variables | Normal n=48 | Hypertensive n=57 | p* |
|---|---|---|---|
| EF % | 72.58±6.48 | 71.08±6.92 | 0.25 |
| mESS, $10^3$ dynes/cm$^2$ | 48.88±12.67 | 61.51±18.57 | <0.001 |
| cESS, $10^3$ dynes/cm$^2$ | 101.87±22.63 | 129.79±33.67 | <0.001 |
| eFS, % | 41.99±5.47 | 40.91±5.81 | 0.33 |
| Observed/predicted eFS | 1.83±2.51 | 2.16±6.96 | 0.96 |
| mFS, % | 33.28±4.42 | 31.78±4.57 | 0.09 |
| Observed/predicted mFS*, % | 30±4.93 | 37±4.15 | 0.08 |
| Median obs/pred mFS | 1.18 | -0.69 | 0.07 |
| 25th percentile obs/pred mFS | -1.23 | -1.66 | 0.08 |
| 75th percentile obs/pred mFS | 2.02 | 1.13 | 0.08 |
| Lateral TDs, cm/sec | 9.18±1.94 | 8.90±2.12 | 0.49 |
| Septal SR, 1/s | -1.25±0.30 | -1.02±0.33 | <0.001 |
| Lateral SR, 1/s | -1.20±0.28 | -1.02±0.41 | 0.01 |
| Septal S, % | -23.29±5.65 | -16.16±5.40 | <0.001 |
| Lateral S, % | -19.31±5.18 | -14.86±8.46 | 0.001 |

Data are presented as mean ± standard deviation and median, percentile values
*- unpaired Student's t test, Mann Whitney U test
EF- ejection fraction, cESS- circumferential end-systolic stress, eFS- endocardial fractional shortening, , mESS- meridional end-systolic stress, mFS- mid-wall fractional shortening, S- systolic strain, SR- systolic strain rate, TDs- tissue Doppler systolic motion

**Table 3. Correlation between the echocardiographic parameters in the control group**

| | mESS | LVMI |
|---|---|---|
| Septal SR, 1/s | r=-0.58 p=0.693 | r=-0.283 p=0.051 |
| Lateral SR, 1/s | r=-0.32 p=0.830 | r=-0.036 p=0.811 |
| Septal S, % | r=0.226 p=0.122 | r=-0.32 p=0.829 |
| Lateral S, % | r=0.138 p=0.349 | r=-0.044 p=0.767 |

LVMI - left ventricle mass index, mESS - meridional end-systolic stress, S - strain, SR - strain rate

**Table 4. Correlation between the echocardiographic parameters in the hypertensive group**

| | mESS | LVMI |
|---|---|---|
| Septal SR, 1/s | r=-0.226 p=0.091 | r=-0.158 p=0.241 |
| Lateral SR, 1/s | r=-0.213 p=0.112 | r=-0.179 p=0.183 |
| Septal S, % | r=-0.129 p=0.338 | r=-0.146 p=0.278 |
| Lateral S, % | r=-0.165 p=0.220 | r=-0.192 p=0.153 |

LVMI - left ventricle mass index, mESS - meridional end-systolic stress, S - strain, SR - strain rate

strain rate measurements, in newly diagnosed and never treated mild to moderate hypertensive patients while standard left ventricular systolic echocardiographic parameters remain normal.

Several studies using standard echocardiographic approaches have reported that longitudinal left ventricular systolic function remains normal in hypertensive patients with depressed circumferential midwall performance (13-16). After the develop-

ment of new echocardiographic modalities, which directly measure myocardial contractility, some conflicting reports have emerged (2, 10). Standard M-mode echocardiographic indices are not much sensitive and reliable in terms of making decision about myocardial contractility in hypertensive patients. In M-mode echocardiographic analysis, we did not determine statistically significant differences between the normotensive and hypertensive subjects with respect to longitudinal and circumferential left ventricular systolic performance (Table 2). There were significant inverse correlations between $_m$ESS and $_e$FS in both normal and hypertensive groups and these results are consistent with those obtained from the study by De Simone et al. (13). In our study, $_m$ESS was not statistically correlated with strain and strain rate measurements in both groups. Therefore, we think that strain and strain rate may be independent of afterload but this relation should be verified in further studies.

By use of strain rate imaging, longitudinal systolic dysfunction was reported in different groups of patients despite normal EF and $_e$FS. Koyama et al. (9) demonstrated early impairment in longitudinal left ventricular systolic function in amyloid patients with normal EF and $_e$FS by use of strain rate analysis, but not by TDV. Ballo et al. (10) recently indicated, by using only TDV together with standard M-mode imaging of the left ventricle and M-mode measurement of atrioventricular plane displacement, that systolic impairment may occur earlier in longitudinal than circumferential performance in hypertension. In strain and strain rate analysis, we determined impaired longitudinal left ventricular systolic function in hypertensive patients despite normal EF and stress-adjusted $_e$FS but we did not obtain similar results in TDV assessment. Therefore, we think that early longitudinal left ventricular systolic dysfunction may be determined by use of strain and strain rate analysis despite other systolic parameters obtained from standard left ventricular M-mode echocardiography remain normal in never treated hypertensive patients.

Although standard M-mode echocardiography tends to overestimate longitudinal systolic performance when the left ventricular wall thickness is increased in hypertensive patients, Saghir et al. (12) reported diminished longitudinal systolic strain and strain rate in hypertensive left ventricular hypertrophy. In that study, LVMI was severely increased in hypertensive patients. We did not find a significant correlation between the LVMI and strain and strain rate measurements. This was probably due to the narrow range of LVMI values in the patient group, which had statistically significant but mild left ventricular hypertrophy.

A recent study investigated whether Doppler tissue imaging (tissue velocity, strain, and strain rate) could be useful to detect subtle left ventricular dysfunction in patients with aortic stenosis and changes in regional myocardial function after aortic valve replacement (AVR). The authors concluded that strain and strain rate parameters seemed to relate to LV function and aortic stenosis severity. They seemed to be superior to tissue velocity and conventional echocardiography in detecting subtle changes in myocardial function after AVR before LV mass and LV function showed improvement (22). In another study (23), the authors sought to define the impact of changes in LV loading conditions on myocardial deformation parameters. They revealed that myocardial deformation parameters change significantly immediately after AVR for aortic stenosis or aortic insufficiency indicating a dependency of determined myocardial deformation parameters on LV preload and afterload (23).

### Limitations of the study

Our study has also some limitations. In our study, we aimed to investigate the impact of hypertension on systolic myocardial function by different echocardiographic techniques. To avoid the effect of various factors, we excluded, subjects with diabetes mellitus, coronary artery disease, obesity and previous treatment for hypertension and/or older than 65 years. The exclusion criteria limited the number of subjects enrolled. The narrow range of LVMI values, the lack of longitudinal systolic function assessment according to different left ventricular geometric patterns were the other main limitations of our study.

## Conclusion

In newly diagnosed and never treated mild to moderate hypertensive patients, early impairment in longitudinal left ventricular systolic function may be documented by SR imaging, which is afterload independent, at a time when the other parameters obtained from standard M-mode echocardiographic analysis remain normal. Therefore, we think that previous studies on left ventricular systolic function in hypertensive patients should be re-interpreted according to tissue Doppler echocardiography modalities.

**Conflict of interest:** None declared.

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