The Egyptian Journal of Hospital Medicine (April 2019) Vol. 75 (3), Page 2467-2474

Strain/Strain Rate Imaging of Impaired Left Atrial Function in Patients with Metabolic Syndrome

Sameh Refaat Hassan Allam, Abd El-Aziz Rezk Hassan Sheredah, Mohammad Al-Deftar, Ahmad Kamal Mohammad Hashem*

Department of Cardiology, Al-Azhar University, Cairo, Egypt

*Corresponding author: Ahmad Kamal Mohammad Hashem; Mobile: 01143279799; Email: Ahmad.binkamal@gmail.com

ABSTRACT

Background: Metabolic syndrome (MS) predisposes to left ventricular dysfunction and heart failure, however, alterations in left atrial (LA) function in MS are unknown. **Objectives:** We aimed to use strain/strain rate (SR) imaging to investigate the effect of MS on LA function. **Subjects and Methods:** This prospective case control study included a total of 100 subjects divided in to 75 metabolic syndrome (MS) patients referred to Al-Azhar university hospital outpatient clinic for evaluation and treatment of hypertension and/or diabetes mellitus and 25 age and sex matched apparently healthy volunteers as a control group. All subjects underwent conventional echocardiographic examination and assessment of LA function by speckle tracking. Partial correlation and multiple stepwise regression analyses were used to determine the risk factors for impaired LA function.

Results: Compared with the controls, the MS patients showed significantly lower levels of mean strain, mean peak systolic SR and mean peak early diastolic SR ($P<0.05$ for all), with no difference in the mean peak late diastolic SR. Central obesity, hypertension, dyslipidemia and uncontrolled diabetes were independent risk factors for impaired LA function.

Conclusion: SR imaging is reliable in assessing LA function in MS patients.

Keywords: Metabolic syndrome, Left atrial function, Speckle tracking, Echocardiography.

INTRODUCTION

Metabolic syndrome (MS) is a condition characterized by the accumulation of multiple risk factors (insulin resistance, hyperglycemia, dyslipidemia, hypertension, visceral obesity) for cardiovascular disease in an individual with a background of obesity and/or lack of exercise [(1)].

Even more with the change of the modern lifestyle and diet structure, incidence of MS increased year by year, it is greatly endangering people's health. However, it is not known whether MS is also associated with abnormal cardiac function. If MS indicates persons who have already developed abnormal left ventricular (LV) function, early recognition of MS would be important [(2)].

Left ventricle diastole occurs in order for the left ventricle (LV) to fill adequately with enough blood, at a low enough pressure, to prevent pulmonary congestion from occurring. This process is referred to as, diastolic function [(3)].

Metabolic syndrome is common and it is associated with increased cardiovascular morbidity and mortality as well as with increased risk of heart failure through multiple complex metabolic reactions most prominent among which are altered insulin signaling, glycoltoxicity, lipotoxicity, increase cytokine activity and intramyocyte and/or interstitial deposition of triacylglycerol plus effect of endothelial dysfunction [(4)].

A 2D strain echocardiographic method has been introduced that measures myocardial deformation by tracking localized acoustic markers frame by frame (speckle tracking). This method has been used for noninvasive assessment of global and regional myocardial strain in the left and the right ventricle, avoiding the angular sensitivity of tissue Doppler echocardiography [(5)].

The Aim of this Study: assessment of left atrial (LA) function in patients with metabolic syndrome by 2D speckle tracking echocardiography.

PATIENTS AND METHODS

This prospective case control study was conducted between March 2018, and March 2019 on (100) subjects divided into 2 groups; group I (The patient group): (75) metabolic syndrome patients who were referred to Al-Azhar University Hospital Outpatient Clinic for evaluation and treatment of hypertension and/or diabetes mellitus and group II (Control Group): (25) age and sex matched healthy volunteers as a control group.

Approval of the ethical committee and a written informed consent from all the subjects were obtained.

Diagnosis of MS: according to International Diabetes Federation (IDF) metabolic syndrome is defined as the presence of central obesity (was

Received:28/1/2019
Accepted:28/2/2019

determined according to the IDF criteria [6] as the waist circumference ≥94 cm for men and ≥80cm for women) plus any two of the following four factors:

- Low level of high-density lipoprotein (HDL) (or specific treatment for this lipid abnormality).
- High triglycerides (or specific treatment for this lipid abnormality).
- Arterial hypertension (or treatment of previously diagnosed hypertension).
- Fasting hyperglycemia (or previously diagnosed diabetes).

Exclusion criteria: It included patients with ejection fraction <55% or with symptoms or sign of heart failure, patients with known coronary artery disease, patients with significant valvular disease, patients with prosthetic mitral valve and patients with atrial fibrillation or other rhythm disturbances.

The following data were collected:

A. Complete and detailed medical History: With attention to hypertension, DM and family history of premature coronary artery disease.

B. Full clinical examination including waist circumference, body surface area [7], heart rate, rhythm, systolic, diastolic blood pressure, heart, and chest auscultation.

C. Conventional echocardiographic Doppler study and 2D speckle tracking were performed using Philips iE33 X Matrix ultrasound machine using X5-1 matrix array transducers (Philips Medical Systems, Andover, USA).

Systolic function assessment

a. Ejection fraction (EF%) and fractional shortening (FS%) were performed to evaluate LV systolic function by 2D echo.

b. LVEDV and LVESV were calculated from the apical 2-and 4-chamber views using a modified biplane Simpson's method.

c. Ejection fraction (EF%) was calculated as percentage changes of volumes of the left ventricle in diastole and systole. The LV ejection fraction (EF%) was automatically calculated as follows: (EF%) = (EDV-ESV)/EDV×100 [8].

Diastolic function assessment

LV diastolic function was evaluated using the four recommended variables for identifying diastolic dysfunction[9].

Assessment of LA function by 2D Speckle Tracking Echocardiography (STE):

Two LV apical views; apical four-chambers and two chambers views were acquired at a frame rate ranging 59–82 frame/s; mean 72+6 frame/s. 5 consecutive cardiac cycles were acquired at end-expiration breath holding and digitally stored on a hard disk for offline analysis.

Offline analysis was performed using Qlab software (version 10, Philips medical systems) using 2D STE software. The LA endocardial border was traced and corrected manually to matches the LA STE (as the program intended for the assessment of LV STE). On the basis of this line, longitudinal strain and strain rate were assessed in the LA walls. The global LA strain obtained from averaging the strain values of 17 LA segments (as the program intended for the assessment of LV STE) were calculated and used for comparisons between control and metabolic syndrome groups[10] **(Figures 1 and 2)**

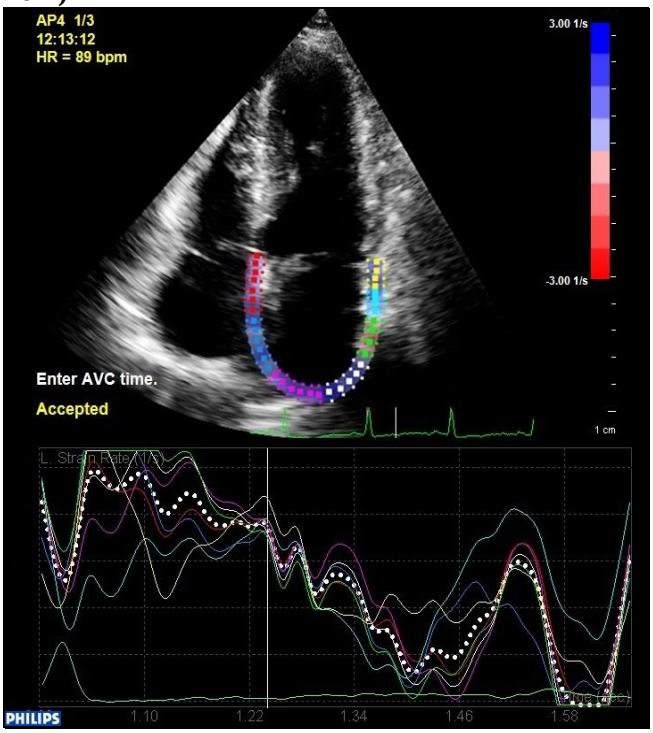

Figure (1): Left atrial function by speckle-tracking echocardiography showing atrial strain rate measurements in a metabolic syndrome patient (apical 4 chamber view).

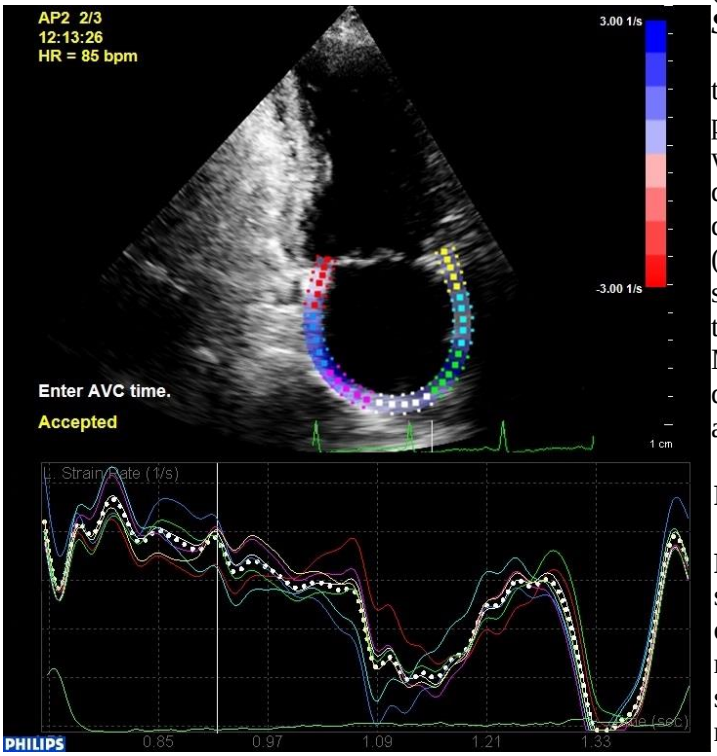

Figure (2): Left atrial function by speckle-tracking echocardiography showing atrial strain rate measurements in a metabolic syndrome patient (apical 2 chamber view).

Statistical analysis

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 20.0 for windows. Data are presented as the mean ± standard deviation (SD). Continuous normally distributed data were compared by the independent sample t test (two-tailed) to detect the differences between the studied groups. Partial correlation was used to study the correlation between the continuous variables. Multiple stepwise regressions was used between different variables, the level of significance was accepted if the *P* value < 0.05.

RESULTS

Regarding clinical data : Table (1) and figure (3): show that there was no statistical significant difference between the two groups (I and II) as regard age or height, but, there was statistical significant difference between the two groups as regard weight, body mass index, waist circumference, hip circumference.

Table (1): Comparison of some clinical data among the studied patients and control groups:

Clinical data	Patients (N = 75)	Control (N = 25)	*P* value
Age (years)	31.89±4.092	30.28 ± 3.482	>0.05
Weight (kg)	82.213±4.9846	67.400 ± 6.2650	<0.001
Height (cm)	170.787± 4.2116	171.160±5.0718	>0.05
BMI (kg/m^2)	28.2467±2.33102	22.9588±1.19339	<0.001
Waist circumference	103.9400±5.06109	77.6000±7.75672	<0.001
Hip circumference	117.5733±5.53471	91.6400±7.48265	<0.001
Waist / hip ratio	0.8841±0.01638	0.8458±0.02267	<0.001
Body surface area	1.9738±.06148	1.7891±10705	<0.001
Systolic BP	129.933±10.2170	106.600±11.9652	<0.001
Diastolic BP	81.333± 7.3674	69.800±8.4755	<0.001
HDL	54.853±9.7255	72.840±7.4815	<0.001
FBG	116.747±18.6338	94.360±5.8799	<0.001
FTGD	179.373±43.4171	89.840±8.7163	<0.001

BSA; body surface area, BMI; body mass index, SD: Standard deviation.
P value > 0.05 = insignificant, P < 0.05 = significant, P < 0.001 = highly significant.

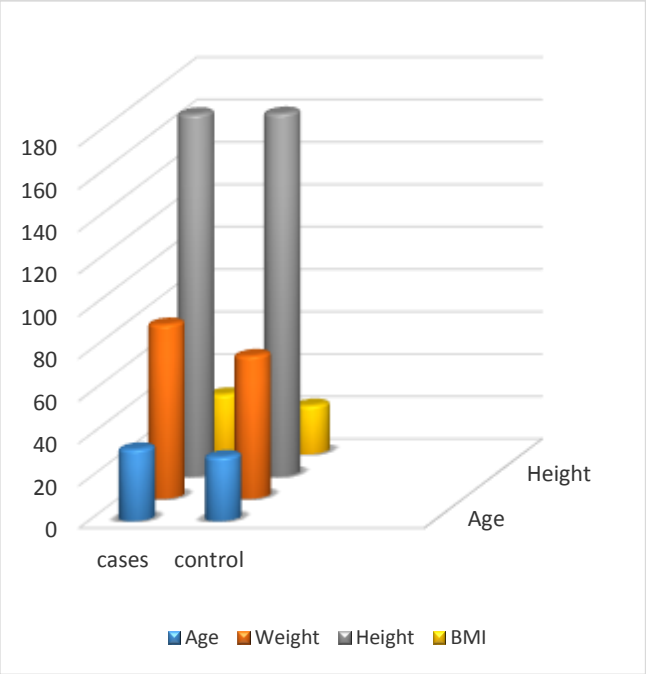

Figure (3): Comparison of some demographic data between cases and control

Regarding Lab investigation and blood pressure: there was statistical significant difference between the two groups as regard lab investigations (Table 2).

Table (2): Comparison of blood pressure and lab investigations among the studied patients and control groups:

Clinical data	Patients (N = 75)	Control (N = 25)	*P* value
Systolic BP	129.933±10.2170	106.600±11.9652	<0.001
Diastolic BP	81.333± 7.3674	69.800±8.4755	<0.001
HDL	54.853±9.7255	72.840±7.4815	<0.001
FBG	116.747±18.6338	94.360±5.8799	<0.001
FTGD	179.373±23.4171	89.840±8.7163	<0.001

HDL: High-density lipoprotein; TG: Triglycerides; SD: Standard deviation, P < 0.001 = highly significant.

Regarding Conventional Echocardiography: LA dimension, LVEDD, LV wall thickness and LV mass were significantly higher in the metabolic syndrome group than the controls, while there were no differences regarding FS, EF and LV mass index. Furthermore, the diastolic function was more impaired in metabolic syndrome patients compared to the controls as evidenced by increasing E / E\ Ratio, LA volume index, TR jet velocity and decreasing septal E\ and Lateral E\ in the metabolic syndrome group (Table 3

Table (3): Comparison of echocardiographic parameters among the studied patients and control groups:

Echo parameters	Patients (N = 75)	Control (N = 25)	*P* value
Aortic dimension	3.007±.3379	2.728 ±.3542	<0.001
Left atrial dimension	3.4560±.24782	3.0120±.19647	<0.001
Inter ventricular septum	0.848±.1389	0.784±.0898	<0.05
Left ventricular end diastolic dimension	4.843 ± .1749	4.788 ± .2555	>0.05
Left ventricular end systolic dimension	3.115 ± .2409	3.088 ± .2651	>0.05
Left ventricular posterior wall dimension	0.796 ± .0667	0.764 ± .0569	>0.05
Ejection fraction by M Mode	65.4072 ± 4.77690	65.2588 ±-4.78522	>0.05
Ejection fraction by two dimensional mode	64.644 ± 4.8300	64.476 ± 4.6824	>0.05
Fraction shortening	35.673 ± 4.4645	35.504 ± 4.3147	>0.05
Left ventricular mass	148.960 ± 15.0139	127.600 ±15.8640	<0.001
Left ventricular mass index	75.526 ± 7.8562	71.697 ± 10.8461	>0.05
E wave	71.631 ± 15.5706	71.080 ± 2.8730	>0.05
A wave	74.213 ±11.4520	54.532 ± 3.9469	<0.001
E/A ratio	0.9699±.35850	1.3028±.07792	<0.001
Septal E prime	6.520 ± .9665	9.132 ± .8892	<0.001
Lateral E prime	9.540 ± 1.1263	13.012 ±1.0717	<0.001
E/E prime	9.0069 ± 2.12198	6.4528 ±.45147	<0.001
Left atrial volume in apical 2 chamber view	53.529 ± 12.4657	40.364 ± 3.2493	<0.001
Left atrial volume in apical 4 chamber view	56.029 ± 8.3771	44.684 ± 2.9639	<0.001
Mean left atrial volume	54.7793±9.57349	42.5240 ± 2.24022	<0.001
Left atrial volume index	27.7583 ± 4.79939	23.8860 ± 2.33072	<0.001

IVS: interventricular septum; **LA**: left atrium; **AO**: Aorta; **PWD**; posterior wall dimension; **End SD**: End systolic diameter; **End DD**: End diastolic diameter; **EF**: Ejection fraction; **FS**: fraction shortening; **E**: E velocity; **A**: A velocity; **MS**: Metabolic syndrome. P value > 0.05 = insignificant, P < 0.05 = significant, P < 0.001 = highly significant.

Analysis of Left atrial deformation data: we found that the mean LS and SSR, considered indicators of the LA reservoir function, were highly significantly lower for the MS patients than for the controls. The mean ESR, an indicator of the LA conduit function, was also highly significantly lower for the MS patients than for the controls. The controls and MS patients did not differ in mean **ASR**, an indicator of LA **booster** function (Table 4).

Table (4): Comparison of speckle tracking echocardiographic parameters among the studied patients and control groups:

Echo parameters	Patients (N = 75)	Control (N = 25)	P-value
Systolic strain rate in apical 2 chamber view	1.2469 ± 0.24287	1.6188 ±.19484	??
Early diastolic (E wave) strain rate in apical 2 chamber view	-1.22240 ± .277741	-1.78640 ±.288457	??
Late diastolic (A wave) strain rate in apical 2 chamber view	-1.5072 ±.12679	-1.4968 ±.10873	??
Longitudinal strain in apical 4 chamber view	21.880±3.4168	28.760±3.1395	??
Systolic strain rate in apical 4 chamber view	1.2796 ±.27820	1.6848 ±.15546	??
Early diastolic (E wave) strain rate in apical 4 chamber view	-1.1597±.22283	-1.7868 ±.14132	??
Late diastolic (A wave) strain rate in apical 4 chamber view	-1.5264 ±.10477	-1.6000 ±.05568	??
Mean longitudinal strain	21.4867 ± 3.42089	28.4200 ± 3.34378	0.001
Mean systolic strain rate	1.2633 ±.25796	1.6518 ±.17114	0.001
Mean early diastolic (E wave) strain rate	-1.1911±.24599	-1.7866 ±.21191	0.001
Mean late diastolic (A wave) strain rate	-1.5168 ±.10462	-1.5484 ±.07659	>0.05

P value > 0.05 = insignificant, P < 0.05 = significant, P < 0.001 = highly significant.

Multiple stepwise regression analyses: were used to determine the risk factors for impaired LA function (Table 5).

Table (5): Multiple stepwise regression analysis of mean strain/strain rate parameters of the left atrium and some clinical characteristics:

Variable	B	SE	β	P-value
Mean longitudinal strain				
Systolic blood pressure	-0.056	0.030	- 0.182	>0.05
Waist /hip ratio	38.736	19.477	0.210	0.05
Fasting triglyceride	-0.023	0.008	-0.276	<0.05
Fasting blood glucose	-0.044	0.019	-0.183	<0.05
Age	-0.171	0.089	-0.160	>0.05
Waist circumference	-0.120	0.046	-0.339	<0.01
Mean systolic strain rate				
Systolic blood pressure	-0.004	1.020	- 0.216	>0.05
Waist /hip ratio	2.261	1.363	0.190	>0.05
Fasting triglyceride	-0.001	0.001	-0.255	<0.05
Fasting blood glucose	-0.003	0.001	-0.172	>0.05
Age	-0.114	0.006	-0.204	>0.05
Waist circumference	-0.005	0.003	-0.227	>0.05
Mean early diastolic strain rate				
Systolic blood pressure	-0.006	0.002	0.254	<0.01
Waist /hip ratio	-2.815	1.382	-0.197	<0.05
Fasting triglyceride	-0.002	0.001	0.318	<0.001
Fasting blood glucose	-0.002	0.001	0.106	>0.05
Age	0.009	0.006	0.106	>0.05
Waist circumference	0.010	0.003	0.370	<0.01

B = unstandardized regression coefficient; **SE** = standard error of the coefficient; **β** = standardized coefficient; **P-value**: significant if < 0.05

The result reveals that central obesity, hypertension, dyslipidemia and diabetes were independent risk factors for impaired LA function, with P value < 0.05 in most parameters.

DISCUSSION

The present study was designed to evaluate left atrial function in metabolic syndrome patients compared to control subjects (case/control study) using 2D-speckle tracking echocardiography based on strain and strain rate imaging parameters: [Longitudinal strain (LS), systolic strain rate (SSR), early diastolic strain rate (ESR), and late diastolic strain rate (LSR)] .

Strain and SR imaging in evaluating LA function:

The novel echocardiographic techniques, such as tissue Doppler imaging in daily development, enhanced the ability to assess regional myocardial function noninvasively[11].

The recently emerged technique, strain/SR imaging, can serve as a method to quantify LA, LV and RV regional myocardial function independent of cardiac rotational motion and a tethering effect [12], as well as to enable quantitative assessment of LA function in patients with paroxysmal atrial fibrillation and atrial septal defect[13].

LA function contributes greatly to LV filling through the following three components: a reservoir phase during systole, a conduit phase during diastole and an active contractile component (when sinus rhythm is present) during late diastole.

In our study we find that:

- The mean LS and SSR, considered indicators of the LA reservoir function, were significantly lower for the MS patients than for the controls, where P-value < 0.001; (highly significant).
- The mean ESR, an indicator of the LA conduit function, was significantly lower for the MS patients than for the controls, where P-value < 0.001; (highly significant).
- The controls and MS patients did not differ in mean **ASR**, an indicator of LA **booster** function.

Also the present study, showed that there was statistical significant difference between the two groups (I and II) as regard weight, body mass index (BMI), waist circumference, hip circumference, fasting plasma glucose, HDL-cholesterol and fasting triglycerides. Also, there was no statistical significant difference between the two groups (I and II) as regard height.

These findings are similar to the findings of **Ning *et al.*[14],** who studied the using of strain/strain rate (SR) imaging to investigate the effect of MS on LA function. They have a total of 177 MS patients and 156 normal subjects underwent echocardiography. They used Strain and SR tissue Doppler imaging values to evaluate LA function. Multiple stepwise regression analyses were used to determine the risk factors for impaired LA function. Compared with the controls, the MS patients showed significantly lower levels of mean strain, mean peak systolic SR and mean peak early diastolic SR (P<0.001 for all), with no difference in the mean peak late diastolic SR. They found that central obesity, hypertension, dyslipidemia and LV diastolic abnormality were independent risk factors for impaired LA function.

The same was found in our study by using multiple stepwise regression analysis of strain/strain rate parameters of the left atrium and clinical characteristics. We found that central obesity, hypertension, dyslipidemia and diabetes were independent risk factors for impaired LA function, with P value < 0.05 in most parameters.

Previous studies have demonstrated that strain, SSR and LA deformation during systole could be used as indices of the LA reservoir function in collecting blood from the pulmonary vein influx to the left atrium and that the mean ESR was assessed in a phase when the left atrium works mainly as a conduit and could be used as an index of LA myocardial conduit function [13,14].

The efficacy of strain/SR imaging, however, has not been determined in patients with MS.

Our study of strain/SR imaging revealed that the LA reservoir and conduit functions were seriously impaired in MS patients, as reflected by a decreased mean S, SSR and ESR.

Impact of MS on LA reservoir and conduit function

The individual components of MS are associated with abnormal cardiac structure and function. These components tend to have synergistic effects on cardiac functions.

Reilly *et al.* [15] demonstrated that the effect of MS on the cardiovascular system is greater than the sum of its components. In our study, we found that impaired LA function in patients with MS was independently associated with hypertension, central obesity, dyslipidemia and insulin resistance. Obesity, particularly central obesity, is an important risk factor for cardiac dysfunction independent of the other components of MS.

Wong *et al.* [16] described a potential pathophysiologic mechanism for the cardiomyopathy of obesity that begins with increased cardiac output, enhanced LV volume and

enlarged LA diameter. Adipose tissue might contribute to circulating angiotensin II, which promotes myocardial tissue growth and influences the aldosterone level, which in turn mediates myocardial fibrosis. Myocardial fibrosis in moderate and severely obese subjects was confirmed by myocardial biopsy.

Our results indicated that central obesity contributes to decreased LA reservoir and conduit function.

Because the impact of hypertension on cardiac structure and function has been widely studied in MS cohorts, the alterations in LA function in patients with hypertension have been thoroughly demonstrated. **Kokubu *et al.*** [17] showed that the impaired LA function in hypertensive patients might be attributable to LA myocardial fibrosis, as shown in an animal study.

We found that systolic BP is the independent factor most responsible for decreased LA reservoir and conduit function.

Although the underlying mechanism of MS that is responsible for increased cardiovascular risk has not been elucidated, the possibilities were reviewed by **Deedwania** [18], who concluded that insulin resistance is the basic mechanism.

The present data support the notion that progressive insulin resistance and alterations in myocardial substrate metabolism lead to myocardial contractile dysfunction associated with obesity[19]. Therefore, diabetes in MS and type 2 diabetes patients might have an important role in cardiac dysfunction .

We found a significant relationship between LA function and diabetes.

Interestingly, we found a weak but independent relationship between LA function and dyslipidemia, which has rarely been demonstrated. Dyslipidemia, an independent risk factor for increased cardiovascular mortality and morbidity [20] can cause vascular endothelial dysfunction, leading to abnormal myocardium infusion and reconstruction of myocardial cells and the interstitium. Therefore, dyslipidemia may have harmful effects on LA function, although the exact mechanisms remain unclear.

Alteration of LA systolic function in MS

The mean LSR was negative during late diastole, which indicates shortening of the LA wall. We found no significant difference in the mean LSR between the control and MS groups, which indicates that MS had no effect on LA myocardial contractility.

Similarly, **Kokubu *et al.*** [17] found no significant difference in LA booster function in hypertensive patients using SR imaging, in contrast to conventional echocardiographic imaging.

Possible reasons for the discrepant results might be that SR imaging reflects regional LA myocardial functions rather than global functions. Compared with the conventional echocardiographic parameters (that is, the LA myocardium and interstitium fibrosis), SR imaging might not be able to detect these subtle changes in the LA wall.

In summary, patients with MS have impaired LA function, and SR imaging is reliable in assessing it. Central obesity, hypertension, dyslipidemia and decreased insulin sensitivity are independent risk factors for impaired LA function; however, the precise mechanisms remain to be elucidated.

CONCLUSION

In conclusion, the current study showed that, metabolic syndrome group have an association with abnormal left atrial performance based on strain and strain rate parameters [Longitudinal strain (LS), systolic strain rate (SSR), early diastolic strain rate (ESR), and late diastolic strain rate (LSR)]. So, patients with metabolic syndrome should receive aggressive therapy to avoid occurrence of heart failure and atrial fibrillation in the future.

Study limitations

Our study included subjects with different onset, severity, and treatment modalities of metabolic syndrome components. The small number of the study participants may have influenced our results.

Rapid events during the cardiac cycle (e.g. isovolumic phases) may disappear altogether, and peak strain rate (SR) may be reduced due to under-sampling. Higher frame rates could reduce the under-sampling problem, although this will result in a reduction of spatial resolution and consequently, less optimal ROI tracking.

Strain, strain rate (SR) and conventional echo Doppler measurements were not measured at the same cardiac cycle; but meticulous care was done to take measurements at cycles with nearly equal R-R interval.

All subjects in our study did not have any signs or symptoms of angina, and had normal findings on electrocardiogram and on 2-D echocardiography, we

could not completely exclude asymptomatic coronary artery disease.

REFERENCES

1. **Harris MF (2013):** The metabolic syndrome. Aust Fam Physician, 42: 524–527.
2. **Briand M, Lemieux I, Dumesnil JG *et al.* (2006):** Metabolic syndrome negatively influences disease progression and prognosis in aortic stenosis. J Am Coll Cardiol., 47(11):2229-36.
3. **Chung C, Shmuylovich L & Kovács S (2015):** What global diastolic function is, what it is not, and how to measure it. Am. J. Physiol.Heart Circ. Physiol., 309:392-406.
4. **Alessi MC, Juhan I (2008):** Metabolic syndrome, haemostasis and thrombosis. Thromb Haemost., 99(6):995 1000.
5. **Blessberger H, Binder T (2010):** Non-invasive imaging: two dimensional speckle tracking echocardiography basic principles. Heart, 96:716-722.
6. **Alberti KG, Zimmet P and Shaw J (2006):** Metabolic syndrome-a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabetic Med., 23(5):469-80.
7. **Du Bois D, Du Bois EF (1916):** A formula to estimate the approximate surface area if height and weight be known". Archives of Internal Medicine, 17 (6): 863-71.
8. **Bulwer JW, Lang RM, Bierig M *et al.* (2009):** Assessment of Left Ventricular Function by Intensivists Using Hand-Held Echocardiography. J Card Fail., 15:782–789.
9. **Nagueh SF, Appleton CP, Gillebert TC *et al.* (2016):** Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr., 29:277-314.
10. **Sirbu C, Herbots L, D'hooge J *et al.* (2006)**: Feasibility of strain and strain rate imaging for the assessment of regional left atrial deformation , Eur J EcEchocardio., 7:199-208.
11. **Borlaug BA, Melenovsky V, Redfield MM *et al.* (2007) :** Impact of arterial load and loading sequence on left ventricular tissue velocities in humans. J Am Coll Cardiol., 50: 1570–1577.
12. **Donal E, Raud-Raynier P, Racaud A *et al.* (2005):** Antitative regional analysis of left atrial function by Doppler tissue imaging-derived parameters discriminates patients with posterior and anterior myocardial infarction. J Am Soc Echocardiogr., 18: 32–38.
13. **Watanabe T, Kawasaki M, Tanaka R *et al.* (2013):** Association among blood pressure control in elderly patients with hypertension, left atrial structure and function and new-onset atrial fibrillation: a prospective 2-year study in 234 patients. Hypertens Res., 36: 799–806.
14. **Ning-ning Fang, Dong-xin Sui, Jin-gui Yu *et al.* (2015):** Strain/strain rate imaging of impaired left atrial function in patients with metabolic syndrome, Hypertension Research, 38, 758–764.
15. **Reilly MP, Rader DJ (2003):** The metabolic syndrome: more than the sum of its parts? Circulation, 108: 1546 –1551.
16. **Wong CY, O'Moore-Sullivan T, Leano R *et al.* (2003):** Alterations of left ventricular myocardial characteristics associated with obesity. Circulation, 110: 3081 –3087.
17. **Kokubu N, Yuda S, Tsuchihashi K *et al.* (2007):** Noninvasive assessment of left atrial function by strain rate imaging in patients with hypertension: a possible beneficial effect of renin-angiotensin system inhibition on left atrial function. Hypertens Res., 30: 13 –21.
18. **Deedwania PC (2002):** Clinical significance of cardiovascular dysmetabolic syndrome. Curr Control Trials Cardiovasc Med., 3: 2-16.
19. **Peterson LR, Herrero P, Schechtman KB *et al.* (2004):** Effect of obesity and insulin resistance on myocardial substrate metabolism and efficiency in young women. Circulation, 109: 2191 –2196.
20. **Gordon DJ, Rifkind BM (1989):** High-density lipoprotein—the clinical implications of recent studies. N Engl J Med., 321: 1311–1316.