

Assessment of Right Ventricular Function by Speckle Tracking Echocardiography in Patients with Metabolic Syndrome

Ibrahim Mohammed Ibrahim^{*}, Attia Morsy Shokr, Mostafa Attia Al-Sawasany

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

Email address:

ibrahim.mohammed198800@gmail.com (I. M. Ibrahim)

^{*}Corresponding author

To cite this article:

Ibrahim Mohammed Ibrahim, Attia Morsy Shokr, Mostafa Attia Al-Sawasany. Assessment of Right Ventricular Function by Speckle Tracking Echocardiography in Patients with Metabolic Syndrome. *Cardiology and Cardiovascular Research*.

Vol. 5, No. 4, 2021, pp. 157-165. doi: 10.11648/j.ccr.20210504.11

Received: September 21, 2021; **Accepted:** October 18, 2021; **Published:** October 28, 2021

Abstract: Metabolic syndrome (MetS) and visceral adiposity are crucial cardio metabolic risk factors. There is evidence of subclinical left ventricular myocardial dysfunction in individuals with metabolic syndrome (MetS). However, the effect of MetS on the right ventricle (RV) is yet unknown. By using 2D Speckle Tracking Echocardiography, we investigated the link between MetS and right ventricle function. This study was conducted on 50 MetS patients and 25 age and gender matched individuals (control group). The MetS is diagnosed when presence of ≥ 3 American Heart Association/National Heart, Lung, and Blood Institute criteria. All individuals had sufficient laboratory assays as well as a thorough 2D examination including tissue Doppler imaging (TDI) and R. V global longitudinal strain (GLS) during the period between November 2019 and December 2020. The metabolic group had a statistically significant lower RV- GLS (-18.27 ± 2.16 in MetS subjects vs. -26.64 ± 3.05 in control subjects, $P < 0.001$), a significantly lower E/A ratio (0.95 ± 0.12 in MetS subjects vs. 1.14 ± 0.15 in controls, $P < 0.001$), and a statistically significant increase in the E/Em ratio (5.66 ± 1.03 in MetS subjects vs. 4.24 ± 0.46 in controls, $P < 0.001$). Other echocardiographic or functional capacity tests revealed no significant differences between the two groups. We concluded that MetS was associated with preclinical right ventricle systolic dysfunction detected by 2D-STE observed with Normal RV by TAPSE and FAC and Normal left ventricular ejection fraction (LVEF) in addition to RV diastolic dysfunction.

Keywords: Echocardiography, Metabolic Syndrome, Right Ventricle, Lipid Profile and Speckle Tracking Echocardiograph

1. Introduction

Metabolic syndrome (Met S) is a massive health problem that combines clinical, biological, and biochemical trials, affecting people worldwide. It consists of elevated blood pressure, atherogenic dyslipidemia, elevated blood glucose, and insulin resistance [1].

The propagation of metabolic syndrome ranges greatly among populations worldwide, ranging from 8% to 84%. The propagation of metabolic syndrome and its components are affected by genetic history, social status, diet, and lifestyle. The incidence of metabolic syndrome varies depending on demographic factors (such as race, age, and gender), geographic area, and the definition standard [2].

A long time ago, the right ventricle (RV) was thought not

to have an essential function in the heart, and therefore it was completely overlooked. But in the last 50 years, RV became recognized for its importance in many physiological and pathological diseases, then had a lot of interest [3].

Over the previous 25 years, technology has advanced significantly in echocardiography. A single test can yield several structural and physiological indices. From one-dimensional to real-time three-dimensional, systolic to diastolic, physiology to pathology, global to regional, the sonographer or clinician may assess RV function in great detail [4].

STE imaging is defined as a non-invasive ultrasound technique that provides an objective and quantifiable assessment of global and regional myocardial function independent of insulation and heart translational motions [5]

Speckle tracking echocardiography is a highly sensitive technique for detecting preclinical systolic abnormalities and mild myocardial dysfunction [6].

This study aimed to investigate RV function by Global longitudinal strain 2D-STE with the metabolic syndrome by 2D Speckle Tracking Echocardiography.

2. Patients and Methods

2.1. Study Area

During the period from November 2019 - December 2020, this study was carried out at Al-Zahar university hospital – Cardiology Department (Cairo- Egypt).

The study included two groups. First one included 50 patients (26 males and 24 females) with metabolic syndrome, while the control group included 25 participants (11 males and 14 females) with no risk factors of the MetS.

We excluded coronary artery disease patients, LV systolic dysfunction (EF<50%), heart failure, congenital heart conditions, atrial fibrillation, moderate to severe valvular heart disease, pericardial heart disease, previous cerebrovascular insult, severe obesity (body mass index>35), sleep apnea syndrome, kidney failure, poor echo window, and chronic diseases, including obstructive lung disease, pulmonary hypertension, connective tissue disorders, liver cirrhosis, and neoplasms. Patients whose RV strain analysis revealed the loss of two or more segments were excluded from the research.

On the other hand, the study protocol was approved by the local ethics council, and patients and volunteers gave their informed written consent before participating in the study.

- 1) Three International Diabetes Federation and American Heart Association/National Heart, Lung, and Blood Institute criteria were used to define the MetS:
- 2) Waist circumference ≥ 102 and 88 cm in men and women, respectively.
- 3) BP $\geq 130/85$ mmHg.
- 4) HDL-cholesterol <40 and 50 mg/dl in men and women, respectively.
- 5) Triglycerides 150 mg/dl or greater.
- 6) Fasting glucose 100 mg/dl or greater.

Height, weight, and waist circumference were measured and body surface area and BMI were calculated for all participants. Fasting glucose, triglycerides, total cholesterol, low- and high-density lipoprotein (HDL) cholesterol, and HbA1c were all measured. Antihypertensive and glucose-lowering medication administration information was also obtained.

In the morning hours, arterial blood pressure readings were acquired using a standard sphygmomanometer by averaging the results of two consecutive measures made in the sitting position within a five-minute interval after the individual had rested for at least five minutes in that posture.

A systolic blood pressure of 140mmHg, a diastolic blood pressure of 90mmHg, and/or current antihypertensive treatment were considered hypertension [7].

HbA1c>6.5%, fasting serum glucose level ≥ 126 mg/dl, and/or current medical therapy with an oral hypoglycemic agent and/or insulin were considered diabetes [8].

2.2. Trans-thoracic Echocardiography

To reduce interobserver variability, all patients were examined by the same physician. Using a Philips ultrasound system affinity, all patients were examined with a transthoracic echo-Doppler examination in the left lateral position. A matrix probe S4-2 with a multi frequency (2 – 4 MHz) was used to examine all patients, and a simultaneous ECG was displayed alongside all records.

Using the Q-lab software available on the echocardiography machine, speckle images analysis was performed. Three cardiac cycles were obtained with the subject holding his breath in each view for image acquisition. For offline analysis, all images were digitally stored. All measurements were made in accordance with the criteria of the American Society of Echocardiography and the European Association of Cardiovascular Imaging [9].

LV ejection fraction was measured using the biplane Simpson method. Using 2-D echocardiography (M-mode), we assessed left ventricular end systolic and diastolic dimensions, left ventricular posterior wall diameter (LVPWD), inter ventricular septal diameter (IVSD), fractional shortening (FS), anomalies in wall motion, and valvular lesions [9].

Pulsed-wave Doppler of mitral to assess trans mitral velocities was obtained sample volume at 1 mm–3 mm, between mitral leaflet tips during diastole to record velocity profile. Mitral inflow assessment was done by measuring peak early (E) and late (A) diastolic filling velocities and E/A ratio. At the mitral annulus level, doppler imaging (TDI) assessment of myocardial systolic and early and late diastolic velocities were examined (results provided are means from lateral and septal walls) [10].

2.3. Assessment of the RV

The RV outflow tract (RVOT) was assessed using 2D echocardiography in the PLAX (RVOT proximal) and PSAX (RVOT distal, RVOT proximal) views, while the apical 4CH view was used to assess the RV basal diameter (RVD1), RV mid-cavity diameter (RVD2), and RV longitudinal dimension (RVD3). The apical 4CH image was used to get the tricuspid plane systolic excursion (TAPSE). The RV fractional area change (FAC) was determined in the apical 4CH view by dividing the difference of RV area (diastolic–systolic) by the RV end-diastolic area [11].

Tricuspid inflow was assessed using Doppler echocardiography, and the peak early diastolic filling velocity (E vel) and peak late diastolic filling velocity (A vel) were measured. The E/A ratio was calculated by dividing the E velocity by the A velocity.

In the apical 4CH view, pulse-wave TDI was utilized to quantify the lateral peak systolic velocity (RV Smv), lateral early and late diastolic velocities (RV Emv and RV Amv),

and the average E/Em ratio [12].

2.4. Two-dimensional Speckle Tracking Echocardiography (2D-STE)

Standard 2D images were obtained in the RV-focused apical views, with a steady electrocardiographic recording. Global systolic myocardial strain were acquired at a heart rate of 74 (± 18) bpm, after adjusting the sector depth, gain, and size,. By reducing the depth and sector width, the frame rate was increased to 76 \pm 24 fps. The images were digitally saved and analysed offline [13].

By monitoring and averaging three consecutive cardiac cycles, we quantified RV strain using a commercially available LV strain software. The RV speckle tracking images included six segments analysis: the RV septal and free walls' basal, mid, and apical regions. In Figure 1, two examples of the strain of the RV six segments and the RV GLS of both groups are displayed. The speckle pattern change in position from the initial one was then used to compute myocardial strain. By averaging the six segments peak systolic values, peak systolic longitudinal strain was computed. Regional thickening or lengthening and regional thinning or shortening were expressed as a positive and negative numbers, respectively [14].

According to the American Society of Echocardiography and the European Association of Cardiovascular Imaging, normal right ventricular global longitudinal strain (GLS) value is -20% [9].

2.5. Statistical Analysis

Continuous data was presented as mean and standard deviation, whereas categorical data was provided as numbers and percentages (SD). The independent student t test or one way ANOVA test were used to compare means between groups, whichever was more convenient. The Pearson's correlation was used for correlation analysis. An SPSS 26 programme was used for all statistical analysis. A p value of less than 0.05 was deemed significant.

3. Results

Our study included two groups; Met S group included 26 males and 24 females (50 patients) and a control group included 11 males and 14 females (25 participants). No significant differences between both groups regarding age and gender.

Demographic and general characteristics are shown in Table 1. All Met S parameters were significantly higher in individuals with MetS than in controls. The levels of HbA1c, total cholesterol, and LDL cholesterol were also shown to be significantly higher in the MetS group.

Table 1. Demographic Characteristics and Clinical Parameters in MetS and Control Subjects.

Variable	Met s (n=50)	Control (n=25)	value - p
Age (y)	40.14 \pm 8.17	41.8 \pm 11.24	0.624
Sex (female, %)	24 (48%)	14 (56%)	0.514
BMI (kg/m ²)	29.18 \pm 2.14	22.04 \pm 1.48	<0.001
Waist circumference, cm			
Women:	10.7 \pm 6.17	81.14 \pm 3.82	<0.001
Men	110.58 \pm 3.602	86.55 \pm 7.076	<0.001
Heart Rate	74.82 \pm 7.81	76.72 \pm 7.81	0.226
SBP (mmHg)	139 \pm 14	104 \pm 13	<0.001
DBP (mmHg)	84 \pm 8	75 \pm 7	<0.001
Plasma Glucose (mg/dL)	178 \pm 89	85 \pm 7	<0.001
Triglycerides (mg/dL)	161 \pm 15	128 \pm 16	<0.001
HDL (mg/dL)			
Women (mg/dL)	37 \pm 6	74 \pm 7	<0.001
Men	36 \pm 5	67 \pm 12	<0.001
LDL (mg/dL)	139 \pm 16	96 \pm 19	<0.001
Cholesterol (mg/dL)	216 \pm 28	177 \pm 13	<0.001
HbA1c (%)	5.85 \pm 0.78	4.9 \pm 61	<0.001

Data shown are mean \pm standard deviation.

Left ventricle diameters and ejection fraction showed no significant differences between both groups (Table 2). The Met S group had a significantly increased relative wall thickness and left atrial diameter (Table 2). The tissue Doppler (sm) parameter of LV systolic function showed normal LV systolic function in Met S patients. However, LV diastolic function parameters (E/A and E/E) were significantly changed (Table 2).

3.1. Assessment of Right Ventricle Diastolic Function by Doppler and Tissue Doppler Echo

As shown in Table 3, there were a significant decline in E/A ratio (0.95 \pm 0.12 in met s vs. 1.14 \pm 0.15 in control, P value<0.001). A highly significant increase in E/e' was reported in MetS (5.66 \pm 1.03) than the control group (4.24 \pm 0.46) (P value<0.001)

The global systolic RV function parameters (TAPSE, FAC) were totally intact in individuals with MetS and did not show a significant difference between the groups (Table 3).

3.2. RV Systolic Function (2D-STE and TDI)

Right ventricular global longitudinal strain (RV GLS) showed a significant decline in the metabolic group compared to controls (-8.27 \pm 2.16 in MetS group vs. -26.64 \pm 3.05 in control subjects, P<0.001) (Table 4).

TDI assessment of RV systolic function showed a non-significant difference between metabolic group and control group regarding average S wave velocity (11.75 \pm 1.70 vs 11.83 \pm 1.16) (Table 4).

Table 2. Left ventricle conventional echocardiography and tissue Doppler data.

Variable	Met s (n=50)	Control (n=25)	p- value
Left ventricular end diastolic dimension	4.78 \pm 0.54	4.82 \pm 0.54	0.664
Left ventricular end systolic dimension	3.10 \pm 43	3.15 \pm 0.44	0.664

Variable	Met s (n=50)	Control (n=25)	p- value
Posterior wall thickness	0.99±0.15	0.8±0.15	<0.001
Left ventricular fraction shorting	34.5±5.02	34.60±4.9	0.91
Left ventricular ejection fraction (%)	63.8±6.35	63±48	0.835
Relative wall thickness (RWT)	0.41±0.09	0.33±0.07	<0.001
Aortic root diameter	2.70±0.43	2.65±0.37	0.611
Left atrial dimension	3.70±0.29	3.22±0.42	<0.001
E (cm/s)	66.88±6.54	65.28±5.09	0.2837
A (cm/s)	60.92±6.33	50.80±4.33	<0.001
E/A ratio	1.0±0.18	1.25±0.13	<0.001
LV. e'	10.01±0.89	12.49±1.02	<0.001
E/e' ratio	6.57±0.65	5.78±1.01	0.002
Mitral s (cm/s)	9.78±2.24	10.14±2.43	0.251

Data are shown as mean±standard deviation.

Table 3. Right ventricle conventional echocardiography and tissue Doppler data.

Variable	Met s (n=50)	Control (n=50)	P- value
RVOT proximal (cm)	2.69±0.28	2.63±0.27	0.138
RVOT distal (cm)	2.14±0.20	2.11±0.23	0.573
RVD1 (basal) (cm)	3.91±0.27	3.20±0.18	<0.001
RVD2 (mid) (cm)	2.81±0.33	2.58±0.27	0.004
RVD3 (longitudinal) (cm)	6.30±0.51	6.11±0.48	0.483
TAPSE (cm)	2.25±0.31	2.30±0.21	0.679
RV ED area (cm ²)	13.31±3.0	13.74±3.6	0.826
RV ES area (cm ²)	7.61±2.32	7.70±2.7	0.902
RV FAC (%)	44.66±6.1	48.62±7.43	0.087
Doppler data			
Tricuspid E velocity (cm.s ⁻¹)	58.32±5.98	54.84±6.23	0.075
Tricuspid A velocity (cm.s ⁻¹)	60.08±4.76	44.92±4.41	<0.001
Tricuspid E/A ratio	0.95±0.12	1.14±0.15	<0.001
Tissue Doppler imaging			
RV e'	10.30±1.11	12.63±1.31	<0.001
RV a'	13.92±1.34	13.77±1.27	0.718
Tricuspid E/e' ratio	5.66±1.03	4.24±0.46	<0.001

Data are shown as mean±standard deviation.

Table 4. Comparison between the two groups as regards the RV function assessed by TDI and strain.

Variable	Met S (n=50)	Control (n=25)	P- value
RV GLS	18.27±2.16	26.64±3.05	<0.001
RV Smv	11.75±1.70	11.83±1.16	0.574

Data are shown as mean±standard deviation

The univariate regression analysis revealed that the predictors of RVGLS were triglycerides (unstandardized B=

0.14, $p < 0.001$), waist circumference (unstandardized B=0.21, $p < 0.001$), systolic BP (unstandardized B=-0.13, $p < 0.001$), and glucose level (unstandardized B=-0.03, $p < 0.001$) (Table 5).

The multivariate regression analysis showed that waist circumference, systolic BP, and glucose level were independent factors in predicting RVGLS (Unstandardized B for waist circumference=-0.089, $p=0.007$; Unstandardized B for Systolic BP=-0.052, $p=0.009$; Unstandardized B for Glucose level=-0.011, $p=0.036$) (Table 5).

Table 5. The univariate and multivariate regression analysis to identify the predictors of Right Ventricular Global Longitudinal Strain (RVGLS).

	Univariate Analysis				Multivariate Analysis			
	Unstand. B	SE	Test	p	Unstand. B	SE	Test	P
Waist circum.	-0.21	0.022	-9.61	<0.001	-0.089	0.032	-2.75	0.007
Systolic BP	-0.13	0.016	-8.27	<0.001	-0.052	0.019	-2.69	0.009
Glucose level	-0.03	0.005	-6.58	<0.001	-0.011	0.005	-2.13	0.036
Triglycerides	-0.14	0.019	-7.25	<0.001	-0.039	0.021	-1.86	0.067
(Intercept)					44.63	2.578	17.31	<.001

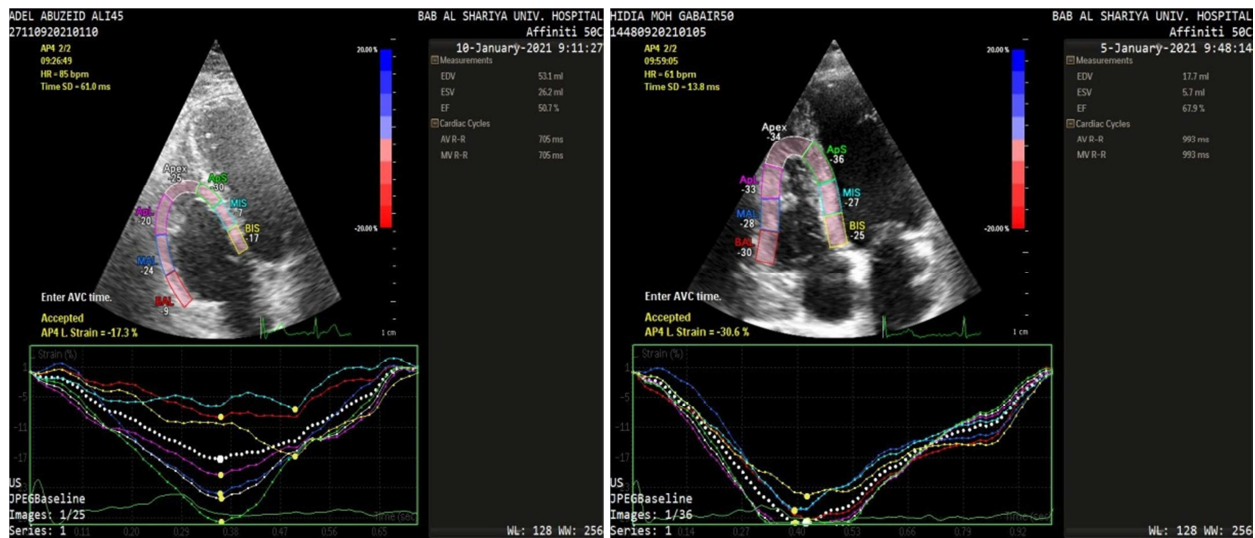


Figure 1. GLS of the right ventricle and strain of the six segments of the right ventricle in one of the Mets (a) and one of the control (b).

4. Discussion

MetS is a growing global concern that can be viewed as a complex condition consisting of a cluster of related elements. Multiple definitions have been proposed to describe the condition; however, according to the International Diabetic Federation (IDF), central obesity has been regarded as the cornerstone of the disorder, along which two more metabolic abnormalities are necessary to make the diagnosis [15, 16].

The peril of the disease can be attributed to its assumingly high prevalence. However, global data on the incidence and prevalence of this disease are neither always readily available nor accurate. Furthermore, there has often been a strong association between MetS and the incidence of T2DM, one of its end results. In fact, according to data provided by the Centers for Disease Control and Prevention (CDC), more than 30% of the adult US population has MetS, while 12% of the US adults have T2DM, with a one-to-three ratio between the prevalence of the two conditions. Strikingly, if we apply the same proportion worldwide, over a billion MetS cases can be expected to exist in the current times, worldwide [17].

With each of its components being a risk factor for a vast range of cardiovascular-related morbidities and mortalities, the relation between MetS and cardiac, including right ventricular dysfunction, has been starting to get more recognized over the last decade [18-20]. Regardless, in comparison with the humongous body of evidence illustrating the link between MetS and left cardiac dynamics, the current knowledge concerning MetS-related right-sided heart problems, is considered defective. Nevertheless, previous work has come up with a number of theories that could lay the ground for future research. For instance, it was suggested by Kranstuber et al. that the hyperglycemia in T2DM would result in an irreversible cross-linkage between glucose and proteins related to cardiac myocytes, leading to advanced glycation end products (AGEs) production, thereby causing myocardial dysfunction [21]. Meanwhile, a similar

reaction was suggested by Bidasee et al., to take place at the intracellular level, causing abnormal myocardial calcium handling and homeostasis [22].

In the MetS group, BMI and waist circumference were significantly higher than the healthy subjects. This is in line with the data from Samiei et al., who concluded significantly greater BMI and waist circumferences amongst participants with MetS [23].

Regarding the distribution of the other three components of MetS, a statistically significant difference was observed between both groups. Likewise, Serrano-Ferrer et al. reported greater percentages of hypertension, hyperglycemia, low HDL and hypertriglyceridemia in the MetS group compared to the control group, respectively [24].

As regards the cardiovascular parameters examined in our study, both SBP and DBP were significantly higher in the MetS group than in the control group. Meanwhile, no significant difference was found between the two groups in terms of heart rate. This was partially in alignment with the demographic criteria observed in the study performed by [25].

As for glucose and lipid regulation indicators, all metabolic parameters were significantly altered amongst the two groups of participants. This almost comes in complete agreement with the findings from the prospective study by Aslan et al., which demonstrated comparable results regarding plasma glucose, HDL, triglycerides, and cholesterol levels, but not LDL levels [26].

In our study, MetS impact on the different parameters obtained by 2D-STE was assessed. We observed no significance between the two groups regarding the conventional echocardiographic parameters related to the left-sided systolic function. Meanwhile, RVGLS was significantly lower in the MetS group. It is considered an accurate measure of the right-ventricular systolic performance, as well as a good and promising prognostic determinant of right ventricular dysfunction [27]. Such an observation corresponds to the observation made by Tadic et al. who conducted a cross-sectional study on 183 subjects

analyzed using 2D-STE examination. In this study, the 2D-RVGLS was significantly lower amongst MetS patients compared to their healthy pairs₁₆. Similarly, Serrano-Ferrer *et al.* found significantly reduced RVGLS percentages amongst 39 MetS patients compared to 40 control subjects [24].

When using univariate regression analysis, all four components of MetS (i.e., waist circumference, dyslipidemia, hypertension, and hyperglycemia) could predict a significant reduction in RVGLS. Interestingly, when applying the multivariate regression analysis, altered triglycerides levels failed to independently correlate with significantly low RVGLS values. The same observation has been made by Tadic *et al.*, where the association between dyslipidemia and RVGLS was lost in the multivariate but not the univariate regression analysis [16].

In this study, BP was significantly higher in MetS patients, which was independently associated with RV functions assessed by two-dimensional strain. This lies in agreement with the study conducted by Hanboly, who found that the global RV systolic strain was significantly reduced in the hypertensive group compared to the control group. This could be due to the fact that in hypertension, the resultant ventricular hypertrophy might contribute to the observed low RVGLS values due to the associated drop in the right-ventricular end-diastolic dimensions [28].

In the current work, we also had the observation that abdominal/central obesity was independently associated with RV dysfunction as inspected by 2D-STE examination. Parallel findings were reported from the MESA study, a large multicentered, cohort that aimed at examining the linkage between the right ventricle morphological and functional characteristics, evaluated by cardiac MRI, and obesity in a sample of 4,127 subjects, who were clinically-free from any cardiovascular morbidities. Indeed, they found that RV mass and end-diastolic volume were higher among obese individuals in comparison to lean participants [29]. Since central obesity is regarded as the cornerstone of MetS. Numerous mechanisms have been suggested in attempt to reveal this pattern of association.

Myocardial lipotoxicity has been closely examined as a plausible underlying mechanism for the development of RV dysfunction in obese subjects. In cases of hyperlipidemia, the heart's uptake of lipid surges, causing accumulation of triglycerides. The heart has the ability to handle a wide range of energy-producing substrates, including glucose, ketone bodies and amino acids. Meanwhile, a rise in fatty acids concentrations in myocardial cells is accompanied by an increase in the rates of their metabolism through β -oxidation. Consequently, a metabolic state of substrates competition (i.e., Randle cycle) between glucose and fatty acids could develop, where glucose metabolism would be suppressed by the progressively increasing rates of fatty acid oxidation, causing less ATP molecules and energy to be produced, as well as raising oxygen consumption levels by the myocardial cells, leading to cardiac dysfunction [30]. Inflammation has been also proposed as a possible route for RV dysfunction in obesity, where high levels of adipocytes-produced cytokines

were found to significantly alter glucose and fatty acid metabolism, cause insulin resistance and initiate myocardial fibrosis and affect cardiac contractility through disrupting intramyocardial calcium homeostasis [31].

Another possible justification was offered by Chahal *et al.* in the MESA study, where the chronic elevation in blood and stroke volumes, as well as in cardiac output that is related to obesity, could significantly alter ventricular dimensions. Although these changes would be initially almost exclusive to the left heart; however, due to the forces of ventricular independence that are directly shared between the two chambers, a close correlation between LV dysfunction and enlarged RV dimensions can be expected [28]. Other possible explanations were suggested in previous studies, including intramyocardial triglycerides deposition, cardiac remodeling and adaptation to body size, and the vasoconstrictive state resulting from the hypoxia related to sleep-disordered breathing commonly seen in obese individuals [29, 32, 33].

Our results demonstrated a clear negative correlation between elevated glucose levels (hyperglycemia) and changes in RV structure and function. This goes along with the observation made by Patscheider *et al.*, who reported subclinical impairment in the right ventricular volumes and function of 87 prediabetic and 43 diabetic male subjects, compared to 207 normoglycemic healthy controls, when assessed with cardiac MRI [34]. Numerous mechanisms have been introduced in order to explain this association. One proposal for the development of RV dysfunction in diabetes was made by Pan *et al.*, who postulated that the diabetic mitochondria might contribute to an abnormal state of relaxation of the pulmonary artery and subsequent development of pulmonary hypertension, by producing an excess of reactive oxygen species, which alter the pulmonary endothelial function [35].

Little work can be found discussing the influence of distorted lipid regulation, commonly known as dyslipidemia, on the right ventricle. In a study conducted by Dalen *et al.*, using tissue Doppler, a significant association could be observed between altered HDL cholesterol levels, one of the lipoproteins that are markedly reduced in MetS, and right ventricular systolic and diastolic parameters [36].

Regarding the TAPSE scoring system, which measures the difference in distance between the right ventricular apex and the tricuspid annulus during the same cardiac cycle, no significant difference was reported between the MetS cases and the controls. These results are consistent with those of Tadic *et al.*, who inspected 327 consecutive subjects divided into four groups; MetS (N=89), hypertensive (N=117), diabetic (N=45), and 76 healthy controls, conflicting results were obtained. In the Serbian observational cross-sectional study, none of the four groups showed any statistical significance regarding their TAPSE measurements₁₆.

In addition, Gopal *et al.* also failed to detect any significant differences between the two groups in terms of their TAPSE measures [37]. These findings disagree with those from Serrano-Ferrer *et al.*, where the TAPSE values were significantly

peculiar between the two divisions of participants [24].

There is no clear justification for such discrepancy in the findings of these studies. However, it has been suggested by Tamborini et al. that the commonly-observed reduction in TAPSE and peak systolic velocity (PSV) in cardiac patients might not be accurate measures of right ventricular dysfunction, especially when compared with other techniques like 3D right-ventricular ejection fraction (RVEF), which could correlate better with the clinical status of those patients [38].

Regarding the right ventricular diastolic function, the MetS group had a significantly lower E/A ratio. Meanwhile, a substantial increase in the E/e' ratio was found amongst the MetS participants when compared to their control pairs. Our findings coincide with those described by Sedaia et al., who reported significantly lower ratios amongst the MetS patients, indicating right ventricular dysfunction and impairment [39].

5. Study Limitations

- 1) The sample size of our study is considered modest in comparison with prior work on the same topic, which might have influenced the magnitude of our findings and their interpretation.
- 2) Only the longitudinal STE parameters were investigated.
- 3) Because of the high interdependence of multiple MetS criteria, determining individual MetS risk factors effect on cardiac remodelling was difficult, which we attempted to address using multivariate analysis.

6. Conclusion

In summary, the current work showed deterioration of the right ventricular functional in subjects with a confirmed diagnosis of MetS, when examined using 2D speckle-tracking echocardiography. Represented by RVGLS, all four components of MetS correlated independently with right ventricular dysfunction, with the exception of alterations in the triglyceride plasma levels.

Ethical Approval

The Research Ethics Committee at the Faculty of Medicine, Al-Azhar University, Cairo, Egypt, granted ethical approval for data collection (No. 0000071).

Conflict of Interest

No conflict of Interest.

References

- [1] Zafar, U., Khaliq, S., Ahmad, H. U., Manzoor, S., & Lone, K. P. (2018). Metabolic syndrome: an update on diagnostic criteria, pathogenesis, and genetic links. *Hormones (Athens, Greece)*, 17 (3), 299–313. <https://doi.org/10.1007/s42000-018-0051-3>.
- [2] Kaur J. (2014). A comprehensive review on metabolic syndrome. *Cardiology research and practice*, 2014, 943162. <https://doi.org/10.1155/2014/943162> (Retraction published *Cardiol Res Pract.* 2019 Jan 31; 2019: 4301528).
- [3] Comunale, G., Peruzzo, P., Castaldi, B., Razzolini, R., Di Salvo, G., Padalino, M. A., & Susin, F. M. (2021). Understanding and recognition of the right ventricular function and dysfunction via a numerical study. *Scientific reports*, 11 (1), 3709. <https://doi.org/10.1038/s41598-021-82567-9>.
- [4] Kossaiy A. (2015). Echocardiographic Assessment of the Right Ventricle, from the Conventional Approach to Speckle Tracking and Three-Dimensional Imaging, and Insights into the "Right Way" to Explore the Forgotten Chamber. *Clinical Medicine Insights. Cardiology*, 9, 65–75. <https://doi.org/10.4137/CMC.S27462>.
- [5] Yang, W. I., & Ha, J. W. (2015). Non-invasive assessment of vascular alteration using ultrasound. *Clinical hypertension*, 21, 25. <https://doi.org/10.1186/s40885-015-0035-4>.
- [6] Morris, D. A., Krisper, M., Nakatani, S., Köhncke, C., Otsuji, Y., Belyavskiy, E., Radha Krishnan, A. K., Kropf, M., Osmanoglu, E., Boldt, L. H., Blaschke, F., Edelmann, F., Haverkamp, W., Tschöpe, C., Pieske-Kraigher, E., Pieske, B., & Takeuchi, M. (2017). Normal range and usefulness of right ventricular systolic strain to detect subtle right ventricular systolic abnormalities in patients with heart failure: a multicentre study. *European heart journal. Cardiovascular Imaging*, 18 (2), 212–223. <https://doi.org/10.1093/ehjci/jew011>.
- [7] Williams, B., Mancia, G., Spiering, W., Agabiti Rosei, E., Azizi, M., Burnier, M., Clement, D. L., Coca, A., de Simone, G., Dominiczak, A., Kahan, T., Mahfoud, F., Redon, J., Ruilope, L., Zanchetti, A., Kerins, M., Kjeldsen, S. E., Kreutz, R., Laurent, S., Lip, G.,... ESC Scientific Document Group (2018). 2018 ESC/ESH Guidelines for the management of arterial hypertension. *European heart journal*, 39 (33), 3021–3104. <https://doi.org/10.1093/eurheartj/ehy339>.
- [8] Cosentino, F., Grant, P. J., Aboyans, V., Bailey, C. J., Ceriello, A., Delgado, V., Federici, M., Filippatos, G., Grobbee, D. E., Hansen, T. B., Huikuri, H. V., Johansson, I., Jüni, P., Lettino, M., Marx, N., Mellbin, L. G., Östgren, C. J., Rocca, B., Roffi, M., Sattar, N.,... ESC Scientific Document Group (2020). 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *European heart journal*, 41 (2), 255–323. <https://doi.org/10.1093/eurheartj/ehz486>.
- [9] Lang, R. M., Badano, L. P., Mor-Avi, V., Afilalo, J., Armstrong, A., Ernande, L., Flachskampf, F. A., Foster, E., Goldstein, S. A., Kuznetsova, T., Lancellotti, P., Muraru, D., Picard, M. H., Rietzschel, E. R., Rudski, L., Spencer, K. T., Tsang, W., & Voigt, J. U. (2015). Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography*, 28 (1), 1–39. e14. <https://doi.org/10.1016/j.echo.2014.10.003>.
- [10] Nagueh, S. F., Appleton, C. P., Gillebert, T. C., Marino, P. N., Oh, J. K., Smiseth, O. A., Waggoner, A. D., Flachskampf, F. A., Pellikka, P. A., & Evangelista, A. (2009). Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography*, 22 (2), 107–133. <https://doi.org/10.1016/j.echo.2008.11.023>.

- [11] Rudski, L. G., Lai, W. W., Afilalo, J., Hua, L., Handschumacher, M. D., Chandrasekaran, K., Solomon, S. D., Louie, E. K., & Schiller, N. B. (2010). Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography*, 23 (7), 685–788. <https://doi.org/10.1016/j.echo.2010.05.010>.
- [12] Zile, M. R., & Brutsaert, D. L. (2002). New concepts in diastolic dysfunction and diastolic heart failure: Part II: causal mechanisms and treatment. *Circulation*, 105 (12), 1503–1508. <https://doi.org/10.1161/hc1202.105290>.
- [13] Voigt, J. U., Pedrizzetti, G., Lysyansky, P., Marwick, T. H., Houle, H., Baumann, R., Pedri, S., Ito, Y., Abe, Y., Metz, S., Song, J. H., Hamilton, J., Sengupta, P. P., Kolias, T. J., d'Hooge, J., Aurigemma, G. P., Thomas, J. D., & Badano, L. P. (2015). Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *European heart journal. Cardiovascular Imaging*, 16 (1), 1–11. <https://doi.org/10.1093/ehjci/jeu184>.
- [14] Il'Giovine, Z. J., Mulder, H., Chiswell, K., Arges, K., Tomfohr, J., Hashmi, A., Velazquez, E. J., Kisslo, J. A., Samad, Z., & Rajagopal, S. (2018). Right Ventricular Longitudinal Strain Reproducibility Using Vendor-Dependent and Vendor-Independent Software. *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography*, 31 (6), 721–732. e5. <https://doi.org/10.1016/j.echo.2018.01.008>.
- [15] Alberti, K. G., Zimmet, P., Shaw, J., & IDF Epidemiology Task Force Consensus Group (2005). The metabolic syndrome—a new worldwide definition. *Lancet (London, England)*, 366 (9491), 1059–1062. [https://doi.org/10.1016/S0140-6736\(05\)67402-8](https://doi.org/10.1016/S0140-6736(05)67402-8).
- [16] Tadic, M., Cuspidi, C., Sljivic, A., Andric, A., Ivanovic, B., Scepanovic, R., Ilic, I., Jozika, L., Marjanovic, T., & Celic, V. (2014). Effects of the metabolic syndrome on right heart mechanics and function. *The Canadian journal of cardiology*, 30 (3), 325–331. <https://doi.org/10.1016/j.cjca.2013.12.006>.
- [17] Saklayen M. G. (2018). The Global Epidemic of the Metabolic Syndrome. *Current hypertension reports*, 20 (2), 12. <https://doi.org/10.1007/s11906-018-0812-z>.
- [18] O'Neill, S., & O'Driscoll, L. (2015). Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obesity reviews: an official journal of the International Association for the Study of Obesity*, 16 (1), 1–12. <https://doi.org/10.1111/obr.12229>.
- [19] Tadic, M., Ivanovic, B., & Grozdic, I. (2011). Metabolic syndrome impacts the right ventricle: true or false?. *Echocardiography (Mount Kisco, N.Y.)*, 28 (5), 530–538. <https://doi.org/10.1111/j.1540-8175.2011.01390.x>.
- [20] Tune, J. D., Goodwill, A. G., Sassoon, D. J., & Mather, K. J. (2017). Cardiovascular consequences of metabolic syndrome. *Translational research: the journal of laboratory and clinical medicine*, 183, 57–70. <https://doi.org/10.1016/j.trsl.2017.01.001>.
- [21] Kranstuber, A. L., Del Rio, C., Biesiadecki, B. J., Hamlin, R. L., Ottobre, J., Gyorke, S., & Lacombe, V. A. (2012). Advanced glycation end product cross-link breaker attenuates diabetes-induced cardiac dysfunction by improving sarcoplasmic reticulum calcium handling. *Frontiers in physiology*, 3, 292. <https://doi.org/10.3389/fphys.2012.00292>.
- [22] Bidasee, K. R., Zhang, Y., Shao, C. H., Wang, M., Patel, K. P., Dincer, U. D., & Besch, H. R., Jr (2004). Diabetes increases formation of advanced glycation end products on Sarco(endo)plasmic reticulum Ca^{2+} -ATPase. *Diabetes*, 53 (2), 463–473. <https://doi.org/10.2337/diabetes.53.2.463>.
- [23] Samiei, N., Bayat, M., Firouzi, A., Dehghani, F., Parsaee, M., Rahimi, S., Ahmadi, S., Pourmojib, M., Ghaemmaghami, Z., Rezaei, Y., & Peighambari, M. M. (2018). Subclinical systolic and diastolic dysfunctions in patients with metabolic syndrome and angiographically normal coronary arteries: An echocardiographic study. *Journal of clinical ultrasound: JCU*, 46 (3), 195–201. <https://doi.org/10.1002/jcu.22568>.
- [24] Serrano-Ferrer, J., Walther, G., Crendal, E., Vinet, A., Dutheil, F., Naughton, G., Lesourd, B., Chapier, R., Courteix, D., & Obert, P. (2014). Right ventricle free wall mechanics in metabolic syndrome without type-2 diabetes: effects of a 3-month lifestyle intervention program. *Cardiovascular diabetology*, 13, 116. <https://doi.org/10.1186/s12933-014-0116-9>.
- [25] Zeller, J., Strack, C., Fenk, S., Mohr, M., Loew, T., Schmitz, G., Maier, L., Fischer, M., & Baessler, A. (2016). Relation Between Obesity, Metabolic Syndrome, Successful Long-Term Weight Reduction, and Right Ventricular Function. *International heart journal*, 57 (4), 441–448. <https://doi.org/10.1536/ihj.15-403>.
- [26] Aslan, E., Sert, A., Buyukinan, M., Pirgon, M. O., Kurku, H., Yilmaz, H., & Odabas, D. (2019). Left and right ventricular function by echocardiography, tissue Doppler imaging, carotid intima-media thickness, and asymmetric dimethyl arginine levels in obese adolescents with metabolic syndrome. *Cardiology in the young*, 29 (3), 310–318. <https://doi.org/10.1017/S1047951118002329>.
- [27] Lu, K. J., Chen, J. X., Profitis, K., Kearney, L. G., DeSilva, D., Smith, G., Ord, M., Harberts, S., Calafiore, P., Jones, E., & Srivastava, P. M. (2015). Right ventricular global longitudinal strain is an independent predictor of right ventricular function: a multimodality study of cardiac magnetic resonance imaging, real time three-dimensional echocardiography and speckle tracking echocardiography. *Echocardiography (Mount Kisco, N.Y.)*, 32 (6), 966–974. <https://doi.org/10.1111/echo.12783>.
- [28] Hanboly, N., 2016. Right ventricle morphology and function in systemic hypertension. *Niger. J. Cardiol.* 13, 11. <https://doi.org/10.4103/0189-7969.173854>.
- [29] Chahal, H., McClelland, R. L., Tandri, H., Jain, A., Turkbey, E. B., Hundley, W. G., Barr, R. G., Kizer, J., Lima, J., Bluemke, D. A., & Kawut, S. M. (2012). Obesity and right ventricular structure and function: the MESA-Right Ventricle Study. *Chest*, 141 (2), 388–395. <https://doi.org/10.1378/chest.11-0172>.
- [30] Sletten, A. C., Peterson, L. R., & Schaffer, J. E. (2018). Manifestations and mechanisms of myocardial lipotoxicity in obesity. *Journal of internal medicine*, 284 (5), 478–491. <https://doi.org/10.1111/joim.12728>.
- [31] Gullestad, L., Ueland, T., Vinge, L. E., Finsen, A., Yndestad, A., & Aukrust, P. (2012). Inflammatory cytokines in heart failure: mediators and markers. *Cardiology*, 122 (1), 23–35. <https://doi.org/10.1159/000338166>.

- [32] Cannavale, G., Francone, M., Galea, N., Vullo, F., Molisso, A., Carbone, I., & Catalano, C. (2018). Fatty Images of the Heart: Spectrum of Normal and Pathological Findings by Computed Tomography and Cardiac Magnetic Resonance Imaging. *BioMed research international*, 2018, 5610347. <https://doi.org/10.1155/2018/5610347>.
- [33] Garg, Sumit & Arora, Shitij & Agarwal, Jawahar. (2018). Influence of BMI on Cardiac Output and Peripheral Blood Flow in Young Adult Males. *JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH*. 12. 10.7860/JCDR/2018/25814.11279.
- [34] Patscheider, H., Lorbeer, R., Auweter, S., Schafnitzel, A., Bayerl, C., Curta, A., Rathmann, W., Heier, M., Meisinger, C., Peters, A., Bamberg, F., & Hetterich, H. (2018). Subclinical changes in MRI-determined right ventricular volumes and function in subjects with prediabetes and diabetes. *European radiology*, 28 (7), 3105–3113. <https://doi.org/10.1007/s00330-017-5185-1>.
- [35] Pan, M., Han, Y., Si, R., Guo, R., Desai, A., & Makino, A. (2017). Hypoxia-induced pulmonary hypertension in type 2 diabetic mice. *Pulmonary circulation*, 7 (1), 175–185. <https://doi.org/10.1086/690206>.
- [36] Dalen, H., Thorstensen, A., Romundstad, P. R., Aase, S. A., Stoylen, A., & Vatten, L. J. (2011). Cardiovascular risk factors and systolic and diastolic cardiac function: a tissue Doppler and speckle tracking echocardiographic study. *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography*, 24 (3), 322–32. e6. <https://doi.org/10.1016/j.echo.2010.12.010>.
- [37] Gopal, D. M., Santhanakrishnan, R., Wang, Y. C., Ayalon, N., Donohue, C., Rahban, Y., Perez, A. J., Downing, J., Liang, C. seng, Gokce, N., Colucci, W. S., Ho, J. E., 2015. Impaired right ventricular hemodynamics indicate preclinical pulmonary hypertension in patients with metabolic syndrome. *J. Am. Heart Assoc.* 4, e001597. <https://doi.org/10.1161/JAHA.114.001597>.
- [38] Tamborini, G., Muratori, M., Brusoni, D., Celeste, F., Maffessanti, F., Caiani, E. G., Alamanni, F., & Pepi, M. (2009). Is right ventricular systolic function reduced after cardiac surgery? A two- and three-dimensional echocardiographic study. *European journal of echocardiography: the journal of the Working Group on Echocardiography of the European Society of Cardiology*, 10 (5), 630–634. <https://doi.org/10.1093/ejechocard/jep015>.
- [39] Sedaia, E., Revenco, V., Gutan, I., Ochisor, V. & Vascenco, A., 2020. The impact of epicardial adipose tissue and right ventricular hypertrophy on diastolic and global function of right ventricle in patients with metabolic syndrome. *Eur. Heart J.* 41. <https://doi.org/10.1093/ehjci/ehaa946.0905>.