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Prevalence of Subclinical Levt Ventricular Diastolic Dysfunction in Patient with Metabolic Syndrome in West Region of the Republic of Macedonia

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Abstract

Background: Metabolic Syndrome (MetS) has been associated with subclinical changes in cardiac structure and function, including left ventricular diastolic dysfunction (LVDD) and is strong risk factors for the future development of clinical heart failure, and specifically increases the risk of heart failure with preserved ejection fraction. To date, the evidence on the prevalence of subclinical LVDD in patient with MetS and relation to components of the MetS, in west region of the Republic of Macedonia are scarce.

Objective: We sought to determine the prevalence of subclinical LVDD and relation to components of the MetS, in patient with MetS in our region.

Methods: We conducted a multicenter observational cross-sectional study. Recruited were 550 consecutive participants,450 with MetS (mean age 50 years,49% women) and 100 controls (no risk factors for MetS; mean 51 years,57% women) , who attended outpatient visits at general cardiology Health Care Clinics in 6 town on western region Republic of Macedonia, during 1 calendar year. Pertcipans underwent echocardiography with tissue Doppler imaging.

Results: Participants with MetS, have significantly increased frequency of subclical LVDD grade 1, in comparation with participants without MetS. (39, 7% vs. 6%, p=0.0005). The overall frequency of subclinical LVDD grade 1, in participants with MetS, was 39, 7%; p=0.0005). Subjects with MetS also had worse measures of diastolic function, including: higher Lev Atrial Volum index {(LAVI), (p=0.00), Lower E/A ratio (p=0.00),lower mean e'(p=0.00) and lower E/ e' ratio(p=0.00), increased Deceleratio time {(DT),(p=0.00)} and Isovolumetric Relaxation time{(IVRT), (p=0.00). Overall, participants with subclinical LVDD, had a worse cardiovascular risk factor profile, including: higher BMI (p=0.001), higher blood pressure{(BP) (p=0.003)}, elevated Weist circumference{(WC)(p=0.001)} and dyslipidemia (p=0.000) in comparation with participants with normal diastolic function. Also, participants with subclinical LVDD,have more risk factors for MetS than participants with normal diastolic function (p=0.002). There was a significant assotiation between subclinical LVDD and: Age (OR=1.108; 95% CI 1.051 -1.168), Females (OR=3.633; 95% CI2.439-5.413), BMI (OR=7.474; 95% CI 4.881-11.443), control of BP (OR=1.763; 95% CI 1.204-2.580) and number of MetS risk factors (OR= 3.609; 95% CI 2.054-6.340).

Conclusions: The prevalence of subclinical LVDD in the patients with MetS, in abscence of coronary disease and other well know heart disease, is considerablye high in western region of the Republic of Macedonia and seem to be significantly associated with age, gender, BMI, Levt Ventricular mass index (LVMI) and number of risk factors for MetS.

Keywords: Metabolic Syndrome; Prevalence; Western Region of the Republic of Macedonija

List of Abbreviations: MetS -Metabolic Syndrome; BW - Body weight; BH -Body height; BMI - Body mass; index; BP - Blood pressure; SBP -Systolic blood pressure; DBP - Diastolic blood pressure; DM - Diabetes Mellitus; WC - Waist circumference; CVD - Cardio-vascular disease; CHD - Coronary heart disease; LV - Levt Ventricular; LVDF - Levt Ventricular Diastolic function; LVDD - Levt Ventricular Diastolic Dysfunction; HF -Heart Failure; HF-nEF -Heart Failure with Normal Ejection Fraction; CVHD -Cardio-vascular

Heart Disease; DF - Diastolic Function; DD - Diastolic Dysfunction; HDL-C - serum High density lipoproteins cholesterol; TG - sserum triglycerides; TDI - tissue Doppler imaging; LVEF - LV ejection fraction; LAVI - Levt atrial volume index; IVRT - Isovolumetric Relaxation Time; DCT - Deceleration Time; ASE - American Society of Echocardiography

Introduction

Since Reaven in 1988 established the clinical importance of the clustering of the metabolic disorders dysglicemia,central adiposity,hypertension and dyslipidemia (low levels of high density lipoprotein cholesterol (HDL-C) and high levels of triglycerides), known as the metabolic syndrome (MetS), many studies, have shown a high risk of cardiovascular disease (CVD) in the presence of MetS [1-3].

Metabolic Syndrome (MetS) has been associated with subclinical changes in cardiac structure and function, including left ventricular diastolic dysfunction (LVDD).Subclinical LVDD has been broadly defined as LVDD without the diagnosis of congestive heart failure and with normal systolic function [4]. Subclinical LVDD is an entity that remains poorly understood, yet has definite clinical significance. Although few original studies have focused on subclinical LVDD. Previous studies have shown that subclinical LVDD, is prevalent and is strong risk factors for the future development of clinical (HF), and specifically increase the risk of heart failure with preserved ejection fraction (HFpEF). In particular, the prognosis of patient with HFpEF, amounting to approximately half the population with HF, has not improved during the past decades [5,6]. Because the development of diastolic HF is associated with progression of lev ventricular diastolic function,preventing LVDD might reduce the incidence of HFpEF [6]. The pathways leading to subclinical LVDD are diverse, and mechanisms of progression to heart failure poorly understood. Because of these findings and the increasing prevalence of heart failure epidemic, it is clear that an understanding of subclinical LVDD is essential to decreasing patient’s morbidity and mortality.

In the MetS, levt ventricular diastolic function (LVDF) appear to worsen in a stepwise fashion with the number of risk factors for MetS [4,7].These findings may account in part for the augmented cardiovascular morbidity and mortality that is associated with MetS [8].

The dramatically increasing prevalence of the MetS, associated with the substantial increase in obesity and diabetes, is therefore, an important public health concern [9].The true prevalence of subclinical LVDD in MetS and relation to components of the MetS are not well defined. To date, the evidence on the prevalence of subclinical LVDD and relation to components of the MetS, in patient with MetS in west region of the Republic of Macedonia are scarce. It would therefore be worthwhile to investigate the prevalence of subclinical LVDD in patient with MetS in our region.

Objective

We sought to determine the prevalence of subclinical LVDD and relation to components of the MetS, in patient with MetS, in our region.

Methods

Study Design

We conducted a multicenter observational cross-sectional study. Recruited were 550 consecutive participants, 450 with MetS and 100 controls without MetS, who attended outpatient visits at general cardiology Health Care Clinics in 6 town on western region Republic of Macedonia, during 1 calendar year (from November 2016 to November 2017). The study is in compliance with the Declaration of Helsinki. All patient that participated in this study were written informed, consent was obtained from all participating patients before they were enrolled into the study.

MetS was defined according to the harmonized definition of the International Diabetes Federation and other organizations, that three or more out of five following criteria are considered as MetS: (1) central adiposity {Waist circumference (WC)} >102 cm in men and >88cm in women); (2) serum HDL-C < 50 mg/dL in women or < 40 mg/dL in men; (3) serum triglyceride levels > 150 mg/dL; (4) SBP ≥ 130mm Hg or DBP ≥ 85mm Hg or use of antihypertensive drugs; (5) the presence of diabetes mellitus (DM) or use of anti-diabetic drugs. Controls without MetS were defined as meeting none of the 5 criteria for MetS [10]. Participants with existing cardiovascular disease (heart failure, LV ejection fraction (LVEF) <50%, coronary artery disease, congenital or acquired valvular heart disease,cardiomyopathies, cardiac wall hypertrophy, cardiac arrhythmias), patient with history of stroke ,were excluded from the study.

All participants underwent a comprehensive medical history and physical examination. Resting heart rate, anthropometrics, blood pressure (obtained after 10 min of rest in the sitting position, expressed as the average of 3 consecutive measurements). Hypertension was defined as a systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg and/or current antihypertensive therapy. Diabetes mellitus was defined as a fasting serum glucose level ≥126 mg/dL and/or current medical therapy with an oral hypoglycemic agent and/or insulin [11,12]. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m^2). Weight was measured with weight balance scales, and height with stadiometer. WC was reported in cm. An overnight fasting blood sample was drawn from each patient to determine: blood glucose, lipid profile tests total serum cholesterol (TC), serum High density lipoproteins cholesterol (HDL-C), serum triglycerides (TG). The sample analysis was performed using standard biochemical analytical methods.

Echocardiographic Measurements

M-mode, two-dimensional and Doppler echocardiography, were performed and/or reviewed by experienced staff cardiologists, compliant with the recommendation of the American Society of Echocardiography (ASE),stored in DICOM format and later reviewed by two experienced echocardiographers. Briefly,the LV (levt ventricular) linear dimensions were measured from a parasternal long-axis view according the recommendations of the ASE [13].The LV mass was calculated with a validated formula and indexed for body surface area(BSA) [14]. The LV relative wall thickness was calculated as follows: (2 x posterior wall thickness) divided by end-diastolic diameter [15]. The LV ejection fraction (EF), was calculated by biplane modified Simpson's rules. From an apical 4-chamber view, transmitral flow was sampled by pulsed-wave Doppler at the level of mitral valve leaflet tips. Peak velocities of the early phase (E) and late phase (A), of the mitral inflow were measured, and their ratio (E/A) was calculated. Levt ventricular myocardial velocities were evaluated by tissue Doppler imaging (TDI). Pulse TDI sample volum was placed at the level of the lateral and septal mitral valve annulus, and peak early diastolic velocities (e') were measured and then averaged. The ration between E and e' (E/ e') was calculated.

Diastolic Function

We used measurements of LA size,tissue Doppler and Doppler of mitral flow as parameters of diastolic dysfunction(DD), and the cut-offs were set according to previously published data and international guidelines [16-18].We defined LA size as normal (< 2.2 cm/m^2), moderately enlarged (2.2–2.79 cm/m^2) and severely enlarged (≥ 2.8 cm/m^2). E/A ratio, the ratio of the E-wave and peak late LV filling (A-wave), were divided into low (< 1.0), normal (1.0–2.0) and high (> 2.0). The early myocardial peak velocity of the mitral annulus, tissue Doppler E' wave (the average of the septal e' and lateral e' measurements), was defined as decreased (< 9 cm/s) or normal (≥ 9 cm/s). E/e' the ratio of peak early LV filling (E-wave) and average tissue Doppler e' wave, was stratified into normal (< 8) and increased (≥ 8). We defined DCT, the deceleration time of early filling velocity, into low (< 140 ms), normal (140–220 ms) and high (> 220 ms).). Isovolumetric relaxation time (IVRT) was reduced (< 60 ms), normal (60–110 ms), or prolonged (> 110 ms). The ratio of the transmitral early and late filling phases (E/A) was calculated as a measure of diastolic function.The ratio of early filling and early myocardial velocity (E/e′) was calculated as a noninvasive index of LV filling pressure.

Definition of Diastolic Dysfunction was as follows

- LAVI > 34 mL/m^2.
- E/A < 0.8; e′ < 8 cm/s;mean E/e′ ≥8: impaired relaxation (DD) of grade I).
- E/A ≤ 1.5; e′ < 8 cm/s ;mean E/e′ 9 - 12: pseudo-normalized pattern (DD of grade II).
- E/A > 2; e′ < 8 cm/s, and mean E/e′ ≥ 13: restrictive patter n (DD of grade III).
- Elevated LV filling pressure was defined as when E/E′ ratio exceeded 14.

Throughout all echocardiographic findings, a consensus reading was again applied.

Statistical Analysis

Baseline clinical characteristics and echocardiographic measures were summarized for participants with and without MetS.The collected data were entered in the software SPSS for Windows, version 19.0, which performed a statistical analysis.The distribution of variables was tested for normality using the Kolmogorov-Smirnov test, and the heterogeneity of variances was evaluated by Levene's test.A simple descriptive analysis was performed for the general characterization of the sample and distribution of variables.Continuous variables were presented as mean ± standard deviation, and categorical variables were presented as frequency (%).Differences between groups were analyzed using the Student t-test, for independent samples. Categorical data were analyzed using the Chi-square (X^2) test. The association between variables was analyzed using logistic regression. A, p value <0.05 was considered statistically significant for a confidence interval of 95%.

Results

A total of 550 subjects were enrolled in our study, including 450 subjects with MetS (mean age 50, 6 years, 49% women), and 100 controls without MetS (mean age 50,1years, 57% women). Baseline characteristics by group are displayed in Table 1.Overall, subjects with MetS had a worse cardiovascular risk factor profile, including higher BMI,higher BP,elevated WC and dyslipidemia.(25,5±3,2 vs. 24,3±0,7 p=0.01;135,7±18,4 vs.118,7±2,2 p=0,04;87,9±10,5 vs. 78,7±3,1 p=0.006; 0,9 ±0,2 vs.1,2±0,6 p=0.00;1,9 ±0,4 vs. 1,4±0,1 p=0.04).

Variables		Met.S (N.450)			Controls (N.100)			p*-value
		N. (%)	Mean	SD	N. (%)	Mean	SD	
Gender	Females	222(49,3)			57(57%)			0.43
	Males	228(50,7)			43(43%)			0.41
Age (year)			50,6	±3,9		50,1	±3,7	0.18
BMI(kg/m^2)			25,5	±3,2		24,3	±0,7	0.01*
SBP(mmHg)			135,7	±18,4		118,7	±2,2	0,04*
DBP(mmHg)			87,9	±10,5		78,7	±3,1	0.006*
D.M.		324 (72)			0(0)			
WC(cm.)		381 (84)	97,5	±8,7	0(0)	84,7	±7,8	0.00*
HDL-chlol(mmol/l)		303 (67)	0,9	±0,2		1,2	±0,6	0.00*
Triglicer(mmol/l).		251 (56)	1,9	±0,4	0(0)	1,4	±0,1	0.04*
Three MetS riskfac.		248 (55)			0(0)			
Four MetS risk fac.		139 (31)			0(0)			
Five MetS risk fac.		63 (14)			0(0)			
LAVI(ml/m^2) >34		179 (39,7)			0(0)			
E (cm/s.)			0,77	±2,2		0,87	±0,12	0.00*
A (cm/s.)			0,63	±0,8		0,54	±0,11	0.00*
E/A ratio <0.8		179 (39,7)			6(6)			
e,(cm/s)			8,1	±0,5		8,5	±0,3	0.01*
E/ e, ratio ≥8		179 (39,7)			6(6)		0.00*	
DT(m/s) >200		179 (39,7)	199,7	±1,2	6(6)	183,3	±20,14	0.00*
IVRT(m/s) >100		179 (39,7)	101,9	±22,1	6(6)	89,5	±10,12	0.00*
LVMI(gr/m^2)			59,5	±1,9		32,1	± 7,5	0.00*

Table 1: Basic demographic, anthropometric, laboratory and echocardiographic characteristics of study population N=550 (Group with Met. S: N=450 and Control Group: N=100)

Fifty five percent (55%) of subjects with MetS met at least three of the established criteria,while fourteen percent (14%) of subjects with MetS met five of the established criteria.

Echocardiographic measures for control and MetS groups are presented in Table 1.There were no differences in LV dimensions and LVEF between groups.Subjects with MetS have greater LV mass index(59,5 ±1,9 vs. 32,1±7,5 p=0.00).Subjects with MetS also had worse measures of diastolic function,including:higher LAVI, lower E/A ratio and lower mean e', lower E/ e' ratio,increased DCT and IVRT (0,77±2,2 vs.0,87±0,12 p=0.00;0,63 ±0,8 vs. 0,54±0,11 p =0.00;39,7% vs.6% p=0.00; 8,1±0,5 vs. 8,5±0,3 p = 0.01; 39,7% vs.6% p=0.00;39,7% vs. 6% p=0.00; 39,7% vs. 6% p=0.00).

As shown in Table 3 and Figure 1, participants with MetS, have significantly increased frequency of subclinical LVDD grade 1, in comparation with participants without MetS.(39,7% vs. 6%, p=0.0005).The overall frequency of subclinical LVDD grade 1,in participants with MetS,was 39,7%; P=0.0005).

Baseline demographic, anthropometric and laboratory characteristics of participants with MetS, stratified by presence of subclinic LVDD, are displayed in Table 2.There was significant changes in relation to frequency of subclinic LVDD between females and males. Females have higher frequency of subclinic LVDD in comparation with males.(68% vs.32%;p=0.001). Participants with subclinic LVDD were older than participants with normal diastolic function (p=0.001). Overall, participants with subclinic LVDD, had a worse cardiovascular risk factor profile, including higher BMI, higher BP, elevated WC and dyslipidemia. (26,9±3,1 vs. 24,6±3,0 p=0.001; 138,3 ±18,0 vs.134,0±18,5 p=0,000; 89,7±10,2 vs. 86,8±10,6 p= 0.003; 99,1±8,8 vs. 94,9±8,0p=0.001;0,85±0,1 vs. 1,0±0,2 p=0.000; 2,1±0,5 vs. 1,7±0,4 p=0.000). Also as shown in Table 2 and Figure 2, participants with subclinic LVDD, have higher number of risk factors for MetS than participants with normal diastolic function(42% vs. 23% p=0.002; 23% vs. 0,7% p=0.001).

As shown in Table 3 and Figure 1, participants with MetS, have significantly increased frequency of subclinical LVDD grade 1, in comparation with participants without MetS. (39,7% vs. 6%, p=0.0005). The overall frequency of subclinical LVDD grade 1,in participants with MetS, was 39,7%; p=0.0005).

Echocardiographic measures for group with subclinic LVDD and group with normal diastolic function among participants with MetS, are presented in Table 4. Participants with subclinic LVDD had worse measures of diastolic function, including: higher LAVI, lower Mitral E peak wave,higher Mitral A peak wave,lower E/A ration,lower mean e,; E/ e, ratio ≥8,increased DT(m/s) >200;increased IVRT(m/s) >100.(0,53±0,1 vs. 0,76±0,1 p=0.00; 0,81±0,13 vs. 0,51 ±0,8 p=0.00; 39,7% vs. 6% p=0.00; 8,1±0,5 vs.

8,5±0,3 p=0.01; 39,7% vs. 6%; p=0.00; 39,7% vs 6% p=0.000; 218,5±24,1 vs.187,4±16,9 p=0.00; 39,7% vs. 6% p=0.000;124,9±15,6 vs.86,7 ±8,38 p=0.00).

Variables		Gr. with Met.S (N.450)						P - value
		Gr. with sub.D.D(n-179)			Gr.with normal.D.F.(n.271)			
		N. (%)	Mean	SD	N. (%)	Mean	SD	
Gender	Females	122 (68)			100 (37%)			0.001*
	Males	57 (32)			171 (63%)			0.004*
Age (year)		114 (64)	51,5	±3,5	201 (74)	50,1	±3,8	0.001*
BMI(kg/m²)			26,9	±3,1		24,6	±3,0	0.001*
SBP(mmHg)			138,3	±18,0		134,0	±18,5	0,000*
DBP(mmHg)			89,7	±10,2		86,8	±10,6	0.003*
D.M.		129 (72)			195 (71)			0.96
WC(cm.)		149 (83)	99,1	±8,8	232 (85)	94,9	±8,0	0.001*
HDL-chlol(mmol/l)		168 (93)	0,85	±0,1	135 (49)	1,0	±0,2	0.000*
Triglicer(mmol/l).		136 (76)	2,1	±0,5	115 (42)	1,7	±0,4	0.000*
Three MetS risk fac.		62 (35)			186 (68)			0.001*
Four MetS risk fac.		76 (42)			63 (23)			0.002*
Five MetS risk fac.		42 (23)			21 (0,7)			0.001*

Table 2: Demographic, antropometric and laboratory characteristics of group with subclinic LVDD (n-179) and group with normal diastolic function (n-271) among patient with Met. S (n.450)

Chi-square: 12,05; p*= 0.0005 Study Group (n-550)					
Gr. with MetS(n-450)			Gr. without MetS(n.100)		
Gr.with subclinic LVDD		Gr.without subclinic LVDD	Gr.with subclinic LVDD	Gr.without subclinic LVDD	total
Count (No)	179	271	6	94	550
Percent (%)	39,7	60,3	6	94	100

Table 3: Frequency of subclinic LVDD among study patient (N.550)
The overall frequency of subclinical LVDD in participants with MetS,was 39,7%. P*<0.05

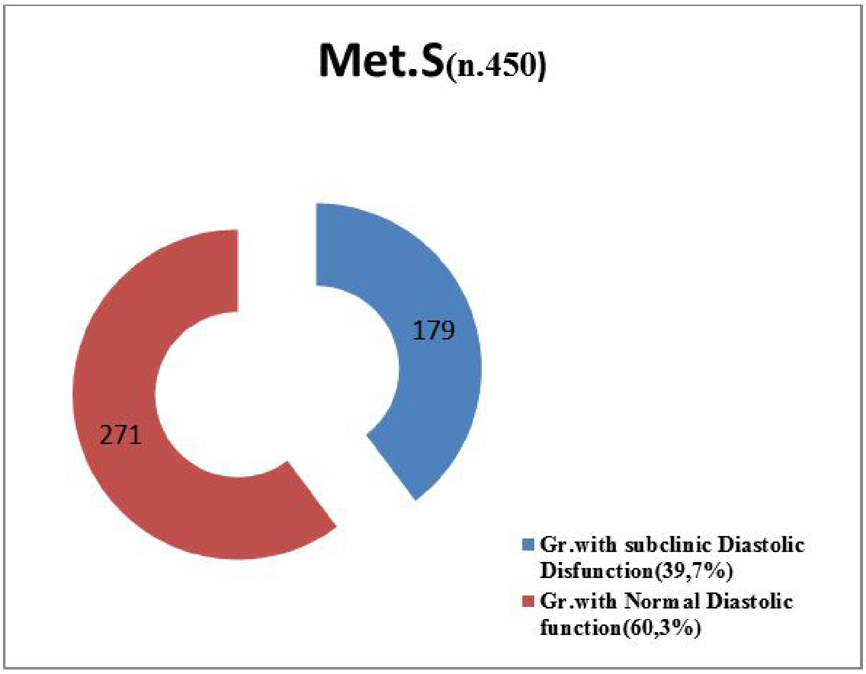

Figure 1: Frequency of subclinic LVDD among patient with Met. S. (N.450)
Frequency of subclinical LVDD in participants with MetS,was 39,7%. P*<0.05 for between group comparation

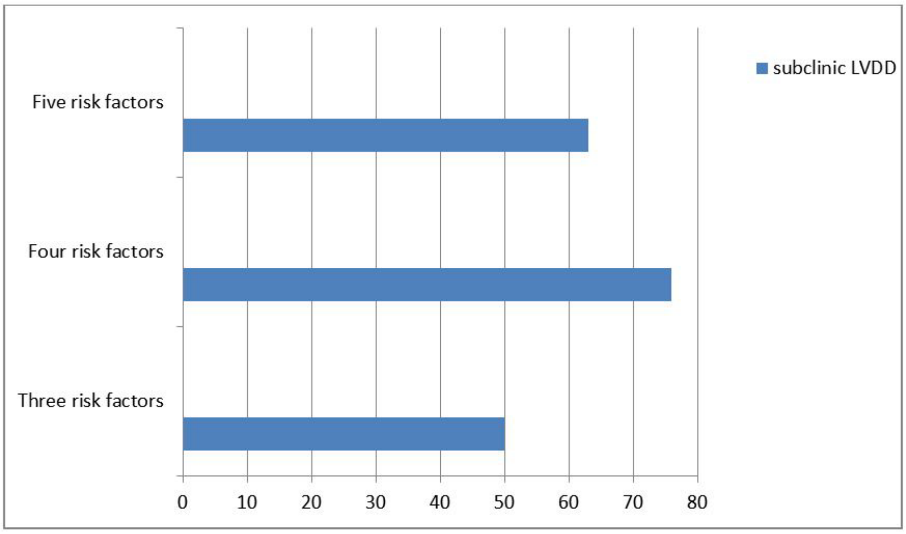

Figure 2: Frequency of subclinic LVDD among patient with different number of risk factors among patient with Met.S. (N.450)
Among patient with Met.S,participants with subclinic LVDD, have higher number of risk factors for MetS than participants with normal diastolic function. P<0.005

Variables	Gr. with Met.S (N.450)						P - value
	Gr. with sub.D.D(n-179)			Gr.with normal.D.F.(n.271)			
	N. (%)	Mean	SD	N. (%)	Mean	SD	
LAVI(ml/m2) >34	179 (39,7)	34,6	±0,5	0 (0)	25,2	±1,3	**0.00***
LVEDD(mm)		4,86	±0,4		4,82	±0,5	0.34
LVESD(mm)		2,93	±0,5		2,96	±0,4	0,79
THS(mm)		1,04	±0,1		1,1	±0,1	0,06
PWTH(mm)		1,0	±0,1		0,9	±0,2	0,34
EF(%)		0,67	±0,12		0,66	±0,6	0,29
FS(%)		0,37	±0,05		0,38	±0,04	0,43
LVMI(gr/m2)		59,71	±2,05		59,47	±1,87	0.18
E (cm/s.)		0,53	±0,1		0,76	±0,1	**0.00***
A(cm/s.)		0,81	±0,13		0,51	±0,8	**0.00***
E/A ratio <0.8	179 (39,7)			6(6)			**0.00***
e,(cm/s)		8,1	±0,5		8,5	±0,3	**0.01***
E/ e, ratio ≥8	179 (39,7)			6(6)			**0.00***
DT(m/s) >200	179 (39,7)	218,5	±24,1	6(6)	187,4	±16,9	**0.00***
IVRT(m/s) >100	179 (39,7)	124,9	±15,6	6(6)	86,7	±8,38	**0.00**

Table 4: Echocardiographic characteristics of group with subclinic LVDD (n-179) and group with normal diastolic function (n-271) among patient with Met. S (n. 450)

	OR	**Sig.**	**95% C.I.for EXP(B)**	
			Lower	**Upper**
AGES	1.108*	.000	1.051	1.168
Females	3.633*	.000	2.439	5.413
BMI	7.474*	.000	4.881	11.443
Contr.BP	1.204*	.004	1.204	2.580
MetS-RF n-five.	2.054*	.000	2.054	6.340

Table 5: Logistic Rgresion Model:Assotiation of subclinic LVDD and;Ages,BMI,Cont. BP and MetS-RF number, in patient with MetS
Significant association of subclinical LVDD and Ages,BMI,Cont.BP and MetS-RF number, were observed among participants with MetS . OR* >1

Association of subclinical LVDD with: demographic, anthropometric and clinical parameters are displayed in Table 5.Ther is a significant association between subclinical LVDD and ages in patient with MetS (OR =1.108, 95% CI 1.051-1.168).There was observed significant association between subclinical (LVDD) and females among patient with MetS. Females, for (OR=3.63; 95% CI 2.439-5.413) have 1.29 times higher risk for sub-clinic LVDD in comparation with males. Significant association between subclinical LVDD and BMI were observed among participants with MetS. Participants with increased BMI, for (OR=7.474; 95% CI 4.881-11.443) have 2.011times higher risk for subclinical LVDD in comparation to participants with normal BMI.Uncontroled BP in patient with MetS,was significantly associated with subclinical LVDD. Participants with subclinical LVDD, for (OR=1.763; 95%CI 1.204-2.580).) have 0.56 times higher risk for subclinical LVDD in comparation to participants with controlled BP. The number of risk factors for MetS, also was associated with subclinical LVDD.For (OR=3.609; 95% CI 2.054-6.340) participants with five RF have 1.28 times higher risk for subclinical LVDD in comparation to participants with three RF.

Discussion

In this study, we observed that the frequency of subclinic LVDD among patient with MetS was significantly increased in comparation to patient without MetS. (39, 7% vs. 6%;p=0.0005, respectively). We found that MetS was associated with subclinical LV diastolic dysfunction as reflected by higher: LAVI , lower E/A ratio,increased E/e, ratio, prolonged DCT and prolonged IVRT, in a sample of individuals without existing cardiovascular disease.These findings suggest that MetS can lead to the development of diastolic dysfunction via mechanisms that are independent of hypertrophy, coronary disease, and potentially lead further insights into the increased cardiovascular risk observed in MetS [19-21].

The influence of gender in the prevalence of LVDD is proved in some but not in all reports [22]. In our study was observed significant gender difference in frequency of of subclinical LVDD among participants with MetS.Females have higher frequency of subclinical LVDD than males. These data are in line with earlier observations [23]. Attention to gender specifies should be a mandatory pre-requisite of clinical and epidemiological research on MetS and cardio-vascular disease, for better knowledge and development of health strategies.

In the present study, in group of MetS, subclinical LVDD was significantly associated with age. A number of previous studies have demonstrated that frequency of subclinical LVDD among patient with MetS significantly increased increasing the age [24]. As the reduced ventricular compliance is secondary to the ageing process,since the ventricular stiffness increases with age and impairs diastolic function altering LV filling pressure 24.Nevertheless,nature of the some Doppler-echocadiographic changes with aging is partially unclear and precise discrimination between pathologic or physiologic changes remain difficult.

Our results are consistent with prior studies showing an association of MetS and increased in LV mass [25]. While elevated BP is one of the important components of MetS, and hypertension is known to lead to increases in LV mass [26]. Previous study, not at all, reported situation of increased in LV mass and elevated BP, whereas Nir Avalon et al.in their study,founded that the association of MetS and increased LV mass, was independent of blood pressure [26,27].

In the present study, BMI, SBP, DBP, and triglycerides were significantly higher in the MetS patients with subclinical LVDD than in the MetS patients without subclinical LVDD, whereas lower high-density lipoprotein cholesterol were significantly decreased in the metabolic syndrome patients with subclinic LVDD than in the metabolic syndrome patients without subclinic LVDD. Our results are consistent with prior studies [27-29]. A cluster of these cardiovascular risk factors may produce latent cardiac diastolic dysfunction in metabolic syndrome.

Levt ventricular diastolic function (LVDF) appear to worsen in a stepwise fashion with the number of risk factors for MetS.In the present study number of risk factors were significantly higher in the metabolic syndrome patients with subclinic LVDD than in the metabolic syndrome patients without subclinic LVDD, Our results are consistent with prior studies [4,7].

The pathophysiological mechanism by which MetS can lead to abnormalities in LV diastolic function is not well understood. In mouse models of diet-induced MetS, increased myocardial oxidative stress has been implicated in the development of diastolic dysfunction, and was associated with both hypertrophy and fibrosis of the myocardium [30]. Animal models of insulin resistance, hypertension, or dyslipidemia have also implicated the development of cardiac fibrosis, abnormal intracellular calcium handling, cardiomyocyte lipotoxicity, mitochondrial dysfunction,impaired endothelial blood flow, increased vascular stiffness, and inflammation [30-32]. While mechanistic inferences cannot be drawn from our observational study, these results support the notion that metabolic heart disease can lead to impaired myocardial relaxation in the absence of. Further studies are needed to elucidate potential mechanisms and potential therapeutic targets.

Several limitations deserve mention. Our study is a cross-sectional observational study, and causal inferences are therefore limited. A larger sample would certainly increase the statistical power of the study, and probably same differences would therefore become more expressive. Healthy controls were selected based on the absence of any MetS criteria. This resulted by design in baseline differences of clinical characteristics between participants with and without MetS. It is therefore possible that residual confounding could in part account for our findings. It was impossible to rule out coronary heart disease as a reason for subclinical LVDD by coronary angiography, because it is difficult to influence asymptomatic patients for an invasive procedure and also from ethical standpoint. This limitation is unavoidable. We do not believe that subtle coronary atheriosclerosis would have an influence in the study results at a significant degree, and will not reduce the values of the basic conclusions of the study as well.

Conclusions

The prevalence of subclinical LVDD in the patients with MetS, in absence of coronary heart disease and other well know heart disease, is considerablye high, in western region of the Republic of Macedonia and seems to be significantly associated with age,gender, BMI,LVM and high number of risk factors for MetS. Attention to high prevalence of subclinical LVDD in the patients with MetS, should be a mandatory pre-requisite of clinical and epidemiological research on MetS and cardio-vascular disease, for better knowledge and development of health strategies for primary prevention of manifested heart failure.

Authorship contributions

Concept-YlberJani; Design–BekimPocesta; Supervision- Atila Rexhepi; Materials-FatmirFerati; DaliLala; Agim Zeqiri; rben Mirto; Data collection/processing-Sotiraq Xhunga ; Artur Serani;Analysis/interpretation-Ylber.Jani.; Atila Rexhepi; Bekim Pocesta; Literature Search-Dali.Lala; Fatmir Ferati; Ylber Jani; Artur Serani. Critical Reviews: Ahmet Kamberi; Atila Rxhepi.

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