Obesity determines right ventricular subclinical dysfunction in middle-aged individuals

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Background: Right ventricular (RV) dysfunction is a relevant prognostic factor in different cardiovascular conditions, but its early determinants remain unclear.

Purpose: This study aimed to identify the main determinants of RV performance through CMR in a large cohort of asymptomatic middle-aged individuals.

Methods: A subgroup of asymptomatic middle-aged participants from the PESA cardiovascular cohort underwent RV assessment by CMR-strain and a comprehensive screening of all possible factors that may influence RV performance (including demographics, cardiometabolic risk factors, physical activity objectively measured by accelerometry, and laboratory parameters). To further understand the mechanism through which RV performance may be affected, subjects additionally underwent stress CMR to assess myocardial perfusion reserve and tissue characterization; 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) to quantify bone marrow metabolic activity, and non-contrast cardiac computed tomography (CT) to measure epicardial adiposity. RV free wall longitudinal strain was calculated through myocardial tagging, and participants were divided into tertiles based on strain values. Age and sex-adjusted trend analyses were conducted, followed by multivariate lineal regression to identify independent predictors of RV strain. Subsequently, mediators of the association between obesity and RV strain were investigated.

Results: 609 individuals (mean age 52.7 years; 82.8% male) were included with a median RV ejection fraction of 59.4% [56.2–62.8] and RV strain -21.3% [-23.5 to -18.3]. After adjusting for age and sex, RV strain positively correlated with body mass index (BMI), waist circumference, non-alcoholic fatty liver disease, fasting glucose, and glycated hemoglobin (HbA1c) and negatively with left ventricular (LV) ejection fraction. Interestingly, bone marrow uptake (surrogate of increased hematopoietic activity) showed a significant positive linear association with RV strain (Table). In multivariable analysis, male sex, BMI, and lower LVEF remained independent predictors of RV strain (Figure). To further understand the association between obesity and RV performance, individuals were recategorized based on BMI tertiles. Higher BMI tertiles were linked to increased bone marrow FDG uptake, lower T1 values, larger epicardial adipose tissue volume, and reduced septal myocardial perfusion reserve, suggesting exacerbated hematopoiesis, myocardial adipose infiltration, epicardial compression and coronary microvascular dysfunction as intermediate mechanisms (Figure).

Conclusions: In asymptomatic middle-aged individuals, obesity emerged as a key determinant of subclinical RV dysfunction, alongside with male sex and LVEF. Increased hematopoietic activity, myocardial adipose infiltration, epicardial compression and coronary microvascular dysfunction were identified as intermediate mechanisms of this association.

	Total N=609	RV strain T1 (-32.4 to -22.6%) N=203	RV strain T2 (-22.6 to -19.6%) N=203	RV strain T3 (-19.6 to -7.8%) N=203	P trend	Beta (95%CI)	Age & Sex adj. P
Demographics and cardiometabolic risk factors							
Age, years	52.7 [49.1;56.2]	53.0 [49.1;56.1]	52.8 [49.0;56.1]	52.3 [49.5;56.4]	0.908		
Female sex	105 (17.2)	69 (34.0)	24 (11.8)	12 (5.9)	**<0.001**	-3.537 (-4.344;-2.731)	**<0.001**
Hypertension	119 (19.5)	37 (18.2)	33 (16.3)	49 (24.1)	0.133		
Dyslipidemia	351 (57.6)	113 (55.7)	117 (57.6)	121 (59.6)	0.422		
Diabetes mellitus	30 (4.9)	6 (3.0)	12 (5.9)	12 (5.9)	0.169		
Current smoking	137 (22.5)	54 (26.6)	46 (22.7)	37 (18.2)	**0.043**	-0.658 (-1.389;0.074)	0.078
BMI, kg/m²	26.8 ± 3.4	25.9 ± 3.5	26.9 ± 3.4	27.6 ± 3.1	**<0.001**	0.130 (0.036;0.224)	**0.007**
WC, cm	94 ± 11.0	91 ± 11.7	95 ± 10.1	97 ± 10.1	**<0.001**	0.045 (0.013;0.077)	**0.006**
NAFLD score, points	-1.9 [-2.5; 1.3]	-2.2 [-2.6;-1.4]	-1.9 [-2.4;-1.3]	-1.7 [-2.3;-1.0]	**<0.001**	0.243 (0.022;0.463)	**0.031**
Moderate-to-vigorous physical activity, min/day	38 [25;56]	35 [25-53]	38 [24-58]	39 [26-56]	0.304		
Laboratory parameters							
Hematocrit, %	43.3 (3.1)	42.4 (3.3)	43.6 (3.2)	44.0 (2.6)	**<0.001**	0.090 (-0.020; 0.210)	0.110
Total cholesterol, mg/dL	210 ± 36.8	214 ± 35.5	208 ± 37.6	207 ± 36.9	**0.023**	-0.007(-0.015;0.001)	0.100
Fasting glucose, mg/dL	91 [85;97]	88 [83;96]	91 [86;97]	92 [85;98]	**0.003**	0.020 (0.0016; 0.039)	**0.034**
HbA1c, %	5.4 [5.2;5.7]	5.4 [5.2;5.7]	5.4 [5.2;5.7]	5.5 [5.2;5.7]	**0.043**	0.646 (0.019;1.272)	**0.044**
C-reactive protein, mg/dL	0.10 [0.06;0.19]	0.09 [0.05;0.16]	0.11 [0.06;0.20]	0.12 [0.06;0.21]	**0.038**	0.558 (-0.600;1.715)	0.345
Cardiac magnetic resonance							
LVEF, %	60.6 [57.2;63.8]	62.0 [58.5;65.2]	60.0 [57.1;63.5]	59.2 [56.4;63.0]	**<0.001**	-0.100 (-0.168;-0.033)	**0.004**
RVEF, %	59.4 [56.2;62.8]	60.6 [57.5;64.0]	59.3 [56.6;62.6]	58.0 [55.5;61.8]	**<0.001**	-0.083(-0.153; -0.014)	**0.019**
RV-PA coupling	0.68 [0.59;0.78]	0.65 [0.56; 0.74]	0.68 [0.60; 0.77]	0.72 [0.62;0.80]	**<0.001**	2.685 (0.251; 5.120)	**0.031**
Native T1, ms (N=561)	1303 [1278;13322]	1308 [1288;1337]	1300 [1275;1332]	1300 [1274;1325]	**0.007**	-0.0009 (-0.009;0.0068)	0.812
^{18F}-FDG PET/MR. Bone marrow uptake							
Bone marrow, SUV max (N=490)	1.93 ± 0.41	1.86 ± 0.38	1.95 ± 0.40	1.99 ± 0.43	**0.012**	0.831 (0.027; 1.635)	**0.043**
Non-contrast cardiac computed tomography							
EAT volume, mL (N=591)	77.3[54.1;111.6]	67.1 [48;96.7]	79.8 [56.1;112.7]	85.4 [59;119.1]	**<0.001**	0.002 (-0.007; 0.010)	0.718
CACS, Agatston (N=595)	8.5 [0.0;56.1]	5.9 [0.0;51.7]	13.8 [0.0;66.4]	8.5 [0.0;42.1]	0.690		

N= 609 asymptomatic participants (median age 53 yo)

Independent predictors of RV strain

	RV free-wall longitudinal strain (%) N=609	
	Beta-Coefficient (CI 95%)	Adjusted p-value
Age (years)	-0.04 (-0.11; 0.03)	0.244
Male	2.89 (2.03; 3.75)	**<0.001**
BMI	0.11 (0.02; 0.20)	**0.022**
Hemoglobin A1c	0.59 (-0.04; 1.21)	0.067
LVEF	-0.10 (-0.17; -0.03)	**0.004**

Potential mechanisms linking obesity with subclinical RV dysfunction