ORIGINAL ARTICLE

Obesity-related adjunctive systo–diastolic ventricular dysfunction in patients with hypertension: echocardiographic assessment with tissue Doppler velocity and strain imaging

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Very few data exist regarding the effect of obesity on both left and right systo–diastolic ventricular function in hypertensive patients. Therefore, the aim of this study was to determine the existence and extent of an obesity-related adjunctive depressive effect on left- and right-ventricular systo–diastolic dysfunction. This study compared non-obese with obese hypertensive patients and evaluated left- and right-ventricular morphological and functional parameters by means of conventional echocardiography and by two new sensitive echocardiographic techniques: tissue Doppler velocity and strain imaging. We selected 248 hypertensive patients and divided them into four groups according to increasing body mass index (BMI). All patients underwent a clinical history and examination and transthoracic echocardiography, including conventional echocardiographic evaluation and tissue Doppler velocity and strain imaging measurements. Conventional echocardiographic evaluation did not reveal an association between ventricular systo–diastolic dysfunction and increasing BMI. In contrast, tissue Doppler velocity and strain imaging measurements emphasized the negative influence of obesity. For measurements in both the left and right ventricle, myocardial early peak diastolic velocities (E_m), the ratio of myocardial early-to-late peak diastolic velocity (E_m/A_m), myocardial peak systolic velocities (S_m), and peak strain and strain rate values significantly decreased with increasing BMI ($P < 0.01$ for all parameters measured), even after adjusting for potential confounding variables. In conclusion, by means of new more sensitive echocardiographic techniques, our study clearly demonstrated the negative impact of obesity on both left- and right-ventricular systo–diastolic function, in terms of adjunctive sub-clinical worsening, in hypertensive patients.

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INTRODUCTION

The prevalence of obesity, defined as a body mass index (BMI) $\geq 30 \text{ kg m}^{-2}$, is dramatically increasing worldwide.^{1,2} Obesity is associated with a higher rate of cardiovascular morbidity and mortality. It is an independent risk factor for the development of heart failure,³ even after accounting for other comorbid conditions that cluster with it, such as diabetes and hypertension.⁴ Moreover, obesity has been associated with heart failure,⁵ left-ventricular dilation, increased left-ventricular wall stress and compensatory (eccentric) left-ventricular hypertrophy.^{6,7}

Impairment of cardiac function has been reported to correlate with BMI and the duration of obesity,^{7,8} with most studies demonstrating abnormal diastolic function,^{9,10} without a consistent association with systolic dysfunction.^{7,8} A condition characterized by chronic left-ventricular volume overload, eccentric hypertrophy and progressive

diastolic impairment, commonly leading to heart failure, have also been described as a unique entity named ‘obesity cardiomyopathy’.⁶ Indeed, obesity has been linked to a spectrum of more minor cardiovascular changes, ranging from hyperdynamic circulation to sub-clinical cardiac structural changes.^{5,6} These early manifestations may be important because treatment to reverse this process is most likely to be effective earlier in the disease. More recently, it has been suggested that even milder degrees of obesity may negatively affect cardiac performance by means of subtle alterations in left-ventricular structure and morphology, and alterations in either sub-clinical or clinical systo–diastolic mechanics.^{4,11,12} In addition, an association between sub-clinical right-ventricular dysfunction and obesity has also been reported.¹³

Furthermore, because these data were mainly derived from studies performed in otherwise healthy subjects with isolated obesity, the

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limitations of this evidence must be recognized. Very few data exist regarding the effect of obesity on left- and right systo-diastolic ventricular function in hypertensive patients.

Therefore, the aim of this study was to evaluate left- and right-ventricular morphological and functional parameters by means of conventional echocardiography and new sensitive echocardiographic techniques—tissue Doppler velocity and strain imaging—in non-obese and obese hypertensive patients.

METHODS

Study characteristics and population

By clinical-instrumental evaluation, we selected 248 patients, referred to our structures with a diagnosis of hypertension (at least three ambulatory resting measurements of systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg), who satisfied the following inclusion criteria:

1. No evidence of diabetes mellitus or other significant systemic diseases other than hypertension and non-syndromal obesity;
2. No evidence of significant organic cardiovascular disease, except hypertensive cardiomyopathy;
3. Presence of normal sinus rhythm with no abnormalities on electrocardiography;
4. Presence of adequate acoustic windows and normal echocardiographic-Doppler parameters other than mitral transvalvular diastolic flow patterns and mild left-ventricular hypertrophy (end-diastolic interventricular septum and posterior wall thickness ≤ 14 and ≤ 13 mm, respectively), without any other underlying etiology;
5. Absence of drug therapy, other than ongoing antihypertensive drug therapy, that was stable for at least 2 months.

Instrumental evaluation

To exclude organic cardiovascular and systemic disease, patients underwent a clinical history and examination, a biochemical analysis, resting and stress electrocardiography and transthoracic echocardiography.

Four groups of hypertensive patients were identified according to their BMI: non-obese (BMI < 25 kg m $^{-2}$; $n=58$), overweight (BMI 25 to 30 kg m $^{-2}$; $n=67$), mildly obese (BMI 30–35 kg m $^{-2}$; $n=63$) and severely obese (BMI > 35 kg m $^{-2}$; $n=60$).

All enrolled patients underwent Doppler echocardiography, with a commercially available standard ultrasound diagnostic system (Vivid 7, GE Vingmed, Horten, Norway), equipped with a 2.5-MHz phased-array transducer. Images were obtained in the standard tomographic views of the left ventricle (parasternal long- and short-axis and apical four chamber, two chamber and long-axis views). All echocardiographic studies were digitally stored for off-line analysis. All measurements were averaged from three cardiac cycles to minimize respiratory variability, and were blind-performed twice by three different and independent expert sonographers (ML, LS and MGB) to minimize intra- and interobserver variabilities, expressed as a coefficient of variation. Left- and right ventricular end-diastolic and end-systolic diameters and septal, posterior, relative, right ventricular free wall thickness were obtained from the bi-dimensional-targeted mono-dimensional echocardiographic tracings in the parasternal long and short-axis scans according to the criteria of the *American Society of Echocardiography guidelines*,^{14,15} and then left-ventricular indexed end-diastolic and systolic volumes, left-ventricular ejection fraction (Simpson's biplane-modified method) and left-ventricular fractional shortening (left-ventricular end diastolic diameter-left-ventricular end-systolic diameter/left-ventricular end-diastolic diameter $\times 100$) were calculated; left-ventricular mass index was determined by Devereux's formula and indexed to height to the power of 2.7.¹⁶ Right ventricular end-diastolic volumes and ejection fraction were calculated from apical four-chamber views using the area-length monoplane method ($V_{RV} = 3/8\pi(\text{area}^2/\text{length})$).

The Doppler's transvalvular parameters measured were mitral E and A wave peak velocities, the ratio of mitral early-to-late peak velocity, and early filling

deceleration and isovolumic relaxation times, obtained in apical four-chamber echocardiographic windows by placing the sample volume at the level of the valve leaflet tips.

The processing of ultrasound and tissue Doppler signals provide a number of sensitive parameters of systolic and diastolic function that are less sensitive to loading and correlate with structural changes such as myocardial fibrosis.¹⁷ Tissue Doppler measurements have also been used to derive myocardial strain and strain rate, which are well-validated descriptors of shortening and lengthening that reflect tissue compressibility.¹¹

Myocardial velocities were recorded by using color tissue Doppler imaging in each apical view, using a high frame rate (120 MHz) and a temporal resolution of 8 ms. Images were recorded and digitized, and derivation and analysis of tissue Doppler velocity profiles were performed off-line, using commercially available computer software (Echopac, GE Vingmed).

Strain and strain rate curves were extracted from color tissue Doppler images using standard software (Echopac, GE Vingmed). Peak strain was defined as the greatest value on the strain curve, and peak strain rate was measured from the strain curve as previously validated.^{18,19}

Briefly, for all patients, mean values of myocardial peak systolic (S_m), early peak diastolic (E_m) and late peak diastolic velocities (A_m) of the septal, lateral, inferior and anterior regions of the mitral annulus were calculated. Values of S_m , E_m and A_m of the lateral region of the tricuspid annulus, and of peak strain and strain rate values of the basal interventricular septum and the basal right ventricular free wall were also obtained. Ratios of mitral and tricuspid annulus myocardial early-to-late peak diastolic velocity (E_m/A_m) were derived, and left-ventricular filling pressures were approximated from the relationship of early-diastolic mitral inflow/mitral annular velocity ratio.

Statistical analysis

Statistical analyses were performed with SPSS/PC for Windows release 11.0 dedicated software (SPSS Inc, Chicago, IL, USA). An estimation of inter-group differences between clinical, echocardiographic and generally quantitative characteristics was performed with an analysis of variance (ANOVA) by Dunnett's *post-hoc* test for multiple comparisons; categorical variables were analyzed by the χ^2 test. Multivariate stepwise linear regression analysis was performed to assess the correlation between echocardiographic variables and BMI adjusted for age, gender, mean blood pressure, left-ventricular mass index, relative wall thickness and right-ventricular free wall thickness. All continuous variables and results are expressed as mean $\pm$ s.d. with categorical variables as frequencies; P -values < 0.05 were considered statistically significant.

RESULTS

Clinical characteristics

Descriptive clinical and echocardiographic characteristics of the four groups of patients are summarized in Table 1. All patients were on antihypertensive therapy. Given that differences in weight, body surface area and BMI reflect the patients' categorization, no other significant variations (age, gender, heart rate, smoking status, systolic-diastolic-mean blood pressure or type of antihypertensive drug therapy) were identified. The results of biochemical analyses (renal function, electrolytes, fasting plasma glucose and lipid profile), and of resting and stress electrocardiography were normal in all patients, with no significant differences between the groups.

Echocardiographic characteristics

With increasing BMI, conventional echocardiography (Table 2) revealed a significant increase only for septal and posterior wall thickness, left-ventricular mass index ($P < 0.001$ for all), relative and right-ventricular free wall thickness ($P < 0.05$ for all). With regard to Doppler transvalvular parameters, only isovolumic relaxation and early filling deceleration times ($P < 0.05$ for all) showed a significant modification. This was likely because of the influence of hemodynamic conditions on mitral early-late peak velocity measurements that

Table 1 Main characteristics of the study population

	Non-obesity (BMI < 25 kg m ⁻² ; n=58)	Overweight (BMI 25 to 30 kg m ⁻² ; n=67)	Mild obesity (BMI 30 to 35 kg m ⁻² ; n=63)	Severe obesity (BMI > 35 kg m ⁻² ; n=60)	P-value
Mean age (years)	53 ± 10	56 ± 12	52 ± 11	58 ± 9	0.41
Male gender (n, %)	27 (47)	33 (49)	30 (48)	34 (57)	0.36
Weight (kg)	69 ± 15	84 ± 14	100 ± 10	126 ± 12	<0.001
Height (cm)	171 ± 9	173 ± 10	170 ± 11	166 ± 9	0.11
Body surface area (m ²)	1.65 ± 0.12	1.89 ± 0.15	2.02 ± 0.18	2.26 ± 0.15	<0.001
BMI (kg m ⁻²)	22.4 ± 1.5	28.6 ± 1.8	32.7 ± 1.4	39.3 ± 3.6	<0.001
Smoking status (n, %)	20 (35)	25 (37)	25 (40)	23 (39)	0.43
Heart rate (b.p.m.)	69 ± 11	70 ± 10	73 ± 8	75 ± 12	0.14
Systolic blood pressure (mm Hg)	129 ± 14	132 ± 12	130 ± 15	134 ± 13	0.61
Diastolic blood pressure (mm Hg)	85 ± 9	84 ± 7	88 ± 9	87 ± 12	0.26
Mean blood pressure (mm Hg)	100 ± 10	102 ± 8	101 ± 11	103 ± 10	0.71
Beta-blockers (n, %)	15 (25)	15 (23)	13 (21)	12 (20)	0.32
Angiotensin-converting enzyme inhibitors (n, %)	35 (60)	41 (61)	41 (65)	35 (59)	0.76
Calcium-channel blockers (n, %)	17 (30)	18 (27)	16 (25)	14 (23)	0.28
Diuretics (n, %)	16 (28)	21 (32)	22 (35)	23 (38)	0.13
Angiotensin II receptor blockers (n, %)	15 (26)	16 (24)	18 (28)	15 (25)	0.66

Abbreviations: BMI, body mass index; b.p.m., beat per minute.

Table 2 Conventional echocardiographic parameters

	Non-obesity (BMI < 25 kg m ⁻² ; n=58)	Overweight (BMI 25 to 30 kg m ⁻² ; n=67)	Mild obesity (BMI 30 to 35 kg m ⁻² ; n=63)	Severe obesity (BMI > 35 kg m ⁻² ; n=60)	P-value
LVEdD (mm)	47.2 ± 3.9	48.6 ± 4.5	48.1 ± 4.9	49.8 ± 5.1	0.16
LVEsD (mm)	26.9 ± 4.2	28.5 ± 4.4	29.0 ± 4.7	28.9 ± 5.0	0.22
FS (%)	34.6 ± 3.9	35.7 ± 4.8	35.2 ± 4.6	34.8 ± 5.2	0.68
LVEdV (ml)	107.2 ± 25.3	108.9 ± 27.1	109.5 ± 30.6	111.8 ± 31.7	0.12
LVEsV (ml)	36.5 ± 11.8	37.9 ± 12.2	38.5 ± 13.0	39.3 ± 13.5	0.20
LVEF (%)	66.7 ± 6.4	67.2 ± 6.0	66.9 ± 7.3	66.5 ± 7.6	0.54
SWT (mm)	11.2 ± 1.04	12.0 ± 1.06	12.5 ± 0.98	12.8 ± 1.12	<0.001
PWT (mm)	10.3 ± 0.89	11.0 ± 1.14	11.4 ± 1.20	11.7 ± 1.15	<0.001
LVMi (g m ^{-2.7})	42.5 ± 14.9	48.7 ± 19.2	54.9 ± 18.6	59.8 ± 22.3	<0.001
RWT (mm)	0.46 ± 0.09	0.48 ± 0.07	0.51 ± 0.06	0.50 ± 0.08	<0.05
RVEdD (mm)	21.6 ± 1.3	22.5 ± 1.2	23.0 ± 1.4	23.8 ± 1.9	0.31
RVFWT (mm)	3.3 ± 0.74	3.8 ± 0.94	3.9 ± 0.78	4.1 ± 1.2	<0.05
RVEdV (ml)	38.2 ± 14.7	40.9 ± 17.7	42.4 ± 18.9	43.9 ± 16.5	0.09
RVEF (%)	53.2 ± 7.3	54.9 ± 5.7	52.8 ± 6.9	51.0 ± 8.3	0.36
E (cm s ⁻¹)	76.5 ± 17.0	74.2 ± 16.5	74.4 ± 18.2	73.7 ± 17.9	0.64
A (cm s ⁻¹)	80.2 ± 15.8	81.3 ± 16.8	82.0 ± 17.4	84.5 ± 16.6	0.49
E/A	0.92 ± 0.3	0.90 ± 0.5	0.89 ± 0.6	0.88 ± 0.9	0.55
IVRT (ms)	94.0 ± 18.7	102.5 ± 17.4	108.7 ± 18.3	117.2 ± 16.1	<0.05
DT (ms)	232.4 ± 26.7	242.6 ± 33.2	254.8 ± 38.7	271.3 ± 45.1	<0.05

Abbreviations: A, mitral late peak velocity; BMI, body mass index; DT, early filling deceleration time; E, mitral early peak velocity; E/A, ratio of mitral early-to-late peak velocity; FS, fractional shortening; IVRT, isovolumic relaxation time; LVEdD, left-ventricular end-diastolic diameter; LVEdV, left-ventricular end-diastolic volume; LVEF, left-ventricular ejection fraction; LVEsD, left-ventricular end-systolic diameter; LVEsV, left-ventricular end-systolic volume; LVMi, left-ventricular mass index; PWT, posterior wall thickness; RVEdD, right-ventricular end-diastolic diameter; RVEdV, right-ventricular end-diastolic volume; RVEF, right-ventricular ejection fraction; RVFWT, right-ventricular free wall thickness; RWT, relative wall thickness; SWT, septal wall thickness.

revealed a mild degree of diastolic dysfunction in the referent group of non-obese hypertensive patients that did not significantly worsen with increasing BMI. These results corroborated that left-ventricular systo-diastolic dysfunction was not associated with obesity in hypertensive patients.

In contrast, tissue Doppler velocity and strain imaging measurements (Table 3) demonstrated and highlighted the negative influence of obesity. For both the left and right ventricles E_m ($P < 0.01$) and the E_m/A_m ratio ($P < 0.001$) significantly decreased with increasing BMI, suggesting an obesity-related diastolic dysfunction; this was confirmed

by the increase of the left-ventricular filling pressures, approximated by the early-diastolic mitral inflow/mitral annular velocity ratio ($P < 0.001$). Furthermore, for both the left and right ventricles, obesity-related systolic dysfunction was also detected; in fact, S_m ($P < 0.01$ and < 0.001 , respectively) and peak strain ($P < 0.001$) and strain rate values ($P < 0.01$ and < 0.001 , respectively) were slightly reduced with increasing BMI.

To avoid the effect of some potentially confounding variables, these were entered into a multivariate linear stepwise regression model. However, even after adjusting for age, gender, mean blood pressure,

Table 3 Tissue Doppler and strain imaging echocardiographic parameters

	Non-obesity (BMI < 25 kg m ⁻² ; n=58)	Overweight (BMI 25 to 30 kg m ⁻² ; n=67)	Mild obesity (BMI 30 to 35 kg m ⁻² ; n=63)	Severe obesity (BMI > 35 kg m ⁻² ; n=60)	P-value
LVS _m (cm s ⁻¹)	7.34 ± 1.7	6.51 ± 1.5	5.72 ± 1.8	4.96 ± 2.0	<0.01
LVE _m (cm s ⁻¹)	7.12 ± 1.6	6.56 ± 1.9	5.78 ± 1.5	5.01 ± 1.5	<0.01
LVA _m (cm s ⁻¹)	7.19 ± 2.0	7.78 ± 1.8	8.06 ± 1.7	8.24 ± 1.9	0.09
LVE _m /LVA _m	0.96 ± 1.9	0.83 ± 1.6	0.67 ± 1.8	0.56 ± 1.9	<0.001
E/LVE _m	10.6 ± 2.0	12.3 ± 2.7	14.4 ± 2.9	16.9 ± 3.2	<0.001
RVS _m (cm s ⁻¹)	9.40 ± 2.1	8.76 ± 1.8	7.69 ± 2.0	6.75 ± 2.2	<0.001
RVE _m (cm s ⁻¹)	9.27 ± 2.3	8.84 ± 1.9	7.95 ± 2.5	7.12 ± 2.1	<0.01
RVA _m (cm s ⁻¹)	8.94 ± 1.6	9.16 ± 1.5	9.55 ± 1.6	9.98 ± 1.8	0.12
RVE _m /RVA _m	1.04 ± 1.5	0.90 ± 1.3	0.78 ± 1.6	0.61 ± 1.4	<0.001
LVS (%)	24.44 ± 3.5	21.23 ± 3.0	19.14 ± 3.6	16.42 ± 3.9	<0.001
LVS _R (LVS ⁻¹)	1.88 ± 0.3	1.76 ± 0.6	1.53 ± 0.4	1.40 ± 0.5	<0.01
RVS (%)	27.56 ± 4.0	24.55 ± 3.8	22.39 ± 3.9	20.14 ± 4.1	<0.001
RVS _R (RVS ⁻¹)	1.91 ± 0.5	1.63 ± 0.7	1.49 ± 0.8	1.31 ± 0.9	<0.001

Abbreviations: BMI, body mass index; E/LVE_m, ratio of mitral early peak velocity/mitral annulus early peak diastolic velocity; LVA_m, mitral annulus late peak diastolic velocity; LVE_m, mitral annulus early peak diastolic velocity; LVE_m/LVA_m, ratio of mitral annulus early-to-late peak diastolic velocity; LVS, basal interventricular septum peak strain value; LVS_m, mitral annulus peak systolic velocity; LVS_R, basal interventricular septum peak strain rate value; RVA_m, tricuspid annulus late peak diastolic velocity; RVE_m, tricuspid annulus early peak diastolic velocity; RVE_m/RVA_m, ratio of tricuspid annulus early-to-late peak diastolic velocity; RVS, basal right-ventricular free wall peak strain value; RVS_m, tricuspid annulus peak systolic velocity; RVS_R, basal right-ventricular free wall peak strain rate value.

Table 4 Multivariate independent predictors of left-ventricular echocardiographic variables in overweight and obese patients

	LVS _m (R ² =0.19)		LVE _m (R ² =0.28)		LVS (R ² =0.26)		LVS _R (R ² =0.32)	
	β	P-value	β	P-value	β	P-value	β	P-value
BMI (kg m ⁻²)	-0.43	<0.01	-0.40	<0.01	-0.38	<0.01	-0.41	<0.01
Age (in years)	-0.18	0.10	-0.20	0.09	-0.16	0.13	-0.13	0.20
Male gender	0.16	0.21	0.19	0.15	0.20	0.13	0.14	0.24
Mean blood pressure (mm Hg)	-0.10	0.31	-0.13	0.26	-0.12	0.28	-0.15	0.22
LVMi (g m ^{-2.7})	-0.21	0.08	-0.24	0.06	-0.20	0.08	-0.22	0.07
RWT (mm)	-0.18	0.10	-0.20	0.08	-0.17	0.12	-0.19	0.09
RVFWT (mm)	-0.02	0.49	-0.06	0.43	-0.10	0.38	-0.08	0.39

Abbreviations: BMI, body mass index; LVE_m, mitral annulus early peak diastolic velocity; LVMi, left-ventricular mass index; LVS, basal interventricular septum peak strain value; LVS_m, mitral annulus peak systolic velocity; LVS_R, basal interventricular septum peak strain rate value; RVFWT, right-ventricular free wall thickness; RWT, relative wall thickness.

Table 5 Multivariate independent predictors of right-ventricular echocardiographic variables in overweight and obese patients

	RVS _m (R ² =0.22)		RVE _m (R ² =0.30)		RVS (R ² =0.18)		RVS _R (R ² =0.29)	
	β	P-value	β	P-value	β	P-value	β	P-value
BMI (kg m ⁻²)	-0.45	<0.01	-0.41	<0.01	-0.39	<0.01	-0.40	<0.01
Age (in years)	-0.16	0.12	-0.21	0.09	-0.15	0.12	-0.19	0.10
Male gender	0.19	0.14	0.22	0.12	0.24	0.09	0.15	0.22
Mean blood pressure (mm Hg)	-0.12	0.28	-0.15	0.22	-0.18	0.17	-0.16	0.19
LVMi (g m ^{-2.7})	-0.14	0.26	-0.14	0.26	-0.10	0.31	-0.07	0.38
RWT (mm)	-0.08	0.40	-0.12	0.36	-0.15	0.32	-0.10	0.38
RVFWT (mm)	-0.26	0.06	-0.23	0.08	-0.25	0.06	-0.20	0.09

Abbreviations: BMI, body mass index; LVMi, left-ventricular mass index; RVE_m, tricuspid annulus early peak diastolic velocity; RVFWT, right-ventricular free wall thickness; RVS, basal right-ventricular free wall peak strain value; RVS_m, tricuspid annulus peak systolic velocity; RVS_R, basal right-ventricular free wall peak strain rate value; RWT, relative wall thickness.

left-ventricular mass index, relative wall thickness and right-ventricular free wall thickness, BMI remained independently related to S_m and E_m , and to peak strain and strain rate values ($P < 0.01$ for all) for both the left and right ventricles (Tables 4 and 5).

Intraobserver differences were $0.4 \pm 0.8 \text{ cm s}^{-1}$ for tissue velocities, $1.8 \pm 1.6\%$ for strain and $0.1 \pm 0.2 \text{ s}^{-1}$ for strain rate. Interobserver

differences were $0.5 \pm 0.9 \text{ cm s}^{-1}$ for tissue velocities, $2.0 \pm 1.6\%$ for strain and $0.2 \pm 0.2 \text{ s}^{-1}$ for strain rate.

DISCUSSION

Diffusion and accuracy confirmation of tissue Doppler imaging compared with conventional echocardiographic techniques for the

identification of early abnormalities in systo–diastolic left-ventricular function have been extensively demonstrated, particularly in hypertensive patients.²⁰ In addition to diagnostic data, tissue Doppler imaging has also been suggested to be able to provide significant prognostic information, incremental to clinical data and standard echocardiographic variables, for risk stratification of hypertensive patients under treatment.²¹ Moreover, the assessment of right-ventricular function, using conventional echocardiographic indexes, is difficult because of the complex geometry involved; consequently, tissue Doppler imaging measurements have been advocated because of their accuracy and reproducibility in this context.

Some recent evidence suggests an association between obesity and ventricular dysfunction, but data regarding this obesity-related effect in hypertensive patients are lacking. Moreover, the manner and the extension of the negative influence of obesity on the diastolic and/or systolic function in the left and right ventricle remains debated and unclear.^{6–13}

To the best of our knowledge, this study represents the first attempt to perform such a complete and detailed echocardiographic evaluation to determine the existence and the extent of an obesity-related adjunctive depressive effect on left- and right systo–diastolic ventricular dysfunction in hypertensive patients with cutting-edge diagnostic techniques, such as tissue Doppler velocity and strain imaging.

Left-ventricular diastolic function

Conventional Doppler echocardiography revealed a mild degree of diastolic dysfunction in the referent group of non-obese hypertensive patients without significant obesity-related modification, probably because of its poor sensitivity due to the influence of hemodynamic conditions. These findings are in agreement with those of other authors studying obese subjects,^{4,11,12,22,23} in particular, they are consistent with the results reported by Ballo *et al.*²⁴ in obese hypertensive patients with normal left-ventricular ejection fraction. Moreover, our data add to the evidence reported by Mureddu *et al.*²⁵ that obesity does not significantly increase the prolonged isovolumic relaxation found in non-obese hypertensive patients.

Tissue Doppler imaging, surely more sensitive, confirmed the early diastolic dysfunction in non-obese hypertensive patients, and also revealed in addition a correlation between the degree of diastolic dysfunction and the BMI of the patients' subgroups. This relationship was particularly highlighted by the evaluation of the early-diastolic mitral inflow/mitral annular velocity and the mitral annulus E_m/A_m ratios, in agreement with the findings of most other authors.^{4,11,12,22,23} Notably, in our study, the variation was quite similar in terms of significance for both of these parameters. This finding, confirmed in two other studies,^{4,12} may suggest that the mitral annulus E_m/A_m ratio, which is more feasible and practical to obtain in routine echocardiographic practice and is equal in sensitivity to the early-diastolic mitral inflow/mitral annular velocity ratio, could be helpful in evaluating diastolic function in these patients.

Left-ventricular morphology and systolic function

Left-ventricular wall thickness and mass indexed to height to the power of 2.7 increased with increasing BMI, reflecting the expected morphological changes according to findings in the existing literature.^{4,11,12,22–24}

Even if left-ventricular ejection fraction values were completely normal with no significant differences between the subgroups, mitral annulus S_m , and more impressively basal interventricular septum peak

strain and peak strain rate values, showed a significant reduction; consequently, these measurements were able to identify and assess the obesity-related sub-clinical left-ventricular systolic dysfunction.

These results challenge previous findings^{7,9,26} and support more recent literature,^{4,11,12,22,24} probably because of the use of newer and more sensitive echocardiographic techniques rather than conventional echocardiographic measurements, such as left-ventricular ejection fraction and fractional shortening, which are relatively insensitive, and thus unable to detect early preclinical changes in left-ventricular function.

Right-ventricular morphology and systo–diastolic function

In previous studies, the relative role of obesity on right-ventricular morphology and function was difficult to identify because of the significant overlap between obesity and obstructive sleep apnea, and as indeed is the role of obesity relative with other covariates, such as diabetes mellitus and hypertension.^{27–31}

In our study, only right-ventricular wall thickness showed a significant variation with increasing BMI and diameter; volume and ejection fraction did not change significantly between subgroups, probably reflecting their insensitivity in assessing early sub-clinical right-ventricular dysfunction.

In contrast, tissue Doppler velocity and strain imaging revealed an obesity-related sub-clinical depressive effect on right-ventricular systo–diastolic function. In fact, tricuspid annulus S_m , basal right ventricular free wall peak strain and peak strain rate values, tricuspid annulus E_m and tricuspid annulus E_m/A_m ratio all showed a significant decrease with increasing BMI, suggesting a consistent early sub-clinical obesity-related worsening of both systolic and diastolic right-ventricular function.

These findings extend the previous data reported by Willens *et al.*,¹² suggesting preserved right-ventricular systolic function in subjects with severe obesity. They also substantially agree with the recent results by Wong *et al.*¹³ that demonstrated the presence of sub-clinical right-ventricular dysfunction in overweight and obese patients, independently of the presence of obstructive sleep apnea, diabetes mellitus, hypertension or other comorbidities.

Conclusion

Our study clearly demonstrated the negative impact of obesity on both left- and right-ventricular systo–diastolic function, in terms of adjunctive sub-clinical worsening, in hypertensive patients. These results were made possible using newer echocardiographic techniques, such as tissue Doppler velocity and strain imaging that are more sensitive, and are thus able to identify and assess obesity-related sub-clinical ventricular dysfunction.

A better understanding of the pathophysiology of obesity-related left- and right-ventricular morphological and functional characteristics will enable us to modify the disease process, resulting in the regression of sub-clinical changes. The newer echocardiographic techniques used in this study can provide a robust tool for the early detection of sub-clinical cardiac functional and structural changes, which seems mandatory for an appropriate assessment of cardiovascular risk. These techniques can also be able to evaluate the natural history of these obesity-related changes and the efficacy of therapeutic interventions over time, including weight loss and the treatment of insulin resistance.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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